

Supporting Information

Total synthesis of diptoindonesin G via a highly efficient domino cyclodehydration/intramolecular Friedel-Crafts acylation/regioselective demethylation sequence

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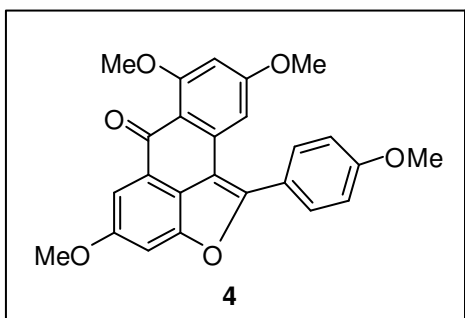
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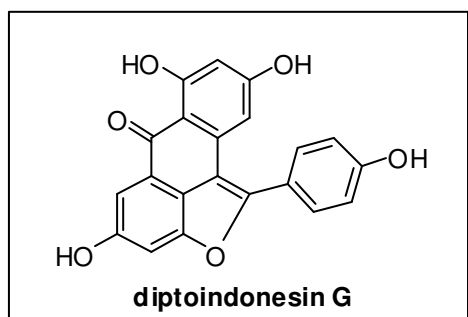
4,7,9-trimethoxy-1-(4-methoxyphenyl)-6H-

anthra[1,9-*bc*]furan-6-one (4)

To a stirred solution of ester **3** (450 mg, 1 mmol) in THF/MeOH/H₂O (3/3/3 mL) was added NaOH

(120 mg, 3 equiv) at rt. After being refluxed for 16 h, the reaction mixture was concentrated in vacuo, acidified with 10% HCl, and extracted with ethyl acetate. The organic layer was dried over MgSO₄ and concentrated under reduced pressure to give the corresponding acid (436 mg, 100%). **3-(3,5-dimethoxyphenyl)-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-carboxylic acid**: ¹H NMR (300 MHz, DMSO-d₆) δ 7.47~7.43 (m, 3H), 7.09 (d, *J* = 2.2 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.51 (dd, *J* = 2.1 Hz, 1H), 6.43 (d, *J* = 2.1 Hz, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.71 (s, 6H); ¹³C NMR (75 MHz, DMSO-d₆) δ 167.4, 160.3, 159.4, 156.8, 154.7, 150.5, 135.4, 127.8, 127.1, 122.3, 120.3, 115.9, 114.1, 112.0, 107.8, 99.7, 98.5, 55.9, 55.2, 55.1; **MS** (EI) *m/z* 434 (M⁺, 100), 419 (26), 375 (7); **HRMS** (EI) calcd for [C₂₅H₂₂O₇]⁺: *m/z* 434.1366, found 434.1367. To a solution of **3** (195 mg, 0.45 mmol) in CH₂Cl₂ (2 mL) was added trifluoroacetic anhydride (0.2 mL, 3 equiv) at 0 °C. After being stirred at rt for 2 h, the reaction mixture was quenched with aq. NaHCO₃ solution and extracted with CH₂Cl₂. The organic layer was dried over MgSO₄, concentrated, and purified by flash column

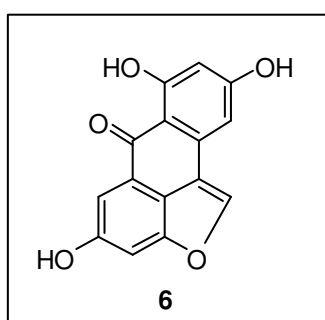
chromatography (hexane:ethyl acetate:dichloromethane = 3:1:2 to 1:1:2) to afford **4** (144 mg, 77%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.88 (d, J = 8.7 Hz, 2H), 7.60 (d, J = 1.3 Hz, 1H), 7.29 (d, J = 2.1 Hz, 1H), 7.22 (d, J = 1.5 Hz, 1H), 7.08 (d, J = 8.7 Hz, 2H), 6.52 (d, J = 2.1 Hz, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.76 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 182.2, 164.6, 163.3, 161.3, 160.0, 155.3, 153.2, 136.3, 130.8, 127.6, 124.9, 123.4, 116.8, 114.4, 109.3, 105.8, 102.4, 100.6, 99.1, 56.6, 56.4, 55.6, 55.5; **MS** (EI) m/z 416 (M^+ , 100), 399 (53), 387 (37), 371 (18); **HRMS** (EI) calcd for $[\text{C}_{25}\text{H}_{20}\text{O}_6]^+$: m/z 416.1260, found 416.1261.



4,7,9-trihydroxy-1-(4-hydroxyphenyl)-6H-anthra[1,9-*bc*]furan-6-one (diptoindonesin G)
from 4

To a solution of **4** (200 mg, 0.48 mmol) in CH_2Cl_2 (17 mL) was added BBr_3 (0.91 mL, 20 equiv) at $-78\text{ }^\circ\text{C}$. After being stirred at rt for 16 h, the reaction mixture was quenched with ice water. The insoluble material was filtered, washed with water and CH_2Cl_2 , and dried to give **diptoindonesin G** (161 mg, 93%). $^1\text{H NMR}$ (500 MHz, $(\text{CD}_3)_2\text{CO}$) δ 9.67 (s, 1H), 9.29 (s, 1H), 9.23 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.54 (s, 1H), 7.35 (s, 1H), 7.26 (s, 1H), 7.12 (d, J = 8.5 Hz, 2H), 6.39 (s,

1H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{CO}$) δ 187.9, 168.5, 164.8, 160.6, 158.5, 157.6, 154.1, 135.7, 131.6, 126.1, 125.3, 122.5, 117.0, 112.2, 109.2, 108.3, 104.7, 103.8, 103.3; **MS** (EI) m/z 360 (M^+ , 100), 321 (6), 303 (7), 247 (6); **HRMS** (EI) calcd for $[\text{C}_{21}\text{H}_{12}\text{O}_6]^+$: m/z 360.0634, found 360.0620.



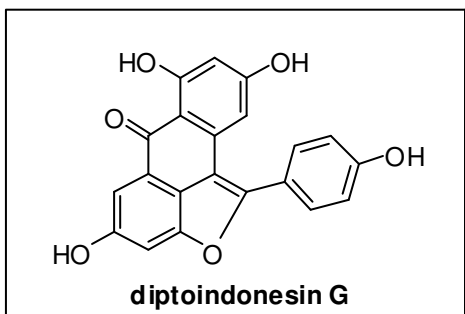
4,7,9-trihydroxy-6H-anthra[1,9-*bc*]furan-6-one (6) from

5

To a solution of **5** (300 mg, 0.88 mmol) in CH_2Cl_2 (5 mL)

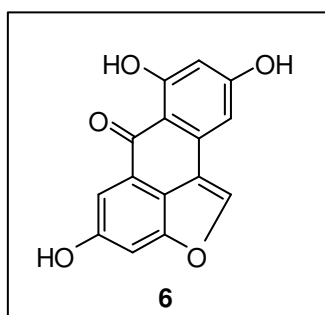
was added BBr_3 (1.2 mL, 15 equiv) at -78°C . After being

stirred at rt for 16 h, the reaction mixture was quenched with ice water. The insoluble material was filtered, washed with water and CH_2Cl_2 , and dried to give **6** (212 mg, 90%). ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{CO}$) δ 13.80 (s, 1H), 9.78 (br s, 1H), 9.28 (br s, 1H), 8.61 (s, 1H), 7.55 (d, $J = 1.7$ Hz, 1H), 7.39 (d, $J = 1.7$ Hz, 1H), 7.07 (d, $J = 1.1$ Hz, 1H), 6.43 (d, $J = 1.3$ Hz, 1H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{CO}$) δ 188.3, 168.0, 165.1, 159.0, 155.2, 145.0, 134.8, 126.2, 123.0, 115.6, 111.9, 109.1, 105.3, 105.2, 103.4; **MS** (EI) m/z 268 (M^+ , 100), 240 (24), 213 (29), 185 (23), 129 (44); **HRMS** (EI) calcd for $[\text{C}_{15}\text{H}_8\text{O}_5]^+$: m/z 268.0372, found 268.0374.



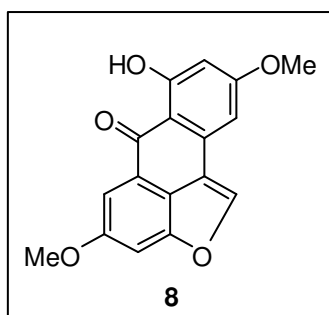
4,7,9-trihydroxy-1-(4-hydroxyphenyl)-6H-anthra[1,9-*bc*]furan-6-one (diptoindonesin G) from 3

To a solution of **3** (77 mg, 0.17 mmol) in CH₂Cl₂ (5 mL) was added BBr₃ (0.5 mL, 30 equiv) at -78 °C. After being stirred at rt for 16 h, the reaction mixture was quenched with ice water. The insoluble material was filtered, washed with water and CH₂Cl₂, and dried to give **diptoindonesin G** (57 mg, 92%).



4,7,9-trihydroxy-6H-anthra[1,9-*bc*]furan-6-one (6) from 7

To a solution of **7** (841 mg, 2.33 mmol) in CH₂Cl₂ (17 mL) was added BCl₃ (4.7 mL, 1 M solution in CH₂Cl₂, 2 equiv) at -78 °C. After being slowly warmed to rt for 1 h, BBr₃ (4.4 mL, 20 equiv) was added at -78 °C. After being stirred at rt for 16 h, the reaction mixture was carefully quenched with ice water. The insoluble material was filtered, washed with water and CH₂Cl₂, and dried to give **6** (582 mg, 93%).



