Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Organocatalytic Approach to δ-Lactones Bearing a Fused Cyclohexenone Scaffold

by

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Supporting Information

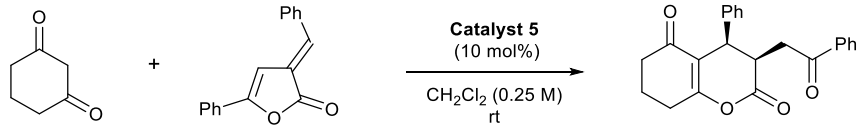
1. General methods

NMR spectra were acquired on a Bruker Ultra Shield 700 instrument, running at 700 MHz for ^{1}H and 176 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR). Mass spectra were recorded on a Bruker Maxis Impact spectrometer using electrospray (ES+) ionization. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and $[\alpha]_D$ values are given in $deg \cdot cm \cdot g^{-1} \cdot dm^{-1}$; concentration *c* is listed in $g \cdot (100\ mL)^{-1}$. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation. The enantiomeric ratio (er) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak IA and ID columns). Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka). (*E*)-3-Alkylidene-5-arylfuran-2(3*H*)-one **4** were prepared according to literature procedures.[1] Cinchona-alkaloid-derived catalysts **5e**[2] and **5d**,**f**[3] were synthesized following the literature procedures.

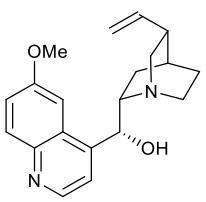
[1] C. G. Wermuth, G. Schlewer, J. J. Bourguignon, G. Maghioros, M. J. Bouchet, C. Moire, J. P. Kan, P. Worms and K. Biziere, *J. Med. Chem.,* 1989, **32**, 528.
[2] W. Yang and D.-M. Du, *Org. Lett*., 2010, **12**, 5450.
[3] B. Vakulya , S. Varga, A. Csámpai and T. Soós, *Org. Lett.,* 2005, **7**, 1967.

2. Screening results

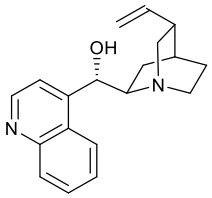
2.1. Catalyst screening



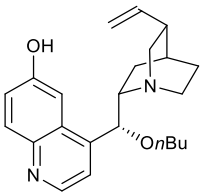
3a + **4a** → **1a**



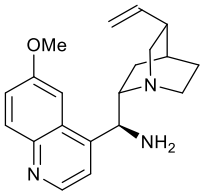
5a
1a: 36% yield
28:72 er



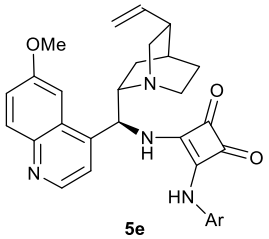
5b
1a: 41% yield
72:28 er



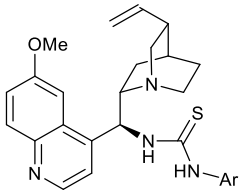
5c
1a: 39% yield
58:42 er



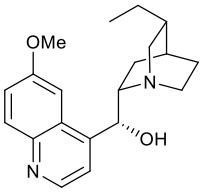
5d
1a: 30% yield
67:33 er



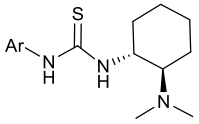
5e
Ar: 3,5-$(CF_3)_2C_6H_3$
1a: 40% yield
87:13 er



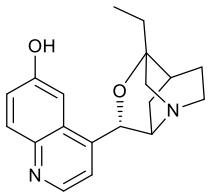
5f
Ar: 3,5-$(CF_3)_2C_6H_3$
1a: 45% yield
91:9 er



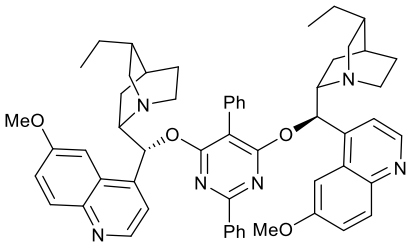
5g
1a: 42% yield
24:76 er



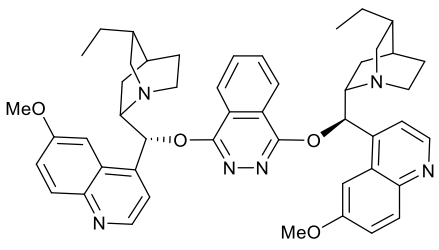
5h
Ar: 3,5-$(CF_3)_2C_6H_3$
1a: 38% yield
10:90 er



5i
1a: 20% yield
28:72 er

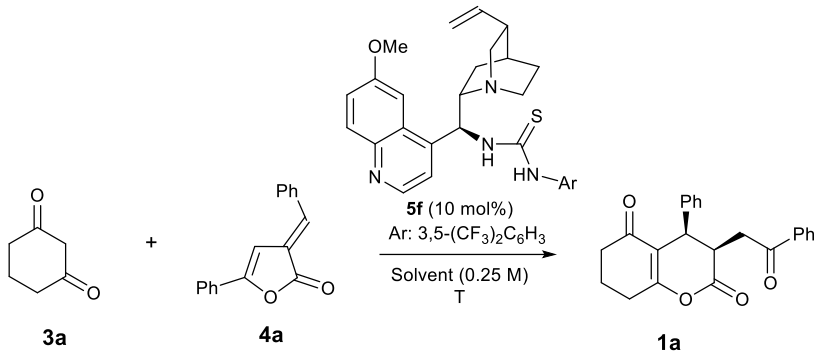


5j
1a: 35% yield
36:64 er



5k
1a: 38% yield
76:24 er

2.2. Reaction conditions screening[a]

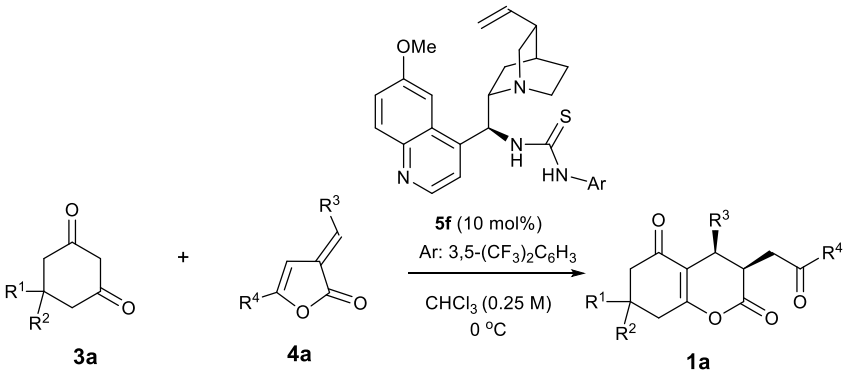


3a + **4a** → **1a**

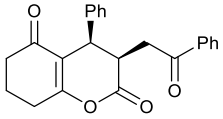
Entry	Solvent	T [°C]	Yield [%][b]	dr[c]	er[d]
1	CH_2Cl_2	rt	52	>20:1	91:9
2	$CHCl_3$	rt	60	>20:1	92:8
3	$ClCH_2CH_2Cl$	rt	43	>20:1	90:10
4	Toluene	rt	31	>20:1	93:7
5	THF	rt	29	>20:1	82:18
6	1,4-Dioxane	rt	32	>20:1	92:8
7	$(CH_3CH_2)_2O$	rt	30	>20:1	76:24
8	CH_3CN	rt	35	>20:1	84:16
9[e]	$CHCl_3$	rt	42	>20:1	92:8
10[f]	$CHCl_3$	rt	44	>20:1	91:9
11	$CHCl_3$	40	45	>20:1	90:10
12	$CHCl_3$	10	58	>20:1	91:9
13	$CHCl_3$	0	65	>20:1	97:3
14	$CHCl_3$	-15	19	>20:1	89:11
15	$CHCl_3$	-40	<5	>20:1	n.d.
16[g]	$CHCl_3$	rt	44	>20:1	91:9
17[h]	$CHCl_3$	rt	50	>20:1	92:8
18[i]	$CHCl_3$	rt	46	>20:1	92:8
19[j]	$CHCl_3$	rt	47	>20:1	91:9

[a] Reactions performed on 0.05 mmol scale using **3a** (1 equiv) and **4a** (1 equiv) in 0.2 mL of the solvent. [b] Isolated yields are given. [c] Determined by ^{1}H NMR of a crude reaction mixture. [d] Determined by a chiral stationary phase HPLC. [e] Reaction was performed in 0.4 mL of $CHCl_3$. [f] Reaction was performed in 0.1 mL of $CHCl_3$. [g] Reaction was performed using **5f** (20 mol%). [h] Reaction was performed using **5f** (5 mol%). [i] Reaction was performed using **3a** (1.5 equiv). [j] Reaction was performed using **4a** (1.5 equiv).

