Supporting Information

A Versatile Solid-Phase Synthesis of Chromenes resembling Classical Cannabinoids

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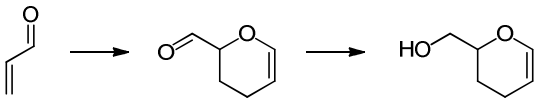
Compounds and solvents were purchased from commercial sources and used without further purification. Merrifield resin was obtained as PL-CMS (0.99 mmol/g, 75–150 µm) from Varian. For TLC aluminum foils layered with silica gel (silica gel 60 F_{254}) produced by Merck were used. Column chromatography was performed employing Merck silica gel 60 under flash conditions. ^{1}H and ^{13}C spectra were measured with Bruker Avance 250, 400 or 500 MHz spectrometers. Chemical shifts were reported in δ (ppm) referenced to residual undeuterated solvents [$CDCl_3$ to 7.26 / 77.00 ppm, acetone-d_6 to 2.05 / 30.83 ppm, MeOD to 3.31 / 39.05 ppm and DMSO-d_6 to 2.50 / 39.43 ppm]. EI-MS and HRMS-spectra were measured with a Finnigan MAT 90 instrument. ESI spectra were recorded on a ESI-TOF MS Mariner TM Biospectrometry Workstation PerSeptive Biosystems. IR spectra were recorded with a Bruker FTIR device IFS 88, Raman spectra with a MultiRAM (Bruker) and both are reported in cm^{-1}. Elemental analyses were performed using a Vario Micro device. Melting points were measured with an OptiMelt (SRS) or a Büchi Melting Point B-545 and are uncorrected. Microwave reactions were performed with a Synthos 3000 (Anton Paar).

General washing procedure for resins: CH_2Cl_2, 2 × H_2O and DMF, 2 × H_2O and THF, 3 × methanol and CH_2Cl_2, 4 × CH_2Cl_2. With 20 mL/g resin each.

Stereochemistry: All compounds are racemic, the drawn stereochemistry refers to the main diastereomer.

3,4-Dihydro-2*H*-pyran-2-methanol *via* 3,4-Dihydro-2*H*-pyran-2-carboxaldehyde:

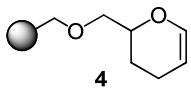


Freshly distilled acrolein (40.0 g, 48.0 mL, 710 mmol) and hydroquinone (50 mg) were distributed in 16 microwave vials á 3 mL. They were heated at first for 100 min at 800 W (140–145 °C), then for 50 min at 850 W (140–156 °C). Afterwards, the contents of the vials was filtered, washed with CH_2Cl_2 and concentrated under reduced pressure to give 3,4-dihydro-2*H*-pyran-2-carboxaldehyde (20.0 g, 50%), pure enough to be immediately used in the next step.

To a solution of $LiAlH_4$ (2.05 g, 55.0 mmol) in THF (80 mL) under nitrogen (stirred for 30 min at r.t.) was added 3,4-dihydro-2*H*-pyran-2-carboxaldehyde (9.40 g, 84.0 mmol) in 20 mL of THF at –78 °C. The mixture was warmed up to –35 °C over the next 3 h and then quenched with acetone and water. A sat. aq solution of K/Na tartrate (100 mL), water (80 mL) and Et_2O (100 mL) were added, the organic layer separated and the aqueous one extracted with Et_2O (3 × 150 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography [CH_2Cl_2/Et_2O (20:1) up to (10:1)] to give 12.1 g (65%) of the product as a colorless oil.[1]

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.60–2.20 (m, 5H, OH+2CH_2), 3.60–3.74 (m, 2H, OCH_2), 3.87–3.98 (m, 1H, CH=), 4.67–4.74 (m, 1H, CH=), 6.39 (d, *J* = 6.1 Hz, 1H, OCH).

Synthesis of DHP-resin 4:[2]



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To a flask containing NaH (2.64 g, 66.0 mmol, 60% in mineral oil) under nitrogen were added dry THF (100 mL) and 3,4-dihydro-2*H*-pyran-2-methanol (7.00 g, 60.0 mmol). The mixture was stirred for 2 h at r.t., before being concentrated under reduced pressure and dissolved in dry DMF (100 mL). The mixture was added to Merrifield resin (suspended in 125 mL of DMF) and the flask was agitated

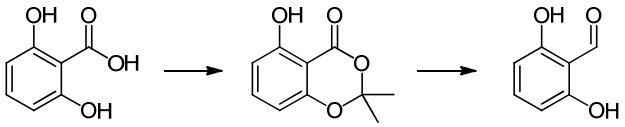
overnight. The solvent was filtered off and the resin washed four times with DMF/H_2O (1/1), three times with DMF and another three times with CH_2Cl_2. Then the resin was dried under vacuum.

Anal. calcd for $C_{70.55}H_{73.82}O_2$: C, 88.84; H, 7.80; O, 3.36; found: C, 88.86; H, 7.86.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 24.6, 72.3, 73.3, 74.0, 100.4, 143.6.

Raman: ν = 3055, 3002, 2977, 2903, 2852, 1651, 1603, 1584, 1450, 1329, 1200, 1183, 1156, 1032, 1002, 622.

6-Hydroxysalicylaldehyde *via* 5-Hydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one:[3,4]



6-HSA

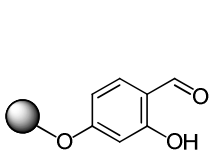
To a solution of 2,6-dihydroxybenzoic acid (9.24 g, 60.0 mmol) and DMAP (366 mg, 3.00 mmol) in DME (45 mL) were added acetone (4.53 g, 5.74 mL, 78.0 mmol) and $SOCl_2$ (9.28 g, 5.67 mL, 78.0 mmol) at 0 °C under nitrogen. Stirring was continued for 1 h at bath temperature, then 23 h at r.t. The reaction was poured into a sat. aqueous solution of $NaHCO_3$ (100 mL) and the aqueous phase was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography [cyclohexane/EtOAc (9:1); R_f = 0.39] to give 9.72 g (84%) of colorless crystals.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.75 (s, 6H, $2CH_3$), 6.34 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar_m-H), 6.64 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar_m-H), 7.41 (t, *J* = 8.2 Hz, 1H, Ar_m-H), 10.34 (s, 1H, OH).

To a solution of 5-hydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (10.1 g, 52.0 mmol) in dry CH_2Cl_2 (52 mL) was added DIBALH (1.2 M solution in toluene, 130 mL, 156 mmol) at –78 °C under nitrogen. Stirring continued for 6 h at bath temperature, after which 5 mL of MeOH were added. The reaction was poured carefully into a 0.5 M solution of HCl (300 mL). 150 mL of Et_2O were added, the organic layer was separated and the aqueous one was extracted with Et_2O (3 × 200 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography [cyclohexane/EtOAc (6:1) up to (3:1); TLC in the latter solvent: R_f = 0.34] to give 5.91 g (82%) of yellow crystals.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.39 (d, *J* = 8.3 Hz, 2H, Ar_m-H), 7.33 (t, *J* = 8.3 Hz, 1H, Ar_m-H), 10.37 (s, 1H, CHO).

General Procedure for Immobilization of Salicylaldehydes:



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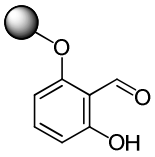


6

DHP-resin **4** was predried overnight at 100 °C, then suspended in a mixture of DCE/toluene (42/18 mL) under nitrogen. 4- or 6-HSA (4.15 g, 30.0 mmol) and PPTS (2.26 g, 9.00 mmol) were added and the mixture agitated at 55 °C overnight. Afterwards, the resin was filtered, washed and dried under vacuum to give resins **5** or **6**.

5: Loading: 0.25–0.43 mmol/g (up to 48% yield)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.3, 26.9, 29.2, 69.3, 72.9, 73.1, 96.0, 103.0, 109.1, 114.8, 135.8, 164.3, 165.1, 194.1.

Raman: ν = 3055, 3002, 2977, 2903, 2852, 1643, 1638, 1603, 1584, 1450, 1329, 1200, 1183, 1156, 1032, 1002, 622.

6: Loading: 0.33–0.46 mmol/g (up to 52% yield)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5, 26.9, 29.3, 69.3, 72.7, 73.2, 96.4, 107.3, 110.3, 114.8, 138.3, 162.0, 194.3.

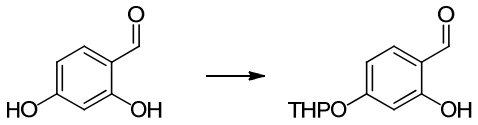
Raman: ν = 3055, 3002, 2976, 2903, 2853, 1644, 1603, 1584, 1450, 1327, 1308, 1200, 1183, 1156, 1032, 1002, 622.

General Procedure for Cleavage:

200 mg of the resin were suspended in 4 mL of a 1:1 mixture of EtOH/DCE or a 6:1 mixture of THF/H_2O. Then PPTS (100 mg, 0.400 mmol) was added and the mixture was agitated at 70 °C overnight. The resin was separated by filtration, washed with 25 mL of EtOAc and the filtrate concentrated under reduced pressure. The crude product was diluted with EtOAc (15 mL) and water (10 mL). The organic layer was separated and the aqueous one extracted twice with EtOAc (15 mL).

The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. After Diels-Alder reaction the crude product was additionally purified by flash chromatography.

2-Hydroxy-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]benzaldehyde (10):



10

2,4-Dihydroxybenzaldehyde (4.14 g, 30.0 mmol) and PPTS (754 mg, 3.00 mmol) were dissolved in CH_2Cl_2 (60 mL) under nitrogen atmosphere. DHP (3.02 g, 3.30 mL, 36.0 mmol) was added and the mixture stirred for 3 h at ambient temperature. Afterwards, 90 mL of a sat. solution of $NaHCO_3$ was added, the organic layer separated and the aqueous one extracted twice with EtOAc (90 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography [cyclohexane/EtOAc (6:1), $R_f = 0.31$] to give colorless crystals (5.63 g, 76%).[5]

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.50–2.20 (m, 6H, $3CH_2$), 3.58–3.67+3.76–3.89 (m, 2H, OCH_2), 5.50 (t, *J* = 2.9 Hz, 1H, OCHO), 6.62 (d, *J* = 2.3 Hz, 1H, Ar_m-H), 6.65 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar_m-H), 7.43 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 9.72 (s, 1 H, CHO), 11.63 (s, 1H, OH).

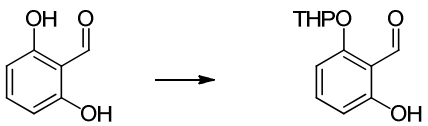
Major Regioisomer:

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4, 24.9, 29.9, 62.1, 96.2, 103.6, 109.4, 115.7, 135.3, 164.1, 164.3, 194.5.

Minor Regioisomer:

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 25.4, 30.6, 63.0, 94.7, 103.0, 108.8, 115.2, 136.0, 164.1, 164.4, 194.2.

2-Hydroxy-6-[(tetrahydro-2*H*-pyran-2-yl)oxy]benzaldehyde (12):



12

2,6-Dihydroxybenzaldehyde (2.07 g, 15.0 mmol) and PPTS (377 mg, 1.50 mmol) were dissolved in CH_2Cl_2 (30 mL) under nitrogen atmosphere. DHP (1.51 g, 1.64 mL, 18.0 mmol) was added and the mixture stirred overnight at ambient temperature. Afterwards, 45 mL of a sat. solution of $NaHCO_3$ were added, the organic layer separated and the aqueous one extracted twice with EtOAc (45 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography [cyclohexane/EtOAc (10:1), $R_f = 0.26$] to give a yellow oil (2.21 g, 67%).

IR (KBr) ν = 2946, 2877, 2944, 1643, 1620, 1582, 1459, 1334, 1240, 1203, 1120, 1059, 1036.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.57–1.76 (m, 3H, $3CH_2$), 1.88–2.04 (m, 3H, $3CH_2$), 3.63 (tdd, *J* = 11.3, 4.0, 1.5 Hz, 1 H, OCH_2), 3.86 (ddd, *J* = 11.5, 11.3, 3.2 Hz, 1H, OCH_2), 5.64 (t, *J* = 3.0 Hz, 1H, OCHO), 6.52 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 6.73 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.48 (t, *J* = 8.4 Hz, 1H, Ar_m-H), 10.44 (s, 1H, CHO), 11.88 (s, 1H, OH).

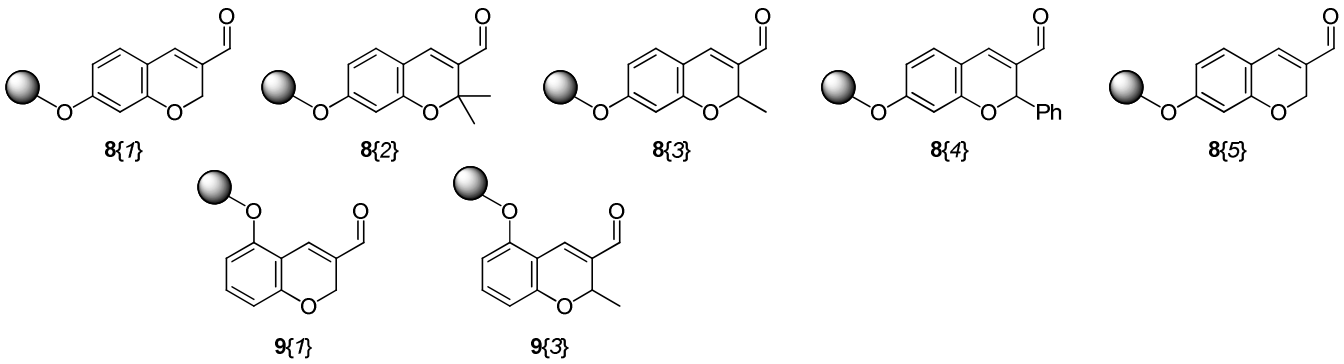
^{13}C NMR (100 MHz, acetone-d_6): δ = 20.2, 26.8, 31.6, 63.6, 98.5, 107.0, 111.6, 113.2, 140.4, 162.1, 165.1, 196.6.

MS (EI, 70 EV): *m/z* (%) = 222 (31) [M^+], 194 (34), 137 (39), 136 (85), 108 (42), 85 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{12}H_{14}O_4$: 222.0892; found 222.0894.

General Procedure for the DOMA condensation (Solid Phase):

1.00 g of the resin was suspended in 1,4-dioxane (10 mL) in a 20 mL vial. Nitrogen was bubbled through for a few minutes, before addition of K_2CO_3 (552 mg, 4.00 mmol) and the Michael acceptor (6.00 mmol). The vial was closed and agitated at 80 °C for 4 d. After the second day another portion of the Michael acceptor (1.0 mmol) was added. At the end of the reaction, the resin was filtered, washed and dried under vacuum. The procedure was repeated a second time if remaining starting material could be detected after cleavage.



8{*1*}: resin is contaminated with ~25% of insoluble side products that complicate analysis but do not matter in the follow-up reactions.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.3, 27.0, 29.2, 63.3, 69.0, 73.0, 95.9, 104.1, 110.5, 114.4, 141.1, 161.4, 189.2.

Raman: ν = 3055, 3002, 2976, 2903, 2854, 1671, 1631, 1604, 1584, 1562, 1450, 1314, 1275, 1200, 1183, 1156, 1032, 1002, 649, 622.

After cleavage: 7-Hydroxy-2*H*-chromene-3-carbaldehyde:

Yield: 65%. Orange solid. For analytical data see solution phase below.

8{*2*}:

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6, 26.8, 27.2 (2C), 29.5, 69.2, 73.1, 79.0, 96.1, 104.6, 110.0, 114.1, 136.6, 142.8, 156.0, 162.1, 190.0.

Raman: ν = 3054, 3003, 2977, 2904, 2853, 1678, 1605, 1584, 1561, 1451, 1332, 1198, 1183, 1157, 1032, 1002.

After cleavage: 7-Hydroxy-2,2-dimethyl-2*H*-chromene-3-carbaldehyde:

Yield: 60–90%. Orange solid. For analytical data see solution phase below.

8{*3*}:

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4, 20.0, 27.3, 29.5, 69.0, 69.8, 73.1, 96.0, 105.0, 110.1, 140.2, 161.7, 189.5.

Raman: ν = 3055, 3002, 2977, 2904, 2853, 1672, 1632, 1604, 1584, 1561, 1450, 1302, 1200, 1183, 1156, 1033, 1002, 622.

After cleavage: 7-Hydroxy-2-methyl-2*H*-chromene-3-carbaldehyde:

Yield: 90%. Yellow solid. For analytical data see solution phase below.

8{*4*}:

Raman ν = 3056, 3001, 2976, 2903, 2854, 1675, 1620, 1604, 1586, 1561, 1451, 1275, 1200, 1182, 1156, 1033, 1003.

After cleavage: 7-Hydroxy-2-phenyl-2*H*-chromene-3-carbaldehyde:

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.42.

Yield: 38% + 27% starting material as an inseparable mixture.

^{1}H NMR (500 MHz, acetone-d_6): δ = 6.24 (s, 1H, OCH), 6.36 (d, J = 2.3 Hz, 1H, Ar_m-H), 6.51 (dd, J = 8.3, 2.3 Hz, 1H, Ar_m-H), 7.25–7.32 (m, 4H, Ar_m-H), 7.34–7.39 (m, 2H, Ar_m-H), 7.66 (s, 1H, =CH), 9.40 (br.s, 1H, OH), 9.62 (s, 1H, CHO).

^{13}C NMR (125 MHz, acetone-d_6): δ = 75.8, 105.4, 111.7, 115.0, 128.4, 130.5 (3C), 132.6, 133.1, 141.4, 132.8, 143.0, 158.4, 164.6, 191.4.

MS (EI, 70eV): *m/z* (%) = 252 (23) [M^+], 223 (100), 175 (13), 165 (29), 152 (19).

HRMS–EI: *m/z* [M^+] calcd for $C_{16}H_{12}O_3$: 252.0786; found: 252.0789.

8{*5*}:

Raman: ν = 3055, 3003, 2977, 2916, 2854, 1659, 1604, 1584, 1565, 1448, 1204, 1156, 1032, 1002 .

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4, 24.7, 27.1, 29.4, 64.2, 69.0, 73.8, 95.9, 103.3, 109.8, 113.1, 130.5, 134.6, 157.2, 161.1, 195.6.

After cleavage: 1-(7-Hydroxy-2*H*-chromen-3-yl)ethanone:

Yield: 50%. Yellow solid. For analytical data see solution phase below.

9{*1*}: resin is contaminated with ~50% of insoluble side products, which give difficulties at analysis.

Raman: ν = 3056, 3001, 2977, 2914, 1722, 1673, 1628, 1603, 1584, 1451, 1309, 1182, 1156, 1032, 1002, 622.

After cleavage: 5-Hydroxy-2*H*-chromene-3-carbaldehyde:

Flash chromatography in cyclohexane/EtOAc (3:1). R_f = 0.30.

Yield: 32% (and 8% 6-HSA). Yellow solid.

^{1}H NMR (400 MHz, MeOD): δ = 4.88 (d, *J* = 0.9 Hz, 2H, OCH_2), 6.32 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 6.41 (dd, *J* = 8.2, 0.9 Hz, 1H, Ar_m-H), 7.11 (t, *J* = 8.2 Hz, 1H, Ar_m-H), 7.73 (d, *J* = 0.9 Hz, 1H, =CH), 9.50 (s, 1H, CHO).

^{13}C NMR (100 MHz, MeOD): δ = 63.5, 108.2, 109.3, 111.9, 130.7, 134.9, 139.0, 157.4, 158.3, 191.7.

MS (EI, 70 eV): *m/z* (%) = 176 (44) [M^+], 147 (69) [$C_9H_7O_2^+$], 138 (67), 137 (58), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{16}H_{22}O_4$: 176.0473; found: 176.0471.

9{*3*}:

Raman: ν = 3056, 3001, 2977, 2914, 1722, 1673, 1628, 1603, 1584, 1451, 1309, 1182, 1156, 1032, 1002, 622.

After cleavage: 5-Hydroxy-2-methyl-2*H*-chromene-3-carbaldehyde:

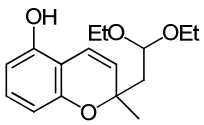
Flash chromatography in cyclohexane/EtOAc (3:1). R_f = 0.50.

Yield: 27% product plus many side products. Yellow solid.

^{1}H NMR (400 MHz, acetone-d_6): δ = 4.88 (d, *J* = 0.9 Hz, 2H, OCH_2), 6.32 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 6.41 (dd, *J* = 8.2, 0.9 Hz, 1H, Ar_m-H), 7.11 (t, *J* = 8.2 Hz, 1H, Ar_m-H), 7.73 (d, *J* = 0.9 Hz, 1H, =CH), 9.50 (s, 1H, CHO).

^{13}C NMR (125 MHz, acetone-d_6): δ = 20.8, 70.8, 109.9, 110.0, 111, 135.5, 136.2, 136.8, 156.9, 157.5, 191.6.

15 (after cleavage of 14a/b):



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Flash chromatography in cyclohexane/EtOAc (3:1). R_f = 0.42.

Yield: 25%. Yellow oil.

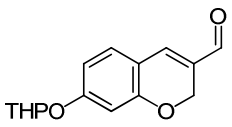
^{1}H NMR (250 MHz, MeOD): δ = 1.146 (t, *J* = 7.1, 3H, CH_3), 1.151 (t, *J* = 7.1, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.99 (dd, *J* = 5.1, 2.3 Hz, 2H, CH_2), 3.40–3.70 (m, 4H, $2CH_2$), 4.77 (t, *J* = 5.1 Hz, 1H, CH), 5.59 (d, *J* = 10.1 Hz, CH=), 6.23 (d, *J* = 8.1 Hz, 1H, Ar_m-H), 6.30 (dd, *J* = 8.1, 0.9 Hz, 1H, Ar_m-H), 6.64 (d, *J* = 10.1 Hz, 1H, =CH), 6.87 (t, *J* = 8.1 Hz, 1H, Ar_m-H).

^{13}C NMR (125 MHz, acetone-d_6): δ = 16.6, 16.7, 27.8, 46.4, 62.2, 62.8, 78.2, 101.6, 109.5, 109.7, 111.3, 118.4, 129.7, 130.7, 155.0, 155.7.

MS (EI, 70 eV): *m/z* (%) = 278 (14) [M^+], 232 (11) [$C_{14}H_{16}O_3^+$], 161 (100), 103 (23), 75 (9), 47 (9).

HRMS–EI *m/z* [M^+] calcd for $C_{16}H_{22}O_4$: 278.1518; found: 278.1519.

General Optimized Procedure for the DOMA Condensation (Solution Phase):



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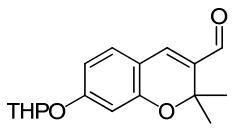
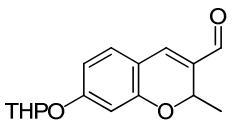
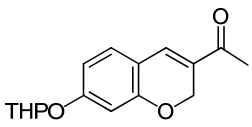


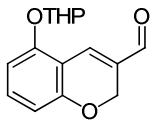
11{*2*}



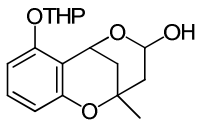
11{*3*}



11{*5*}



13{*1*}



14b

To a solution of 2-hydroxy-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]benzaldehyde or 2-hydroxy-6-[(tetrahydro-2*H*-pyran-2-yl)oxy]benzaldehyde (3.00 mmol) and K_2CO_3 (207 mg, 1.50 mmol) in 1,4-dioxane (6 mL) was added the Michael acceptor (4.50 mmol). The mixture was heated for 3 d at 80 °C. After half of the time another portion of the Michael acceptor (1.00 mmol) was added. The reaction was quenched by adding a sat. aqueous solution of $NaHCO_3$ (15 mL) and EtOAc (15 mL), then the aqueous layer was separated and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried, concentrated under reduced pressure and purified by flash chromatography.

7-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-2*H*-chromene-3-carbaldehyde (11{*1*}):

Flash chromatography in cyclohexane/EtOAc (6:1). R_f = 0.26. Yield: 89%. Yellow crystals.

Mp 174 °C (cyclohexane).

IR (DRIFT): ν = 3306, 3070, 2943, 2877, 1666, 1611, 1561, 1494, 1461, 1439, 1402, 1372, 1352, 1273, 1202, 1169, 1123, 1106.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.54–2.06 (m, 6H, $3CH_2$), 3.56–3.67+3.79–3.91 (m, 2H, OCH_2), 5.01 (s, 2H, OCH_2), 5.43 (t, *J* = 2.9 Hz, 1H, OCHO), 6.59 (d, *J* = 2.2 Hz, 1H, Ar_m-H), 6.65 (dd, *J* = 8.4, 2.2 Hz, 1H, Ar_m-H), 7.12 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.21 (s, 1H, =CH), 9.51 (s, 1H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 25.0, 30.0, 62.1, 63.4, 96.2, 104.2, 110.6, 114.5, 129.2, 130.4, 141.5, 157.7, 161.5, 189.5.

MS (EI, 70 eV): *m/z* (%) = 260 (1) [M^+], 174 (15) [$C_{10}H_8O_3^+$], 147 (7), 85 (11), 58 (22), 43 (100).