7-hydroxy-4,9-dimethoxy-6H-anthra[1,9-*bc*]furan-6-one

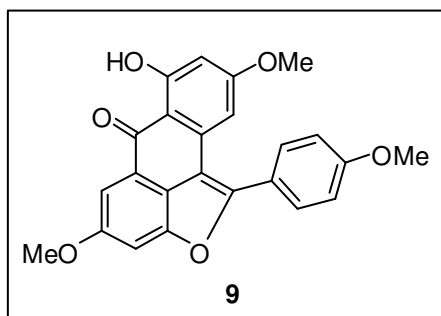
(8)

To a solution of **7** (1.01 g, 2.8 mmol) in CH₂Cl₂ (10 mL) was added BCl₃ (14 mL, 5 equiv) at -78 °C. After being stirred at rt for 16 h, the reaction mixture was quenched with ice water. The volatiles were removed under reduced pressure. The insoluble material was filtered, washed with water, and dried to give **8** (788 mg, 95%). ¹H NMR (300 MHz, CDCl₃) δ 13.80 (s, 1H), 8.09 (s, 1H), 7.59 (d, *J* = 1.4 Hz, 1H), 7.29 (d, *J* = 1.4 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.47 (d, *J* = 2.2 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 187.7, 167.3, 165.4, 160.4, 154.2, 143.0, 133.2, 125.4, 123.6, 115.0, 112.0, 106.6, 104.3, 103.7, 100.8, 56.7, 55.8; MS (EI) *m/z* 296 (M⁺, 100), 281 (16), 267 (27), 253 (16), 225 (15), 126 (14); HRMS (EI) calcd for [C₁₇H₁₂O₅]⁺: *m/z* 296.0685, found 296.0683.

General procedure for direct arylation of 8:

To a mixture of **8** (50 mg, 0.17 mmol), appropriate aryl halide (2 equiv), Pd(OAc)₂ (4 mg, 10 mol %), PCy₃HBF₄ (13 mg, 20 mol %), and K₂CO₃ (35 mg, 1.5 equiv) was added DMA (3 mL) containing pivalic acid (52 mg, 3 equiv) at rt. After being stirred at 100 °C for 1 h, the reaction mixture was cooled to rt. The mixture was concentrated in vacuo to give the residue which was purified by flash column chromatography

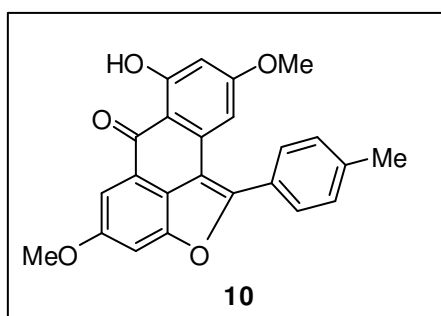
(hexane:ethyl acetate:dichloromethane = 15:1:2) to afford **9~13**.



7-hydroxy-4,9-dimethoxy-1-(4-methoxyphenyl)-

6H-anthra[1,9-*bc*]furan-6-one (9): The reaction with 4-bromoanisole (43 μ L, 2 equiv) gave **9** (57 mg, 83%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.86 (d,

$J = 8.7$ Hz, 2H), 7.56 (s, 1H), 7.25 (s, 1H), 7.21 (d, $J = 1.8$ Hz, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 6.45 (s, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.80 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 187.3, 167.5, 165.1, 161.5, 159.8, 156.7, 153.1, 134.3, 130.5, 126.0, 125.1, 123.0, 114.6, 112.2, 108.9, 105.4, 103.9, 102.6, 100.6, 56.6, 55.6, 55.6; **MS** (EI) m/z 402 (M^+ , 100), 387 (28), 316 (6), 273 (7); **HRMS** (EI) calcd for $[\text{C}_{24}\text{H}_{18}\text{O}_6]^+$: m/z 402.1103, found 402.1104.

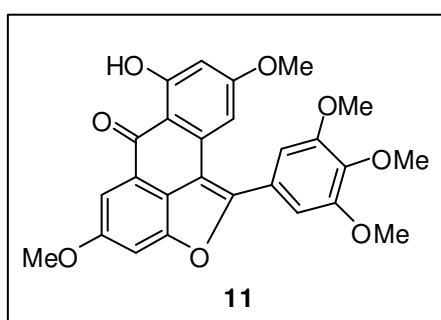


7-hydroxy-4,9-dimethoxy-1-p-tolyl-6H-

anthra[1,9-*bc*]furan-6-one (10): The reaction with 4-bromotoluene (42 μ L, 2 equiv) gave **10** (51 mg, 78%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.82 (d,

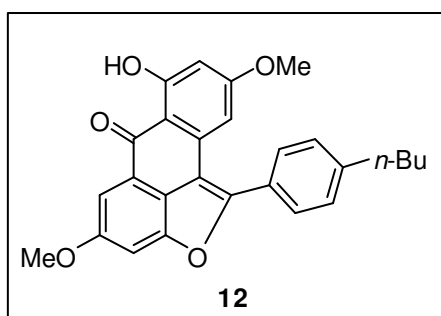
$J = 8.1$ Hz, 2H), 7.59 (d, $J = 1.7$ Hz, 1H), 7.38 (d, $J = 8.0$ Hz, 2H), 7.28 (d, $J = 1.8$ Hz, 1H), 7.25 (d, $J = 2.5$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 3.96 (s, 3H), 3.81 (s, 3H), 2.48

(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 187.3, 167.4, 165.0, 159.8, 156.6, 153.0, 141.0, 134.0, 129.7, 128.7, 127.7, 125.7, 125.1, 112.0, 109.2, 105.4, 103.8, 102.7, 100.5, 56.5, 55.5, 21.7; **MS** (EI) m/z 386 (M^+ , 100), 371 (20), 357 (6), 300 (6); **HRMS** (EI) calcd for $[\text{C}_{24}\text{H}_{18}\text{O}_5]^+$: m/z 386.1154, found 386.1156.



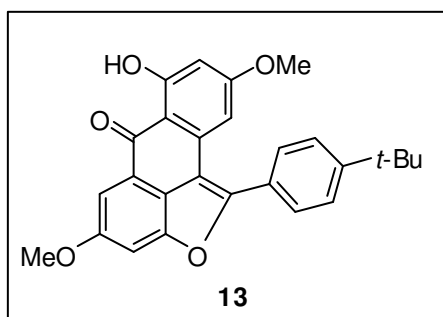
7-hydroxy-4,9-dimethoxy-1-(3,4,5-trimethoxyphenyl)-6H-anthra[1,9-*bc*]furan-6-one (11): The reaction with 5-bromo-1,2,3-trimethoxybenzene (84 mg, 2 equiv) gave **11** (33

mg, 42%). ^1H NMR (300 MHz, CDCl_3) δ 7.61 (s, 1H), 7.41 (d, $J = 2.1$ Hz, 1H), 7.30 (s, 1H), 7.19 (s, 2H), 6.47 (d, $J = 1.9$ Hz, 1H), 3.98 (s, 3H), 3.97 (s, 3H), 3.96 (s, 6H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 187.3, 167.7, 165.3, 160.0, 156.1, 153.7, 153.0, 140.2, 134.0, 125.8, 125.7, 125.3, 112.1, 109.4, 106.2, 105.7, 103.9, 103.7, 100.3, 61.3, 56.6, 56.5, 55.7; **MS** (EI) m/z 462 (M^+ , 100), 447 (42), 387 (4), 231 (4); **HRMS** (EI) calcd for $[\text{C}_{26}\text{H}_{22}\text{O}_8]^+$: m/z 462.1315, found 462.1316.



1-(4-butylphenyl)-7-hydroxy-4,9-dimethoxy-6H-anthra[1,9-*bc*]furan-6-one (12): The reaction

with 1-bromo-4-butylbenzene (60 μ L, 2 equiv) gave **9** (32 mg, 44%). **^1H NMR** (300 MHz, CDCl_3) δ 14.17 (s, 1H), 7.84 (d, J = 7.7 Hz, 2H), 7.62 (s, 1H), 7.38 (d, J = 7.8 Hz, 2H), 7.29 (s, 1H), 7.27 (d, J = 0.7 Hz, 1H), 6.47 (s, 1H), 3.96 (s, 3H), 3.80 (s, 3H), 2.73 (t, J = 7.5 Hz, 2H), 1.74~1.65 (m, 2H), 1.46~1.39 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, CDCl_3) δ 187.2, 167.3, 165.0, 159.8, 156.6, 153.0, 146.0, 134.0, 129.0, 128.7, 127.8, 125.7, 125.1, 112.0, 109.2, 105.4, 103.8, 102.6, 100.6, 56.5, 55.5, 35.7, 33.4, 22.4, 14.0; **MS** (EI) m/z 428 (M^+ , 100), 385 (42), 299 (13), 271 (7); **HRMS** (EI) calcd for $[\text{C}_{27}\text{H}_{24}\text{O}_5]^+$: m/z 428.1624, found 428.1627.