3. Asymmetric synthesis of bicyclic δ-lactones 1 – general procedure

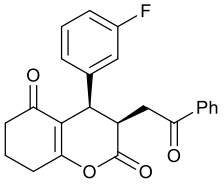


An ordinary screw-cap vial was charged with a magnetic stirring bar, the corresponding 1,3-cyclohexanedione **3** (0.1 mmol, 1 equiv), (*E*)-3-arylidene-5-arylfuran-2(3*H*)-one **4a** (0.1 mmol, 1 equiv), the catalyst **5f** (0.01 mmol, 0.1 equiv) and $CHCl_3$ (0.4 mL). The reaction was stirred at 0°C and monitored by ^1H NMR spectroscopy. After 72 h the crude reaction mixture was directly purified by FC on silica gel to afford a target product **1**.



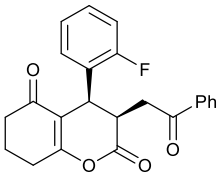
1a (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 1)

Following the general procedure, **1a** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 65% yield as a pale-yellow oil (>20:1 dr). ^1H NMR (700 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.58 – 7.52 (m, 1H), 7.46 – 7.39 (m, 2H), 7.26 – 7.21 (m, 3H), 7.06 – 7.02 (m, 2H), 4.31 (d, *J* = 7.3 Hz, 1H), 3.83 (ddd, *J* = 7.4, 6.6, 6.0 Hz, 1H), 3.36 (dd, *J* = 18.3, 6.0 Hz, 1H), 2.80 (dd, *J* = 18.3, 6.6 Hz, 1H), 2.75 – 2.67 (m, 2H), 2.42 (ddd, *J* = 23.4, 8.3, 4.9 Hz, 2H), 2.16 – 2.06 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.9, 195.9, 168.9, 166.6, 137.8, 136.5, 133.6, 129.2 (2C), 128.8 (2C), 128.3 (2C), 128.1, 128.0 (2C), 119.1, 40.0, 38.8, 36.8, 36.0, 27.3, 20.8. HRMS calculated for $[C_{23}H_{20}O_4+H]^+$: 361.1434; found: 361.1440. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 13.9 min, τ_{minor} = 15.0 min (97:3 er). $[\alpha]^{20}_D$ = -64.1 (*c* = 1.2, $CHCl_3$).



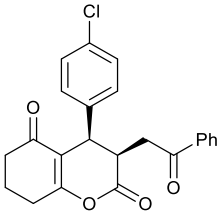
1b (3*R*,4*R*)-4-(3-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 2)

Following the general procedure, **1b** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 62% yield as a pale-yellow oil (>20:1 dr). ^1H NMR (700 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 2H), 7.61 – 7.52 (m, 1H), 7.47 – 7.37 (m, 2H), 7.22 (td, *J* = 8.0, 5.9 Hz, 1H), 6.94 (tdd, *J* = 8.4, 2.5, 0.9 Hz, 1H), 6.83 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.76 (dt, *J* = 9.6, 2.1 Hz, 1H), 4.32 (d, *J* = 7.3 Hz, 1H), 3.83 (dt, *J* = 7.3, 6.3 Hz, 1H), 3.39 (dd, *J* = 18.2, 5.9 Hz, 1H), 2.80 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.77 – 2.65 (m, 2H), 2.51 – 2.35 (m, 2H), 2.18 – 2.05 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.7, 195.8, 168.5, 166.9, 163.2 (d, *J* = 247.6 Hz), 140.4 (d, *J* = 6.9 Hz), 136.4, 133.7, 130.8 (d, *J* = 8.3 Hz), 128.8 (2C), 128.2 (2C), 123.7 (d, *J* = 2.9 Hz), 118.7, 115.1 (d, *J* = 10.5 Hz), 115.0 (d, *J* = 11.2 Hz), 39.9, 38.6, 36.7, 35.9, 27.3, 20.8. HRMS calculated for $[C_{23}H_{19}FO_4+H]^+$: 379.1341; found: 379.1342. The er was determined by HPLC using a Chiralpak ID column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 31.7 min, τ_{minor} = 28.8 min (94:6 er). $[\alpha]^{20}_D$ = -66.3 (*c* = 0.8, $CHCl_3$).



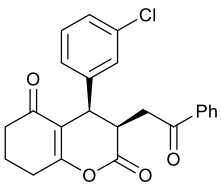
1c (3*R*,4*R*)-4-(2-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 3)

Following the general procedure, **1c** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 64% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ ^{1}H NMR (700 MHz, Chloroform-*d*) δ 7.85 – 7.81 (m, 2H), 7.56 – 7.51 (m, 1H), 7.44 – 7.38 (m, 2H), 7.24 – 7.19 (m, 1H), 7.06 – 6.98 (m, 3H), 4.63 (d, *J* = 7.8 Hz, 1H), 3.86 (dt, *J* = 7.9, 6.3 Hz, 1H), 3.40 (dd, *J* = 18.3, 6.2 Hz, 1H), 2.87 (ddd, *J* = 18.3, 6.4, 0.8 Hz, 1H), 2.77 – 2.66 (m, 2H), 2.49 – 2.36 (m, 2H), 2.20 – 2.03 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.7, 195.9, 168.3, 167.4, 161.0 (d, *J* = 245.7 Hz), 136.5, 133.5, 130.2, 129.8 (d, *J* = 8.4 Hz), 128.7 (2C), 128.2 (2C), 125.0 (d, *J* = 3.3 Hz), 124.4 (d, *J* = 14.8 Hz), 117.0, 116.0 (d, *J* = 22.5 Hz), 39.3, 36.8, 35.7, 33.5, 27.4, 20.8. HRMS calculated for $[C_{23}H_{19}FO_4+H]^+$: 379.1341; found: 379.1349. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 21.7 min, τ_{minor} = 15.8 min (98:2 er). $[\alpha]^{20}_D$ = -121.4 (*c* = 0.6, $CHCl_3$).



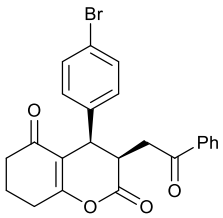
1d (3*R*,4*R*)-4-(4-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 4)

Following the general procedure, **1d** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 63% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.46 – 7.40 (m, 2H), 7.25 – 7.19 (m, 2H), 7.00 – 6.95 (m, 2H), 4.30 (d, *J* = 7.4 Hz, 1H), 3.84 – 3.81 (m, 1H), 3.39 (dd, *J* = 18.3, 5.8 Hz, 1H), 2.77 (dd, *J* = 18.3, 6.7 Hz, 1H), 2.75 – 2.65 (m, 2H), 2.49 – 2.36 (m, 2H), 2.20 – 2.04 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.7, 195.9, 168.6, 166.8, 136.4, 136.3, 133.9, 133.7, 129.5 (2C), 129.4 (2C), 128.8 (2C), 128.2 (2C), 118.8, 39.8, 38.3, 36.7, 35.9, 27.3, 20.8. HRMS calculated for $[C_{23}H_{19}ClO_4+H]^+$: 395.1045; found: 395.1049. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 14.1 min, τ_{minor} = 19.7 min (92:8 er). $[\alpha]^{20}_D$ = -48.2 (*c* = 0.7, $CHCl_3$).