MS (FAB^+): *m/z* (%) = 261 (45) [MH^+], 217 (18), 177 (100) [$C_{10}H_{11}O_3^+$], 176 (52) [$C_{10}H_{10}O_3^+$], 154 (56), 137 (36), 136 (46), 85 (56).

HRMS–FAB: *m/z* [MH^+] calcd for $C_{15}H_{17}O_4$: 261.1127; found: 261.1124.

2,2-Dimethyl-7-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2*H*-chromene-3-carbaldehyde (11{*2*}):

Flash chromatography in cyclohexane/CH_2Cl_2 (2:3) to CH_2Cl_2. Latter R_f = 0.40. Yield: 44%. Brown solid, slightly impure but attempts of further purification by recrystallization failed.

IR (DRIFT): ν = 3318, 3072, 2944, 2874, 2730, 1885, 1780, 1666, 1607, 1563, 1499, 1436, 1359, 1331, 1275, 1161, 1114, 1037.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.56 (s, 6H, $2CH_3$), 1.50–2.00 (m, 6H, $3CH_2$), 3.55–3.68+3.74–3.88 (m, 2H, OCH_2), 5.51 (t, *J* = 2.9 Hz, 1H, OCHO), 6.51 (d, *J* = 2.3 Hz, 1H, Ar_m-H), 6.64 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar_m-H), 7.26 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.34 (s, 1H, =CH), 9.43 (s, 1H, CHO).

^{13}C NMR (100 MHz, acetone-d_6): δ = 20.4, 26.8, 28.0 (2C), 31.8, 63.6, 80.3, 98.0, 105.7, 111.9, 115.7, 132.0, 138.5, 144.0, 157.4, 163.8, 191.7.

MS (FAB^+): *m/z* (%) = 289 (19) [MH^+], 206 (18) [$C_{11}H_{14}O_3^+$], 205 (71) [$C_{11}H_{13}O_3^+$], 204 (49) [$C_{11}H_{12}O_3^+$], 203 (23), 189 (45), 85 (100).

HRMS–FAB: *m/z* [MH^+] calcd for $C_{17}H_{21}O_4$: 289.1440; found: 289.1443.

2-Methyl-7-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2*H*-chromene-3-carbaldehyde (11{*3*}):

Flash chromatography in cyclohexane/EtOAc (6:1). R_f = 0.27. Yield: 75%. Orange oil.

2 Diastereomers not separable ~1:1.

IR (KBr): ν = 2944, 2872, 2712, 1670, 1608, 1559, 1494, 1441, 1391, 1325, 1301, 1271, 1230, 1203, 1168, 1121, 1102, 1074, 1036, 1022.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.28+1.29 (d, *J* = 6.5 Hz, 3H, CH_3), 1.55–2.00 (m, 6H, $3CH_2$), 3.55–3.67+3.74–3.88 (m, 2H, OCH_2), 5.31 (q, *J* = 6.5 Hz, 1H, CH), 5.48–5.63 (m, 1H, OCHO), 6.55–6.58 (m, 1H, Ar_m-H), 6.68 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar_m-H), 7.29 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.42 (s, 1H, =CH), 9.52 (s, 1H, CHO).

^{13}C NMR (100 MHz, acetone-d_6): δ = 20.37+20.40, 21.20+21.24, 26.8+28.5, 31.79+31.84, 63.5+63.6, 71.5+71.6, 97.9+98.1, 106.2+106.3, 112.1+112.2, 115.92+115.94, 132.3, 135.75+135.77, 141.56+141.62, 157.58+157.60, 163.5+163.6, 191.3.

MS (FAB$^+$): *m/z* (%) = 275 (28) [MH^+], 191 (100) [$C_{11}H_{11}O_3^+$], 190 (46) [$C_{11}H_{10}O_3^+$], 175 (15), 85 (85).

HRMS–FAB: *m/z* [MH^+] calcd for $C_{16}H_{19}O_4$: 275.1283; found: 275.1280.

1-[7-{(Tetrahydro-2*H*-pyran-2-yl)oxy}-2*H*-chromen-3-yl]ethanone (11{*5*}):

Flash chromatography in cyclohexane/EtOAc (6:1). R_f = 0.26. Yield: 67%. Yellow crystals.

Mp 83–85 °C.

IR (Diamant-ATR) ν = 2934, 2870, 1654, 1633, 1609, 1340, 1286, 1271, 1253, 1201, 1179, 1142, 1108, 1047, 1021.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52–2.00 (m, 6H, $3CH_2$), 2.35 (s, 3H, CH_3), 3.60 (tdd, *J* = 10.2, 4.3, 1.1 Hz, 1H, OCH_2), 3.80 (tdd, *J* = 11.5, 9.5, 3.2 Hz, 1H, OCH_2), 4.89 (d, *J* = 1.1 Hz, 2H, OCH_2), 5.48 (t, *J* =3.3 Hz, 1H, OCHO), 6.54 (d, *J* = 2.3 Hz, 1H, Ar_m-H), 6.66 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar_m-H), 7.23 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.55 (s, 1H, CH=).

^{13}C NMR (100 MHz, Acetone-d_6): δ = 20.4, 26.0, 26.8, 31.8, 63.5, 65.8, 98.0, 105.6, 112.2, 116.8, 129.9, 132.2, 135.6, 158.7, 162.6, 196.8.

MS (EI, 70 EV): *m/z* (%) = 274 (7) [M^+], 190 (100), 147 (48), 85 (14).

HRMS–EI: *m/z* [MH^+] calcd for $C_{16}H_{18}O_4$: 274.1205; found: 274.1207.

5-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-2*H*-chromene-3-carbaldehyde (13{*1*}):

Flash chromatography in cyclohexane/EtOAc (20:1). R_f = 0.17. Yield: 43% (+20% SM). Pale yellow crystals.

IR (ATR): v = 2934, 2876, 2812, 1657, 1627, 1600, 1575, 1468, 1397, 1343, 1307, 1286, 1256, 1234, 1204, 1187, 1164, 1117, 1049, 1035, 1019.

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.58–1.77 (m, 3H, $3CH_2$), 1.89–1.96 (m, 2H, CH_2), 2.02–2.10 (m, 1H, CH_2), 3.61 (tdd, *J* = 11.3, 4.1, 1.2 Hz, 1H, OCH_2), 3.83 (tdd, *J* = 21.3, 19.9, 3.2 Hz, 1H, OCH_2), 4.91 (dAB-sys., *J* = 14.1, 1.1 Hz, 2H, OCH_2), 5.57 (d, *J* = 3.1 Hz, 1H, OCHO), 6.51 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 6.78 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 7.27 (t, *J* = 8.2 Hz, 1H, Ar_m-H), 7.81 (s, 1H, CH=), 9.64 (s, 1H, CHO).

^{13}C NMR (125 MHz, acetone-d_6): δ = 20.4, 26.8, 31.8, 63.6, 64.2, 98.3, 109.5, 111.1, 113.4, 139.9, 132.3, 137.7, 156.7, 158.7, 191.6.

MS (EI, 70 eV): *m/z* (%) = 260 (13) [M^+], 176 (75), 147 (31), 85 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_4$: 260.1049; found: 260.1048.

2-Methyl-7-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2,3,4,6-tetrahydro-2,6-methanobenzo[*b*][1,5] dioxocin-4-ol (14b):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.27. Yield: 69%. Colorless crystals.

Diastereomeric mixture (3 : 2).

IR (ATR): v = 3329, 2927, 1703, 1588, 1462, 1344, 1284, 1235, 1194, 1181, 1160, 1122, 1096, 1057, 1022.

MS (EI, 70 eV): *m/z* (%) = 306 (5) [M^+], 222 (65), 204 (16), 161 (54), 160 (100), 85 (65), 85 (30), 43 (83).

HRMS–EI: *m/z* [M^+] calcd for $C_{17}H_{22}O_5$: 306.1467; found: 306.1465.

Major Diastereomer:

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.403 (s, 3H, CH_3), 1.52–1.71 (m, 6H, 3CH_2), 1.81–1.86 (m, 2H, CH_2), 2.09 (dt, *J* = 13.3, 3.8 Hz, 2H, CH_2), 2.09 (s, 1H, OH), 3.49–3.58 (m, 1H, OCH_2), 3.81 (ddd, *J* = 11.4, 9.7, 3.1 Hz, 1H, OCH_2), 5.20 (d, *J* = 6.5 Hz, 1H, OCH), 5.28–5.32 (m, 1H, OCHO), 5.43 (t, *J* = 3.2 Hz, 1H, OCHO), 6.41 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 6.64 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 7.10 (t, *J* = 8.2 Hz, 1H, Ar_m-H).

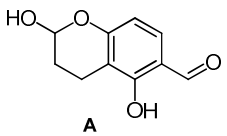
^{13}C NMR (125 MHz, acetone-d_6): δ = 20.6, 27.0, 29.9, 32.0, 36.5, 48.1, 63.4, 63.5, 76.0, 91.2, 98.5, 109.0, 110.7, 113.2, 131.3, 156.8, 158.7.

Minor Diastereomer:

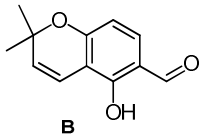
^{1}H NMR (500 MHz, acetone-d_6): δ = 1.400 (s, 3H, CH_3), 1.52–1.71 (m, 6H, 3 CH_2), 1.81–1.86 (m, 2H, CH_2), 2.00 (dt, *J* = 13.8, 2.5 Hz, 2H, CH_2), 2.09 (s, 1H, OH), 3.49–3.58 (m, 1H, OCH_2), 3.93 (ddd, *J* = 11.4, 9.7, 3.1 Hz, 1H, OCH_2), 5.17 (d, *J* = 6.5 Hz, 1H, OCH), 5.28–5.32 (m, 1H, OCHO), 5.45 (t, *J* = 3.2 Hz, 1H, OCHO), 6.38 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 6.63 (d, *J* = 8.2 Hz, 1H, Ar_m-H), 7.09 (t, *J* = 8.2 Hz, 1H, Ar_m-H).

^{13}C NMR (125 MHz, acetone-d_6): δ = 20.5, 27.02, 29.9, 32.1, 36.5, 48.1, 63.3, 63.4, 76.0, 91.2, 97.8, 107.6, 110.2, 112.5, 131.3, 156.7, 158.6.

Side reactions under DOMA-Conditions of Acrolein/Senecialdehyde with Unprotected 4-HSA:



A



B

2,5-Dihydroxychroman-6-carbaldehyde (A):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.40. Yield: 50%. Yellow crystals.

Mp 76–79 °C.

IR (ATR) v = 3447, 3106, 2875, 2543, 1622, 1580, 1485, 1422, 1373, 1275, 1235, 1176, 1142, 1124, 1083.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.88–2.04 (m, 2H, CH_2), 2.69–2.74 (m, 3H, CH_2), 5.67 (bs, 1H, OCHO), 6.32 (br. s, 1H, OH), 6.45 (d, *J* = 8.6 Hz, 1 H, Ar_m-H), 7.47 (d, *J* = 8.6 Hz, 1 H, Ar_m-H), 9.75 (s, 1H, CHO), 11.85 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 15.8, 28.1, 94.7, 111.7, 111.8, 116.4, 134.7, 162.1, 163.0, 197.3.

MS (EI, 70 eV): *m/z* (%) = 194 (86) [M^+], 166 (63), 151 (50), 138 (28), 55 (75), 39 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{10}H_{10}O_4$: 194.0579; found: 194.0578.

5-Hydroxy-2,2-dimethyl-2*H*-chromene-6-carbaldehyde (B):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.63. Yield: 12% + 40% starting material.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.45 (s, 6H, $2CH_3$), 5.77 (d, *J* = 10.0 Hz, 1H, CH=), 6.47 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 6.65 (d, *J* = 10.0 Hz, 1H, CH=), 7.54 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 9.76 (s, 1H, CHO), 11.81 (s, 1H, OH).

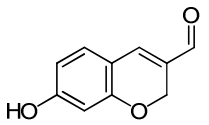
^{13}C NMR (125 MHz, acetone-d_6): δ = 29.5 (2C), 79.9, 110.4, 111.1, 116.5, 117.2, 130.9, 137.1, 160.2, 162.2, 197.5.

MS (EI, 70 eV): *m/z* (%) = 204 (20) [M^+], 189 (100), 187 (30).

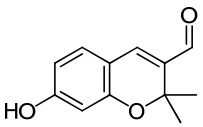
HRMS–EI: *m/z* [M^+] calcd for $C_{10}H_{10}O_4$: 204.0786; found: 204.0784.

General Procedure for THP-Cleavage (Solution Phase):

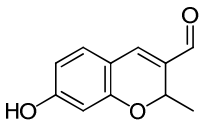
To a solution of the THP ether (0.75 mmol) in methanol (11 mL) was added *p*-TsOH•H_2O (29 mg, 0.15 mmol) and stirring continued for 3 h. The crude mixture was concentrated under reduced pressure, diluted with EtOAc (20 mL) and water (25 mL), the organic layer was separated and the aqueous one extracted twice with EtOAc (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure and purified by flash chromatography.



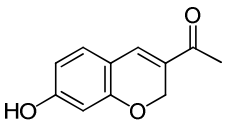
C-8{*1*}



C-8{*2*}



C-8{*3*}



C-8{*5*}

7-Hydroxy-2*H*-chromene-3-carbaldehyde (C-8{*1*}):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.30. Yield: 80%. Orange solid.

Mp 191–201 °C (CH_2Cl_2/EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.88 (d, J = 0.9 Hz, 2H, OCH_2), 6.28 (d, J = 2.1 Hz, 1H, Ar_m-H), 6.45 (dd, J = 8.3, 2.3 Hz, 1H, Ar_m-H), 7.21 (d, J = 8.3 Hz, 1H, Ar_m-H), 7.52 (d, J = 0.6 Hz, 1H, =CH), 9.47 (s, 1H, CHO), 10.30 (bs, 1H, OH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 63.2, 103.1, 110.4, 113.0, 128.0, 131.8, 142.3, 157.7, 162.9, 190.3.

MS (EI, 70eV): *m/z* (%) = 176 (100) [M^+], 147 (84) [M^+–CHO], 137 (36).

HRMS–EI: *m/z* [M^+] calcd for $C_{10}H_8O_3$: 176.0473; found: 176.0475.

7-Hydroxy-2,2-dimethyl -2*H*-chromene-3-carbaldehyde (C-8{*2*}):

Flash chromatography in cyclohexane/EtOAc (4:1). R_f = 0.25. Yield: 78%. Brown solid.

Mp 143 °C (cyclohexane/EtOAc = 3:1).

IR (ATR): ν = 2919, 1645, 1609, 1550, 1455, 1379, 1359, 1249, 1193, 1160, 1128, 1100.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.55 (s, 6H, $2CH_3$), 6.31 (d, J = 2.3 Hz, 1H, Ar_m-H), 6.47 (dd, J = 8.3, 2.3 Hz, 1H, Ar_m-H), 7.19 (d, J = 8.3 Hz, 1H, Ar_m-H), 7.30 (s, 1H, =CH), 9.00–9.22 (bs, 1H, OH), 9.40 (s, 1H, CHO).

^{13}C NMR (100 MHz, acetone-d_6): δ = 27.9 (2C), 80.2, 104.9, 111.2, 114.3, 132.5, 137.7, 144.4, 157.8, 164.6, 191.5.

MS (EI, 70 eV): *m/z* (%) = 204 (18) [M^+], 189 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{12}H_{12}O_3$: 204.0786; found: 204.0790.

7-Hydroxy-2-methyl -2*H*-chromene-3-carbaldehyde (C-8{*3*}):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.39. Yield: 70%. Yellow solid.

Mp 157 °C (cyclohexane/EtOAc = 3:1).

IR (ATR): ν = 2926, 1638, 1603, 1550, 1393, 1361, 1280, 1165, 1095.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.27 (d, J = 6.5 Hz, 3H, CH_3), 5.28 (q, J = 6.5 Hz, 1H, OCH), 6.36 (d, J = 2.3 Hz, 1H, Ar_m-H), 6.50 (dd, J = 8.3, 2.3 Hz, 1H, Ar_m-H), 7.22 (d, J = 8.3 Hz, 1H, Ar_m-H), 7.39 (s, 1H, =CH), 9.12 (s, 1H, OH), 9.49 (s, 1H, CHO).

^{13}C NMR (100 MHz, acetone-d_6): δ = 21.1, 71.5, 105.3+105.4, 111.4+111.5, 114.6, 132.8, 134.9, 142.0, 158.0, 164.2+164.3, 191.2.

MS (EI, 70 eV): *m/z* (%) = 190 (26) [M^+], 175 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{11}H_{10}O_3$: 190.0630; found: 190.0631.

7-Hydroxy-2-methyl -2*H*-chromene-3-carbaldehyde (C-8{*5*}):

Flash chromatography in cyclohexane/EtOAc (2:1). R_f = 0.39. Yield: 95%. Yellow solid.

Mp 189–190 °C.

^{1}H NMR (500 MHz, acetone-d_6): δ = 2.33 (s, 3H, CH_3), 4.87 (d, *J* = 1.1 Hz, 2H, OCH_2), 6.33 (d, *J* = 2.2 Hz, 1H, Ar_m-H), 6.49 (dd, *J* = 8.3, 2.2 Hz, 1H, Ar_m-H), 7.17 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 7.53 (s, 1H, =CH), 9.01 (s, 1H, OH).

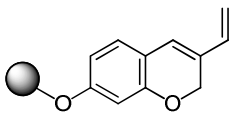
^{13}C NMR (100 MHz, acetone-d_6): δ = 25.9, 65.8, 104.7, 111.5, 115.2, 129.0, 132.7, 136.0, 159.1, 163.4, 196.7.

MS (EI, 70 eV): *m/z* (%) = 190 (60) [M^+], 175 (14), 147 (100), 43 (42).

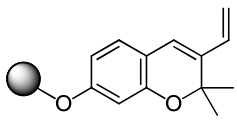
HRMS–EI: *m/z* [M^+] calcd for $C_{11}H_{10}O_3$: 190.0630; found: 190.0632.

General Procedure for the Wittig reaction (Solid Phase):

Methyl triphenylphosphonium bromide (1.79 g, 5.00 mmol) was suspended in dry THF (14 mL) under nitrogen and cooled to –25 °C. *n*-BuLi (3.10 mL, 5.00 mmol, 1.6 M solution in hexanes) was added (yellow color) and the mixture stirred for 2 h (–25 °C up to r.t.). Afterwards, it was cooled to –35 °C and added to the resin (1.65 g), which was previously suspended in 12 mL of dry THF, also cooled to –35 °C. The reaction was allowed to warm up to r.t. over the next 2 h. Then it was quenched with water (2 mL), washed and dried under vacuum.



16{*1*}



16{*2*}

16{*1*}:

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4, 27.1, 29.4, 65.4, 68.7, 72.8, 95.9, 103.8, 109.9, 112.0, 115.7, 154.8, 158.1.

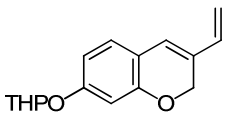
Raman: ν = 3056, 3003, 2977, 2906, 2855, 1633, 1603, 1584, 1450, 1271, 1182, 1032, 1002.

16{*2*}:

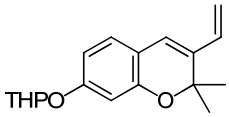
^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5, 26.6 (2C), 27.2, 29.5, 68.6, 70.12, 73.1, 95.9, 104.2, 109.2, 114.6, 118.6, 158.2.

Raman: ν = 3054, 3003, 2977, 2905, 2854, 1604, 1584, 1568, 1451, 1183, 1032, 1002.

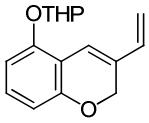
General Procedure for the Wittig reaction (Solution Phase):



17{*1*}



17{*2*}



Wittig of 13{*2*}

Methyl triphenylphosphonium bromide (714 mg, 2.00 mmol) was suspended in dry THF (6 mL) under nitrogen and cooled to –20 °C. *n*-BuLi (1.25 mL, 1.6 M solution in hexane, 2.0 mmol) was added and the mixture stirred for 1 h (–20 °C up to 0 °C). Afterwards, the carbaldehyde (0.85 mmol) was added at –20 °C in 5 mL of THF. The reaction was allowed to warm up to r.t. over the next hour, before being quenched with water (0.5 mL). A saturated aqueous solution of NH_4Cl (15 mL) and EtOAc (15 mL) were added, the aqueous layer separated and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried, concentrated under reduced pressure and purified by flash chromatography. The products undergo dimerization on silica gel and/or refrigerated.

7-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-3-vinyl-2*H*-chromene 17{*1*}:

Flash chromatography in cyclohexane/EtOAc (12:1). R_f = 0.41. Yield: 80%. Colorless oil.

IR (KBr): ν = 3392, 2947, 2871, 2874, 1726, 1616, 1501, 1440, 1356, 1270, 1203, 1161, 1104, 1076, 1021.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.56–2.10 (m, 6H, $3CH_2$), 3.57–3.65 (m, 1H, OCH_2), 3.89 (ddd, *J* = 11.5, 9.0, 3.2 Hz, 1H, OCH_2), 4.94 (s, 2H, OCH_2), 4.97 (d, *J* = 17.8 Hz, 1H, $=CH_2$), 5.11 (d, *J* = 11.1

Hz, 1H, =CH_2), 5.38 (t, *J* = 3.3 Hz, 1H, OCHO), 6.35 (s, 1H, CH=), 6.42 (dd, *J* = 17.8, 11.1 Hz, 1H, =CH), 6.56 (s, 1H, Ar_m-H), 6.56–6.62 (m, 1H, Ar_m-H), 6.88–6.98 (m, 1H, Ar_m-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8, 25.1, 30.2, 62.1, 65.3, 96.3, 104.0, 109.6, 112.2, 116.5, 123.5, 127.5, 128.3, 134.8, 154.8, 158.1.

MS (FAB^+): *m/z* (%) = 175 (17) [$C_{11}H_{11}O_2^+$], 174 (40) [MH^+–THP; $C_{11}H_{10}O_2^+$], 173 (29), 85 (THP, 100).

2,2-Dimethyl-7-[(tetrahydro-2*H*-pyran-2-yl)oxy]-3-vinyl-2*H*-chromene 17{*2*}:

Flash chromatography in cyclohexane/EtOAc (10:1). R_f = 0.50. Yield: 87%. Colorless oil.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.46 (s, 6H, $2CH_3$), 1.52–2.00 (m, 6H, $3CH_2$), 3.46–3.64 (m, 1H, OCH_2), 3.77–3.90 (m, 1H, OCH_2), 5.10 (dd, *J* = 11.0, 1.4 Hz, 1H, =CH_2), 5.40 (t, *J* = 2.9 Hz, OCHO), 5.53 (dd, *J* = 17.3, 1.4 Hz, 1H, =CH_2), 6.43 (ddd, *J* = 17.3, 11.0, 1.4 Hz, 1H, CH=), 6.47 (d, *J* = 2.3 Hz, 1H, Ar_m-H), 6.51 (s, 1H, =CH), 6.54 (dd, *J* = 8.3, 2.3 Hz, 1H, Ar_m-H), 6.97 (d, *J* = 8.3 Hz, 1H, Ar_m-H).

5-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-3-vinyl-2*H*-chromene (Wittig of 13{*2*}):

Flash chromatography in cyclohexane/EtOAc (20:1); R_f = 0.50. Yield: 74%. Colorless oil.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.52–2.10 (m, 6H, $3CH_2$), 3.51–3.64 (m, 1H, OCH_2), 3.82 (ddd, *J* = 11.5, 9.1, 3.4 Hz, 1H, OCH_2), 4.92 (s, 2H, OCH_2), 5.17 (d, *J* = 11.0 Hz, 1H, =CH_2), 5.23 (d, *J* = 11.0 Hz, 1H, =CH_2), 5.47 (t, *J* = 2.4 Hz, 1H, OCHO), 6.45 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 6.57 (dd, *J* = 17.8, 11.0 Hz, 1H, =CH), 6.70 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 6.83 (s, 1H, CH=), 7.04 (t, *J* = 8.3 Hz, 1H, Ar_m-H).

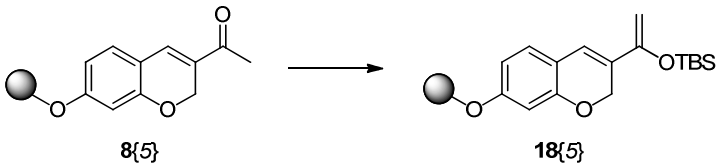
^{13}C NMR (50 MHz, acetone-d_6): δ = 19.8, 26.2, 31.8, 63.0, 65.9, 97.8, 109.2, 110.0, 114.1, 120.0, 130.5, 136.3. Determined via CH-COSY, no quaternary Cs.

MS (EI, 70 eV): *m/z* (%) = 258 (16) [M^+], 174 (100), 153 (40), 136 (21), 107 (33), 89 (28), 77 (53).

HRMS–EI *m/z* [M^+] calcd for $C_{16}H_{18}O_3$: 258.1256; found: 258.1257.

Procedure for the Enol-Ether Formation (Solid Phase):

The resin (2.50 g) was solvated in anhydrous CH_2Cl_2 (25 mL) and degassed with nitrogen for 5 min. Et_3N (2.08 mL, 1.52 g, 15.0 mmol) was added, followed by TBSOTf (1.70 mL, 1.98 g, 7.50 mmol) at –30 °C. Afterwards, the reaction was agitated for 16 h, in which the temperature was allowed to rise to r.t. The resin was filtered and washed as described above.