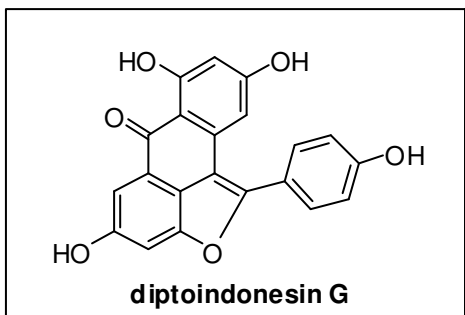


1-(4-*tert*-butylphenyl)-7-hydroxy-4,9-dimethoxy-6H-anthra[1,9-*bc*]furan-6-one (13**):**

The reaction with 1-bromo-4-*tert*-butylbenzene (59 μ L, 2 equiv) gave **9** (41 mg, 56%). **^1H NMR**

(300 MHz, CDCl_3) δ 7.89 (d, J = 8.4 Hz, 2H), 7.62 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.31 (s, 1H), 7.30 (s, 1H), 3.97 (s, 3H), 3.83 (s, 3H), 1.41 (s, 9H); **^{13}C NMR** (75 MHz, CDCl_3) δ 187.4, 167.6, 165.2, 159.9, 156.7, 154.3, 153.2, 134.2, 128.6, 127.8, 126.1, 125.9, 125.3, 112.2, 109.4, 105.6, 103.9, 103.1, 100.6, 56.6, 55.6, 35.3, 31.4, 14.3; **MS** (EI) m/z 428 (M^+ , 100), 413 (60), 381 (19), 185 (36); **HRMS** (EI) calcd for

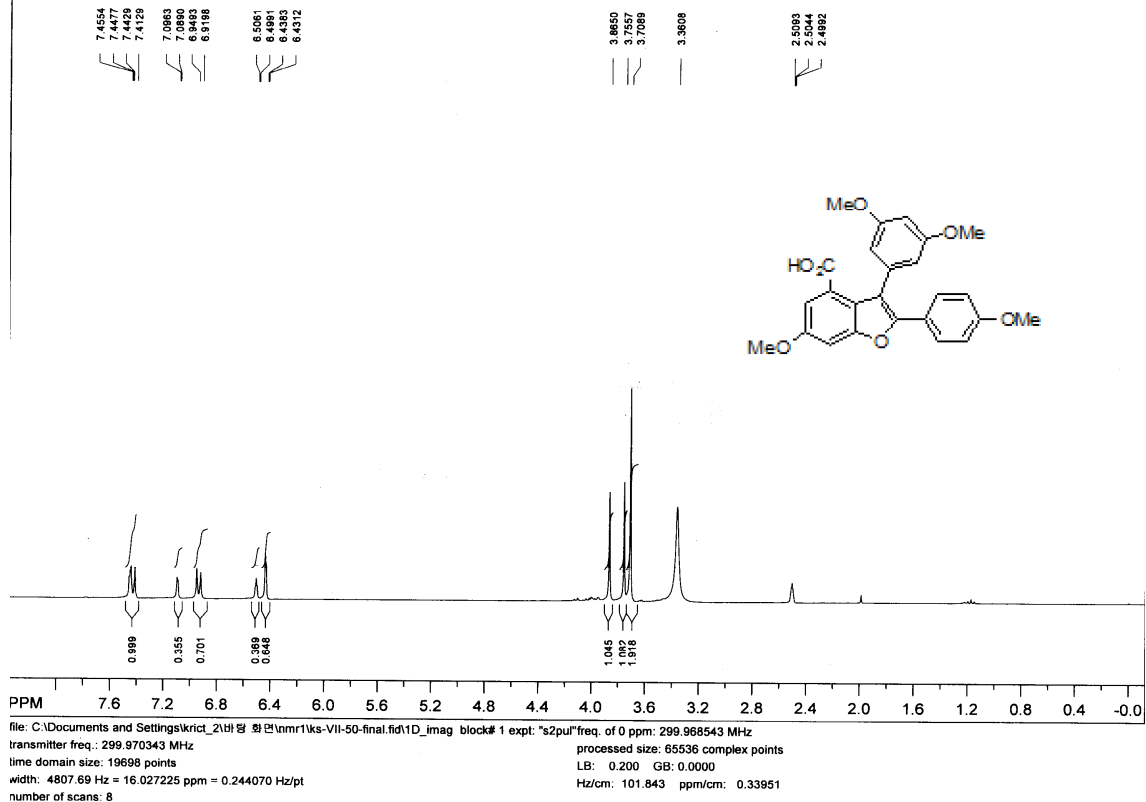
[C₂₇H₂₄O₅]⁺: *m/z* 428.1624, found 428.1623.



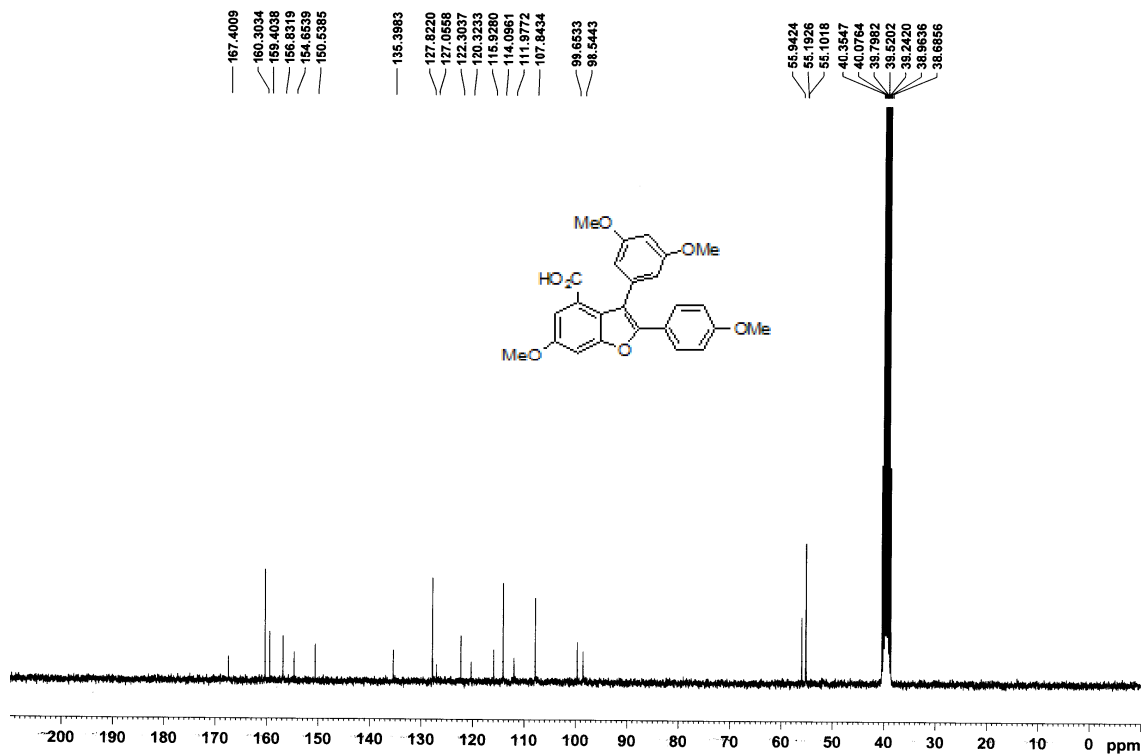
**4,7,9-trihydroxy-1-(4-hydroxyphenyl)-6*H*-
anthra[1,9-*bc*]furan-6-one (diptoindonesin G)
from **9****

To a solution of **9** (50 mg, 0.12 mmol) in CH₂Cl₂ (2 mL) was added BBr₃ (0.11 mL, 10 equiv) at -78 °C. After being stirred at rt for 16 h, the reaction mixture was quenched with ice water. The insoluble material was filtered, washed with water and CH₂Cl₂, and dried to give **diptoindonesin G** (42mg, 93%).