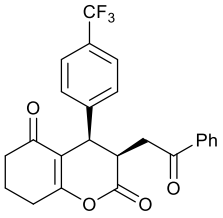
1e (3*R*,4*R*)-4-(3-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 5)

Following the general procedure, **1e** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 61% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.59 – 7.55 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.22 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 1.9 Hz, 1H), 6.92 (dt, *J* = 7.6, 1.5 Hz, 1H), 4.29 (d, *J* = 7.4 Hz, 1H), 3.84 (q, *J* = 6.6 Hz, 1H), 3.38 (dd, *J* = 18.2, 5.9 Hz, 1H), 2.79 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.77 – 2.70 (m, 2H), 2.43 (qdd, *J* = 16.8, 8.2, 5.0 Hz, 2H), 2.18 – 2.07 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.6, 195.7, 168.4, 166.8, 139.8, 136.3, 135.0, 133.6, 130.4, 128.7 (2C), 128.2, 128.1 (2C), 128.0, 126.1, 118.4, 39.7, 38.4, 36.6, 35.8, 27.2, 20.6. HRMS calculated for $[C_{23}H_{19}ClO_4+H]^+$: 395.1045; found: 395.1052. The er was determined by HPLC using a Chiralpak ID column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 30.7 min, τ_{minor} = 28.4 min (93:7 er). $[\alpha]^{20}_D$ = -55.7 (*c* = 0.7, $CHCl_3$).



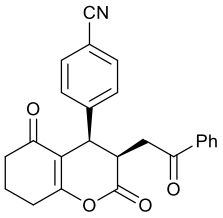
1f (3*R*,4*R*)-4-(4-Bromophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 6)

Following the general procedure, **1f** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 60% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.57 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.40 – 7.36 (m, 2H), 6.95 – 6.91 (m, 2H), 4.29 (d, *J* = 7.3 Hz, 1H), 3.83 (q, *J* = 6.6 Hz, 1H), 3.39 (dd, *J* = 18.3, 5.9 Hz, 1H), 2.77 (dd, *J* = 18.3, 6.6 Hz, 1H), 2.74 – 2.67 (m, 2H), 2.49 – 2.36 (m, 2H), 2.19 – 2.05 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.7, 195.8, 168.6, 166.8, 137.0, 136.3, 133.7, 132.4 (2C), 129.7 (2C), 128.8 (2C), 128.2 (2C), 122.0, 118.7, 39.7, 38.4, 36.7, 35.9, 27.3, 20.8. HRMS calculated for $[C_{23}H_{19}BrO_4+H]^+$: 439.0540; found: 439.0549. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 14.6 min, τ_{minor} = 20.7 min (96:4 er). $[\alpha]^{20}_D$ = -41.7 (*c* = 0.8, $CHCl_3$).



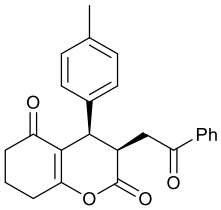
1g (3*R*,4*R*)-4-(4-Trifluoromethylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 7)

Following the general procedure, **1g** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 54% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.57 (td, *J* = 7.4, 1.3 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.40 (d, *J* = 7.4 Hz, 1H), 3.87 (q, *J* = 6.7 Hz, 1H), 3.40 (dd, *J* = 18.3, 5.9 Hz, 1H), 2.75 (dd, *J* = 18.4, 6.8 Hz, 1H), 2.74-2.71 (m, 2H), 2.47 – 2.36 (m, 2H), 2.19 – 2.05 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.5, 195.8, 168.5, 167.1, 142.1, 136.3, 133.8, 130.3 (q, *J* = 32.5 Hz), 128.9 (2C), 128.5 (2C), 128.2 (2C), 126.3 (q, *J* = 3.3 Hz, 2C), 124.0 (q, *J* = 272.5 Hz), 118.5, 39.7, 38.7, 36.7, 35.9, 27.3, 20.7. HRMS calculated for $[C_{24}H_{19}F_3O_4+H]^+$: 429.1309; found: 429.1312. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 12.4 min, τ_{minor} = 17.0 min (94:6 er). $[\alpha]^{20}_D$ = -42.3 (*c* = 0.5, $CHCl_3$).



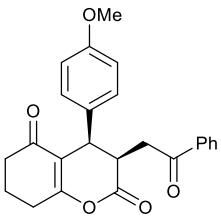
1h (3*R*,4*R*)-4-(4-Cyanophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 8)

Following the general procedure, **1h** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 61% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.87 – 7.78 (m, 2H), 7.60 – 7.56 (m, 1H), 7.56 – 7.54 (m, 2H), 7.49 – 7.34 (m, 2H), 7.20 – 7.12 (m, 2H), 4.41 (dt, *J* = 7.4, 1.2 Hz, 1H), 3.87 (td, *J* = 7.1, 5.7 Hz, 1H), 3.40 (dd, *J* = 18.2, 5.8 Hz, 1H), 2.78 – 2.68 (m, 3H), 2.43 (dddd, *J* = 52.5, 16.8, 8.5, 4.9 Hz, 2H), 2.20 – 2.04 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.3, 195.7, 168.2, 167.3, 143.5, 136.2, 133.9, 133.0 (2C), 128.9 (4C), 128.2 (2C), 118.4, 118.1, 112.1, 39.5, 38.9, 36.6, 35.8, 27.3, 20.7. HRMS calculated for $[C_{24}H_{19}NO_4+H]^+$: 386.1387; found: 386.1390. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 13.7 min, τ_{minor} = 21.0 min (95.5:4.5 er). $[\alpha]^{20}_D$ = -61.2 (*c* = 0.5, $CHCl_3$).



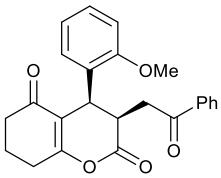
1i (3*R*,4*R*)-4-(4-Methylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 9)

Following the general procedure, **1i** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 62% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.87 – 7.83 (m, 2H), 7.58 – 7.51 (m, 1H), 7.45 – 7.39 (m, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 4.26 (dd, *J* = 7.4, 1.4 Hz, 1H), 3.81 (dt, *J* = 7.3, 6.2 Hz, 1H), 3.36 (dd, *J* = 18.3, 6.0 Hz, 1H), 2.81 (dd, *J* = 18.3, 6.4 Hz, 1H), 2.75 – 2.64 (m, 2H), 2.47 – 2.35 (m, 2H), 2.29 (s, 3H), 2.18 – 2.02 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.9, 195.8, 169.3, 168.8, 166.6, 150.3, 136.4, 135.4, 133.7, 129.0 (2C), 128.8 (2C), 128.3 (2C), 122.3 (2C), 119.0, 39.9, 38.2, 36.7, 36.0, 27.3, 21.3, 20.7. HRMS calculated for $[C_{24}H_{22}O_4+H]^+$: 375.1591; found: 375.1582. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 11.9 min, τ_{minor} = 14.0 min (>99.5:0.5 er). $[\alpha]^{20}_D$ = -38.3 (*c* = 0.8, $CHCl_3$).