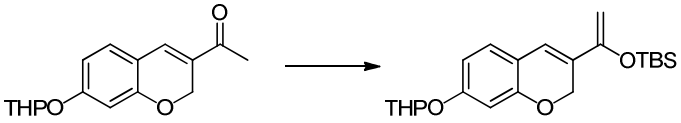


8{*5*} **18**{*5*}

18{*5*}:

Raman: ν = 3055, 3002, 2903, 2857, 1604, 1584, 1448, 1203, 1183, 1156, 1032, 1003.

Procedure for the Enol-Ether Formation (Solution Phase):



11{*5*} **19**{*5*}

To a solution of ketone **11**{*5*} (274 mg, 1.00 mmol) and Et_3N (304 mg, 0.42 mL, 3.00 mmol) in anhydrous CH_2Cl_2 under nitrogen atmosphere was added TBSOTf (396 mg, 0.34 mL, 1.50 mmol) at 0 °C. The reaction was stirred and allowed to warm up to r.t. over the next 3 h. Afterwards, it was diluted with Et_2O (10 mL) and a saturated solution of $NaHCO_3$ (15 mL). The organic layer was separated and the aqueous one extracted three times with Et_2O (15 mL). The combined organic layers were dried, concentrated and rapidly purified by flash chromatography, as decomposition could be observed on silica gel [cyclohexane/EtOAc (20:1), R_f = 0.50] to give 283 mg (73%) of a colorless oil.

19{*5*}:

IR (KBr) ν = 2952, 2857, 1614, 1570, 1501, 1462, 1345, 1320, 1288, 1256, 1203, 1162, 1142, 1123, 1109, 1077, 1023.

^{1}H NMR (250 MHz, acetone-d_6): δ = 0.24 (s, 6H, $2CH_3$), 1.03 (s, 9H, $3CH_3$), 1.50–2.02 (m, 6H, $3CH_2$), 3.63–3.51 (m, 1H, OCH_2), 3.82 (ddd, J = 11.1, 8.8, 3.0 Hz, 1H, OCH_2), 4.39–4.45 (m, 2H, $=CH_2$), 4.87 (s, 2H, OCH_2), 5.41 (br. s, 1H, OCHO), 6.53 (bs, 1H, Ar_m-H), 6.59 (dd, J = 8.3, 2.2 Hz, 1H, Ar_m-H), 6.81 (s, 1H, =CH), 7.02 (d, J = 8.3 Hz, 1H, Ar_m-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –3.4 (2C), 19.9, 26.9, 27.2 (3C), 31.9, 63.3, 66.9, 93.6, 97.9, 105.5, 111.6, 117.9, 121.9, 128.2, 129.9, 154.3, 154.3, 156.6, 160.3.

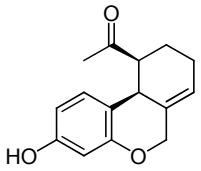
MS (EI, 70 eV): *m/z* (%) = 388 (7) [M^+], 248 (43), 233 (25), 205 (19), 147 (21), 85 (100), 75 (45), 57 (33).

HRMS–EI: *m/z* [M^+] calcd for $C_{22}H_{32}O_4Si$: 388.2070; found: 388.2068.

General Procedure for the Diels-Alder Reaction (Solid Phase):

The resin (500 mg) was dried overnight at 90 °C. It was suspended in toluene (5 mL) in a vial and nitrogen was bubbled through for 10 min. The dienophile (5.00 mmol) was added, the vial closed and the reaction agitated at 80 °C for 2 days. The resin was filtered, washed and dried under vacuum to be immediately cleaved.

1-(3-Hydroxy-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-10-yl)ethanone (21{*1,1*}):



21{*1,1*}

Yield for Wittig, Diels-Alder and cleavage: 95%. *Endo*/*Exo* = 4:1.

Flash chromatography in cyclohexane/EtOAc (2:1).

Exo-Isomer: R_f = 0.20

^{1}H NMR (250 MHz, acetone-d_6): δ = 2.00–2.24 (m, 4H, $2CH_2$), 2.35 (s, 3H, CH_3), 2.75 (ddd, *J* = 12.0, 9.2, 2.7 Hz, 1H, CH), 3.97 (bdd, *J* = 9.2, 2.3 Hz, 1H, CH), 4.38–4.50 (m, 2H, OCH_2), 5.89 (bd, *J* = 2.6 Hz, 1H, CH=), 6.21 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.32 (dd, *J* = 8.6, 2.5 Hz, 1H, Ar_m-H), 6.63 (dd, *J* = 8.6, 1.0 Hz, 1H, Ar_m-H), 8.17 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.4, 28.1, 37.4, 55.5, 72.2, 105.1, 110.2, 118.6, 125.8, 130.0, 133.8, 157.7, 158.6, 213.0.

MS (EI, 70 eV): *m/z* (%) = 244 (48) [M^+], 201 (43) [$C_{13}H_{13}O_2^+$], 173 (23), 89 (14), 58 (20), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_3$: 244.1099; found: 244.1098.

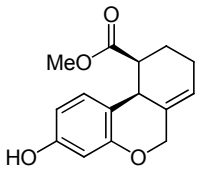
Endo-Isomer: R_f = 0.15

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.84 (s, 3H, CH_3), 1.93–2.22 (m, 4H, $2CH_2$), 3.63–3.55 (m, 1H, CH), 3.73–3.82 (m, 1H, CH), 4.40 (s, 2H, OCH_2), 5.67–5.74 (m, 1H, CH=), 6.24 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.39 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 7.02 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.13 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 23.6, 26.5, 37.7, 51.5, 71.9, 105.2, 110.6, 118.2, 124.7, 129.4, 133.0, 158.1, 158.5, 209.1.

MS (ESI$^-$): *m/z* (%) = 275 (100) [MH^-+MeOH], 261 (47) [MH^-+NH_4^+], 243 (34) [MH^-], 175 (50).

Methyl 3-hydroxy-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-10-carboxylate (21{*1,2*}):



21{*1,2*}

Yield for Wittig, Diels-Alder and cleavage: 90%. *Endo*/*Exo* = 2:1.

Flash chromatography in cyclohexane/EtOAc (2:1).

Exo-Isomer: R_f = 0.62 (1:1)

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.66–2.24 (m, 4H, CH_2), 2.46 (ddd, *J* = 12.3, 9.5, 3.0 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 3.84–3.94 (m, 1H, CH), 4.43 (s, 2H, OCH_2), 5.86–5.94 (m, 1H, CH=), 6.22 (d, *J* = 2.6 Hz, 1H, Ar_m-H), 6.35 (dd, *J* = 8.5, 2.6 Hz, 1H, Ar_m-H), 6.77 (dd, *J* = 8.5, 0.9 Hz, 1H, Ar_m-H), 8.22 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 26.0, 28.8, 38.4, 48.7, 53.3, 72.1, 105.2, 110.4, 118.3, 126.1, 129.7, 133.4, 157.8, 158.7, 178.5.

MS (FAB$^+$): *m/z* (%) = 260 (76) [M^+, $C_{15}H_{16}O_4^+$], 229 (22), 213 (29), 201 (60) [$C_{13}H_{13}O_2^+$], 199 (61) [$C_{13}H_{11}O_2^+$], 185 (29) [$C_{13}H_{13}O^+$], 173 (49), 161 (37), 149 (50), 133 (75), 105 (62), 91 (100).

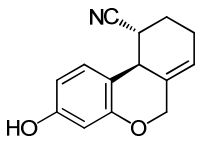
Endo-Isomer: R_f = 0.52 (1:1)

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.90–2.20 (m, 4H, $2CH_2$), 3.35 (s, 3H, OCH_3), 3.50 (td, *J* = 5.8, 3.7 Hz, 1H, CH), 3.80–3.73 (m, 1H, CH), 4.38 (s, 2H, OCH_2), 5.70–5.76 (m, 1H, CH=), 6.22 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.35 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 7.01 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.09 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 23.7, 26.6, 37.7, 44.3, 52.1, 71.8, 105.1, 110.2, 117.8, 124.8, 129.4, 132.4, 158.1, 158.5, 173.8.

MS (FAB$^+$): *m/z* (%) = 260 (24) [M$^+$, $C_{15}H_{16}O_4^+$], 255 (16), 201 (12) [$C_{13}H_{13}O_2^+$], 123 (45), 107 (48), 95 (60), 81 (66).

3-Hydroxy-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-10-carbonitrile (21{*1,3*}):



21{*1,3*}

Yield for Wittig, Diels-Alder and cleavage: 90%. *Endo*/*Exo* = 4:5.

Flash chromatography in cyclohexane/EtOAc (3:1).

Exo-Isomer: R_f = 0.31

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.95–2.03 (m, 1H, CH_2), 2.17–2.27 (m, 3H, CH_2), 2.80 (ddd, *J* = 12.1, 9.6, 2.8 Hz, 1H, NC-CH), 3.82 (bqd, *J* = 9.6, 2.8 Hz, 1H, CH), 4.42 (s, 2H, OCH_2), 5.94 (br. q, *J* = 2.8 Hz, 1H, =CH), 6.26 (d, *J* = 2.6 Hz, 1H, Ar_m-H), 6.47 (dd, *J* = 8.6, 2.6 Hz, 1H, Ar_m-H), 7.62 (d, *J* = 8.6 Hz, 1H, Ar_m-H), 8.34 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 25.2, 28.5, 33.7, 39.0, 72.0, 105.3, 110.6, 116.9, 125.2, 126.8, 129.8, 132.6, 158.0, 159.3.

MS (EI, 70 eV): *m/z* (%) = 166 (17), 143 (24), 128 (13), 109 (100). No M$^+$.

Endo-Isomer: R_f = 0.15.

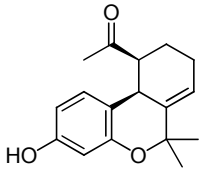
^{1}H NMR (500 MHz, acetone-d_6): δ = 1.96–2.04 (m, 1H, CH_2), 2.15–2.30 (m, 2H, CH_2), 2.35–2.45 (m, 1H, CH_2), 3.79-3.82 (m, 1H, NC-CH), 3.84–3.88 (m, 1H, CH), 4.40 (AB-sys., *J* = 11.7 Hz, 2 H, OCH_2), 5.91 (bd, *J* = 1.9 Hz, 1H, =CH), 6.28 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.48 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 7.17 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.30 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 22.5, 25.2, 32.2, 37.3, 70.3, 104.3, 110.1, 114.5, 120.2, 125.2, 129.5, 131.1, 157.5, 158.0.

MS (EI, 70 eV): *m/z* (%) = 227 (2) [M$^+$], 149 (12), 109 (51), 66 (68), 65 (56), 46 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{14}H_{13}NO_2$: 227.0946; found: 227.0945.

1-(3-Hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-10-yl)ethanone (21{*2,1*}):



21{*2,1*}

Yield for Wittig, Diels-Alder and cleavage: 50%. *Endo*/*Exo* = 7:10.

Flash chromatography in cyclohexane/EtOAc (4:1).

Exo-Isomer: R_f = 0.52 (2:1)

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.41 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.02–2.18 (m, 4H, $2CH_2$), 2.37 (s, 3H, CH_3), 2.89 (ddd, *J* = 11.9, 8.8, 3.0 Hz, 1H, CH), 3.92 (qd, *J* = 8.8, 2.5 Hz, 1H, CH), 5.74–5.78 (m, 1H, CH=), 6.25 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.34 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 6.64 (dd, *J* = 8.4, 1.1 Hz, 1H, Ar_m-H), 8.12 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.3, 27.5, 28.5, 30.0, 30.1, 35.3, 54.2, 79.4, 106.0, 110.0, 119.5, 120.8, 128.5, 141.3, 156.6, 158.7, 212.4.

MS (EI, 70 eV): *m/z* (%) = 272 (29) [M^+], 257 (100), 215 (35), 187 (21), 109 (21), 65 (26), 59 (24), 46 (38), 43 (87).

HRMS–EI: *m/z* [M^+] calcd for $C_{17}H_{20}O_3$: 272.1412; found: 272.1414.

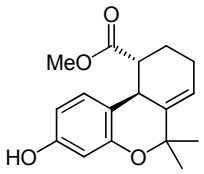
Endo-Isomer: R_f = 0.45 (2:1). Not stable, decomposition and isomerization to *exo*-diastereomer.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.31 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 1.95–2.20 (m, 4H, $2CH_2$), 3.52–3.62 (m, 1H, CH), 3.73–3.83 (m, 1H, CH), 5.69 (bd, *J* = 2.6 Hz, 1H, CH=), 6.24 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.36 (dd, *J* = 8.3, 2.4 Hz, 1H, Ar_m-H), 6.99 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 8.11 (s, 1H, OH).

MS (EI, 70 eV): *m/z* (%) = 272 (1) [M^+], 257 (1), 101 (9), 64 (30), 58 (35), 46 (100), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{17}H_{20}O_3$: 272.1412; found: 272.1414.

Methyl 3-hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-10-carboxylate (21{*2,2*}):



21{*2,2*}

Yield for Wittig, Diels-Alder and cleavage: 35%. *Endo*/*Exo* = 1:1.

Flash chromatography in cyclohexane/EtOAc (3:1).

Exo-Isomer: $R_f = 0.24$

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.40 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.65–1.76 (m, 1H, CH_2), 1.94–2.02 (m, 1H, CH_2), 2.12–2.19 (m, 2H, CH_2), 2.64 (ddd, *J* = 12.1, 9.2, 3.1 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 3.79–3.84 (m, 1H, CH), 5.77 (td, *J* = 4.7, 2.7 Hz, 1H, CH=), 6.26 (d, *J* = 2.6 Hz, 1H, Ar_m-H), 6.37 (dd, *J* = 8.5, 2.6 Hz, 1H, Ar_m-H), 6.79 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.21 (bs, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 25.9, 28.1, 28.5, 28.9, 36.4, 47.2, 53.3, 79.5, 106.1, 110.2, 119.3, 121.1, 128.0, 140.8, 156.6, 158.9, 178.3.

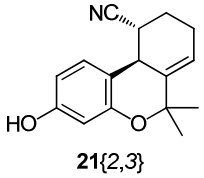
MS (EI, 70 eV): *m/z* (%) = 288 (3) [M^+], 273 (18), 101 (9), 64 (22), 58 (35), 46 (70), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{17}H_{20}O_4$: 288.1362; found: 288.1366.

Endo-Isomer: $R_f = 0.19$. Not stable. Decomposition after a few hours in solution.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.30 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.86–2.20 (m, 4H, $2CH_2$), 3.38 (s, 3H, OCH_3), 3.54 (td, *J* = 5.5, 4.0 Hz, 1H, CH), 3.55–3.85 (m, 1H, CH, exact location due to impurities not detected), 5.69 (d, *J* = 3.1 Hz, 1H, CH=), 6.21 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.34 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 6.98 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.07 (s, 1H, OH).

3-Hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-10-carbonitrile (21{*2,3*}):



21{*2,3*}

Yield for Wittig, Diels-Alder and cleavage: 50%. *Endo*/*Exo* = 1:10.

Flash chromatography in cyclohexane/EtOAc (4:1).

Exo-Isomer: $R_f = 0.24$

IR (ATR, platinum) ν = 3329, 2978, 2937, 2248, 1622, 1589, 1506, 1456, 1310, 1296, 1160, 1139, 1121.

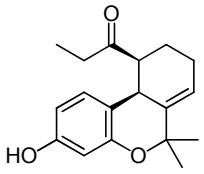
^{1}H NMR (250 MHz, acetone-d_6): δ = 1.39 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.84–2.01 (m, 1H, CH_2), 2.08–2.27 (m, 3H, CH_2), 3.00 (ddd, *J* = 11.5, 9.1, 3.1 Hz, 1H, NC-CH), 3.73 (bdd, *J* = 9.1, 2.2 Hz, 1H, CH), 5.80–5.88 (m, 1H, =CH), 6.28 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.47 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 7.51 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.32 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 25.0, 27.6, 28.28, 28.34, 32.4, 37.3, 79.2, 106.2, 110.3, 117.7, 121.7, 125.1, 128.2, 139.6, 156.6, 159.4.

MS (EI, 70 eV): *m/z* (%) = 255 (43) [M^+], 187 (100), 174 (27), 173 (29).

HRMS–EI: *m/z* [M^+] calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1258.

1-(3-Hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-10-yl)propan-1-one (21{*2,4*}):



21{*2,4*}

Yield for Wittig, Diels-Alder and cleavage: 70%. *Endo*/*Exo* = 8:5.

Flash chromatography in cyclohexane/EtOAc (4:1).

Exo-Isomer: $R_f = 0.26$

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.09 (t, *J* = 7.2 Hz, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.10–2.20 (m, 2H, CH_2), 2.40–2.90 (m, 4H, $2CH_2$), 3.59–3.65 (m, 1H, CH), 3.92–4.00 (m, 1H, CH), 5.74–5.80 (m, 1H, =CH), 6.24 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.33 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 6.60 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.15 (s, 1H, OH).

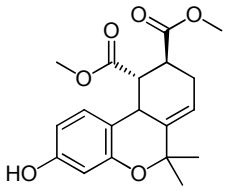
MS (EI, 70 eV): *m/z* (%) = 286 (12) [M^+], 271 (46) [$C_{17}H_{19}O_2$], 201 (20), 161 (14), 153 (13), 109 (12), 101 (25), 98 (17), 83 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{18}H_{22}O_3$: 286.1569; found: 286.1567.

Endo-Isomer: R_f = 0.22

^{1}H NMR (250 MHz, acetone-d_6): δ = 0.74 (t, *J* = 7.3 Hz, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.90–2.20 (m, 6H, $3CH_2$), 3.56–3.66 (m, 1H, CH), 3.70–3.80 (m, 1H, CH), 5.64–5.70 (m, 1H, =C*H*), 6.24 (d, *J* = 2.9 Hz, 1H, Ar_m-H), 6.34 (dd, *J* = 8.4, 2.9 Hz, 1H, Ar_m-H), 6.97 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.15 (s, 1H, OH).

Dimethyl 3-hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-9,10-dicarboxylate (21{*2,5*}):



21{*2,5*}

Yield for Wittig, Diels-Alder and cleavage: 32%. *Endo*/*Exo* = 1:1.

Flash chromatography in cyclohexane/EtOAc (3:1). *Exo*-Isomer and *Endo*-Isomer: R_f = 0.21. Not separable.

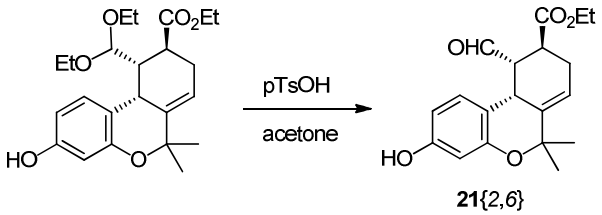
^{1}H NMR (500 MHz, acetone-d_6): δ = 1.27 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 2.31–2.46 (m, 3H, CH_2), 2.51–2.58 (m, 1H, CH_2), 2.80 (dd, *J* = 11.4, 9.5 Hz, 1H, CH), 2.85 (dd, *J* = 10.7, 5.3 Hz, 1H, CH), 3.16 (tt, *J* = 3.8, 3.1 Hz, 1H, CH), 3.42 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.67–3.71 (m, 1H, CH), 3.72 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.81 (dd, *J* = 5.3, 3.4 Hz, 1H, CH), 3.83–3.88 (m, 1H, CH), 5.66 (tt, *J* = 4.3, 3.1 Hz, 1H, =CH)+5.78 (tt, *J* = 5.3, 2.5 Hz, 1H, =CH), 6.24+6.28 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.37+6.40 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 6.88+6.97 (dd, *J* = 8.5, 0.9 Hz, 1H, Ar_m-H), 8.11+8.25 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 27.69, 27.73, 28.5, 28.9, 26.1+29.1, 33.1+37.7, 41.0, 45.0, 46.0, 49.9, 52.7, 53.2, 53.4, 78.4+79.5, 105.9+106.4, 110.0+110.4, 117.6+118.6, 118.5+119.3, 128.0+128.3, 139.0+141.2, 156.5+156.7, 158.5+159.1, 173.3, 175.3, 176.7.

MS (EI, 70 eV): *m/z* (%) = 346 (27) [M^+], 331 [M^+–CH_3] (99), 271 (100), 187 (23), 109 (30), 65 (53), 46 (98).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{22}O_6$: 346.1416; found: 346.1419.

Ethyl 10-formyl-3-hydroxy-6,6-dimethyl-8,9,10,10a-tetrahydro-6H-benzo[c]chromene-9-carboxylate (21{*2,6*}):



21{*2,6*}

100 mg (approx. 0.29 mmol) of the crude cleaved product were dissolved in 10 mL of acetone. *p*-TsOH•H_2O (40 mg, 0.21 mmol) was added and the mixture was stirred for 2 h at r.t. The solvent was removed under reduced pressure and the residue dissolved in EtOAc (10 mL) and water (10 mL). The organic layer was separated and the aqueous one extracted twice with EtOAc (10 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and purified by flash chromatography [cyclohexane/EtOAc (4:1)].

Yield: 29%. *Endo*/*Exo* = 5:4. After Wittig, Diels-Alder, cleavage and acetal deprotection, based on isolated yield of *endo*-diastereomer and calculated *exo*-diastereomer according to their ratio after cleavage (losses on chromatography).

Endo-Isomer: R_f = 0.52 (2:1)

IR (KBr) ν = 3415, 2981, 2931, 2849, 1719, 1621, 1595, 1507, 1456, 1372, 1280, 1237, 1175, 1138, 1114, 1052, 1026.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.28 (t, *J* = 7.1 Hz, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.27 (quin d, *J* = 19.1, 3.7 Hz, 1H, CH_2), 2.54–2.70 (m, 1H, CH_2), 3.24–3.32 (m, 1H, CH), 3.51–3.59 (m, 1H, **CH**-CHO), 3.75–3.84 (m, 1H, benzylic-CH), 4.13–4.30 (m, 2H, OCH_2), 5.80 (td, *J* = 6.3, 3.0 Hz, 1H, CH=), 6.30 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.50 (dd, *J* = 7.7, 2.5 Hz, 1H, Ar_m-H), 7.15 (d, *J* = 7.7 Hz, 1 H, Ar_m-H), 8.29 (s, 1H, OH), 9.16 (s, 1H, CHO).

^{13}C NMR (100 MHz, acetone-d_6): δ = 15.5, 24.6, 27.0, 27.3, 31.9, 39.6, 52.5, 62.5, 77.8, 105.9, 111.0, 114.9, 121.6, 130.0, 139.0, 156.7, 159.1, 175.1, 203.7.

MS (EI, 70 eV): *m/z* (%) = 330 (1) [M^+], 149 (11), 83 (40), 57 (35), 46 (66), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{22}O_5$: 330.1467; found: 330.1468.

Exo-Isomer: 0.45 (2:1)

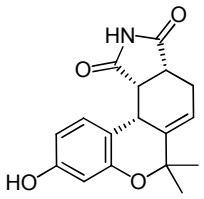
^{1}H NMR (250 MHz, acetone-d_6): δ = 1.20 (t, J = 7.1 Hz, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 2.20–2.51 (m, 2H, CH_2), 2.92 (td, J = 10.4, 5.4 Hz, 1H, CH), 3.17 (ddd, J = 11.0, 9.0, 2.3 Hz, 1H, **CH**-CHO), 3.85 (bd, J = 7.9 Hz, 1H, CH-benzylic), 4.09 (qd, J = 7.1, 2.4 Hz, 2H, OCH_2), 5.76 (td, J = 5.2, 2.6 Hz, 1H, CH=), 6.30 (d, J = 2.5 Hz, 1H, Ar_m-H), 6.42 (dd, J = 8.4, 2.5 Hz, 1H, Ar_m-H), 6.96 (dd, J = 8.4, 1.1 Hz, 1 H, Ar_m-H), 8.24 (s, 1H, OH), 10.15 (d, J = 2.3 Hz, 1H, CHO).

^{13}C NMR (63 MHz, acetone-d_6): δ = 15.4, 28.7, 28.8, 29.6, 35.2, 42.7, 53.5, 62.4, 80.0, 106.5, 110.3, 119.1, 119.3, 128.5, 141.8, 156.9, 159.1, 175.0, 205.2.

MS (EI, 70 eV): *m/z* (%) = 330 (3) [M^+], 315 (9), 149 (13), 83 (23), 57 (39), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{22}O_5$: 330.1467; found: 330.1465.

9-Hydroxy-6,6-dimethyl-3a,4,11b,11c-tetrahydrochromeno[4,3-e]isoindole-1,3(2*H*,6*H*)-dione (21{*2,7*}):



21{*2,7*}

Yield for Wittig, Diels-Alder and cleavage: 23%. *Endo*/*Exo* = 1:0.

Flash chromatography in cyclohexane/EtOAc = 2:3.

Endo-Isomer: R_f = 0.26. Yellow solid. Similar structures can be found in reference [6].