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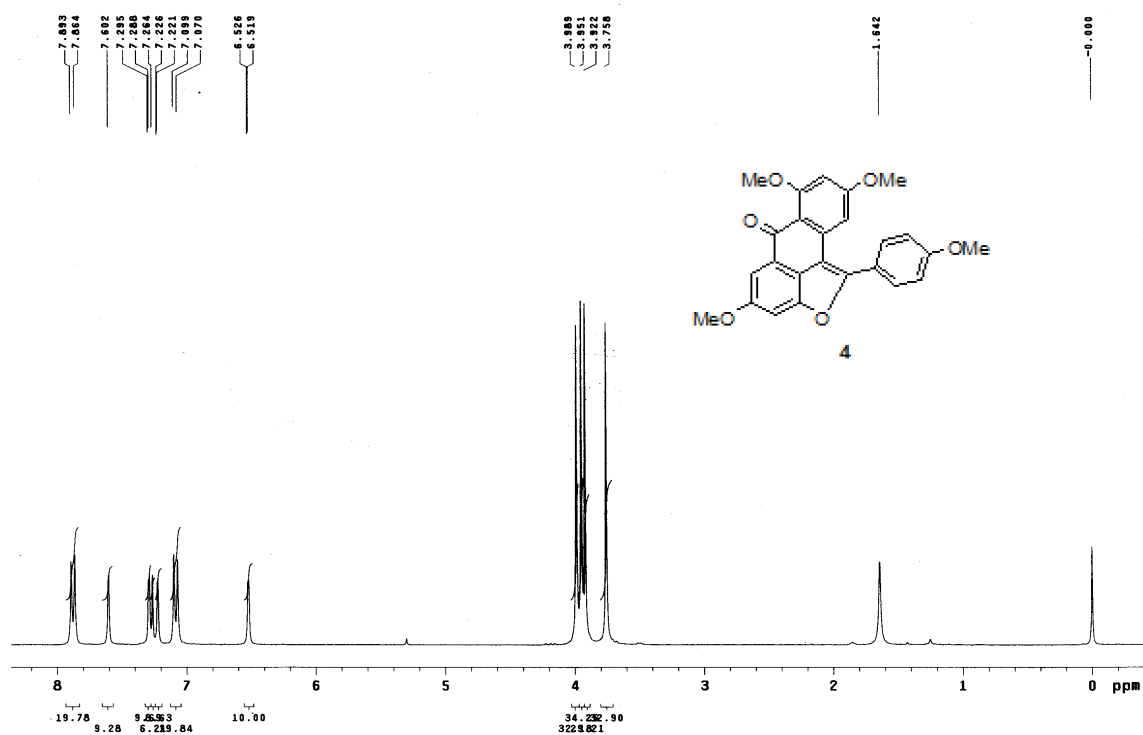
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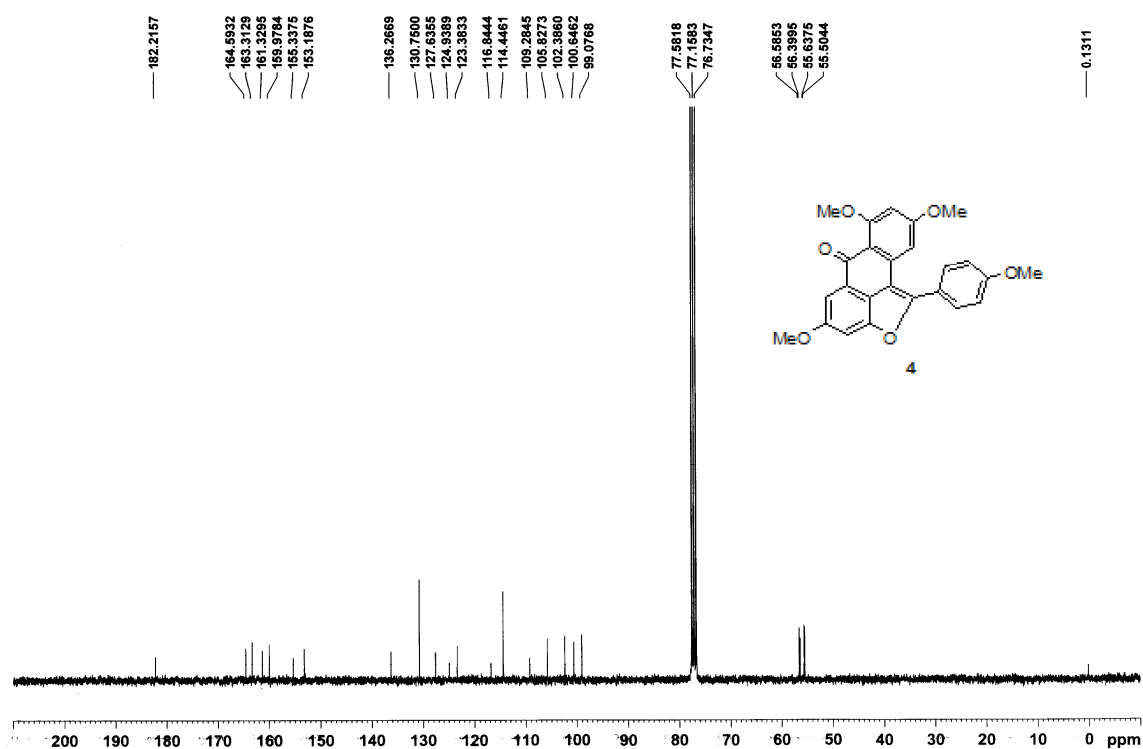
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