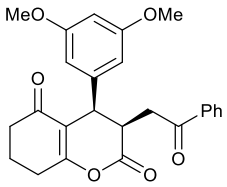
1j (3*R*,4*R*)-4-(4-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 10)

Following the general procedure, **1j** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 58% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.58 – 7.51 (m, 1H), 7.43 (dd, *J* = 8.3, 7.3 Hz, 2H), 6.98 – 6.94 (m, 2H), 6.81 – 6.75 (m, 2H), 4.26 (d, *J* = 7.3 Hz, 1H), 3.82 – 3.78 (m, 1H), 3.76 (s, 3H), 3.37 (dd, *J* = 18.3, 5.9 Hz, 1H), 2.81 (dd, *J* = 18.3, 6.6 Hz, 1H), 2.73 – 2.67 (m, 2H), 2.48 – 2.34 (m, 2H), 2.16 – 2.05 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.0, 196.0, 169.0, 166.4, 159.3, 136.5, 133.6, 129.7, 129.0 (2C), 128.8 (2C), 128.3 (2C), 119.3, 114.6 (2C), 55.4, 40.2, 38.1, 36.8, 36.0, 27.3, 20.8. HRMS calculated for $[C_{24}H_{22}O_5+H]^+$: 391.1540; found: 391.1549. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 15.9 min, τ_{minor} = 21.8 min (98:2 er). $[\alpha]^{20}_D$ = -64.3 (*c* = 0.6, $CHCl_3$).



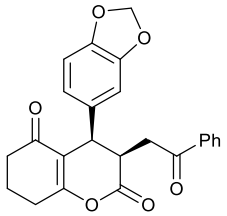
1k (3*R*,4*R*)-4-(2-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 11)

Following the general procedure, **1k** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 68% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.7 Hz, 2H), 7.55 – 7.47 (m, 1H), 7.43 – 7.35 (m, 2H), 7.18 (ddd, *J* = 8.1, 7.4, 1.7 Hz, 1H), 7.11 – 7.01 (m, 1H), 6.86 – 6.65 (m, 2H), 4.54 (s, 1H), 3.78 (td, *J* = 7.9, 5.0 Hz, 1H), 3.58 (s, 3H), 3.39 – 3.28 (m, 1H), 2.80 (d, *J* = 17.8 Hz, 1H), 2.65 (t, *J* = 5.3 Hz, 2H), 2.37 (qdd, *J* = 16.6, 8.3, 5.0 Hz, 2H), 2.14 – 1.97 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.1, 196.4, 168.7, 157.4, 136.7, 133.3 (2C), 129.1, 128.6 (3C), 128.1 (3C), 125.4, 121.2, 110.5, 54.4, 37.0, 35.7 (2C), 27.5, 20.8 (2C). HRMS calculated for $[C_{24}H_{22}O_5+H]^+$: 391.1540; found: 391.1544. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 17.6 min, τ_{minor} = 15.5 min (96:4 er). $[\alpha]^{20}_D$ = -71.3 (*c* = 0.7, $CHCl_3$).



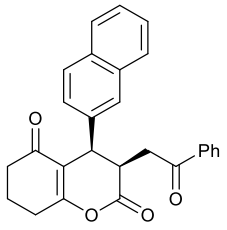
1l (3*R*,4*R*)-4-(3,5-Dimethoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 12)

Following the general procedure, **1l** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 70% yield as a pale-yellow oil (10:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.45 – 7.39 (m, 2H), 6.74 (d, J = 8.2 Hz, 1H), 6.56 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.49 (d, *J* = 2.2 Hz, 1H), 4.25 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.81 (s, 3H), 3.79 (td, *J* = 7.4, 5.3 Hz, 1H), 3.61 (s, 3H), 3.36 (dd, *J* = 18.3, 5.2 Hz, 1H), 2.86 (dd, *J* = 18.3, 7.4 Hz, 1H), 2.74 – 2.64 (m, 2H), 2.42 (ddd, *J* = 19.8, 8.3, 4.9 Hz, 2H), 2.17 – 2.05 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.1, 196.0, 169.1, 166.4, 149.2, 148.6, 136.5, 133.7, 130.2, 128.8 (2C), 128.2 (2C), 119.3, 119.1, 111.8, 111.6, 56.0, 55.8, 40.2, 38.1, 36.8, 35.9, 27.3, 20.8. HRMS calculated for $[C_{25}H_{24}O_6+H]^+$: 421.1646; found: 421.1655. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 18.4 min, τ_{minor} = 21.9 min (91:9 er). $[\alpha]^{20}_D$ = -58.1 (*c* = 0.8, $CHCl_3$).



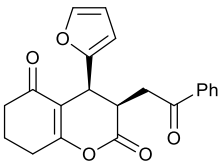
1m (3*R*,4*R*)-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 13)

Following the general procedure, **1m** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 57% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.59 – 7.55 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.22 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 1.9 Hz, 1H), 6.92 (dt, *J* = 7.6, 1.5 Hz, 1H), 4.29 (d, *J* = 7.4 Hz, 1H), 3.84 (q, *J* = 6.6 Hz, 1H), 3.38 (dd, *J* = 18.2, 5.9 Hz, 1H), 2.79 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.77 – 2.70 (m, 2H), 2.43 (qdd, *J* = 16.8, 8.2, 5.0 Hz, 2H), 2.18 – 2.07 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.6, 195.7, 168.4, 166.8, 139.8, 136.3, 135.0, 133.6, 130.4, 128.7 (2C), 128.2, 128.1 (2C), 128.0, 126.1, 118.4, 39.7, 38.4, 36.6, 35.8, 27.2, 20.6. HRMS calculated for $[C_{24}H_{20}O_6+H]^+$: 405.1333; found: 405.1336. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 13.5 min, τ_{minor} = 14.8 min (98:2 er). $[\alpha]^{20}_D$ = -61.8 (*c* = 0.8, $CHCl_3$).



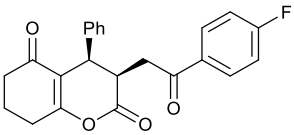
1n (3*R*,4*R*)-4-(Naphthalen-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 14)

Following the general procedure, **1n** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 75% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) 7.83 – 7.77 (m, 3H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.54 – 7.49 (m, 2H), 7.46 – 7.42 (m, 2H), 7.37 (dd, *J* = 8.3, 7.3 Hz, 2H), 7.15 (dd, *J* = 8.5, 1.9 Hz, 1H), 4.48 (d, *J* = 7.5 Hz, 1H), 3.92 (dt, *J* = 7.4, 6.3 Hz, 1H), 3.38 (dd, *J* = 18.2, 6.0 Hz, 1H), 2.84 (dd, *J* = 18.3, 6.5 Hz, 1H), 2.81 – 2.68 (m, 2H), 2.50 – 2.34 (m, 2H), 2.19 – 2.06 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.0, 196.0, 169.0, 166.7, 136.4, 135.3, 133.6, 133.0, 129.2, 128.7 (2C), 128.2 (2C), 128.1, 127.7, 127.2, 126.5, 126.3, 125.6, 119.0, 100.1, 40.0, 39.0, 36.8, 36.1, 27.4, 20.8. HRMS calculated for $[C_{27}H_{22}O_4+H]^+$: 411.1591; found: 411.1592. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 16.3 min, τ_{minor} = 21.5 min (96:4 er). $[\alpha]^{20}_D$ = -74.2 (*c* = 1.0, $CHCl_3$).