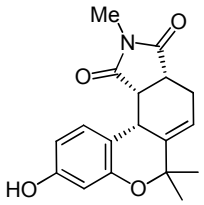
^{1}H NMR (400 MHz, acetone-d_6): δ = 1.30 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 2.20–2.27 (m, 1H, CH_2), 2.70 (ddd, J = 15.0, 7.4, 1.6 Hz, 1H, CH_2), 3.26 (ddd, J = 8.5, 7.6, 1.6 Hz, 1H, CH), 3.59 (td, J = 6.5, 3.1 Hz, 1H, CH-benzylic), 3.64 (dd, J = 8.5, 6.5 Hz, 1H, CH), 5.90 (td, J = 7.4, 3.1 Hz, 1H, CH=), 6.28 (d, J = 2.5 Hz, 1H, Ar_m-H), 6.47 (dd, J = 8.5, 2.5 Hz, 1H, Ar_m-H), 7.22 (d, J = 8.5 Hz, 1 H, Ar_m-H), 8.15 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.0, 28.0, 28.6, 31.4, 35.8, 43.2, 47.3, 77.8, 106.4, 110.7, 116.5, 120.0, 130.5, 147.1, 156.7, 158.7, 178.7, 181.6.

MS (EI, 70 eV): *m/z* (%) = 299 (12) [M^+], 280 (26), 187 (13), 109 (10), 101 (25), 64 (20), 59 (42), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{17}H_{17}NO_4$: 299.1158; found: 299.1155.

9-Hydroxy-2,6,6-trimethyl-3a,4,11b,11c-tetrahydrochromeno[4,3-e]isoindole-1,3(2*H*,6*H*)-dione (21{*2,8*}):



21{*2,8*}

Yield for Wittig, Diels-Alder and cleavage: 27%. *Endo*/*Exo* = 1:0.

Flash chromatography in cyclohexane/EtOAc = 2:1.

Endo-Isomer: R_f = 0.10. Colorless solid.

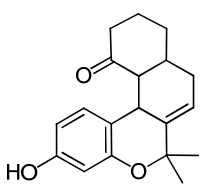
^{1}H NMR (400 MHz, acetone-d_6): δ = 1.26 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 2.21–2.29 (m, 1H, CH_2), 2.71 (s, 3H, CH_3), 2.73 (ddd, *J* = 15.0, 7.5, 1.6 Hz, 1H, CH_2), 3.25 (t, *J* = 7.3 Hz, 1H, CH), 3.60–3.66 (m, 2H, 2CH), 5.85 (td, *J* = 7.3, 3.0 Hz, 1H, CH=), 6.29 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.48 (dd, *J* = 8.3, 2.5 Hz, 1H, Ar_m-H), 7.25 (d, *J* = 8.3 Hz, 1 H, Ar_m-H), 8.16 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 25.5, 26.1, 28.1, 28.5, 35.9, 37.9, 42.0, 46.2, 77.8, 106.4, 110.7, 116.4, 120.0, 130.5, 147.1, 156.7, 158.8, 178.0, 180.9.

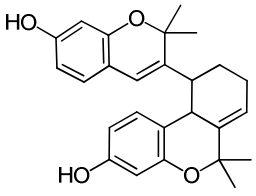
MS (EI, 70 eV): *m/z* (%) = 313 (1) [M^+], 64 (34), 58 (34), 46 (100), 43 (86).

HRMS–EI: *m/z* [M^+] calcd for $C_{18}H_{19}NO_4$: 313.1314; found: 313.1315.

3-Hydroxy-6,6-dimethyl-8a,9,10,11,12a,12b-hexahydro-6*H*-naphtho[2,1-*c*]chromen-12(8*H*)-one (21{*2,9*}):



21{*2,9*}



DImerization after deprotection of unreacted **16**{*2*}

Yield of dimerization product: 31%. Single diastereomer.

Flash chromatography in cyclohexane/EtOAc (4:1) up to (2:1).

21{*2,9*}: R_f = 0.44. Mixture. Only traces of product.

Recognizable signals in ^{1}H NMR (250 MHz, acetone-d_6): δ = 2.64–2.76 (m, 1H, CH), 3.65–3.75 (m, 1H, CH), 4.63 (d *J* = 11.0 Hz, 1H, CH), 5.78–5.80 (m, 1H, CH=), 7.09 (d, *J* = 8.4 Hz, 1H, Ar_m-H).

MS (EI, 70 eV): *m/z* (%) = 338 (2), 323 (3), 286 (2), 283 (4), 202 (3), 189 (7), 187 (6), 161 (15), 101 (24), 59 (39), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{22}O_3$: 298.1569; found: 298.1566.

Dimerization product: R_f = 0.38.

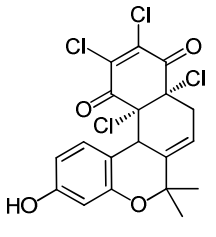
^{1}H NMR (400 MHz, acetone-d_6): δ = 1.30 (s, 6H, CH_3), 1.44 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.41–2.20 (m, 4H, CH_2), 3.32–3.38 (m, 1H, CH), 3.91–3.99 (m, 1H, CH), 5.75–5.80 (m, 1H, CH=), 6.08 (s, 1H, CH=), 6.14 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.19 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.21 (dd, *J* = 8.1, 2.4 Hz, 1H, Ar_m-H), 6.32 (dd, *J* = 8.4, 2.4 Hz, 1H, Ar_m-H), 6.47 (d, *J* = 8.1 Hz, 1H, Ar_m-H), 7.05 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 7.96 (s, 1H, OH), 8.18 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 23.2, 26.9, 27.1, 27.9, 28.2 (2C), 39.0, 39.5, 78.2, 80.4, 104.8, 105.4, 109.4, 110.2, 117.6, 118.0, 121.5, 122.2, 128.4, 129.6, 135.6, 139.8, 155.1, 156.2, 158.1, 159.5.

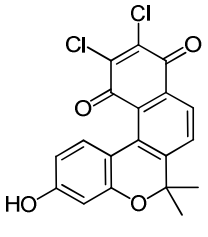
MS (EI, 70 eV): *m/z* (%) = 404 (19) [M^+], 402 (47), 400 (36), 387 (63), 385 (69), 211 (23), 202 (67), 187 (100), 43 (41).

HRMS–EI: *m/z* [M^+] calcd for $C_{26}H_{28}O_4$: 404.1988; found: 404.1984.

8a,10,11,12a-tetrachloro-3-hydroxy-6,6-dimethyl-8,8a-dihydro-6*H*-naphtho[2,1-*c*]chromene-9,12(12a*H*,12b*H*)-dione (21{*2,10*}):



21{*2,10*}



Side Product

Yield for Wittig, Diels-Alder and cleavage: 11% + 8% side product. *Endo*/*Exo* = 1:1.

Flash chromatography in cyclohexane/EtOAc (2:1). *Exo*- and e*ndo*-isomer not separable.

Exo- and *endo*-isomer: R_f = 0.21

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.30 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.98 (ddd, *J* = 19.6, 4.4, 2.2 Hz, 1H, CH_2), 3.44 (ddd, *J* = 19.6, 3.1, 2.2 Hz, 1H, CH), 4.56–4.62 (m, 1H, CH), 5.83 (td, *J* = 4.4, 3.1 Hz, 1H, CH=), 6.36 (d, *J* = 2.6 Hz, 1H, Ar_m-H), 6.41 (dd, *J* = 8.6, 2.6 Hz, 1H, Ar_m-H), 7.55 (d, *J* = 8.6 Hz, 1H, Ar_m-H), 8.35 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.4, 28.2, 38.9, 42.4, 78.3, 79.6, 80.5, 106.6+106.7, 109.9+110.0, 113.6, 116.9, 131.3, 140.5, 142.0, 143.7, 158.8, 159.4+159.5, 180.4, 183.3.

MS (EI, 70 eV): *m/z* (%) = 450 (9), 448 (16), 447 (7), 446 (11) [M^+], 415 (29), 414 (39), 413 (100), 412 (22), 411 (71), 189 (16), 188 (58), 187 (74).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{14}Cl_4O_4$: 445.9646; found: 445.9644.

Side-Product: R_f = 0.16. Purity: 75%

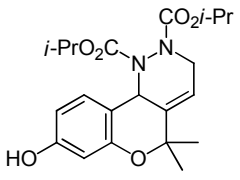
^{1}H NMR (400 MHz, acetone-d_6): δ = 1.58 (s, 6H, $2CH_3$), 6.47 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.50 (dd, *J* = 8.6, 2.5 Hz, 1H, Ar_m-H), 7.45 (d, *J* = 8.6 Hz, 1H, Ar_m-H), 7.78 (d, *J* = 8.0 Hz, 1H, Ar_m-H), 8.01 (d, *J* = 8.0 Hz, 1H, Ar_m-H), 8.93 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 27.9 (2C), 80.0, 106.6, 111.4, 115.0, 127.4, 128.9, 130.3, 133.3, 134.3, 134.6, 142.0, 146.8, 151.6, 157.7, 162.2, 177.7, 179.1.

MS (EI, 70 eV): *m/z* (%) = 451 (3), 449 (5), 447 (4), 414 (7), 412 (24), 411 (10), 410 (11), 399 (18), 398 (10), 397 (37), 396 (10), 395 (29), 376 (28), 375 (11), 374 [M^+, $C_{19}H_{12}O_4Cl_2$] (34), 361 (66), 360 (23), 359 (100), 253 (41), 189 (60). Higher masses probably due to impurities.

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{12}Cl_2O_4$: 374.0113; found: 374.0112.

Diisopropyl 8-hydroxy-5,5-dimethyl-5,10b-dihydro-1*H*-chromeno[4,3-*c*]pyridazine-1,2(3*H*)-dicarboxylate (21{*2,11*}):



21{*2,11*}

Yield for Wittig, Diels-Alder and cleavage: 30%.

Flash chromatography in cyclohexane/EtOAc (3:1). R_f = 0.21.

2 Rotamers in a ratio of ~ 4:1.

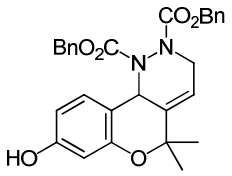
^{1}H NMR (500 MHz, acetone-d_6): δ = 0.92–1.21 (m, 12H, 4CH_3), 1.34 (s, 3H, CH_3, major), 1.35 (s, 3H, CH_3, minor), 1.38 (s, 3H, CH_3, minor), 1.40 (s, 3H, CH_3, major), 3.57 (bd, *J* = 17.0 Hz, 1H, CH_2, major), 3.66–3.75 (m, 1H, CH_2, minor), 4.17 (bd, *J* = 20.0 Hz, 1H, CH_2, major), 4.31 (bd, *J* = 14.0 Hz, 1H, CH_2, minor), 4.64 (sept, *J* = 6.2 Hz, 1H, CH, major), 4.73 (sept, *J* = 6.2 Hz, 1H, CH, minor), 4.89 (sept, *J* = 6.2 Hz, 1H, CH, major), 5.64 (bs, 1H, CH), 5.77 (d, *J* = 6.7 Hz, 1H, Ar_m-H, minor), 5.89 (d, *J* = 5.2 Hz, 1H, Ar_m-H, major), 6.08 (bs, 1H, CH=), 6.29 (bdd, *J* = 8.2, 1.7 Hz, 1H, Ar_m-H, major), 7.17 (bd, *J* = 8.2 Hz, 1H, Ar_m-H, major), 7.29 (bd, *J* = 8.2 Hz, 1H, Ar_m-H, minor), 8.15 (bs, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 23.0+23.2+23.4 (4C), 27.5, 27.6, 43.6, 53.5, 70.1+70.3+71.1+72.1 (2C), 79.3, 104.8+105.0, 109.6+109.8, 115.1, 119.2, 129.8, 137.9, 155.7, 156.5, 158.2, 160.0+160.1. Broad and multiple signals due to hindered rotation.

MS (EI, 70 eV): *m/z* (%) = 404 (5) [M^+], 275 (11), 109 (33), 65 (59), 63 (16), 46 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{21}H_{28}N_2O_6$: 404.1947; found: 404.1950.

Dibenzyl 8-hydroxy-5,5-dimethyl-5,10b-dihydro-1*H*-chromeno[4,3-*c*]pyridazine-1,2(3*H*)-dicarboxylate (21{*2,12*}):



21{*2,12*}

Yield for Wittig, Diels-Alder and cleavage: 48%.

Flash chromatography in cyclohexane/EtOAc (4:1) up to 2:1. TLC in the latter R_f = 0.40.

2 Rotamers in a ratio of ~ 3:1. Structure confirmed by CH+HHCOSY.

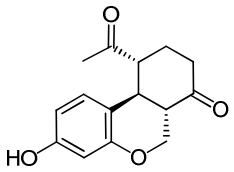
^{1}H NMR (400 MHz, acetone-d_6): δ = 1.46+1.48 (s, 3H, CH_3), 1.50+1.53 (s, 3H, CH_3), 3.80+3.92 (bd, *J* = 17.3 Hz, 1H, CH_2), 4.46 (bd, *J* = 12.7 Hz, 1H, CH_2), 4.98 (bs, *2*H, OCH_2), 5.27 (bs, *2*H, OCH_2), 5.80 (bs, 1H, CH), 5.93+6.03 (bs+bd, *J* = 5.3 Hz, 1H, CH=), 6.20–6.28+6.44 (m+bd, *J* = 7.7 Hz, 2H, Ar_m-H), 7.17 (d, *J* = 8.8 Hz, 1H, Ar_m-H), 7.22–7.48 (m, 10H, Ar_m-H), 8.27 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 27.5, 27.3, 44.06+44.11, 53.9+54.0, 69.2+68.3, 69.8, 79.3+79.8, 104.9+105.1, 109.7+109.8, 114.8, 119.1, 129.3+129.7+129.78+129.81+130.0+130.17+130.22+ 130.4 (13C), 138.2+138.8, 156.0+156.4, 158.3, 160.1 (2C).

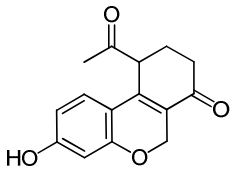
MS (EI, 70 eV): *m/z* (%) = 500 (1) [M^+], 365 (15), 321 (11), 187 (19), 91 (100)

HRMS–EI: *m/z* [M^+] calcd for $C_{29}H_{28}N_2O_6$: 500.1947; found: 500.1950.

10-Acetyl-3-hydroxy-8,9,10,10a-tetrahydro-6*H*-benzo[c]chromen-7(6a*H*)-one (24{*5,1*}):



24{*5,1*}



26{*5,1*}

Yield for enol-ether formation, Diels-Alder and cleavage (DCE/EtOH): 35% of **24**{*5,1*} (*endo*/*exo* = 1:2), 15% of **26**{*5,1*} and 20% starting material (DOMA-product).

Flash chromatography in cyclohexane/EtOAc (2:1), TLC in (1:1).

Exo-**24**{*5,1*}: R_f = 0.27

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.88–1.98 (m, 1H, CH_2), 2.05–2.30 (m, 3H, CH_2), 2.62 (s, 3H, CH_3), 2.93 (ddd, *J* = 5.9, 5.7, 3.2 Hz, 1H, CH next to OCH_2), 3.53 (ddd, *J* = 5.9, 5.8, 4.2 Hz, 1H, CH), 3.76 (dd, *J* = 5.9, 5.9 Hz, 1H, CH-benzylic), 3.94 (dd, *J* = 10.9, 3.2 Hz, 1H, OCH_2), 4.63 (dd, *J* = 10.9, 5.7 Hz, 1H, OCH_2), 6.23 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.36 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 6.96 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.27 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 25.94 (CH_2), 31.58 (CH_3), 38.39 (CH), 39.49 (CH_2), 47.22 (CH), 52.17 (CH), 65.39 (OCH_2), 105.05 (CH, C-Ar_m), 110.31 (CH, C-Ar_m), 114.94 (C, C-Ar_m), 130.14 (CH, C-Ar_m), 157.41 (C, C-Ar_m), 159.18 (C, C-Ar_m), 208.59 (CO), 21.89 (CO).

MS (EI, 70 eV): *m/z* (%) = 260 (100) [M^+], 217 (13), 190 (20), 148 (29), 101 (22), 59 (28), 43 (38).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_5$: 260.1049; found: 260.1052.

Endo-**24**{*5,1*}: R_f = 0.23. Not separable from **26**{*5,1*}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.24–2.50 (m, 4H, $2CH_2$), 2.36 (s, 3H, CH_3), 4.22–4.26 (m, 1H, CH), 4.79 (dd, *J* = 13.8, 1.4 Hz, 1H, OCH_2), 4.95 (d, *J* = 13.8 Hz, 1H, OCH_2), 6.37 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.50 (dd, *J* = 8.6, 2.4 Hz, 1H, Ar_m-H), 7.286(d, *J* = 8.6 Hz, 1 H, Ar_m-H), 9.07 (bs, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.7, 34.9, 49.1, 64.6, 105.1, 111.6, 115.8, 125.1, 129.2, 146.86 (C=), 159.6, 163.3, 195.9. (C=O) + CH_3 not detected due to NMR-solvent.

MS (EI, 70 eV): *m/z* (%) = 260 (100) [M^+], 258 (55) [M^+], 216 (42), 215 (62), 149 (51), 148 (76), 147 (92), 101 (42), 59 (42), 43 (69).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_4$: 260.1049; found: 260.1050.

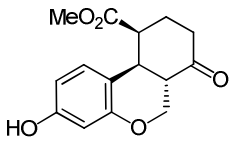
26{*5,1*}: R_f = 0.23. Not separable from **24**{*5,1*}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.24–2.50 (m, 4H, $2CH_2$), 2.37 (s, 3H, CH_3), 3.06 (td, *J* = 5.8, 2.8 Hz, 1H, CH), 3.36 td, *J* = 11.4, 3.1 Hz, 1H, CH), 4.01 (d, *J* = 10.8, 3.2 Hz, 1H, OCH_2), 4.22–4.26 (m, 1H, CH), 4.69 (dd, *J* = 10.8, 2.8 Hz, 1H, OCH_2), 6.20 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.28 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 6.61 (d, *J* = 8.5 Hz, 1 H, Ar_m-H), 8.26 (bs, 1H, OH).

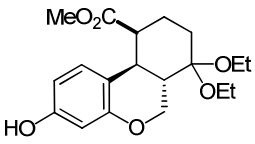
^{13}C NMR (100 MHz, acetone-d_6): δ = 23.3, 29.5, 38.3, 40.9, 54.4, 66.2, 105.1, 109.9, 113.2, 129.4, 158.3, 159.9, 208.3, 211.1. One C was not detected, presumable because of isochronous signals.

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{14}O_4$: 258.0892; found: 258.0890.

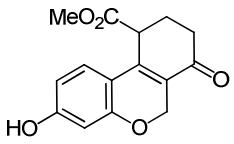
Methyl 3-hydroxy-7-oxo-6a,7,8,9,10,10a-hexahydro-6*H*-benzo[*c*]chromene-10-carboxylate (24{*5,2*}):



24{*5,2*}



25{*5,2*}



26{*5,2*}

Yield for enol-ether formation, Diels-Alder and cleavage (DCE/EtOH): 51% of **24**{*5,2*} (*endo*/*exo* = 2:1), 22% of **25**{*5,2*}, 7% of **26**{*5,2*} and 20% starting material (DOMA-product).

Flash chromatography in cyclohexane/EtOAc (2:1).

Exo-**24**{*5,2*}: R_f = 0.25

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.91–1.98 (m, 1H, CH_2), 2.09–2.19 (m, 1H, CH_2), 2.28–2.49 (m, 2H, CH_2), 2.95 (ddd, *J* = 6.4, 6.3, 3.3 Hz, 1H, CH), 3.34 (ddd, *J* = 6.9, 6.9, 4.1 Hz, 1H, CH), 3.67–3.75

(m, 1H, CH-benzylic), 3.73 (s, 3H, OCH_3), 3.95 (dd, *J* = 10.9, 3.3 Hz, 1H, OCH_2), 4.61 (dd, *J* = 10.9, 6.4 Hz, 1H, OCH_2), 6.24 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.38 (dd, *J* = 8.3, 2.4 Hz, 1H, Ar_m-H), 6.98 (d, *J* = 8.3 Hz, 1 H, Ar_m-H), 8.29 (bs, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 26.6, 39.4, 39.5, 45.6, 47.6, 53.2, 65.3, 105.0, 110.4, 114.5, 130.2, 157.2, 159.4, 176.2. Ketone C=O was not detected.

MS (EI, 70 eV): *m/z* (%) = 276 (8) [M^+], 147 (11), 129 (44), 101 (39), 75 (17), 64 (17), 59 (51), 46 (70), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_5$: 276.0998; found: 276.0996.

Endo-**24**{*5,2*}: R_f = 0.13. Yellow solid.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.81–1.93 (m, 1H, CH_2), 2.22–2.32 (m, 2H, CH_2), 2.43–2.52 (m, 1H, CH_2), 3.02 (ddd, *J* = 5.8, 3.0, 2.8 Hz, 1H, CH), 3.41 (td, *J* = 11.8, 3.3 Hz, 1H, CH), 3.76 (s, 3H, OCH_3), 4.05 (dd, *J* = 10.8, 3.0 Hz, 1H, OCH_2), 4.04–4.09 (m, 1H, CH-benzylic), 4.70 (dd, *J* = 10.8, 2.8 Hz, 1H, OCH_2), 6.20 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.31 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 6.68 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.28 (bs, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 23.7, 38.3, 40.9, 45.7, 48.9, 53.3, 66.1, 105.2, 110.0, 113.1, 129.3, 158.1, 159.2, 176.0, 208.0.

MS (EI, 70 eV): *m/z* (%) = 276 (2) [M^+], 259 (4), 129 (19), 101 (27), 87 (21), 58 (30), 57 (52), 46 (40), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{16}O_5$: 276.0998; found: 276.1000.

25{*5,2*}: R_f = 0.40

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.16 (t, *J* = 7.1 Hz, 3H, CH_3), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3), 1.43–1.51 (m, 1H, CH_2), 1.70–1.85 (m, 2H, CH_2), 1.93–1.99 (m, 1H, CH_2), 2.42–2.48 (m, 1H, CH), 2.63 (td, *J* = 12.0, 4.3 Hz, 1H, CH), 3.10 (dd, *J* = 11.5, 4.3 Hz, 1H, CH), 3.49 (q, *J* = 7.1 Hz, 1H, OCH_2), 3.54 (q, *J* = 7.1 Hz, 1H, OCH_2), 3.58 (s, 3H, OCH_3), 4.09–4.18 (m, 2H, OCH_2), 6.23 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.27 (dd, *J* = 8.3, 2.4 Hz, 1H, Ar_m-H), 6.73 (d, *J* = 8.3 Hz, 1 H, Ar_m-H), 8.15 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 16.6 (2C), 27.6, 30.0, 37.9, 40.2, 49.0, 52.5, 56.3, 56.5, 64.7, 101.2, 104.7, 109.4, 117.2, 131.9, 156.7, 159.3, 177.1.

MS (EI, 70 eV): *m/z* (%) = 350 (3) [M^+], 155 (16), 101 (36), 91 (14), 75 (24), 59 (61), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{19}H_{26}O_6$: 350.1927; found: 350.1931.

26{*5,2*}: R_f = 0.20

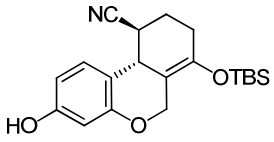
^{1}H NMR (400 MHz, acetone-d_6): δ = 2.32–2.62 (m, 4H, 2CH_2), 3.69 (s, 3H, OCH_3), 4.02–4.07 (m, 1H, CH), 4.86 (AB-sys., *J* = 13.9 Hz, 2H, OCH_2), 6.37 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.52 (dd, *J* = 8.6, 2.4 Hz, 1H, Ar_m-H), 7.28 (d, *J* = 8.6 Hz, 1H, Ar_m-H), 9.08 (bs, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 27.4, 35.1, 41.4, 53.7, 64.6, 105.0, 111.6, 115.6, 124.6, 129.2, 145.7, 159.6, 163.4, 173.5, 196.0.

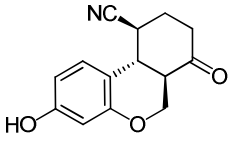
MS (EI, 70 eV): *m/z* (%) = 276 (100), 274 [M^+] (55), 216 (40), 215 (23), 190 (18), 160 (17), 148 (29), 147 (45), 43 (23).

HRMS–EI: *m/z* [M^+] calcd for $C_{15}H_{14}O_5$: 274.0841; found: 274.0835.

3-Hydroxy-7-oxo-6a,7,8,9,10,10a-hexahydro-6*H*-benzo[*c*]chromene-10-carbonitrile (24{*5,3*}):



23{*5,3*}



24{*5,3*}

Yield for enol-ether formation, Diels-Alder and cleavage (THF/water): 15% of **23**{*5,3*} and 10% of **24**{*5,3*} (*endo*/*exo* = 0:1), and 8% of starting material (DOMA-product).

General Procedure for TBS-cleavage:

To the TBS-protected enol-ether (0.014 mmol) in acetonitrile (1 mL) was added TBAF•3H_2O (9 mg, 0.028 mmol). The mixture was stirred for 2 h at r.t. Then brine was added (10 mL), followed by extraction with Et_2O (3 × 10 mL). The combined organic layers were dried, concentrated and purified by flash chromatography.

Flash chromatography in cyclohexane/EtOAc (4:1) up to (2:1). TLC in the latter.