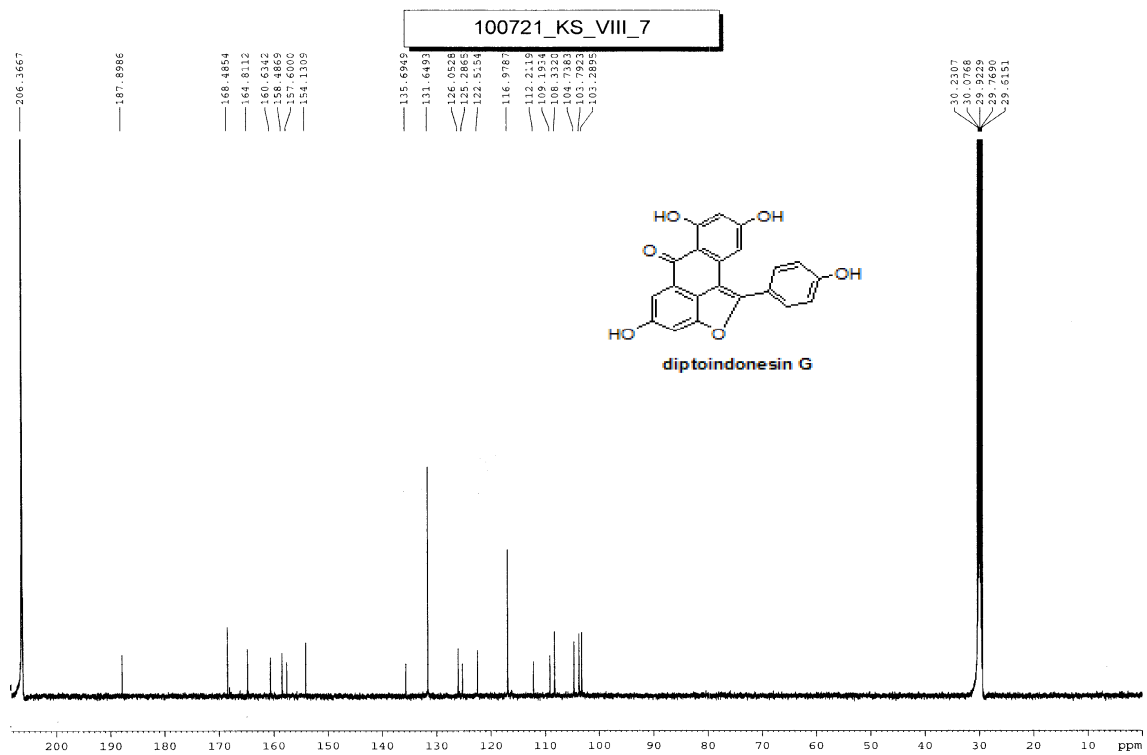
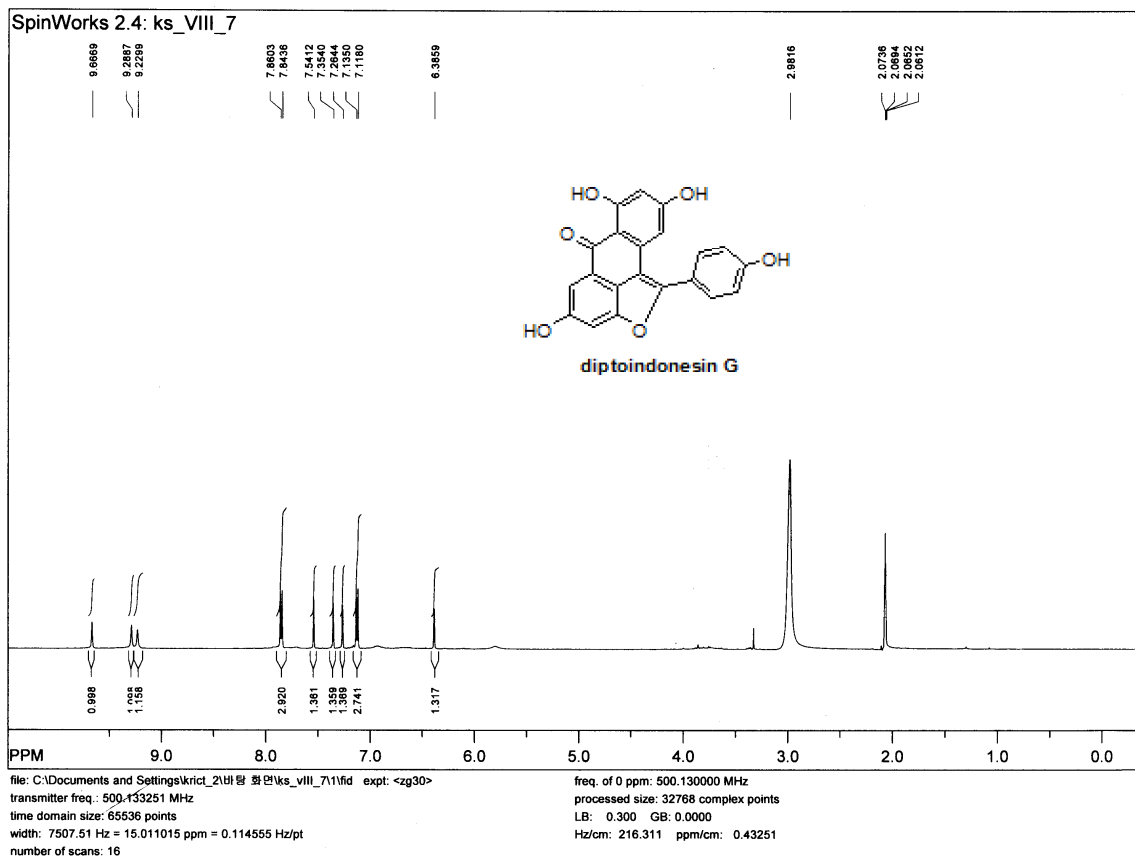
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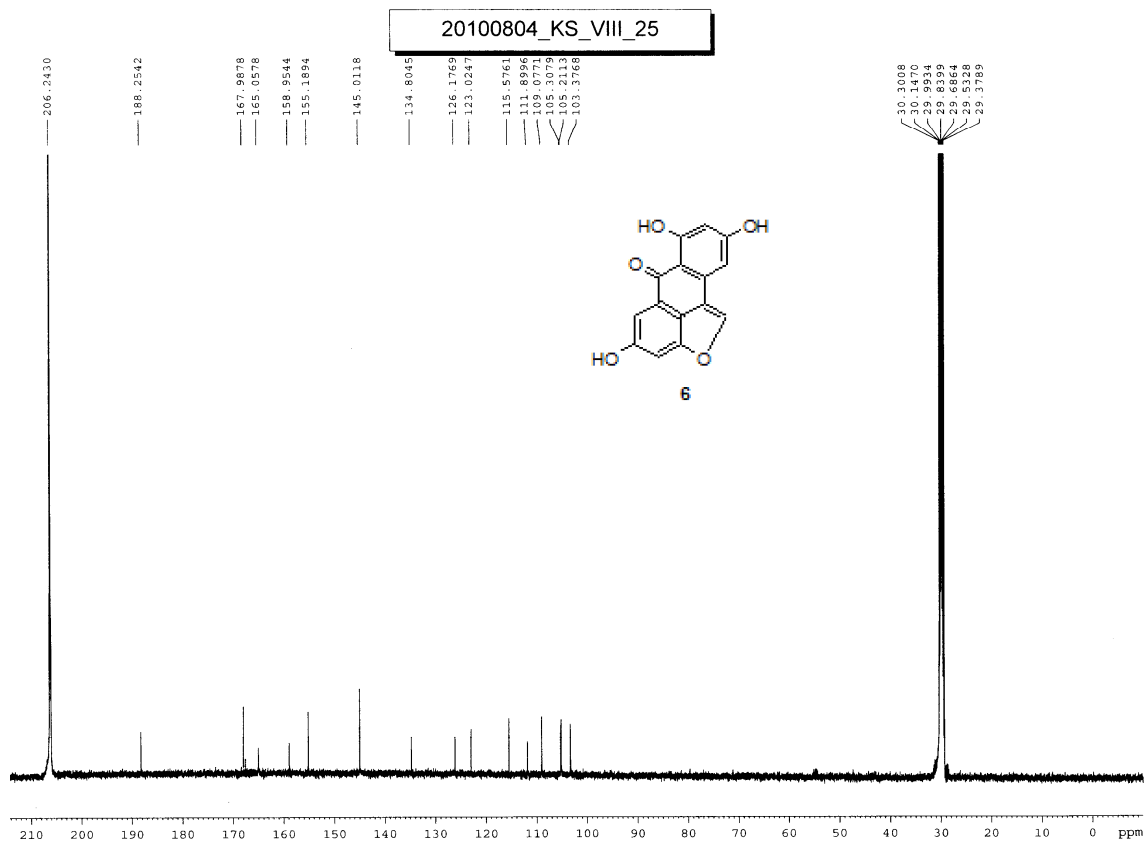
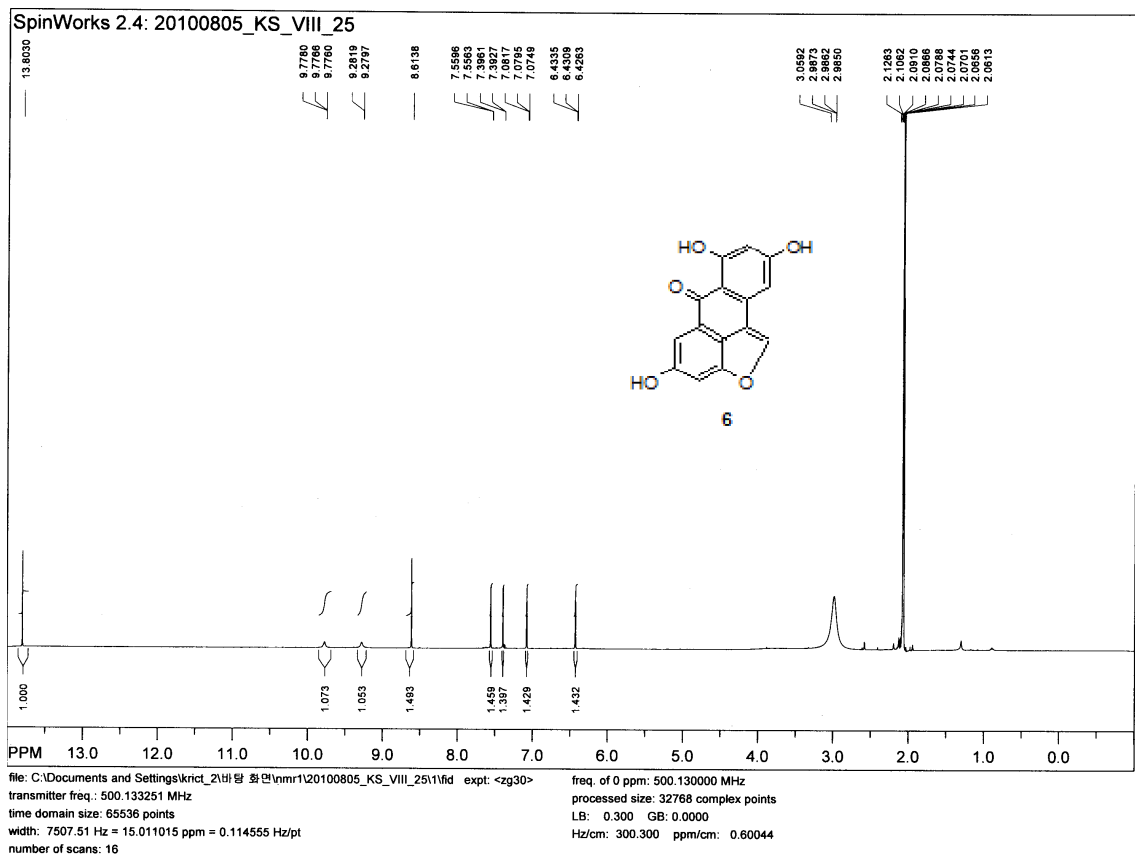
Pulse Sequence: s2pu1