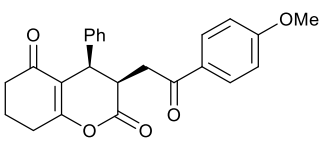
1o (3*R*,4*S*)-4-(Furan-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 15)

Following the general procedure, **1o** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 69% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H), 7.59 – 7.54 (m, 1H), 7.47 – 7.42 (m, 2H), 7.28 (dd, *J* = 1.9, 0.8 Hz, 1H), 6.23 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.11 (dd, *J* = 3.3, 0.8 Hz, 1H), 4.44 (dd, *J* = 6.9, 1.2 Hz, 1H), 3.74 (td, *J* = 6.7, 5.7 Hz, 1H), 3.52 (dd, *J* = 18.3, 5.8 Hz, 1H), 2.87 (dd, *J* = 18.3, 6.6 Hz, 1H), 2.73 – 2.60 (m, 2H), 2.44 (ddd, *J* = 7.4, 5.6, 3.2 Hz, 2H), 2.18 – 2.02 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.8, 195.7, 168.4, 167.4, 150.9, 142.7, 136.5, 133.6, 128.8 (2C), 128.3 (2C), 116.2, 110.6, 108.6, 38.9, 36.6, 36.0, 32.4, 27.3, 20.7. HRMS calculated for $[C_{21}H_{18}O_5+H]^+$: 351.1227; found: 351.1234. The er was determined by HPLC using a Chiralpak ID column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 30.6 min, τ_{minor} = 33.1 min (98:2 er). $[\alpha]^{20}_D$ = -63.5 (*c* = 0.8, $CHCl_3$).



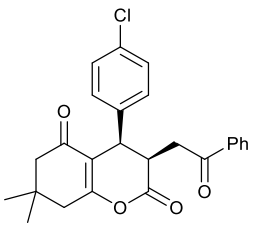
1p (3*R*,4*R*)-3-(2-(4-Fluorophenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Following the general procedure, **1p** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 64% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.90 – 7.79 (m, 2H), 7.26 – 7.22 (m, 3H), 7.09 (t, *J* = 8.5 Hz, 2H), 7.03 (dd, *J* = 7.5, 1.9 Hz, 2H), 4.29 (d, *J* = 7.3 Hz, 1H), 3.82 (q, *J* = 6.6 Hz, 1H), 3.31 (dd, *J* = 18.1, 6.0 Hz, 1H), 2.75 (dd, *J* = 18.2, 6.5 Hz, 1H), 2.73 – 2.63 (m, 2H), 2.48 – 2.35 (m, 2H), 2.18 – 2.03 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 195.9, 195.3, 168.9, 166.6, 166.0 (d, *J* = 245.7 Hz), 137.8, 132.9 (d, *J* = 3.2 Hz), 131.0, 130.9, 129.3 (2C), 128.0, 127.9 (2C), 119.1, 116.0, 115.8, 40.1, 38.9, 36.8, 36.0, 27.3, 20.8. HRMS calculated for $[C_{23}H_{19}FO_4+H]^+$: 379.1341; found: 379.1344. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 14.5 min, τ_{minor} = 16.8 min (96:4 er). $[\alpha]^{20}_D$ = -72.3 (*c* = 0.7, $CHCl_3$).



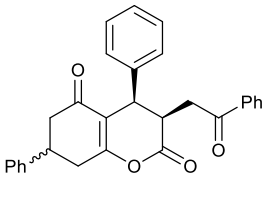
1q (3*R*,4*R*)-3-(2-(4-Methoxyphenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Following the general procedure, **1q** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 61% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.88 – 7.69 (m, 2H), 7.26 – 7.21 (m, 3H), 7.05 – 7.02 (m, 2H), 6.90 – 6.86 (m, 2H), 4.29 (dd, *J* = 7.2, 1.3 Hz, 1H), 3.85 (s, 3H), 3.82 (td, *J* = 6.9, 5.7 Hz, 1H), 3.29 (dd, *J* = 18.1, 5.8 Hz, 1H), 2.75 (dd, *J* = 18.1, 6.8 Hz, 1H), 2.73 – 2.67 (m, 2H), 2.47 – 2.34 (m, 2H), 2.21 – 1.99 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 195.9, 195.3, 169.1, 166.6, 163.9, 137.9, 130.6 (2C), 129.6, 129.2 (2C), 128.0 (2C), 127.9, 119.2, 113.9 (2C), 55.6, 40.1, 38.8, 36.8, 35.5, 27.3, 20.8. HRMS calculated for $[C_{24}H_{22}O_5+H]^+$: 391.1540; found: 391.1551. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 22.0 min, τ_{minor} = 26.7 min (93:7 er). $[\alpha]^{20}_D$ = -63.1 (*c* = 0.5, $CHCl_3$).



1r (3*R*,4*R*)-4-(4-Chlorophenyl)-7,7-dimethyl-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

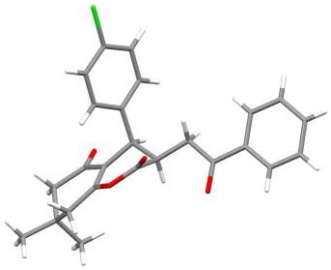
Following the general procedure, **1r** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 85% yield as a pale-yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 2H), 7.59 – 7.54 (m, 1H), 7.47 – 7.40 (m, 2H), 7.24 – 7.21 (m, 2H), 7.02 – 6.92 (m, 2H), 4.29 (dd, *J* = 7.5, 1.5 Hz, 1H), 3.82 (dt, *J* = 7.2, 6.2 Hz, 1H), 3.38 (dd, *J* = 18.2, 5.9 Hz, 1H), 2.77 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.63 – 2.50 (m, 2H), 2.39 – 2.20 (m, 2H), 1.18 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.7, 195.7, 168.7, 165.2, 136.4, 136.3, 133.9, 133.7, 129.5 (2C), 129.3 (2C), 128.8 (2C), 128.2 (2C), 117.5, 50.6, 41.0, 39.9, 38.2, 35.9, 32.8, 28.8, 28.2. HRMS calculated for $[C_{25}H_{23}ClO_4+H]^+$: 423.1358; found: 423.1350. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 13.0 min, τ_{minor} = 23.0 min (92:8 er). $[\alpha]^{20}_D$ = -101.6 (*c* = 0.8, $CHCl_3$).



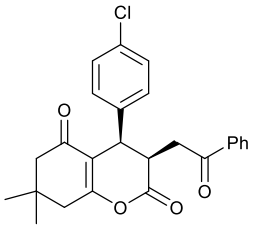
1s (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4,7-diphenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Following the general procedure, **1s** was isolated by FC on silica (hexane/AcOEt from 100:1 to 100:4) in 69% yield as a pale-yellow oil (1.2:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (ddd, *J* = 8.4, 2.7, 1.3 Hz, 2H, diaA+diaB), 7.58 – 7.53 (m, 1H, diaA+diaB), 7.43 (dd, *J* = 8.3, 7.1 Hz, 2H, diaA+diaB), 7.40 – 7.33 (m, 2H, diaA+diaB), 7.31 – 7.27 (m, 2H, diaA+diaB), 7.26 – 7.21 (m, 4H, diaA+diaB), 7.13 – 7.09 (m, 2H, diaA), 7.06 – 7.00 (m, 2H, diaB), 4.38 – 4.34 (m, 1H, diaA+diaB), 3.88 (dtd, *J* = 7.4, 6.1, 3.2 Hz, 1H, diaA+diaB), 3.57 (ddt, *J* = 12.3, 10.0, 4.6 Hz, 1H, diaB), 3.46 – 3.41 (m, 1H, diaA), 3.39 (dd, *J* = 18.2, 5.9 Hz, 1H, diaA), 3.37 (dd, *J* = 18.2, 5.9 Hz, 1H, diaB), 3.01 – 2.95 (m, 1H, diaA+diaB), 2.95 – 2.89 (m, 1H, diaA+diaB), 2.83 (dd, *J* = 18.3, 6.6 Hz, 1H, diaA), 2.77 – 2.61 (m, 2H, diaA), 2.70 (d, *J* = 12.3 Hz, 1H, diaB), 2.66 (dd, *J* = 22.9, 12.3 Hz, 1H, diaB), 2.62 (d, *J* = 12.4 Hz, 1H, diaB). ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.9 (diaA), 196.8 (diaB), 195.1 (diaA), 195.0 (diaB), 168.9 (diaA), 168.8 (diaB), 165.9 (diaA), 165.5 (diaB), 142.0 (diaA), 141.95 (diaB), 137.8 (diaA), 137.5 (diaB), 136.4 (diaA+diaB), 133.6 (diaA+diaB), 129.3 (2C, diaA), 129.2 (2C, diaB), 129.1 (2C, diaA), 129.0 (2C, diaB), 128.8 (2C, diaA+diaB), 128.2 (2C, diaA+diaB), 128.1 (diaA), 128.1 (diaB), 128.0 (2C, diaA+diaB), 127.5 (diaA), 127.5 (diaB), 126.8 (2C, diaA), 126.8 (2C, diaB), 118.9 (diaA), 118.7 (diaB), 43.8 (diaA), 43.7 (diaB), 40.0 (diaA), 39.9 (diaB), 39.2 (diaA), 39.0 (diaB), 38.8 (diaA), 38.7 (diaB), 36.1 (diaA), 36.0 (diaB), 35.0 (diaA), 34.8 (diaB). HRMS calculated for $[C_{29}H_{24}O_4+H]^+$: 437.1748; found: 437.1750. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; diaA: τ_{major} = 90.5 min, τ_{minor} = 47.2 min (89:11 er); diaB: τ_{major} = 72.8 min, τ_{minor} = 56.4 min (90:10 er). $[\alpha]^{20}_D$ = -35.9 (*c* = 0.9, $CHCl_3$).