Exo-**23**{*5,3*}: R_f = 0.60

^{1}H NMR (500 MHz, acetone-d_6): δ = 0.19 (s, 3H, $SiCH_3$), 1.20 (s, 3H, $SiCH_3$), 0.98 (s, 9H, 3CH_3), 2.15–2.05 (m, 1H, CH_2), 2.20–2.31 (m, 2H, CH_2), 2.35–2.45 (m, 1H, CH_2), 3.84 (ddd, *J* = 11.4, 9.3, 3.0 Hz, 1H, NC-CH), 3.85 (bd, *J* = 9.3 Hz, 1H, CH), 4.13 (d, *J* =11.5 Hz, 1H, OCH_2), 5.07 (d, *J* = 11.5 Hz, 1H, OCH_2), 6.27 (d, *J* = 2.6 Hz, 1H, Ar_m-H), 6.45 (dd, *J* = 8.6, 2.6 Hz, 1H, Ar_m-H), 7.57 (d, *J* = 8.6 Hz, 1H, Ar_m-H), 8.30 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = –2.9, –2.8, 19.8, 27.1 (3C), 28.4, 30.3, 33.3, 39.0, 64.8, 105.4, 110.4, 111.0, 117.7, 124.9, 129.3, 148.0, 158.3, 159.2.

MS (EI, 70 eV): *m/z* (%) = 357 (7) [M^+], 301 (26), 300 (100), 273 (29), 248 (18), 73 (20).

HRMS–EI: *m/z* [M^+] calcd for $C_{20}H_{27}NO_3Si$: 357.1760; found: 357.1761.

Exo-**24**{*5,3*}: R_f = 0.20. Yield for TBS-cleavage: 60%.

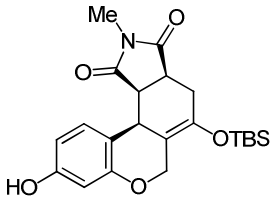
^{1}H NMR (500 MHz, acetone-d_6): δ = 2.05–2.21 (m, 2H, CH_2), 2.35–2.46 (m, 1H, CH_2), 2.54–2.63 (m, 1H, CH_2), 3.04 (ddd, *J* = 5.8, 5.6, 3.3 Hz, 1H, CH), 3.74 (dd, *J* = 6.0, 5.6 Hz, 1H, CH), 3.81 (ddd, *J* = 6.3, 6.0, 3.7 Hz, 1H, CH), 4.00 (dd, *J* = 11.1, 3.3 Hz, 1H, OCH_2), 4.66 (d, *J* = 11.1, 5.8 Hz, 1H, OCH_2), 6.25 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.44 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 7.19 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.40 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.7, 32.2, 39.1, 39.7, 47.2, 65.1, 105.1, 110.6, 112.4, 122.8, 130.6, 157.4, 159.9. C=O not detected.

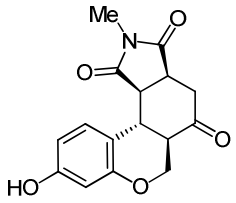
MS (EI, 70 eV): *m/z* (%) = 243 (7) [M^+], 189 (62), 175 (20), 149 (26), 148 (61), 147 (73).

HRMS–EI: *m/z* [M^+] calcd for $C_{14}H_{13}NO_3$: 243.0895; found: 243.0895.

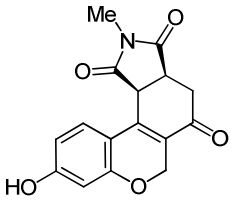
9-Hydroxy-2-methyl-3a,4,5a,6-tetrahydrochromeno[4,3-*e*]isoindole-1,3,5(2*H*,11b*H*,11c*H*)-trione (24{*5,8*}):



23{*5,8*}



24{*5,8*}



26{*5,8*}

Yield for enol-ether formation, Diels-Alder and cleavage (THF/water): 20% of *exo*-**23**{*5,8*} and 12% of **24**{*5,8*} (*endo*/*exo* = 4:5), and 10% of **26**{*5,8*}.

Flash chromatography in cyclohexane/EtOAc (1:1). *Exo*- and *endo*-diastereomers not separable.

TBS-cleavage of *endo*-**23**{*5,8*} gives 35% of a diastereomeric mixture (*endo*/*exo* = 1:3).

Endo-**23**{*5,8*}: R_f = 0.32. In a mixture with *exo*-**24**{*5,8*}.

^{1}H NMR (500 MHz, acetone-d_6): δ = 0.12 (s, 3H, $SiCH_3$), 1.19 (s, 3H, $SiCH_3$), 0.95 (s, 9H, 3 CH_3), 2.61–2.65 (m, 2H, CH_2), 2.74 (s, 3H, CH_3), 3.31 (ddd, *J* = 8.7, 6.3, 3.2 Hz, 1H, CH), 3.52 (dd, *J* = 8.7 6.1 Hz, 1H, CH), 3.68 (d, *J* = 6.1 Hz, 1H, CH-benzylic), 4.25 (d, *J* = 13.1 Hz, 1H, OCH_2), 4.64 (d, *J* = 13.1 Hz, 1H, OCH_2), 6.31 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.48 (dd, *J* = 8.3, 2.5 Hz, 1H, Ar_m-H), 7.20 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 8.16 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = –3.4, –2.9, 19.6, 25.8, 27.0 (3C), 31.6, 35.9, 42.3, 46.6, 64.8, 105.8, 111.1, 113.6, 116.9, 131.2, 145.5, 158.5, 159.6, 177.7, 180.7.

MS (EI, 70 eV): *m/z* (%) = 415 (10) [M^+], 386 (24), 357 (25), 358 (100), 273 (15), 167 (15).

HRMS–EI: *m/z* [M^+] calcd for $C_{22}H_{29}NO_5Si$: 415.1815; found: 415.1816.

Exo-**24**{*5,8*}: R_f = 0.09. In admixture with *endo*-**24**{*5,8*}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.43 (ddd, *J* = 14.1, 10.6, 4.2 Hz, 1H, CH), 2.79 (m, 1H, CH_2), 2.83 (s, 3H, CH_3), 3.02 (dd, *J* = 17.9, 8.3 Hz, 1H, CH_2), 3.61 (ddd, *J* = 9.5, 8.3, 2.0 Hz, 1H, CH), 3.73 (dd, *J* = 11.1, 10.6 Hz, 1H, OCH_2), 3.78 (dd, *J* = 14.1, 6.0 Hz, 1H, CH-benzylic), 4.06 (dd, *J* = 9.5, 6.0 Hz, 1H, CH), 4.49 (dd, *J* = 11.1, 4.2 Hz, 1H, OCH_2), 6.24 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.47 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar_m-H), 7.37 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.24 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 25.9, 36.3, 37.9, 39.3, 42.2, 46.7, 66.4, 104.9, 110.4, 113.7, 131.7, 157.4, 158.8, 177.4, 180.2, 209.3.

Endo-**24**{*5,8*}: R_f = 0.09

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.54 (dd, *J* = 13.8, 3.9 Hz, 1H, CH_2), ~2.85 (s, 3H, CH_3), 3.09 (ddd, *J* = 10.2, 6.6, 4.5 Hz, 1H, CH), 3.15 (dd, *J* = 13.8, 8.6 Hz, 1H, CH_2), 3.58–3.64 (m, 1H, CH), 3.68–3.82 (m, 2H, CH+OCH_2), 4.11 (dd, *J* = 6.6, 6.3 Hz, 1H, CH) 4.24 (dd, *J* = 11.2, 4.3 Hz, 1H, OCH_2), 6.27 (d, *J* = 2.5 Hz, 1H, Ar_m-H), 6.44 (dd, *J* = 8.4, 2.5 Hz, 1H, Ar_m-H), 7.11 (d, *J* = 8.4 Hz, 1H, Ar_m-H), 8.21 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 25.9, 35.4, 40.0, 43.4, 44.5, 48.0, 66.4, 105.1, 110.8, 114.0, 131.5, 157.5, 158.1, 177.4, 179.7, 208.0.

MS (EI, 70 eV): *m/z* (%) = 301 (100) [M^+], 190 (24), 189 (32), 148 (22), 147 (37).

HRMS–EI: *m/z* [M^+] calcd for $C_{16}H_{15}NO_5$: 301.0950; found: 301.0950.

26{*5,8*}: R_f = 0.17

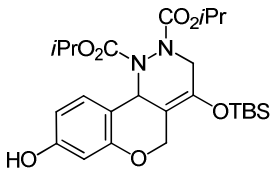
^{1}H NMR (500 MHz, acetone-d_6): δ = 2.77 (dd, J = 16.8, 8.3 Hz, 1H, CH_2), 2.86 (dd, J = 16.8, 6.0 Hz, 1H, CH_2), 2.89 (s, 3H, CH_3), 3.74–3.81 (m, 1H, CH), 4.61 (bd, J = 7.9 Hz, 1H, CH), 4.64 (dd, J = 13.8, 2.0 Hz, 1H, OCH_2), 4.96 (d, J = 13.8 Hz, 1H, OCH_2), 6.36 (d, J = 2.4 Hz, 1H, Ar_m-H), 6.58 (dd, J = 8.7, 2.4 Hz, 1H, Ar_m-H), 7.72 (d, J = 8.7 Hz, 1H, Ar_m-H), 9.16 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 26.3, 35.8, 39.9, 41.6, 64.6, 104.6, 111.2, 115.3, 125.0, 132.5, 142.5, 160.0, 163.6, 175.9, 179.3, 192.8.

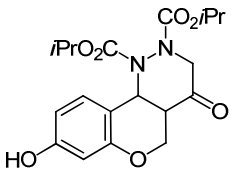
MS (EI, 70 eV): *m/z* (%) = 299 (7) [M^+], 242 (8), 213 (6), 150 (10), 141 (30), 101 (29), 59 (56), 43 (100).

HRMS–EI: *m/z* [M^+] calcd for $C_{16}H_{13}NO_5$: 299.0794; found: 299.0795.

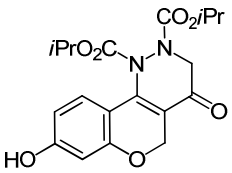
Diisopropyl 8-hydroxy-4-oxo-3,4,4a,5-tetrahydro-1*H*-chromeno[4,3-*c*]pyridazine-1,2(10*bH*)-dicarboxylate (24{*5,11*}):



23{*5,11*}



24{*5,11*}



26{*5,11*}

Yield for enol-ether formation, Diels-Alder and cleavage (THF/water): 20% of *exo*-**23**{*5,8*} and 12% of **24**{*5,8*} (*endo*/*exo* = 4:5), and 10% of **26**{*5,8*}.

Flash chromatography in cyclohexane/EtOAc (4:1) up to (2:1). TLC in the latter.

TBS-cleavage of **23**{*5,11*} gives 43% of **26**{*5,11*}.

23{*5,11*}: R_f = 0.53

^{1}H NMR (500 MHz, acetone-d_6): δ = 0.22 (s, 6H, $2CH_3$), 0.99 (s, 9H, $3CH_3$), 1.20–1.35 (m, 12H, $4CH_3$), 3.74 (br. d, J = 6.2 Hz, 1H, CH_2), 4.33 (br. d, J = 6.2 Hz, 1H, CH_2), 4.47 (dd, J = 11.5, 1.6 Hz, 1H, OCH_2), 4.73 (sept, J = 6.3 Hz, 1H, CH), 5.02 (sept, J = 6.2 Hz, 1H, CH), 5.07 (d, J = 11.5 Hz, 1H, OCH_2), 5.81 (bs, 1H, CH), 6.20 (d, J = 2.4 Hz, 1H, Ar_m-H), 6.40 (dd, J = 8.3, 2.4 Hz, 1H, Ar_m-H), 7.24 (d, J = 8.3 Hz, 1H, Ar_m-H), 8.23 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = –3.2, –3.1, 19.7, 22.8, 23.2, 23.3 (2C), 26.9 (3C), 46.8, 54.3, 64.5, 71.5, 72.2, 104.4, 109.0, 109.5, 116.0, 130.5, 145.2, 156.0, 158.1, 159.9 (2C).

MS (EI, 70 eV): *m/z* (%) = 506 (76) [M^+], 419 (100), 403 (41), 390 (78), 377 (39), 348 (76).

HRMS–EI: *m/z* [M^+] calcd for $C_{25}H_{38}N_2O_7Si$: 506.2448; found: 506.2447.

24{*5,11*}: R_f = 0.26

^{1}H NMR (500 MHz, acetone-d_6): δ = 1.18–1.39 (m, 12H, 4CH_3), 3.12–3.19 (m, 1H, CH), 4.86 (d, *J* = 17.0 Hz, 1H, CH_2), 4.10 (dd, *J* = 11.5, 2.7 Hz, 1H, OCH_2), 4.27 (d, *J* = 17.0 Hz, 1H, CH_2), 4.73–4.85 (m, 2H, CH+OCH_2), 5.04 (sept, *J* = 6.2 Hz, 1H, CH), 5.96 (d, *J* = 7.8 Hz, 1H, CH), 6.20 (d, *J* = 2.4 Hz, 1H, Ar_m-H), 6.45 (dd, *J* = 8.5, 2.4 Hz, 1H, Ar_m-H), 7.35 (d, *J* = 8.5 Hz, 1H, Ar_m-H), 8.40 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 23.0, 23.1, 23.2, 23.4, 46.0, 53.7, 55.2, 65.2, 71.6, 72.7, 104.7, 110.9, 112.2, 132.0, 155.7, 159.0, 160.1 (2C), 201.7.

MS (EI, 70 eV): *m/z* (%) = 392 (19) [M^+], 249 (17), 189 (18), 101 (32), 71 (34), 59 (56); 46 (77), 43 (100).

HRMS–EI: *m/z* [M^+] calcd $C_{19}H_{24}N_2O_7$: 392.1584; found: 392.1581.

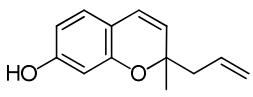
26{*5,11*}: R_f = 0.17.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.20 (s, 6H, 2CH_3), 1.22 (s, 6H, 2CH_3), 4.72–4.94 (m, 6H, CH_2, OCH_2, 2CH), 6.35 (d, *J* = 2.2 Hz, 1H, Ar_m-H), 6.51 (dd, *J* = 8.3, 2.2 Hz, 1H, Ar_m-H), 7.20 (d, *J* = 8.3 Hz, 1H, Ar_m-H), 7.67 (s, 1H, OH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 23.2 (4C), 56.7, 65.5, 71.5, 71.6, 104.7, 111.7, 115.1, 126.5, 133.1, 136.4, 157.5, 159.4, 163.8 (2C), 193.4.

MS (EI, 70 eV): *m/z* (%) = 322 (5), 379 (11), 205 (10), 191 (16), 166 (13), 149 (45), 101 (21), 83 (31), 71 (49), 57 (43), 43 (100). No [M^+] detected.

2-Allyl-2-methyl-2*H*-chromen-7-ol: Side Product from DOMA Condensation after Wittig Reaction:



Flash chromatography in cyclohexane/EtOAc (4:1). R_f = 0.42

Isolated from the **21{*2,X*}** series in amounts between 5–10%.

IR (ATR): ν = 3382, 3076, 2978, 2929, 1701, 1618, 1505, 1456, 1302, 1216, 1155, 1118, 1042.

^{1}H NMR (250 MHz, acetone-d_6): δ = 1.34 (s, 3H, CH_3), 2.42 (bdd, *J* = 7.1, 1.1 Hz, 2H, CH_2), 5.03 (t, *J* = 1.1 Hz, 1H, =CH), 5.06–5.12 (m, 1H, =CH), 5.48 (d, *J* = 9.8 Hz, 1H, =CH), 5.87 (qt, *J* = 10.3, 7.2 Hz, 1H, =CH), 6.26 (bd, *J* = 2.4 Hz, 1H, Ar_m-H), 6.33 (dd, *J* = 8.1, 2.4 Hz, 1H, Ar_m-H), 6.35 (bd, *J* = 9.8 Hz, 1H, =CH), 6.85 (d, *J* = 8.1 Hz, 1H, Ar_m-H), 8.40 (s, 1H, OH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 27.2, 46.9, 79.6, 105.1, 109.6, 115.6, 119.3, 124.4, 127.8, 129.0, 135.3, 156.2, 160.5.

MS (EI, 70 eV): *m/z* (%) = 202 (2) [M^+], 161 (100) [$C_{10}H_9O_2$].

HRMS–EI: *m/z* [M^+] calcd for $C_{13}H_{14}O_2$: 202.0994; found: 202.0993.

References:

[1] Modified according to: Zhang, S.; Zhen, J.; Reith, M. E. A.; Dutta, A. K. *Bioorg. Med. Chem.* **2006**, *14*, 3953.

[2] Yu, X.; Wang, S.; Chen, F. *J. Comb. Chem.* **2008**, *10*, 605.

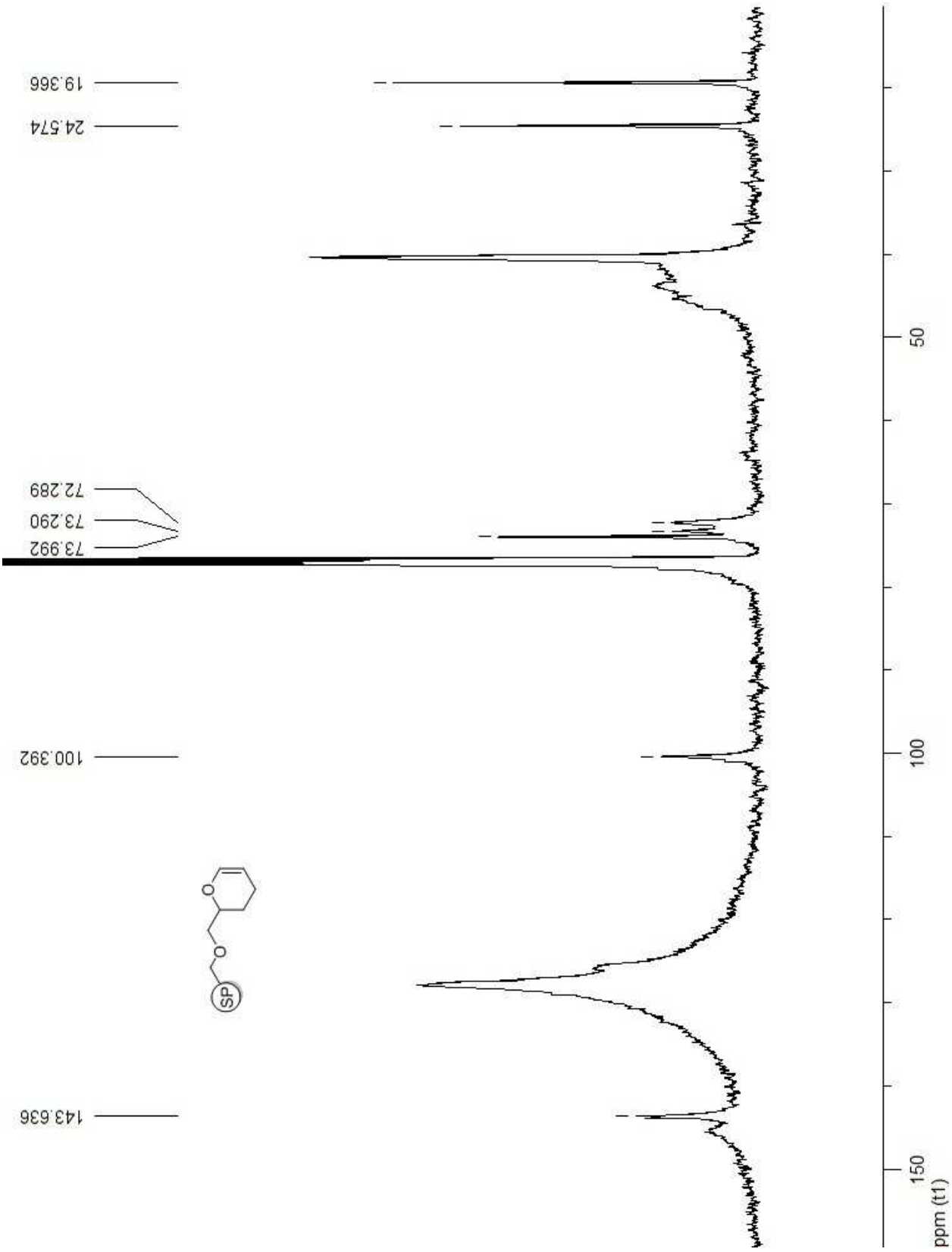
[3] Uchiyama, M.; Ozawa, H.; Takuma, K.; Matsumoto, Y.; Yonehara, M.; Hiroya, K.; Sakamoto, T. *Org. Lett.* **2006**, *8*, 5517.

[4] Bajwa, M.; Jennings, M. P. *J. Org. Chem.* **2006**, *71*, 3646.

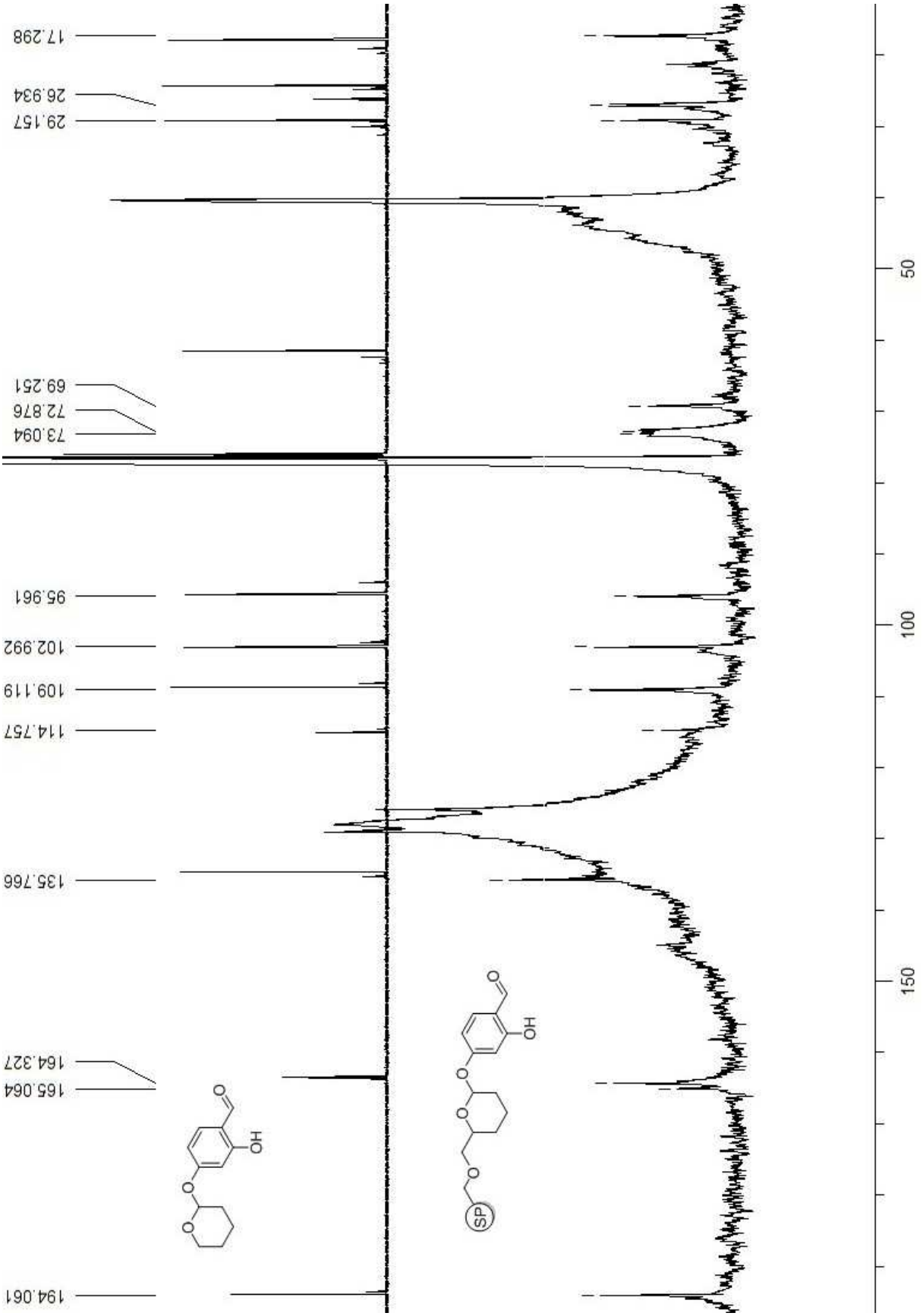
[5] Burke, T. R. Jr.; Nelson, W. L. *J. Med. Chem.* **1979**, 22, 1535.

[6] Oh, S.; Jang, H. J.; Ko, S. K.; Ko, Y.; Park, S. B. *J. Comb. Chem.* **2010**, *12*, 548–558.