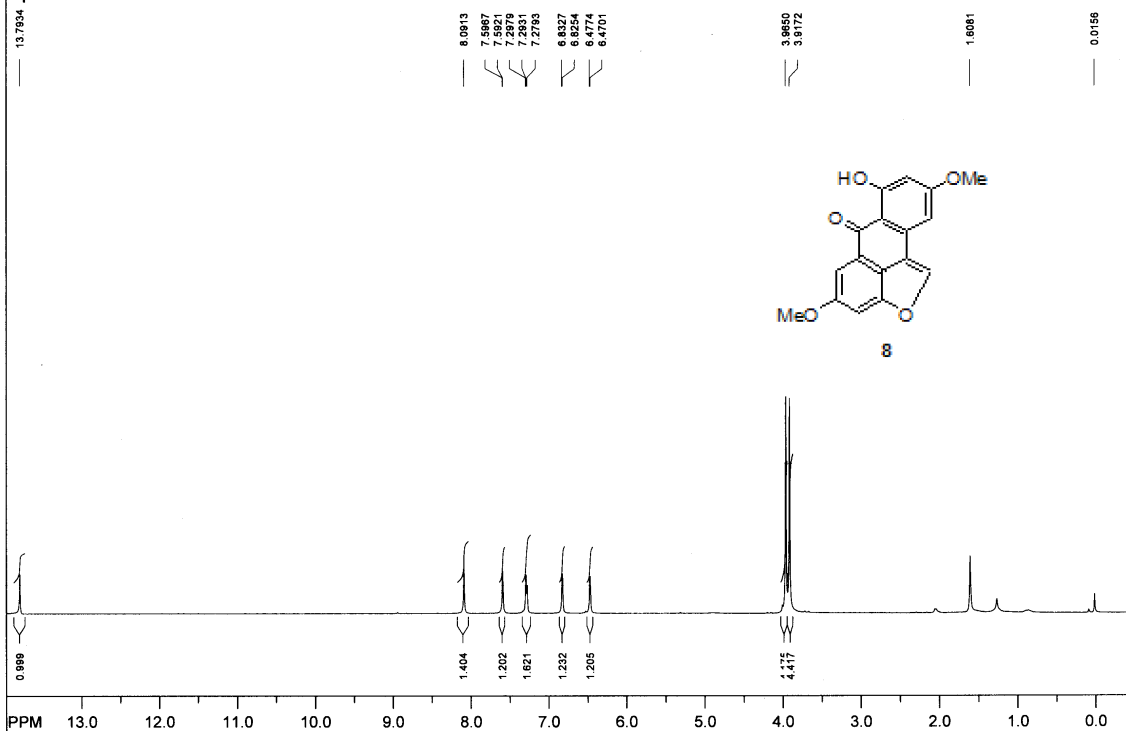
KS_VII_55







SpinWorks 2.4: ks-VIII-32f



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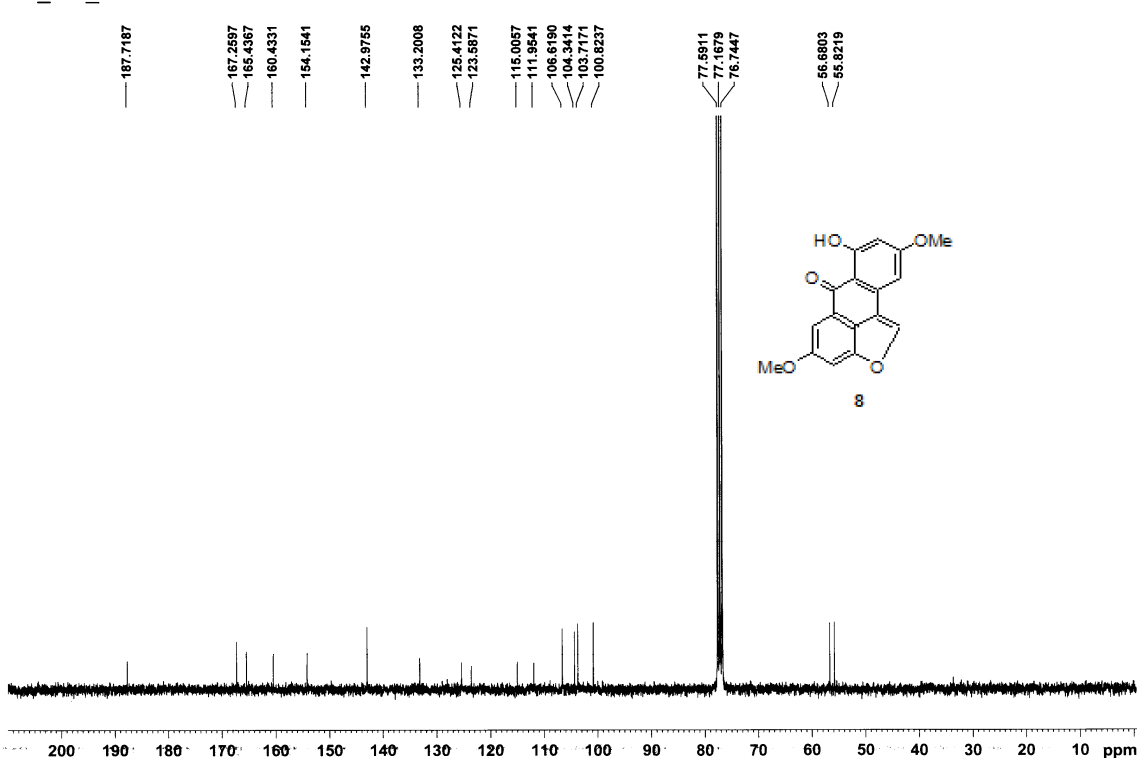
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processed size: 65536 complex points

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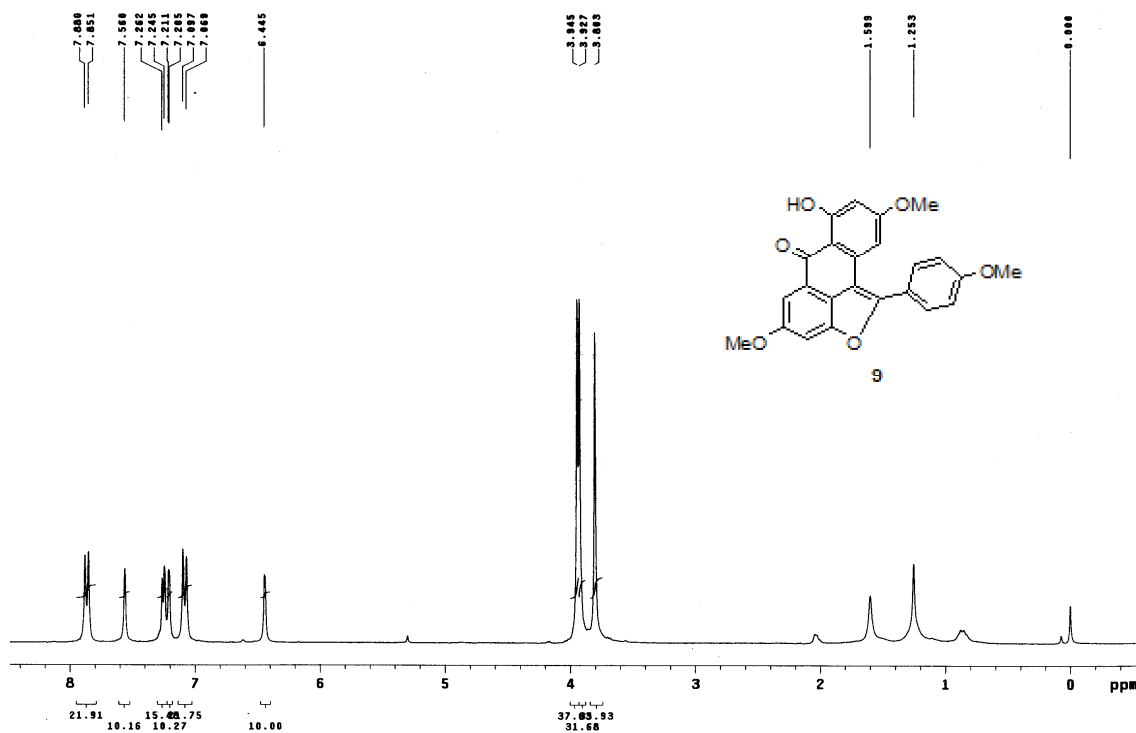
KS_VIII_32



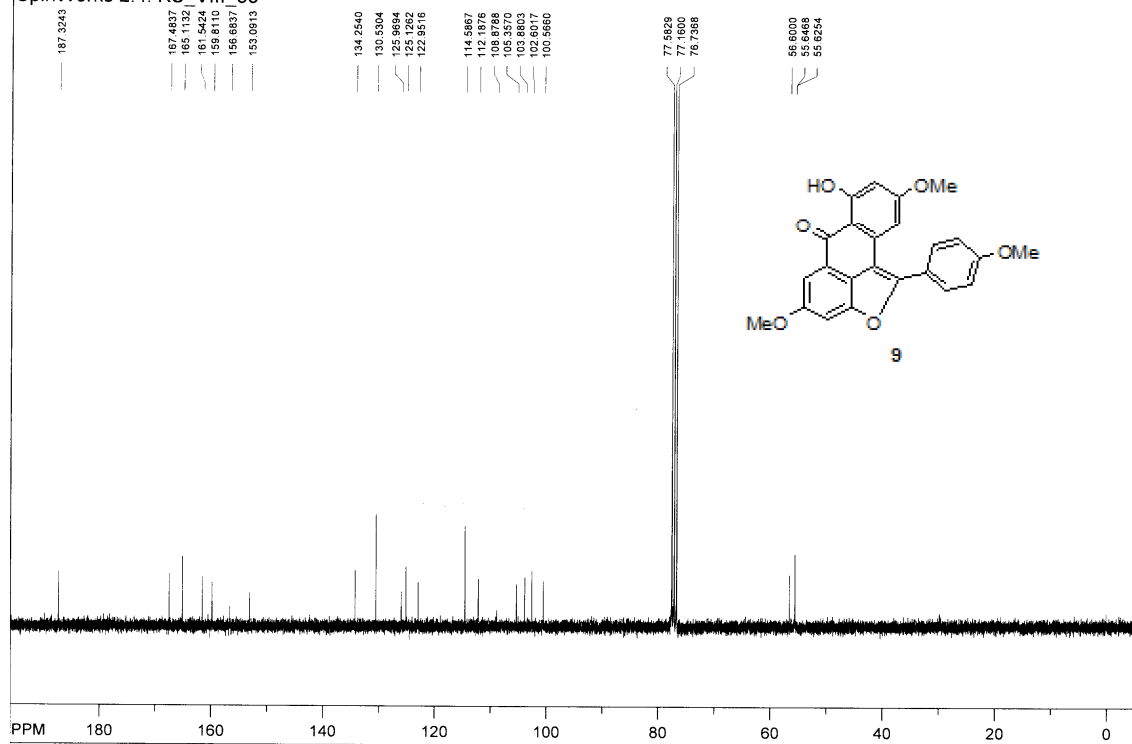
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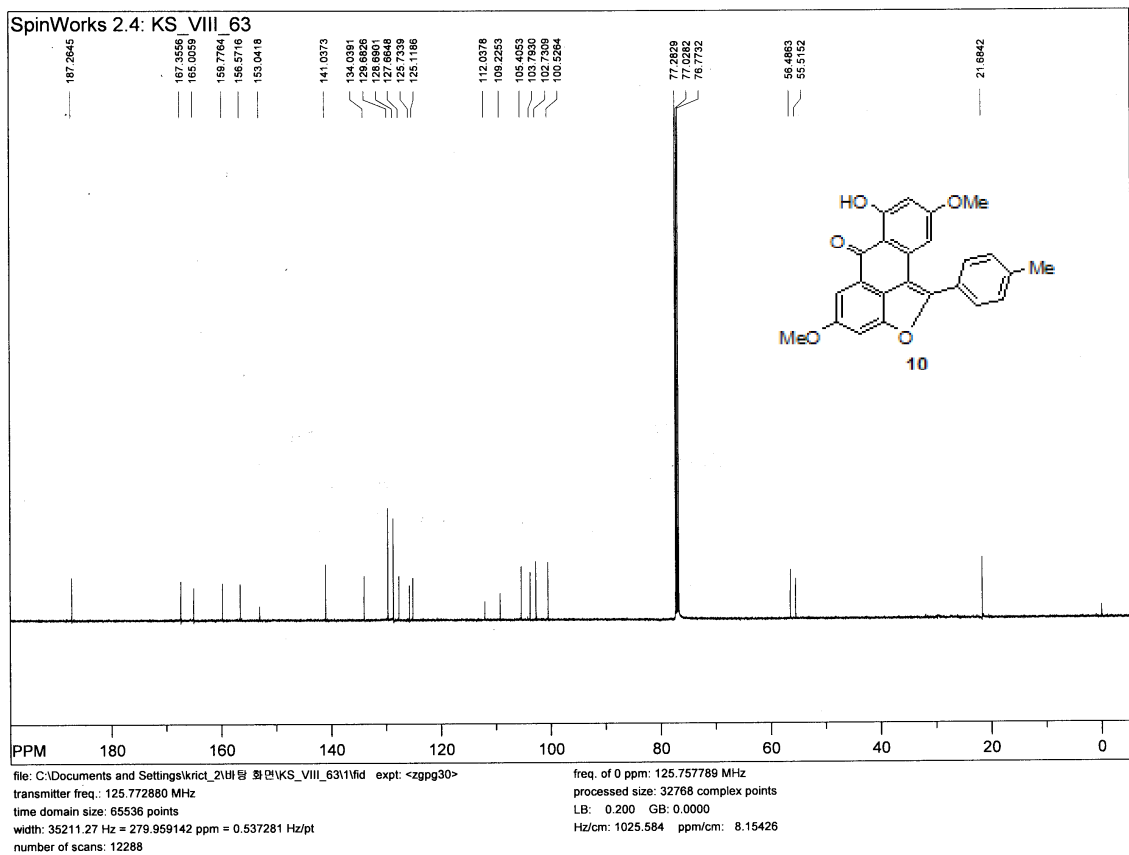
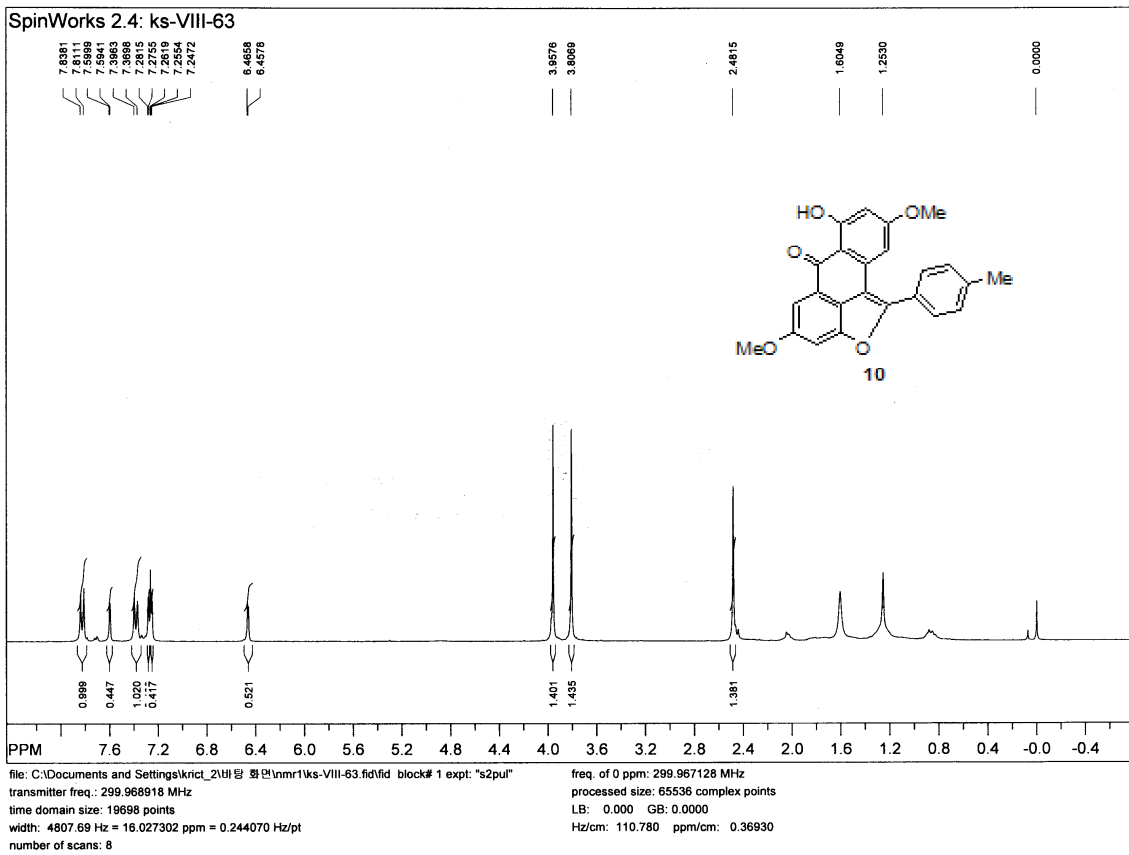