4. Crystal and X-ray data for (3*R*,4*R*)-4-(4-chlorophenyl)-7,7-dimethyl-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (1s)



≡



1s

Formula $C_{25}H_{23}O_4Cl$, orthorhombic, space group *P* $2_12_12_1$, *Z* = 4, cell constants a = 5.8155(2) Å, b = 11.5974(3) Å, c = 31.3321(10) Å, V = 2113.18(11) Å^3. The data was collected on a XtaLAB Synergy, Dualflex, Pilatus 300K diffractometer at 100 K using PhotonJet micro-focus X-ray Source Cu-Kα (*λ* =1.54184 Å) as a source of radiation. The integration of the data yielded a total of 15558 reflections to a θ angle of 72.10°, of which 4088 were independent (R_{int} = 6.36%,) and 3620 were greater than 2σ(F^2). The final anisotropic full-matrix least-squares refinement on F^2 with 273 variables converged at R_1 = 6.15%, for the observed data and wR_2 = 15.93% for all data. The hydrogen atoms were placed in calculated positions and refined isotropically by using a riding model. The goodness-of-fit was 1.097.

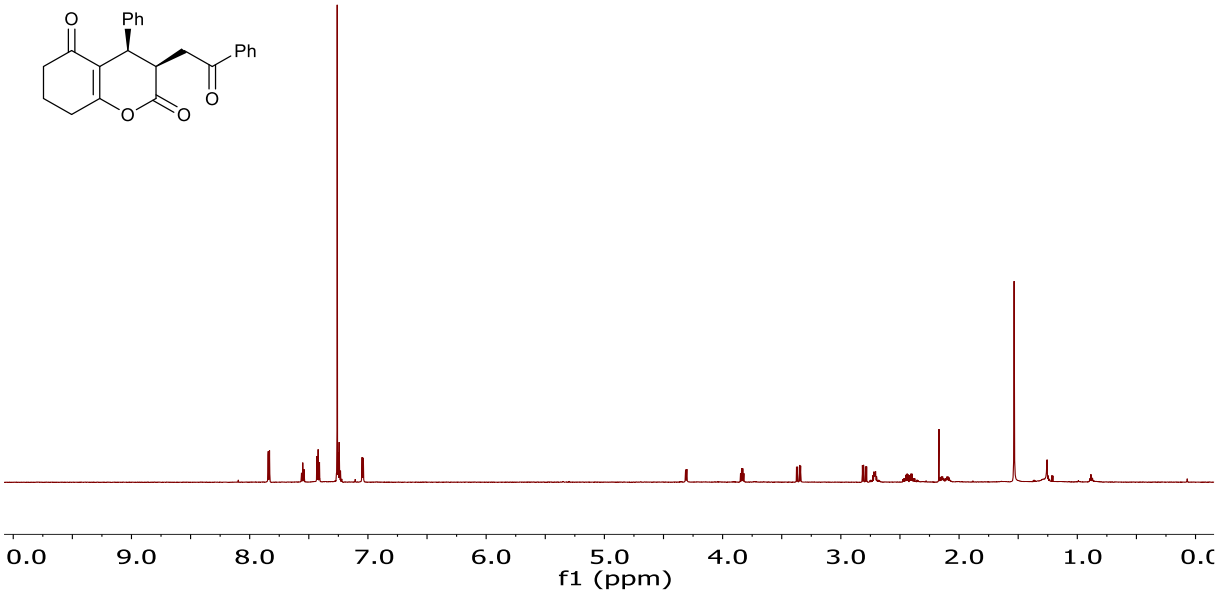
The absolute configuration of X was determined from anomalous scattering, by calculating the by calculating the Flack parameter: 0.022(13) from 1311 selected quotients (Parsons' method).

CCDC 1555933 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures.

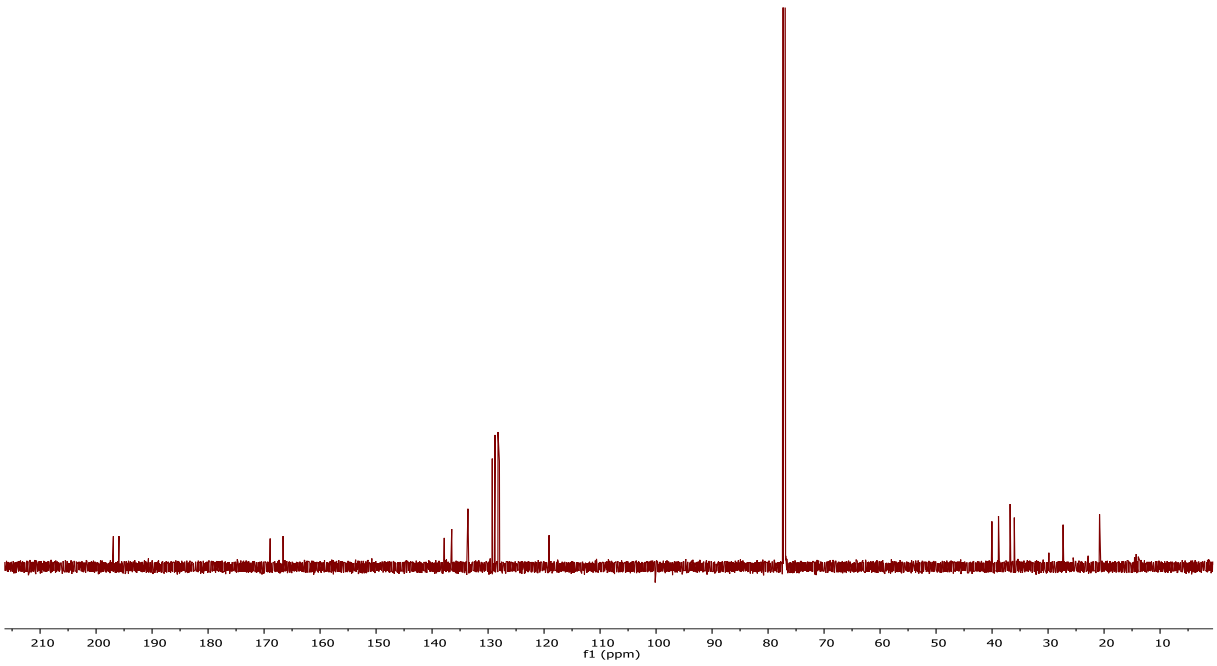
5. NMR data

1a (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 1)