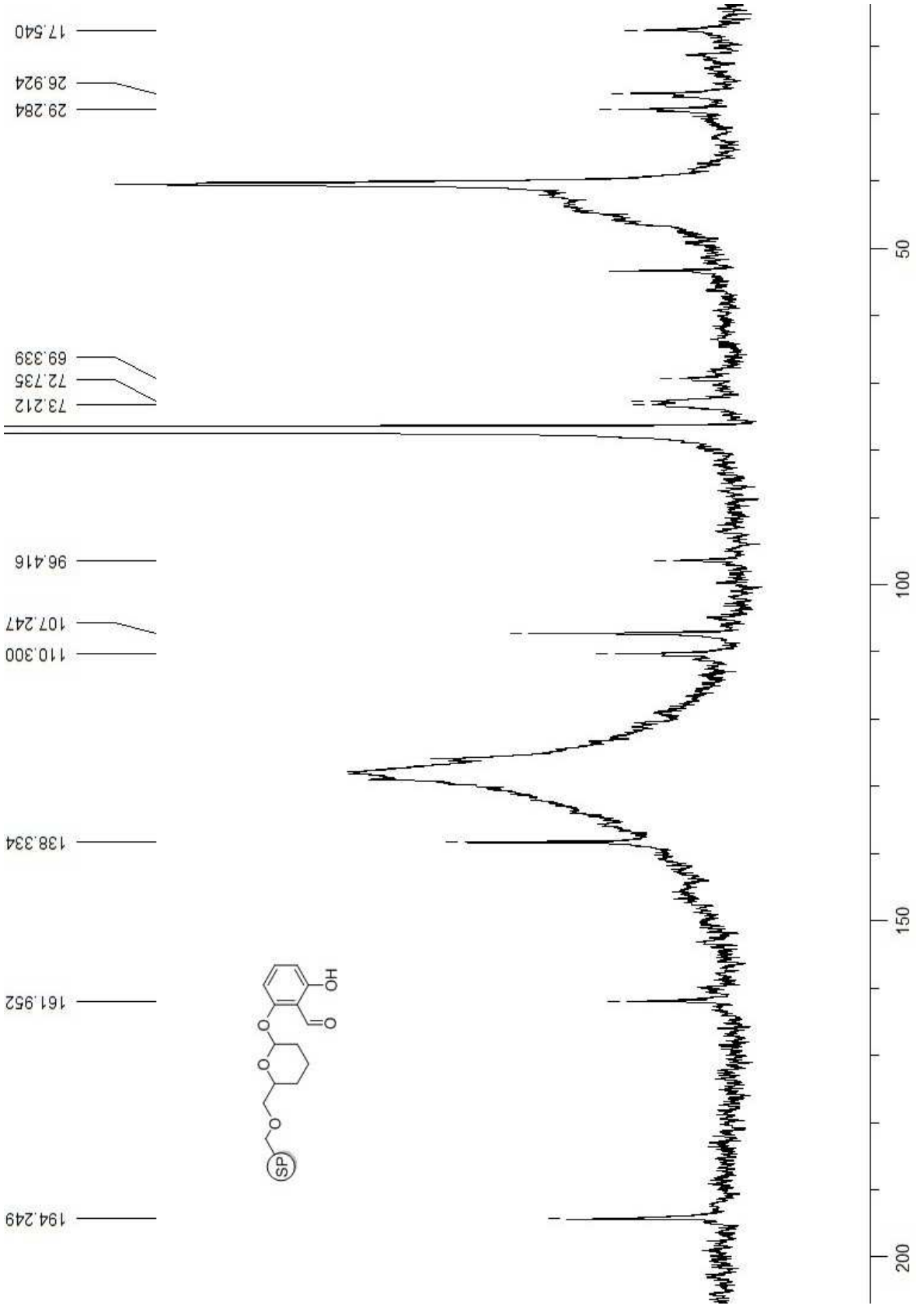
THP-Linker **4**:


19.366
24.574
72.289
73.290
73.992
100.392
143.636
SP
50
100
150
ppm (t1)

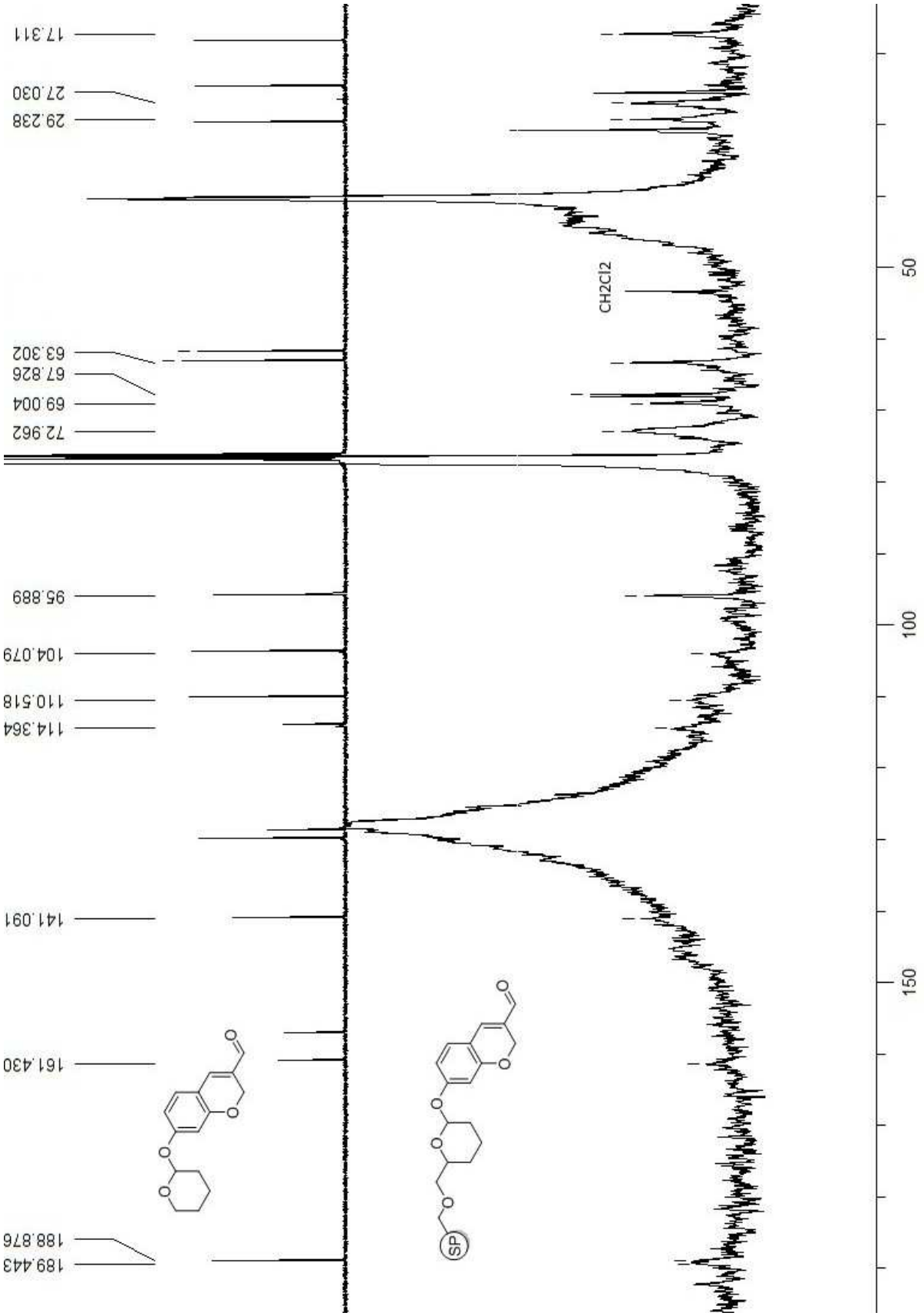
2-Hydroxy-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]benzaldehyde and immobilized 4-HSA **5**:



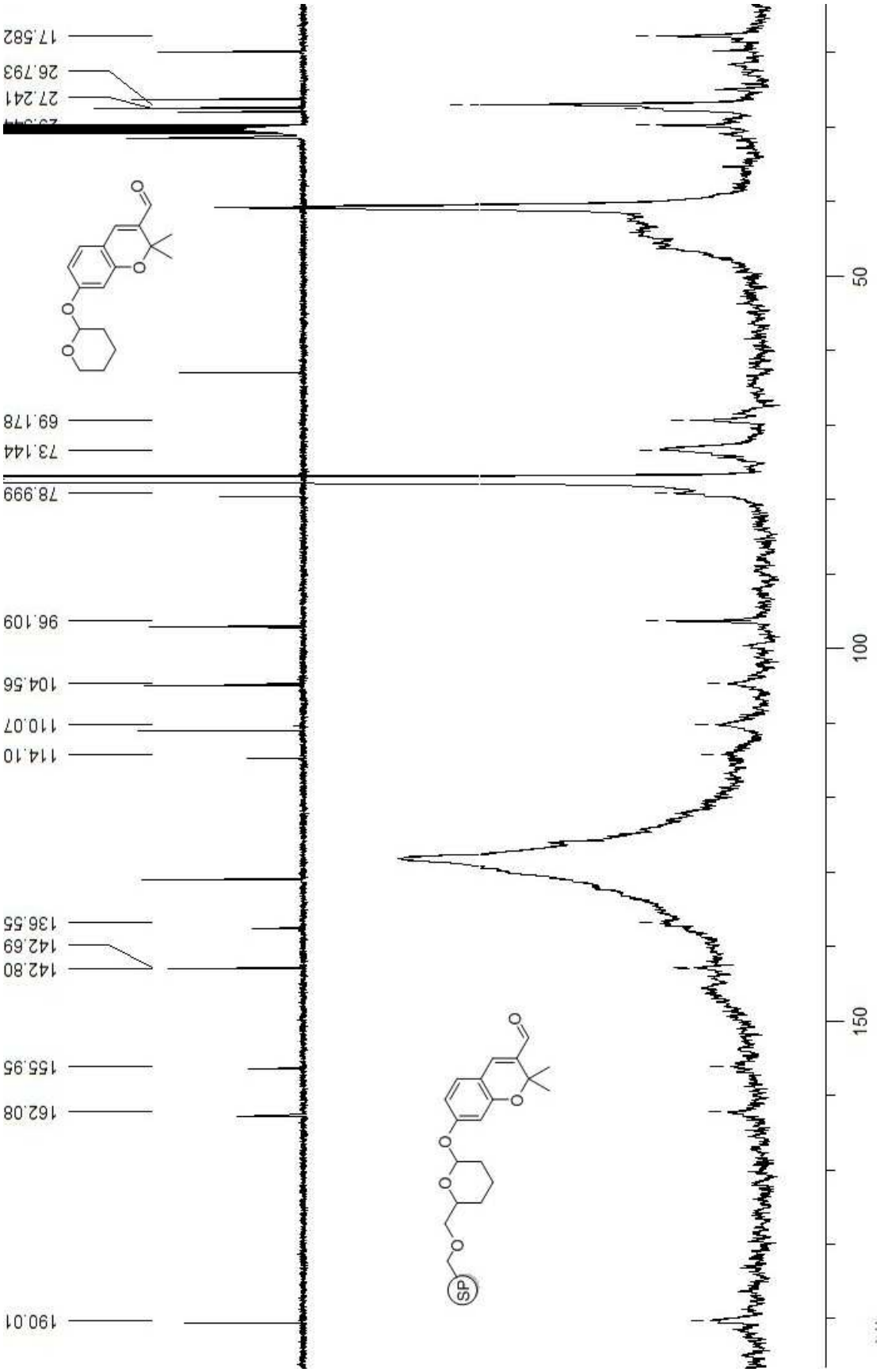
Immobilized 6-HSA **6**: (Peak at 53.31 = CH_2Cl_2)



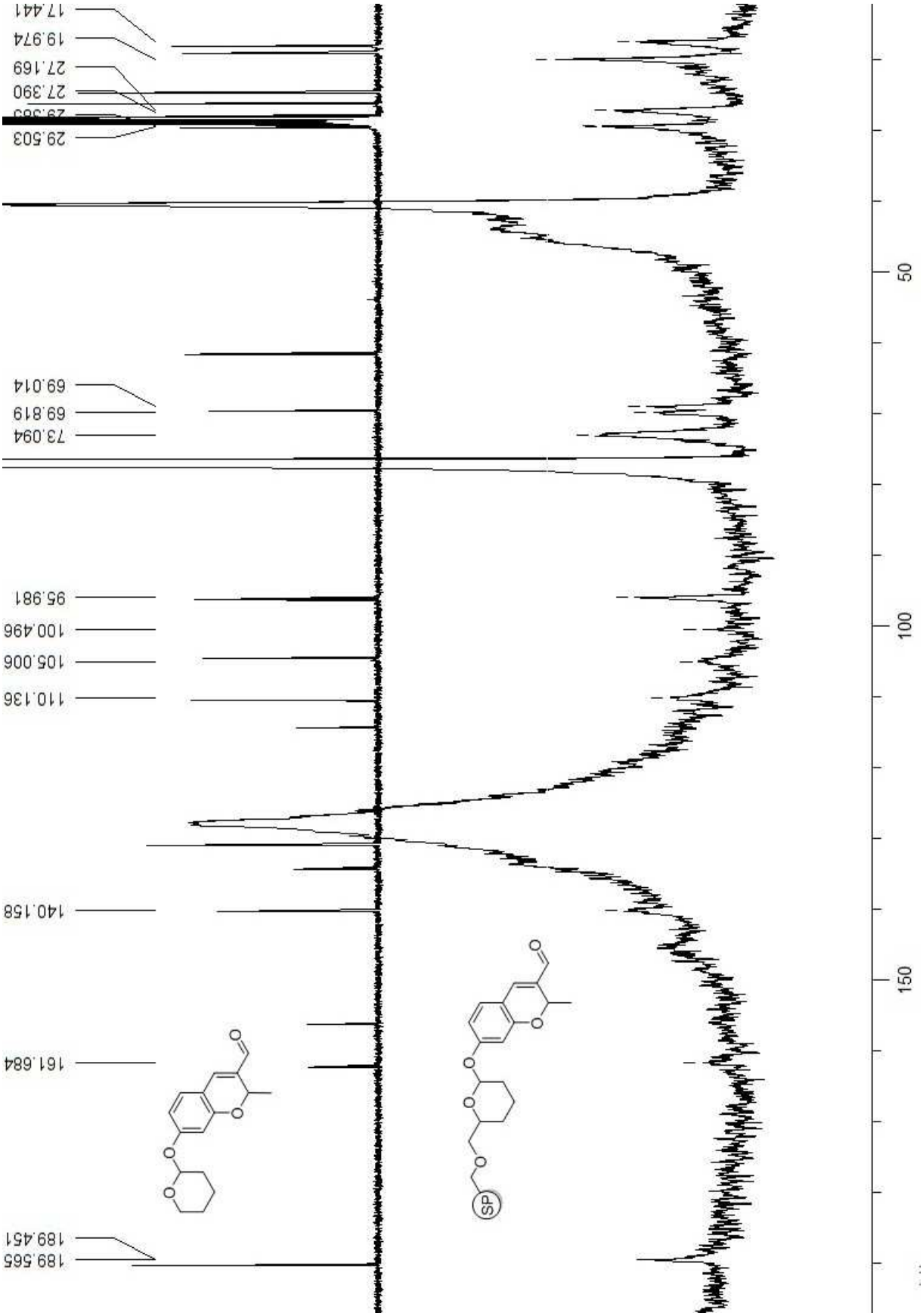
DOMA: **11**{*1*} and **8**{*1*}: (Peak at 53.31 = CH_2Cl_2)



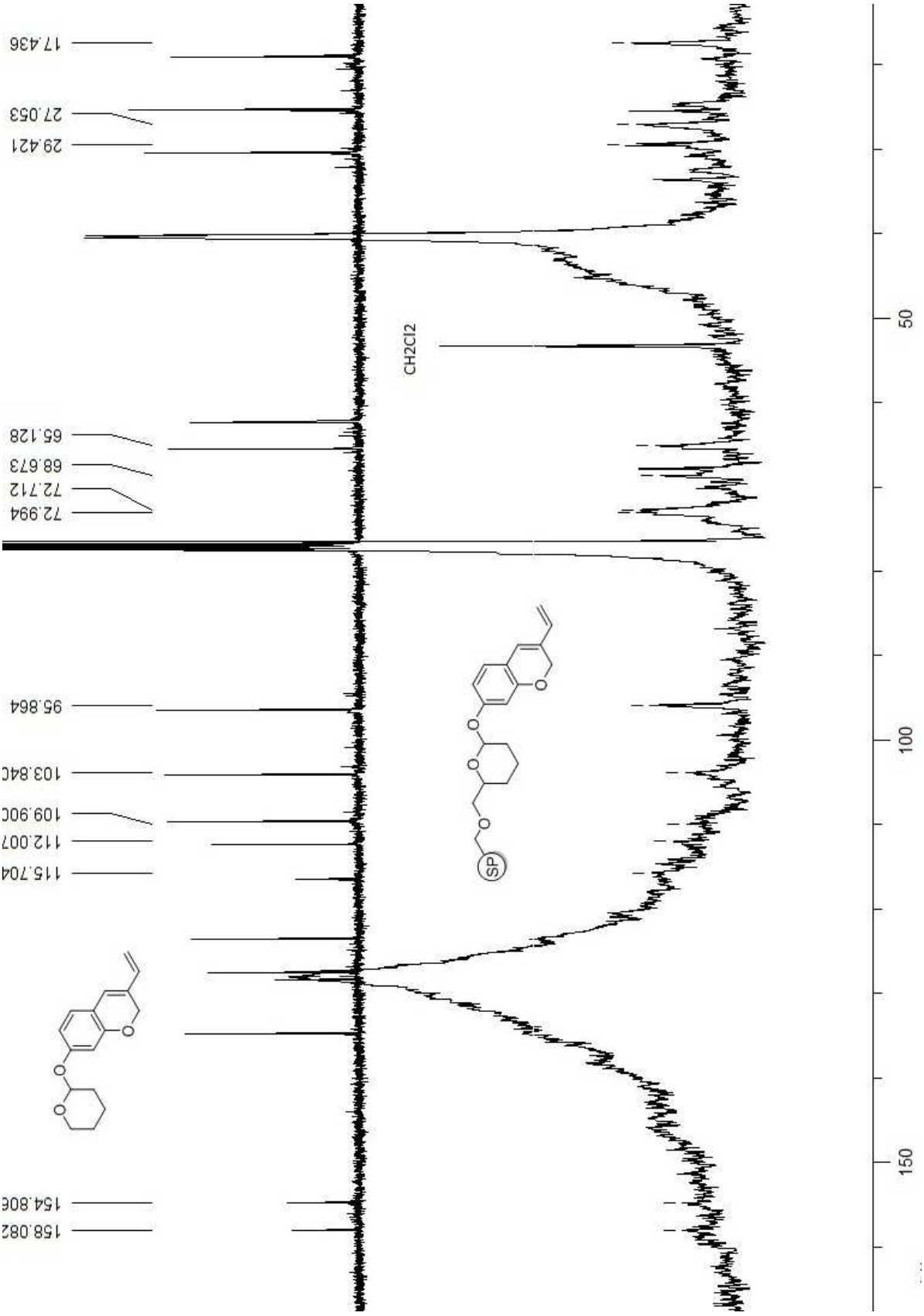
DOMA: **11**{*2*} and **8**{*2*}:



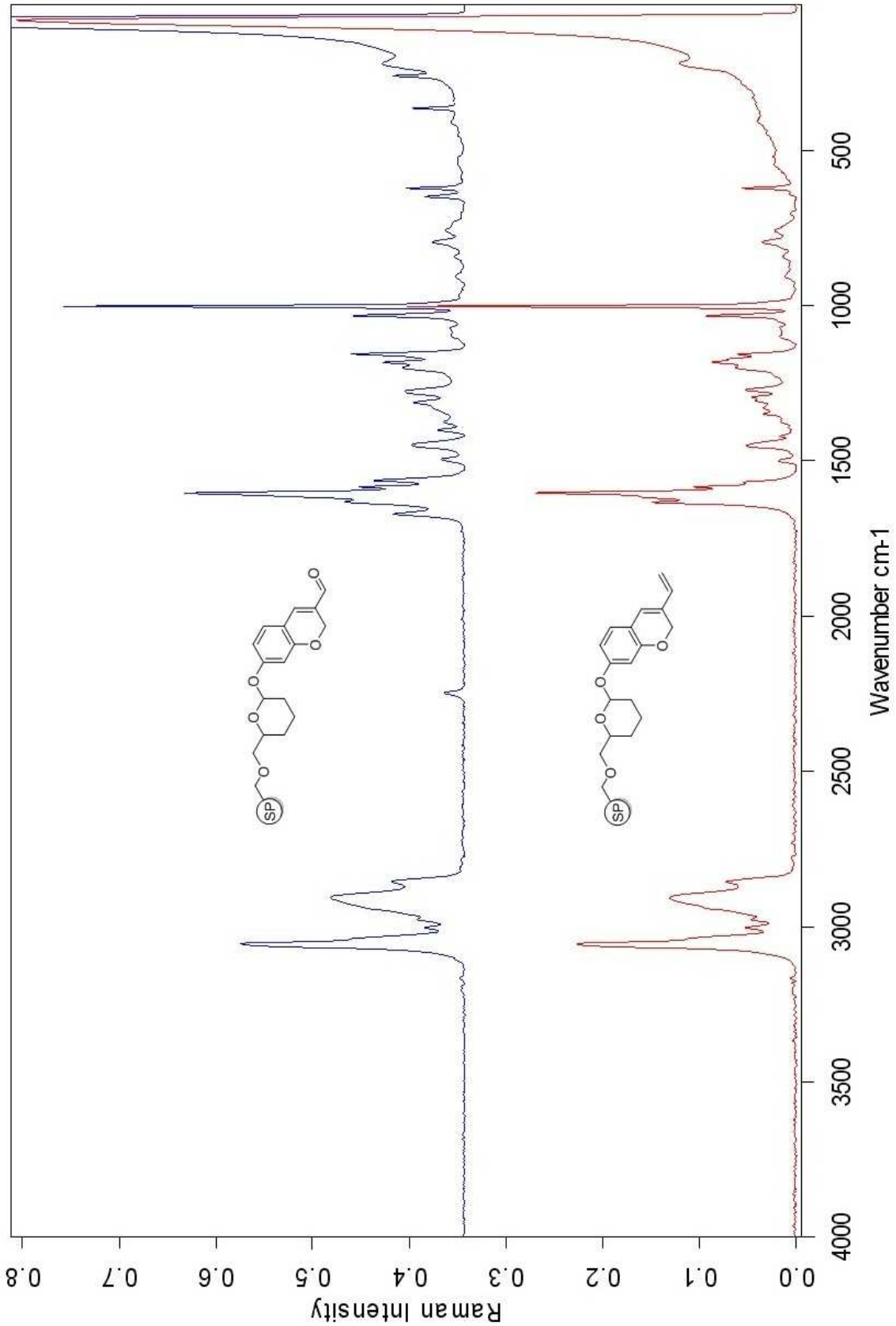
DOMA: **11**{*3*} and **8**{*3*}:



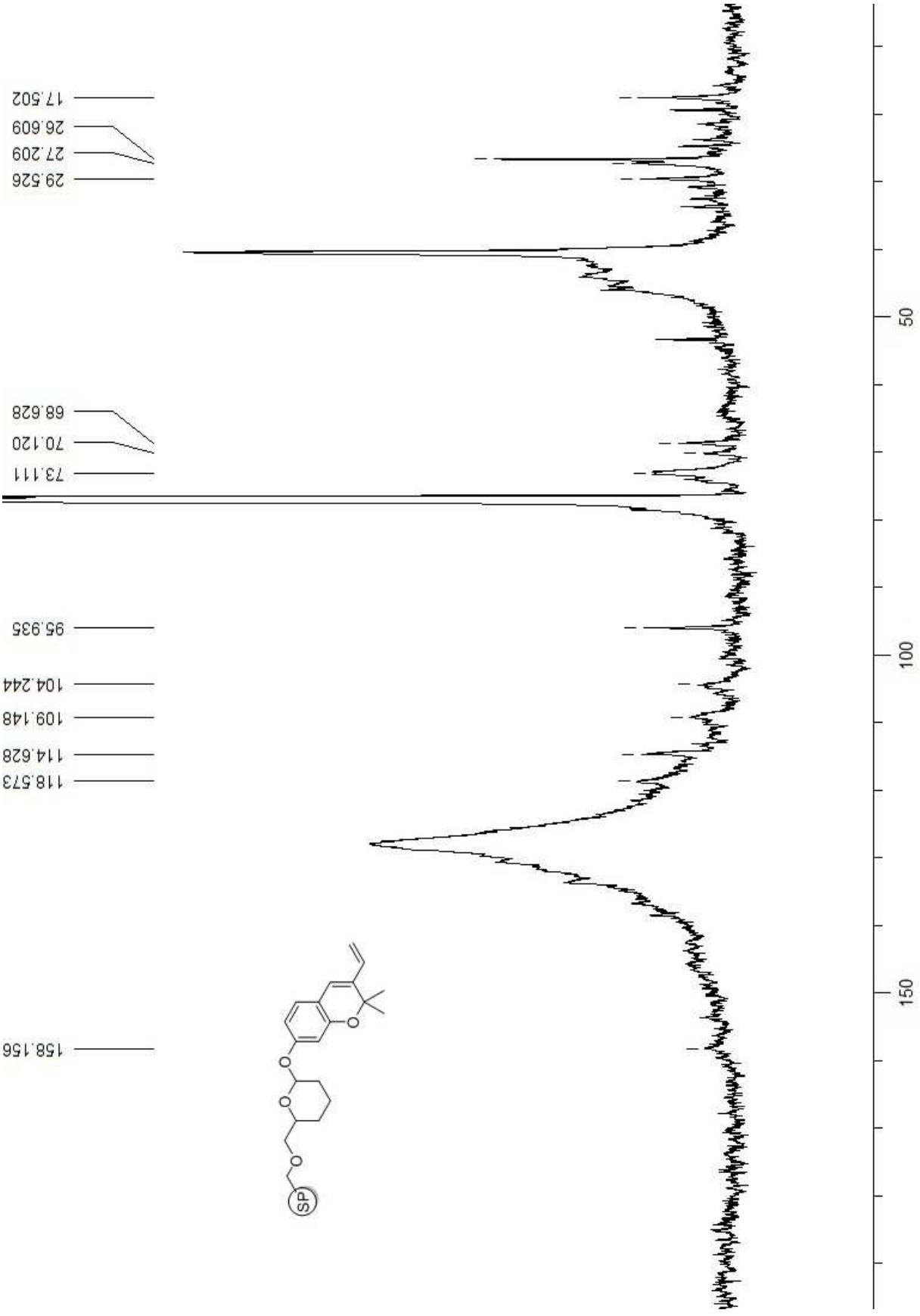
Wittig: **17**{*1*} and **16**{*1*}: (Peak at 53.31 = CH_2Cl_2)