SpinWorks 2.4: KS_VIII_33

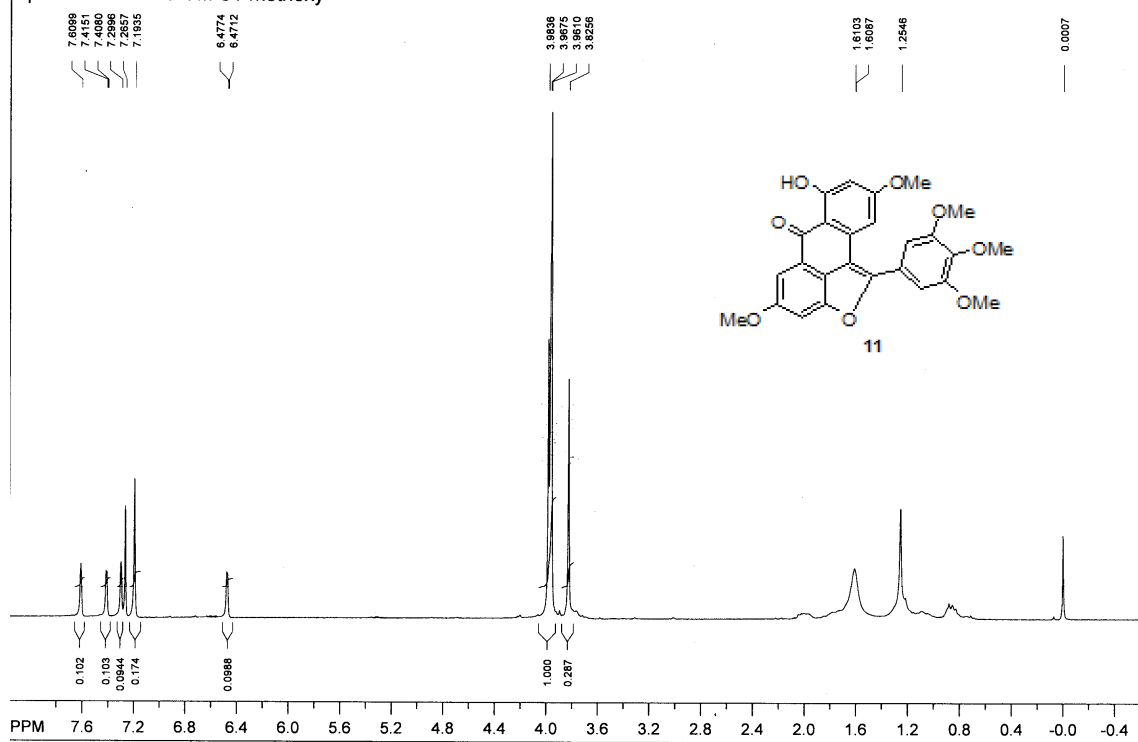


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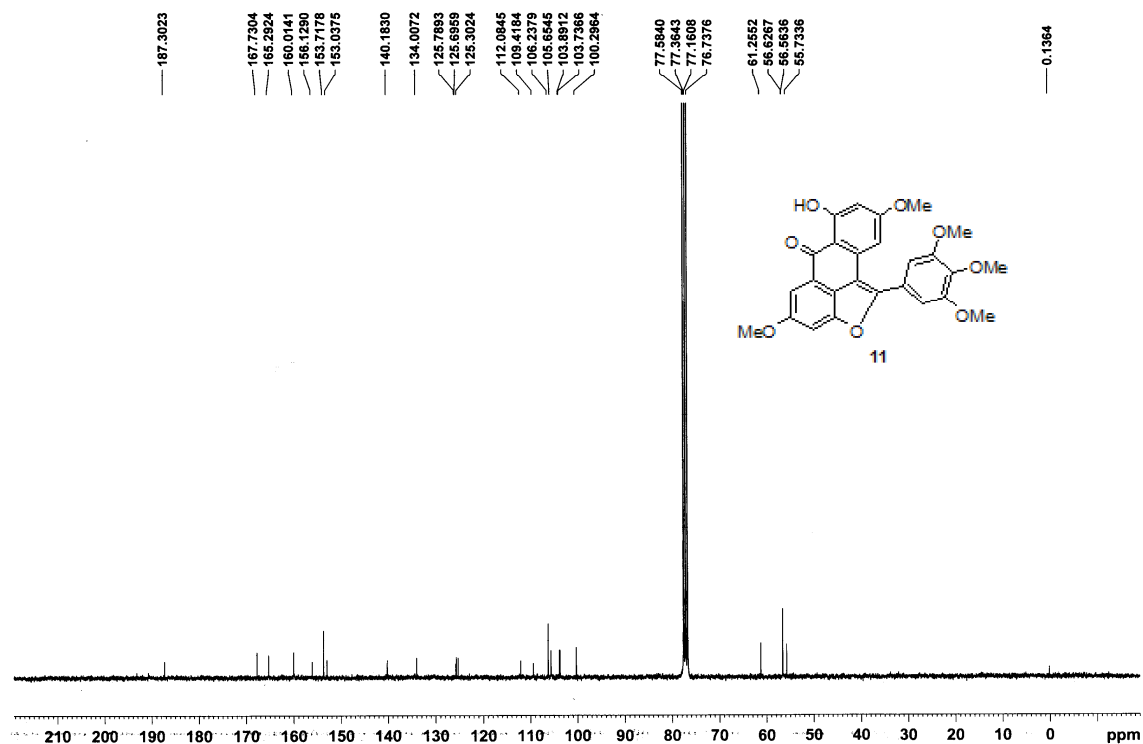