^{1}H NMR

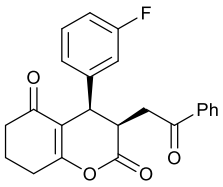


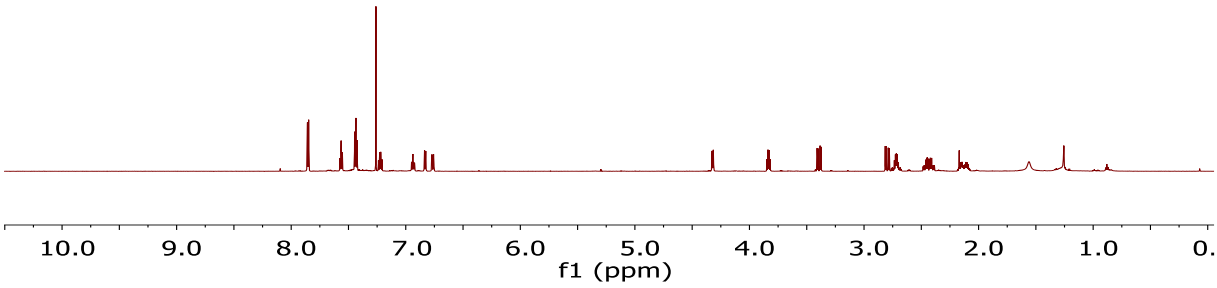
^{13}C NMR



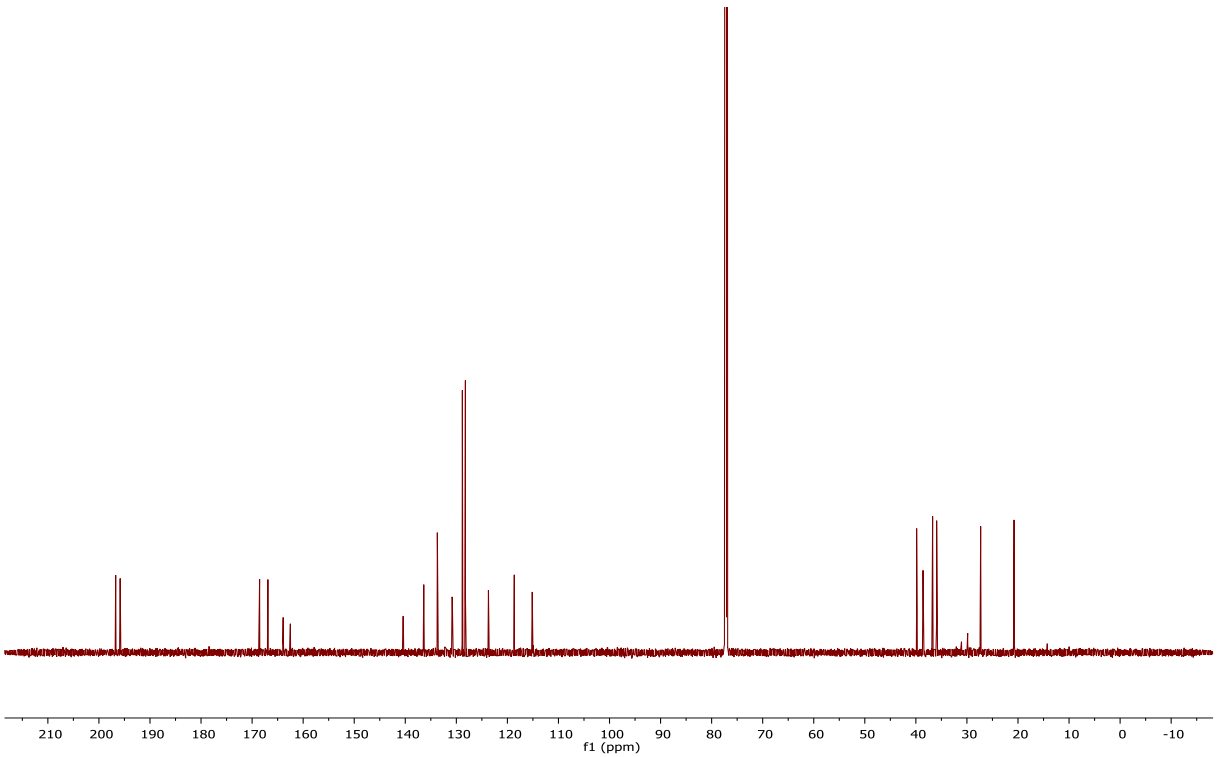
1b 4-(3-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-3,4,7,8-tetrahydro-2*H*-chromene-2,5(6*H*)-dione (Table 2, entry 2)