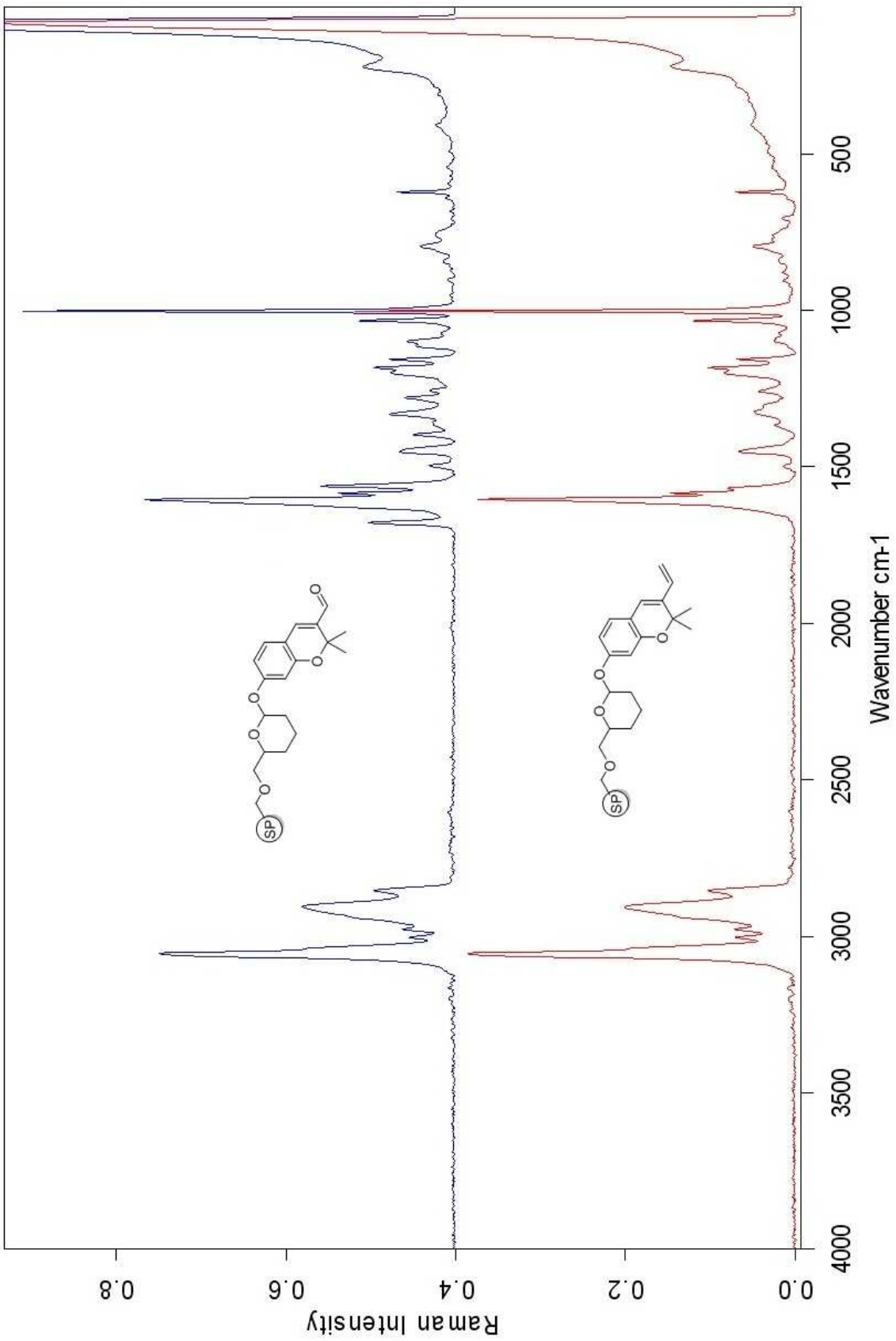
Wittig: **8**{*1*} to **16**{*1*}:



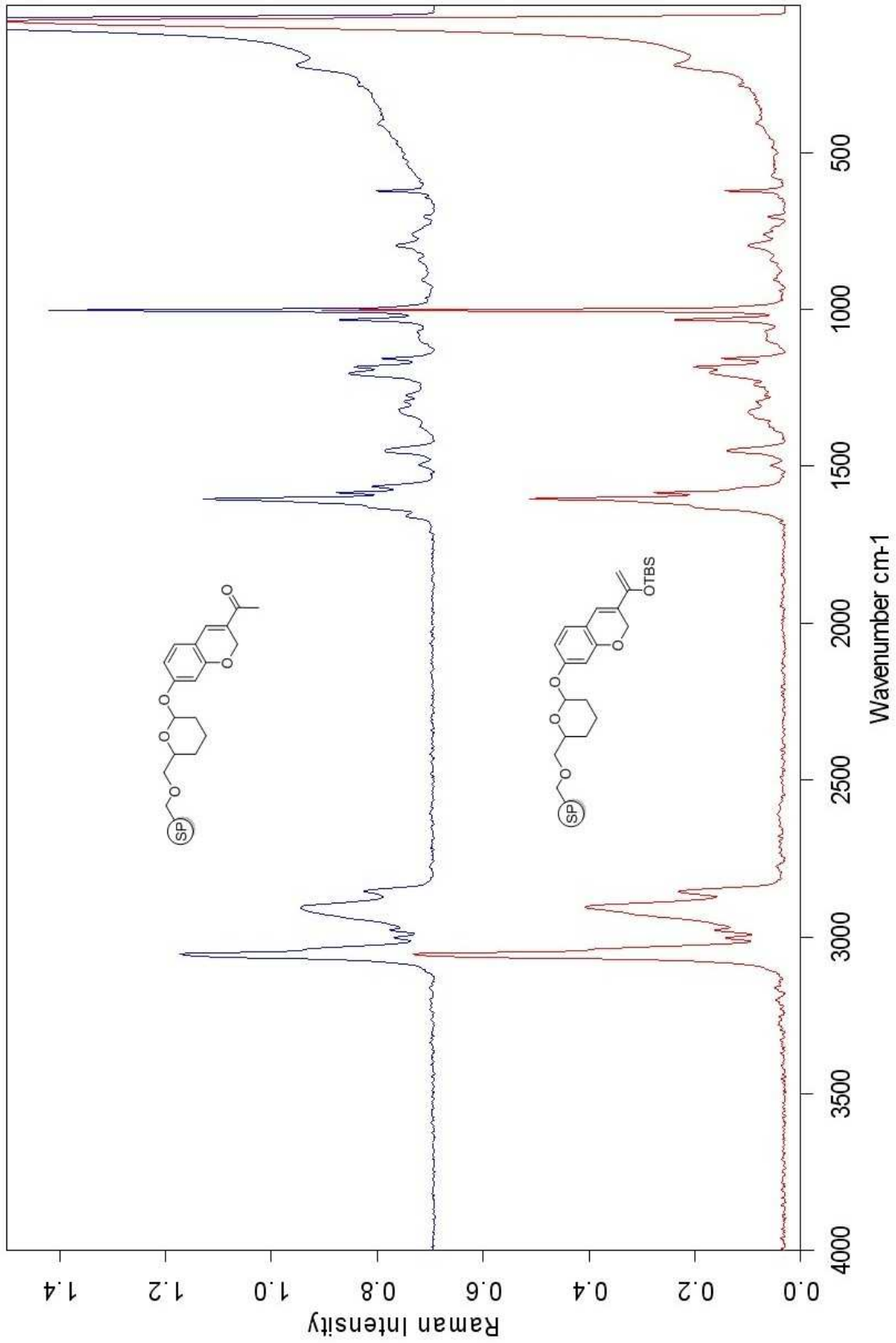
Wittig: **16**{*2*}:


17.502
26.609
27.209
29.526
68.628
70.120
73.111
95.935
104.244
109.148
114.628
118.573
158.156
50
100
150
SP

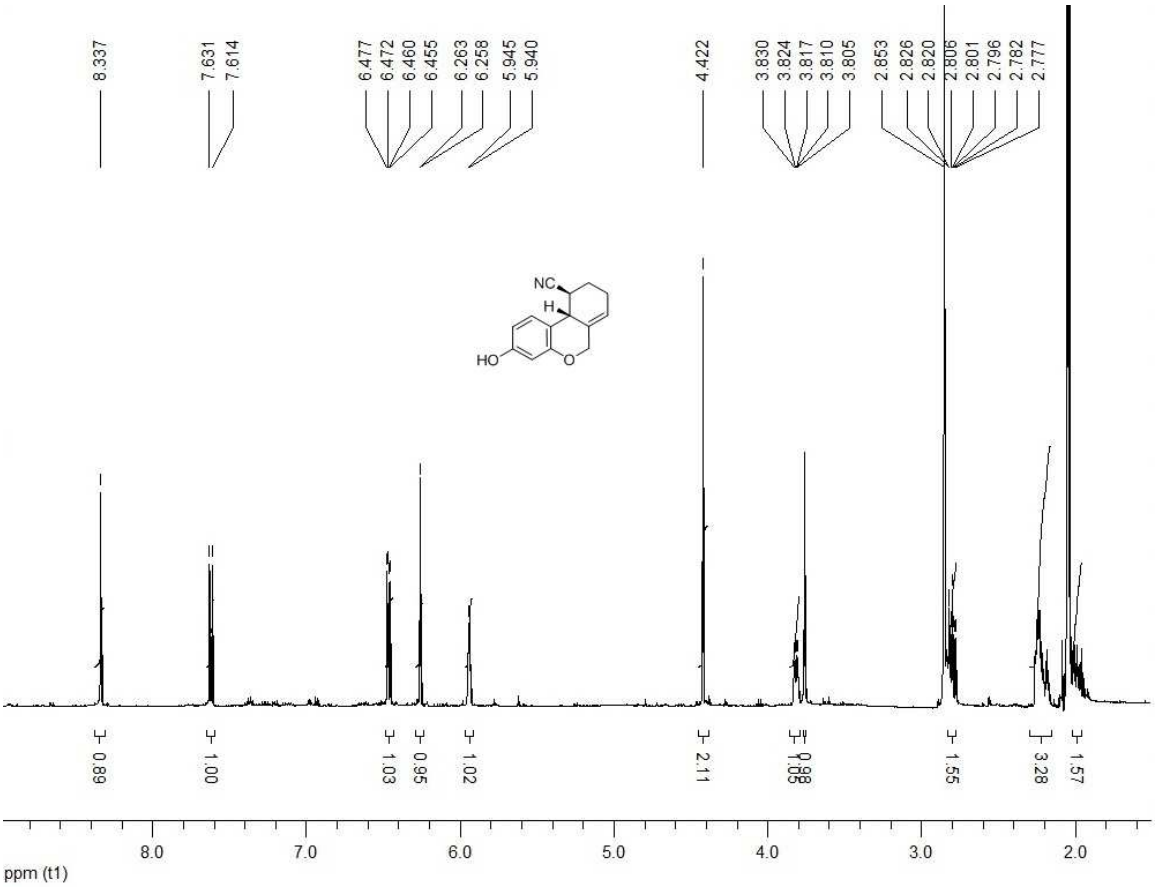
Wittig: **8**{*2*} to **16**{*2*}:

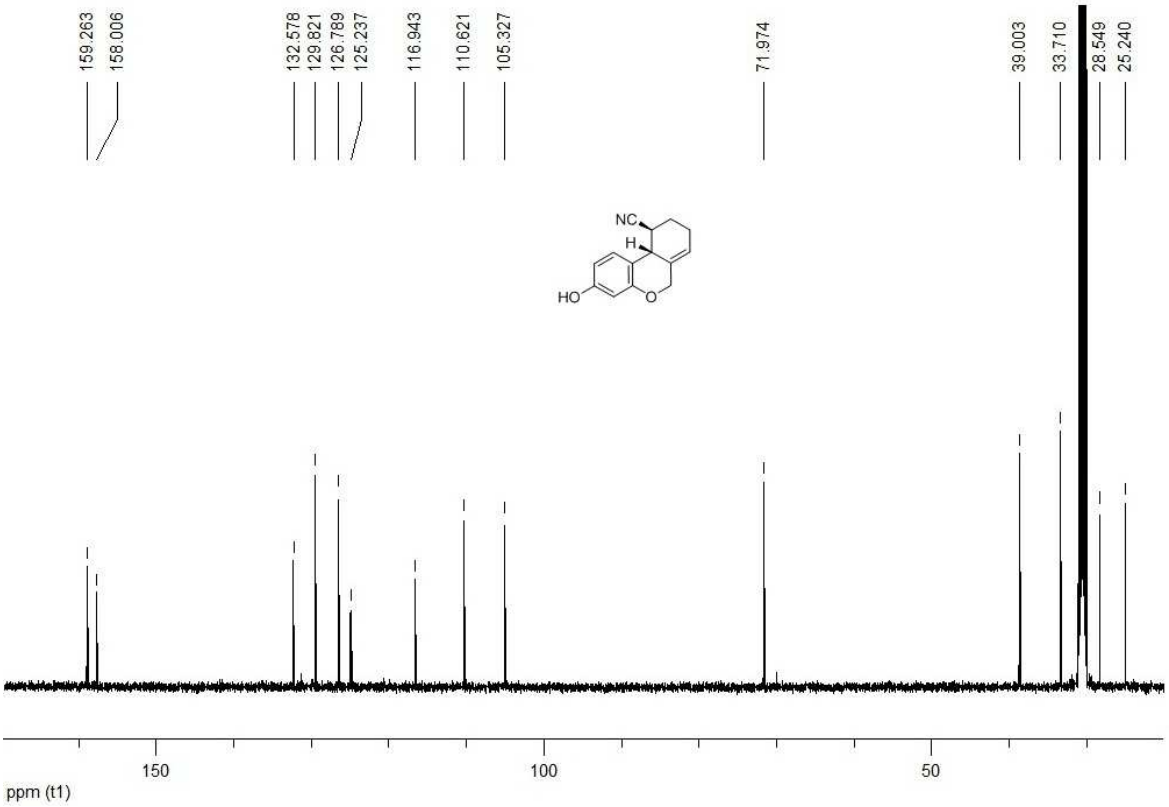


Enol-Ether: **8**{*5*} to **11**{*5*}:

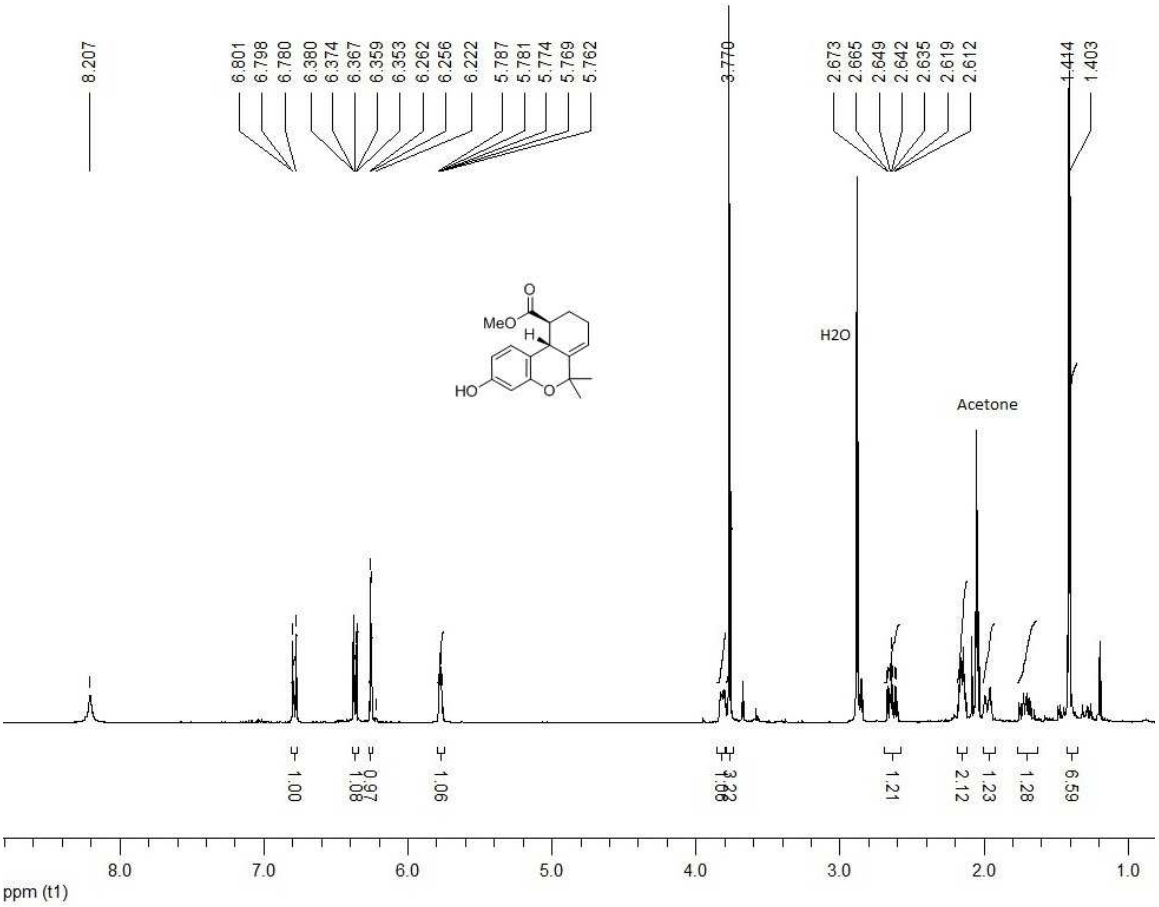


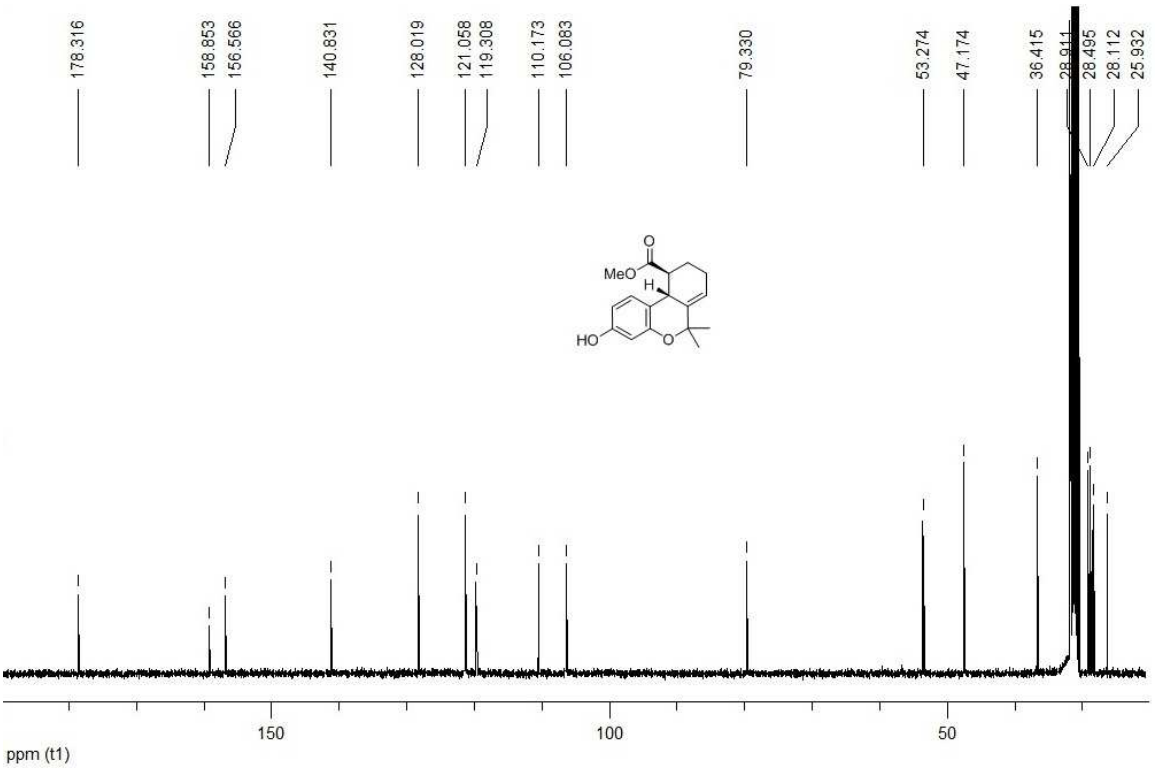
21{*1,3*}:


8.337
7.631
7.614
6.477
6.472
6.460
6.455
6.263
6.258
5.945
5.940
4.422
3.830
3.824
3.817
3.810
3.805
2.853
2.826
2.820
2.806
2.801
2.796
2.782
2.777
NC
H
HO
O
0.89
1.00
1.03
0.95
1.02
2.11
3.08
1.55
3.28
1.57
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

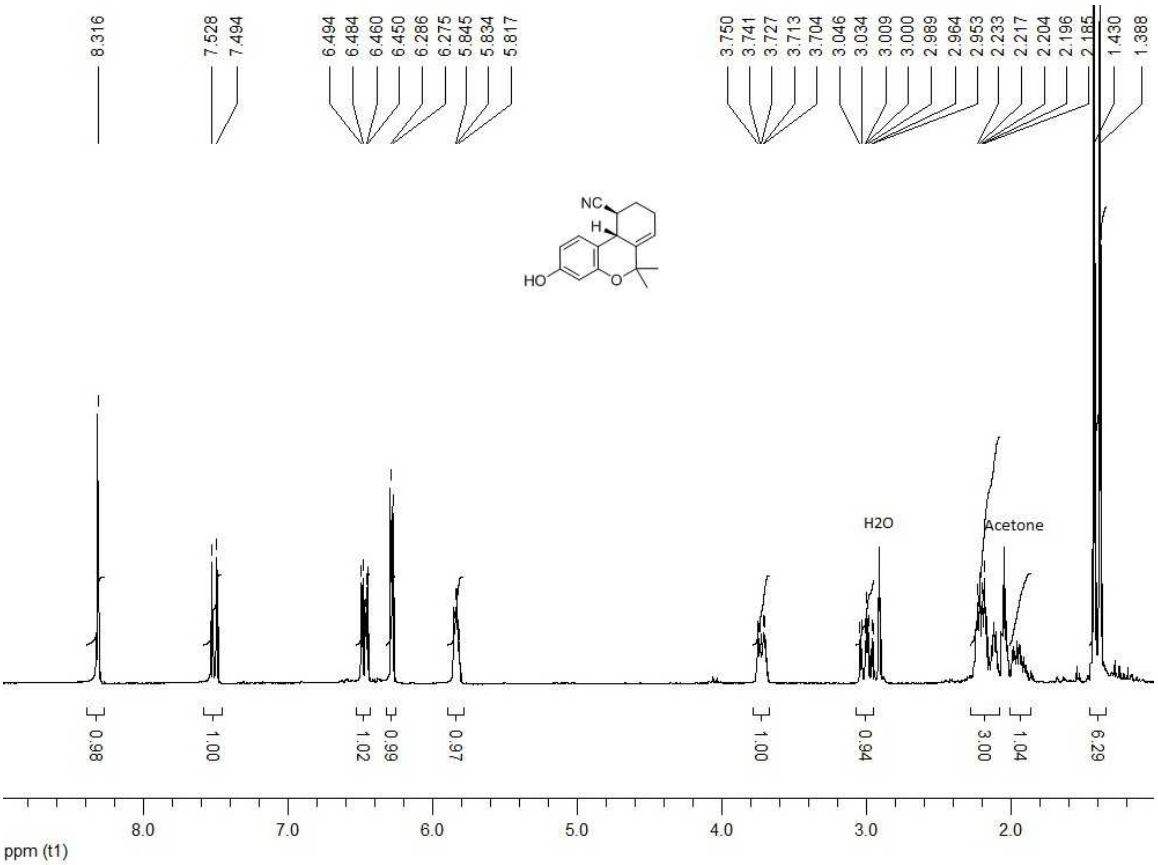

159.263
158.006
132.578
129.821
126.789
125.237
116.943
110.621
105.327
71.974
39.003
33.710
28.549
25.240
NC
H
HO
O
150
100
50
ppm (t1)