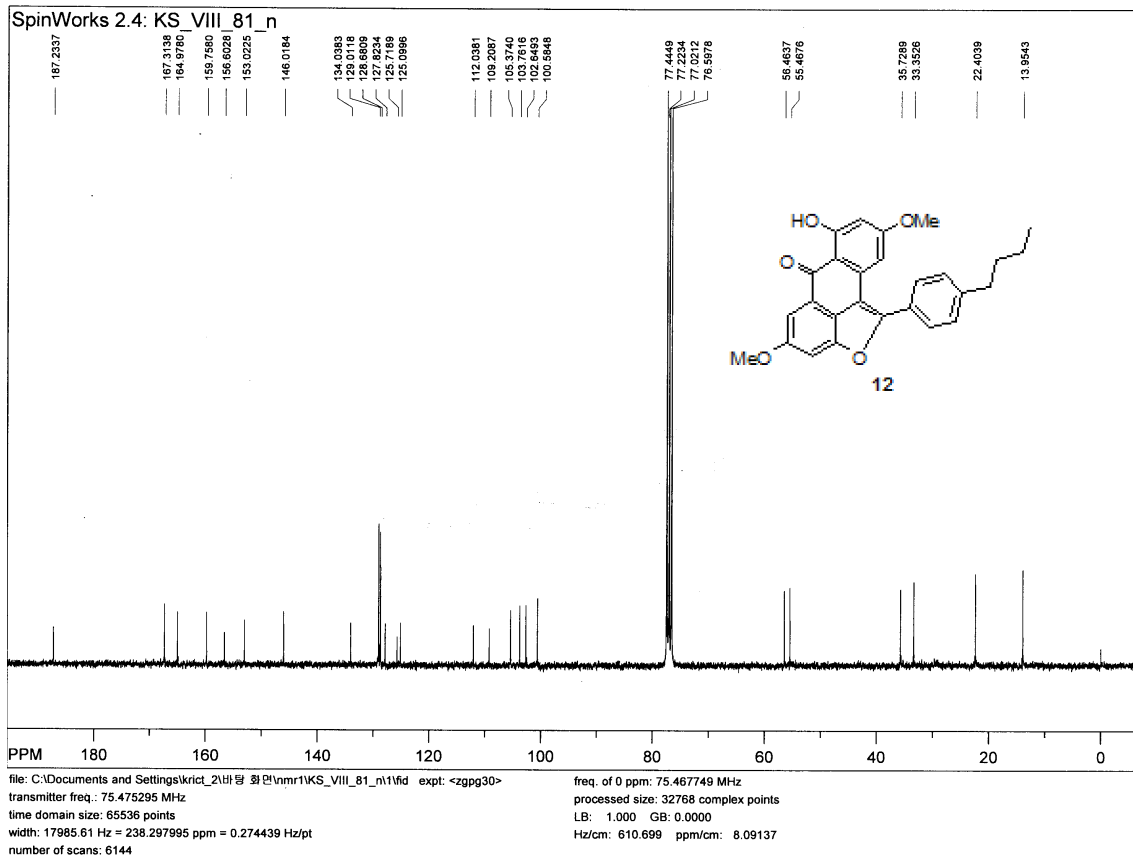
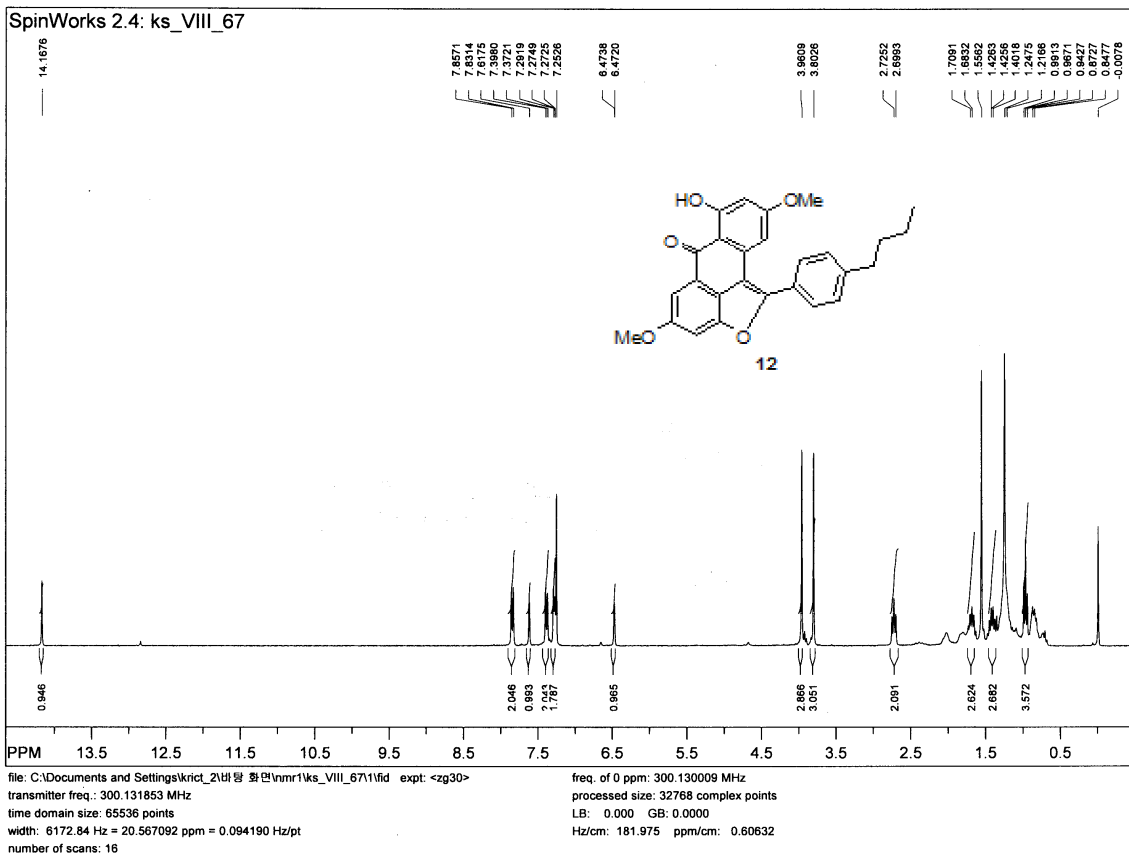
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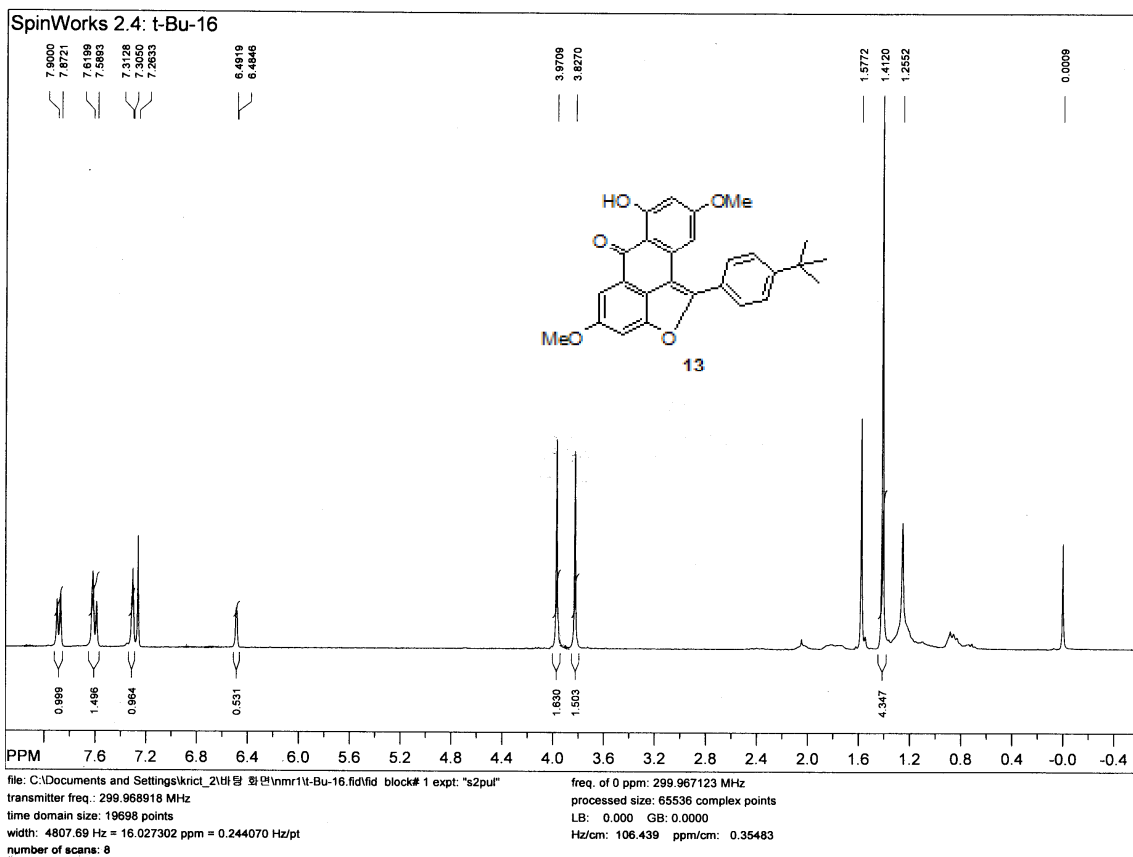


file: C:\Documents and Settings\kric12\바탕 화면\nmr1\ks-VIII-81-methoxy1.fid\fid block# 1 expt: "s2pul" freq. of 0 ppm: 299.967123 MHz
 transmitter freq.: 299.968918 MHz processed size: 65536 complex points
 time domain size: 19698 points LB: 0.200 GB: 0.0000
 width: 4807.69 Hz = 16.027302 ppm = 0.244070 Hz/pt Hz/cm: 105.307 ppm/cm: 0.35106
 number of scans: 8

KS_VIII_81_M







KS_VIII_81_t