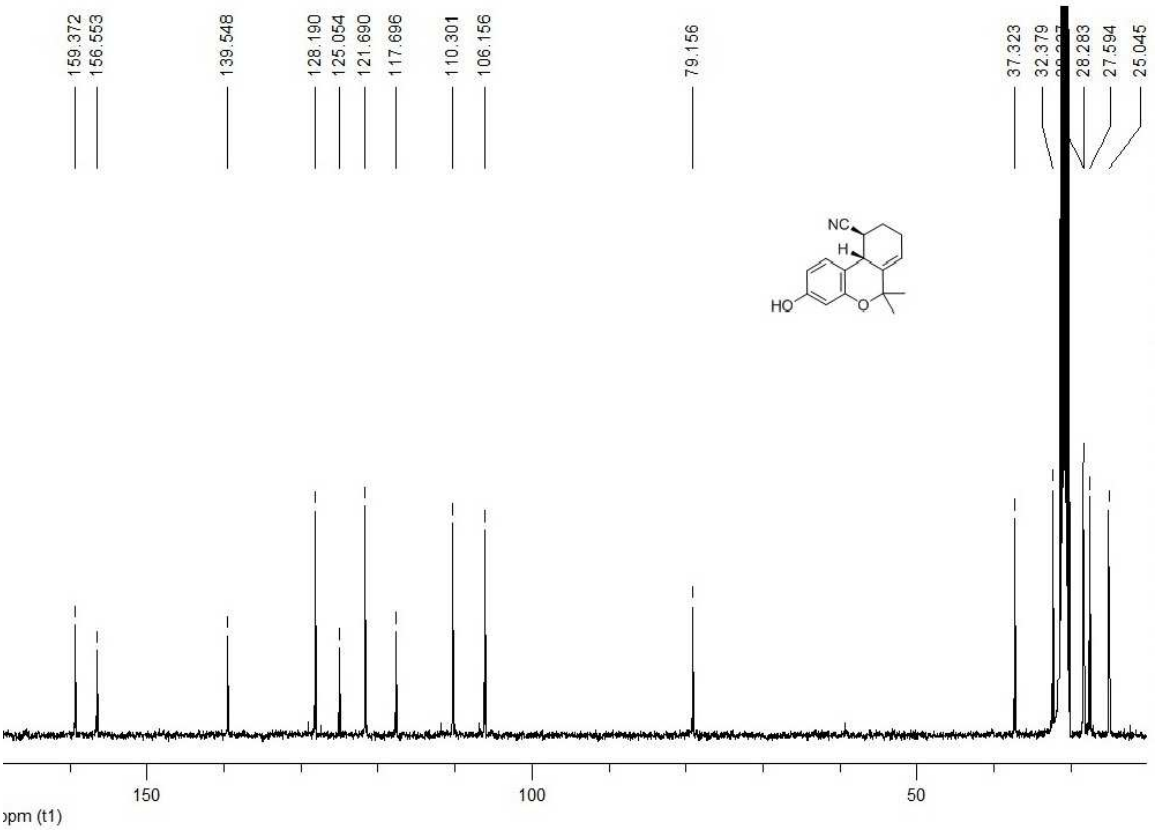
21{*2,2*}:


8.207
6.801
6.798
6.780
6.380
6.374
6.367
6.359
6.353
6.262
6.256
6.222
5.787
5.781
5.774
5.769
5.762
3.770
2.673
2.665
2.649
2.642
2.635
2.619
2.612
1.444
1.403
MeO
H
HO
O
H2O
Acetone
1.00
1.08
0.97
1.06
3.38
3.36
1.21
2.12
1.23
1.28
6.59
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

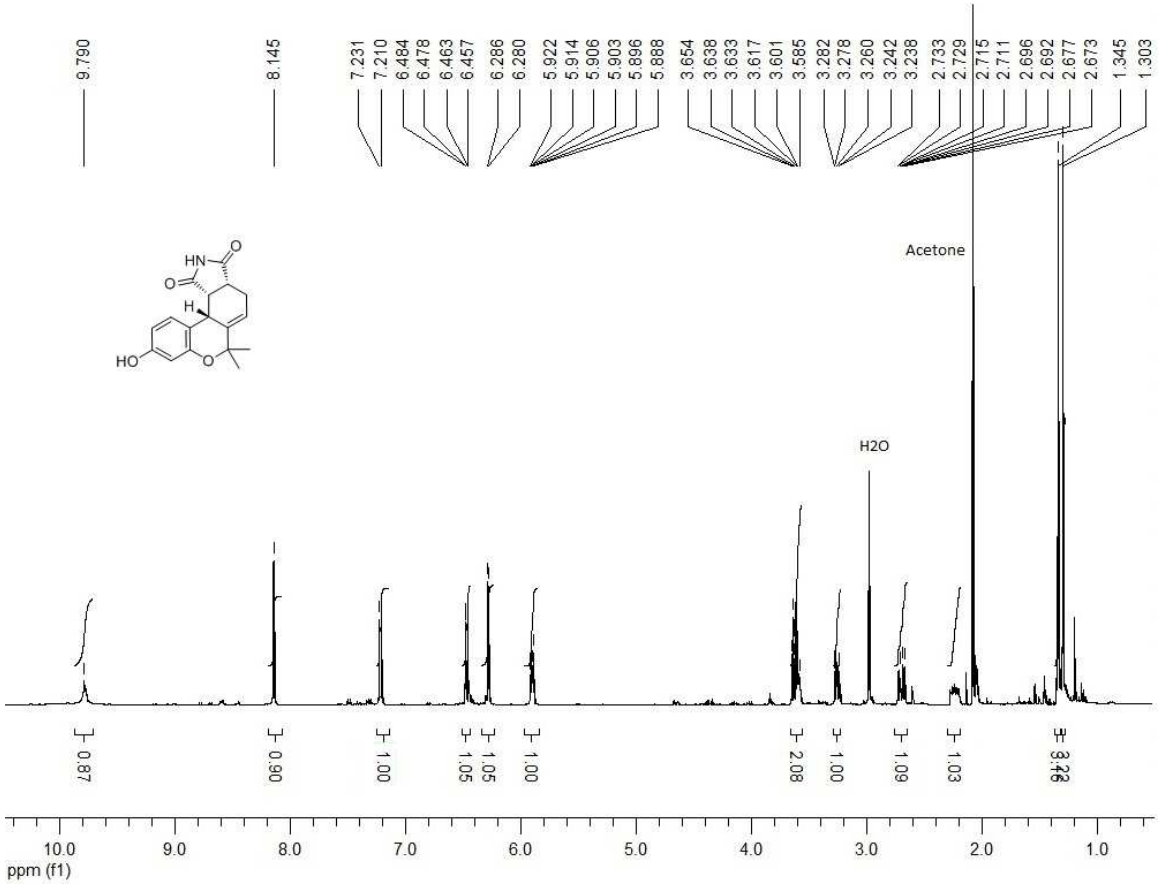

178.316
158.853
156.566
140.831
128.019
121.058
119.308
110.173
106.083
79.330
53.274
47.174
36.415
28.911
28.495
28.112
25.932
MeO
H
HO
O
150
100
50
ppm (t1)

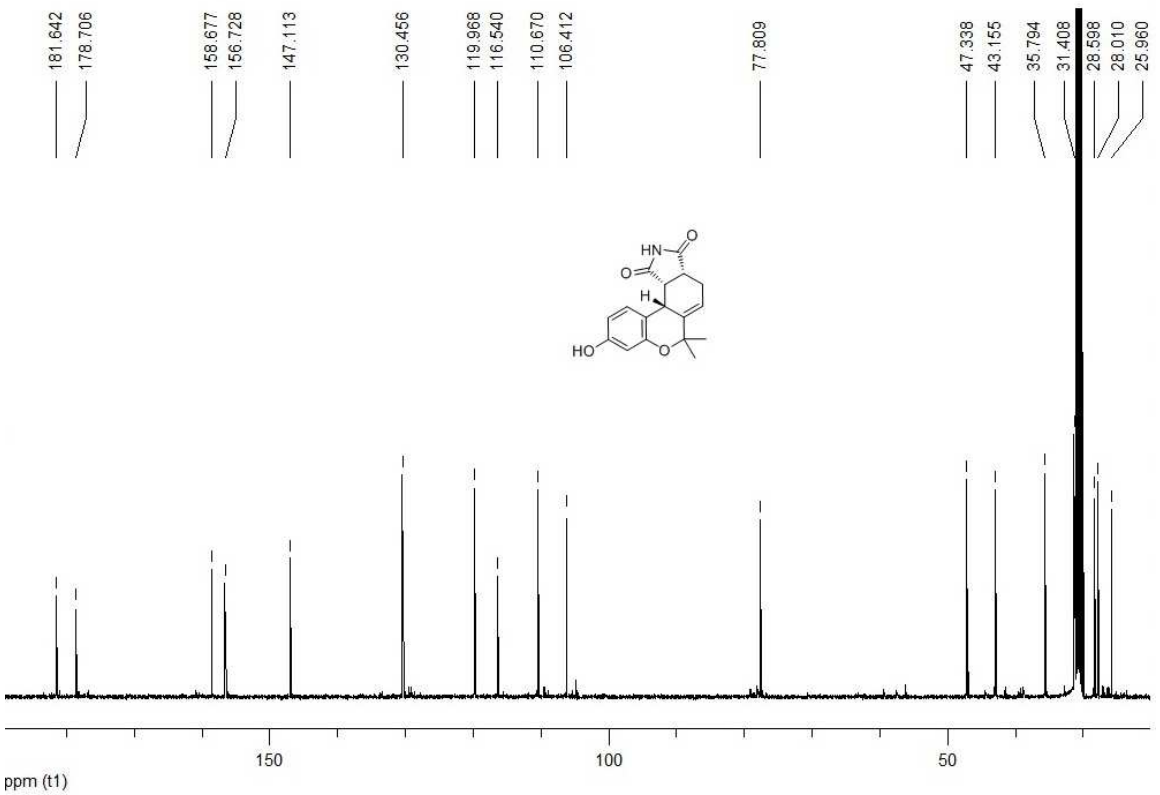
21{*2,3*}:


8.316
7.528
7.494
6.494
6.484
6.460
6.450
6.286
6.275
5.845
5.834
5.817
3.750
3.741
3.727
3.713
3.704
3.046
3.034
3.009
3.000
2.989
2.964
2.953
2.233
2.217
2.204
2.196
2.185
1.430
1.388
NC
H
HO
O
H2O
Acetone
0.98
1.00
1.02
0.99
0.97
1.00
0.94
3.00
1.04
6.29
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

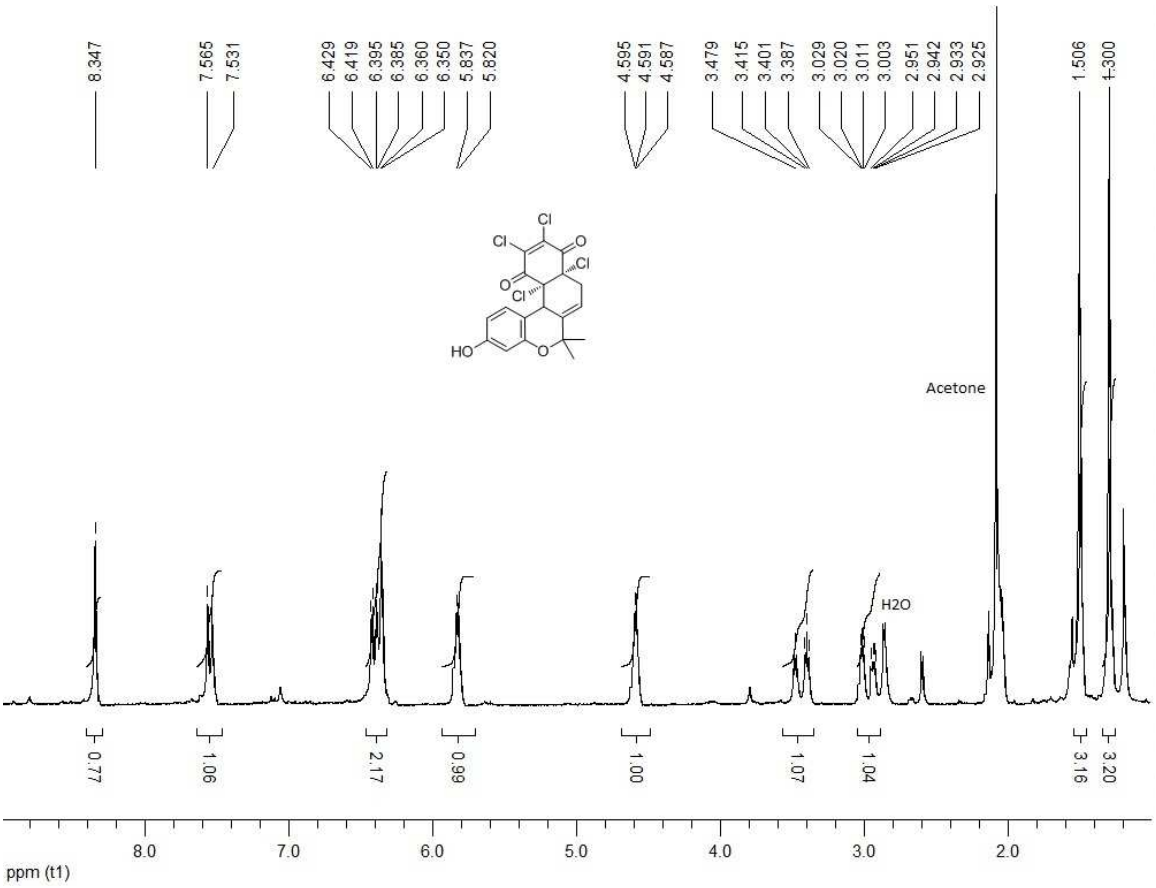

159.372
156.553
139.548
128.190
125.054
121.690
117.696
110.301
106.156
79.156
37.323
32.379
28.283
27.594
25.045
NC
H
HO
O
150
100
50
ppm (t1)

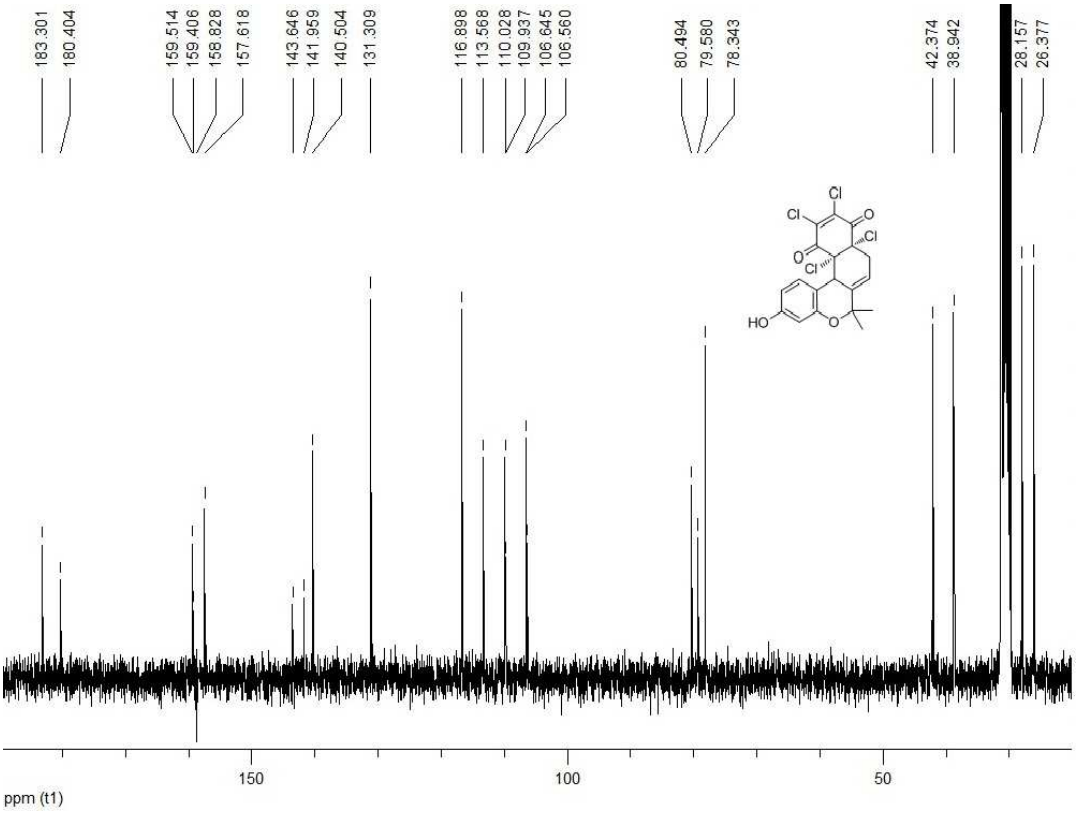
21{*2,7*}:


9.790
8.145
7.231
7.210
6.484
6.478
6.463
6.457
6.286
6.280
5.922
5.914
5.906
5.903
5.896
5.888
3.654
3.638
3.633
3.617
3.601
3.585
3.282
3.278
3.260
3.242
3.238
2.733
2.729
2.715
2.711
2.696
2.692
2.677
2.673
1.345
1.303
Acetone
H2O
HN
O
O
H
HO
O
0.87
0.90
1.00
1.05
1.05
1.00
2.08
1.00
1.09
1.03
3.26
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

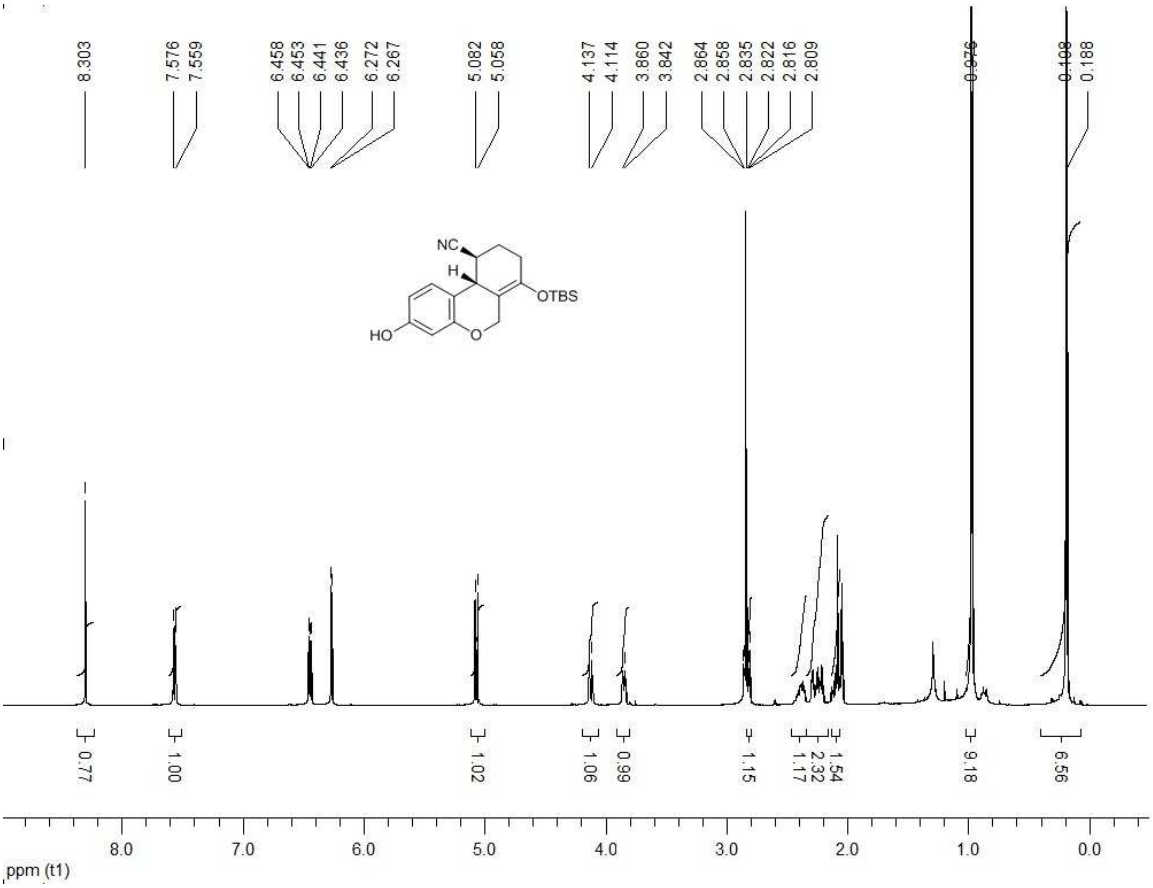

181.642
178.706
158.677
156.728
147.113
130.456
119.968
116.540
110.670
106.412
77.809
47.338
43.155
35.794
31.408
28.598
28.010
25.960
HN
O
O
H
HO
O
150
100
50
ppm (t1)

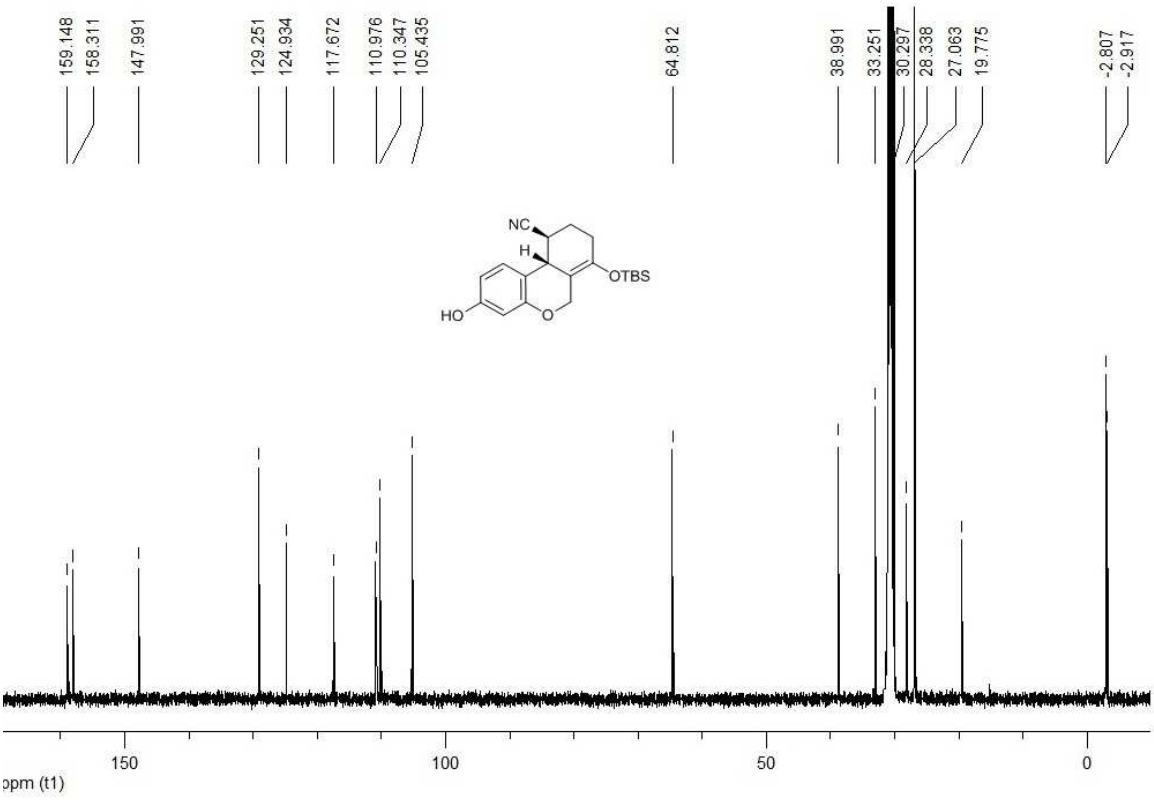
21{*2,10*}:


8.347
7.565
7.531
6.429
6.419
6.395
6.385
6.360
6.350
5.837
5.820
4.595
4.591
4.587
3.479
3.415
3.401
3.387
3.029
3.020
3.011
3.003
2.951
2.942
2.933
2.925
1.506
1.300
Acetone
H2O
0.77
1.06
2.17
0.99
1.00
1.07
1.04
3.16
3.20
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)


183.301
180.404
159.514
159.406
158.828
157.618
143.646
141.959
140.504
131.309
116.898
113.568
110.028
109.937
106.645
106.560
80.494
79.580
78.343
42.374
38.942
28.157
26.377
150
100
50
ppm (t1)

21{*5,3*}:


8.303
7.576
7.559
6.458
6.453
6.441
6.436
6.272
6.267
5.082
5.058
4.137
4.114
3.860
3.842
2.864
2.858
2.835
2.822
2.816
2.809
0.076
0.108
0.188
NC
H
OTBS
HO
O
0.77
1.00
1.02
1.06
0.99
1.15
1.17
2.32
1.54
9.18
6.56
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


159.148
158.311
147.991
129.251
124.934
117.672
110.976
110.347
105.435
64.812
38.991
33.251
30.297
28.338
27.063
19.775
-2.807
-2.917
NC
H
OTBS
HO
O
150
100
50
0
ppm (t1)