^{1}H NMR



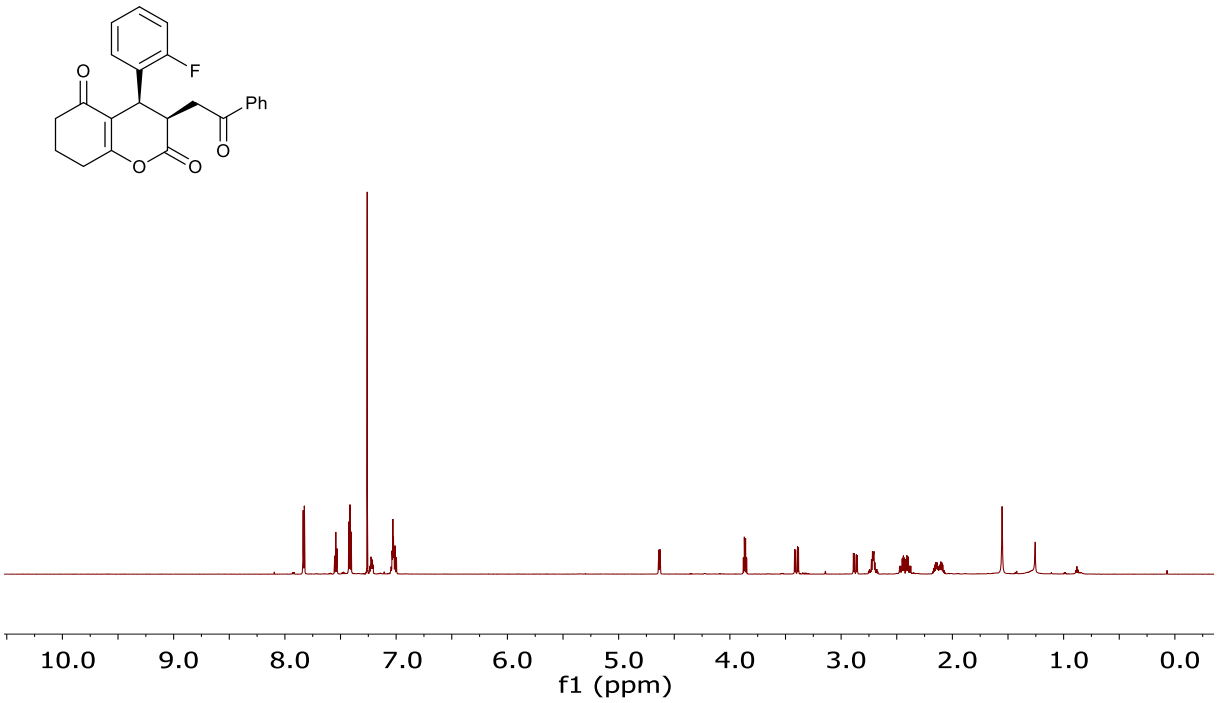


^{13}C NMR

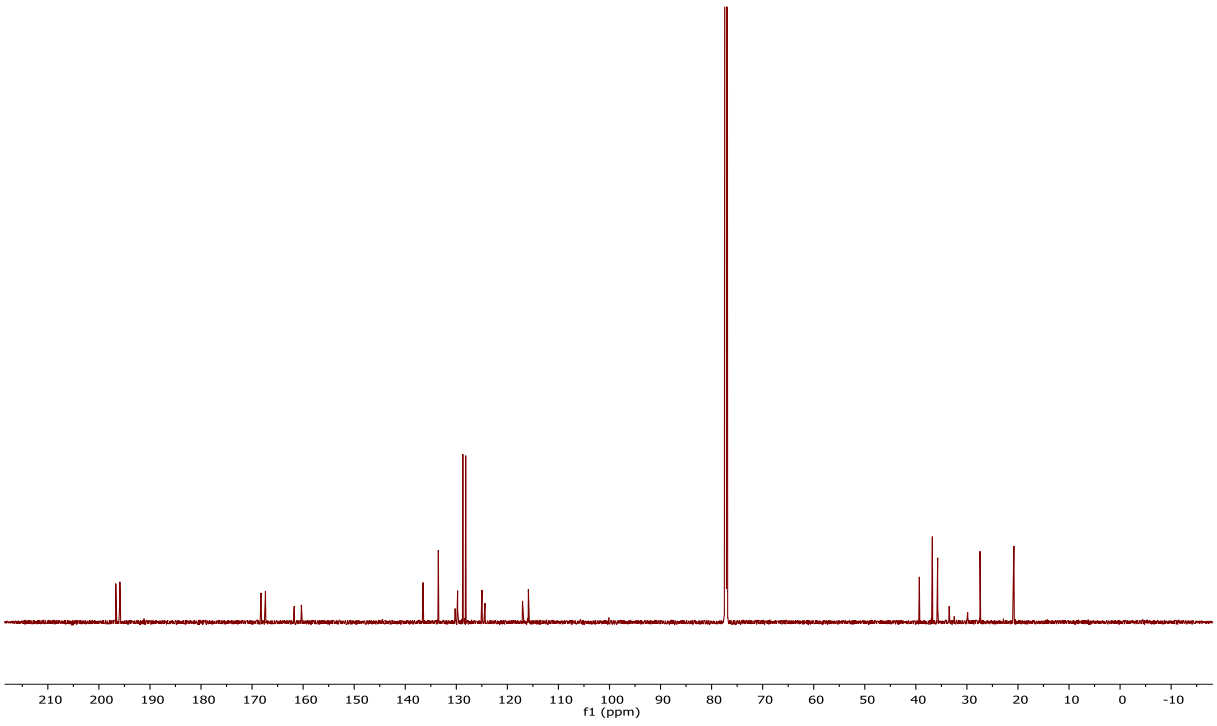


1c (3*R*,4*R*)-4-(2-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 3)

^{1}H NMR

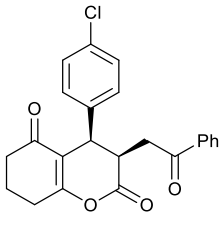


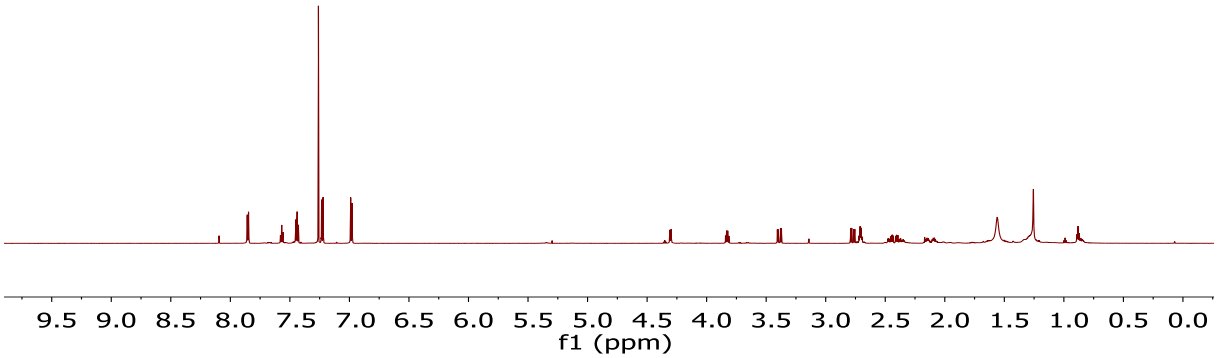
^{13}C NMR



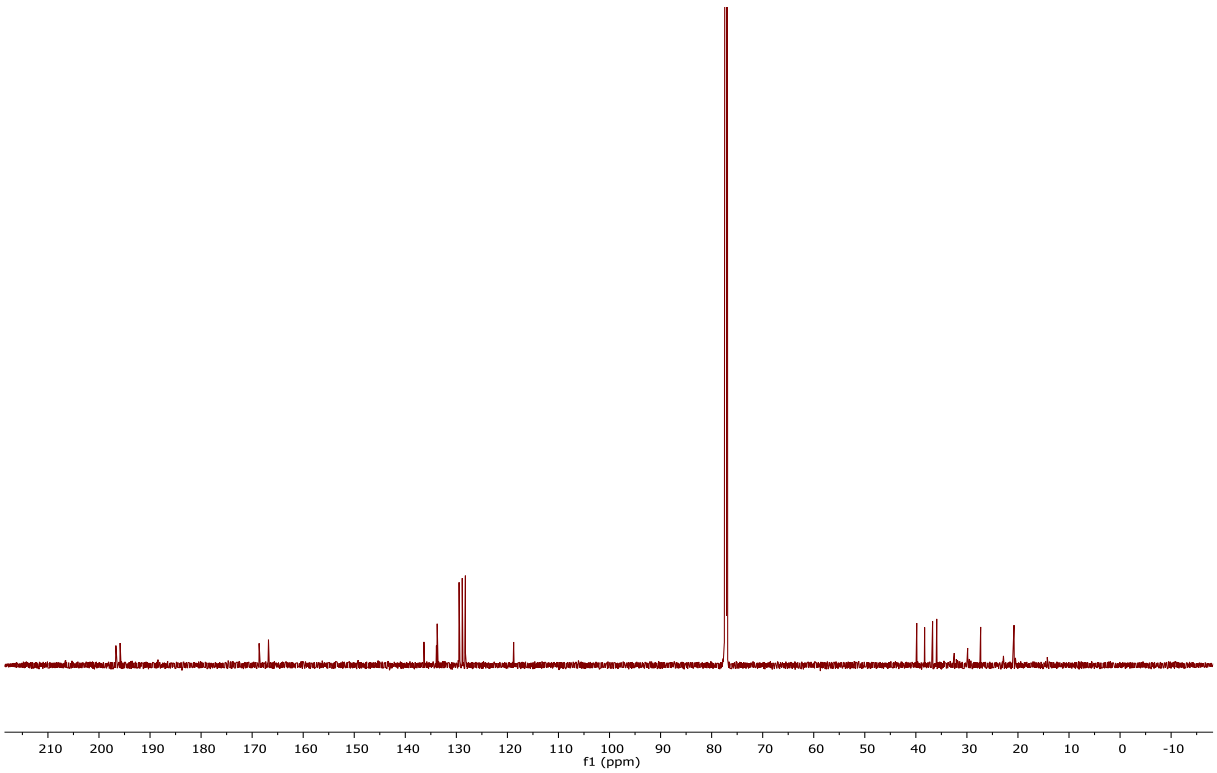
1d (3*R*,4*R*)-4-(4-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 4)

^{1}H NMR



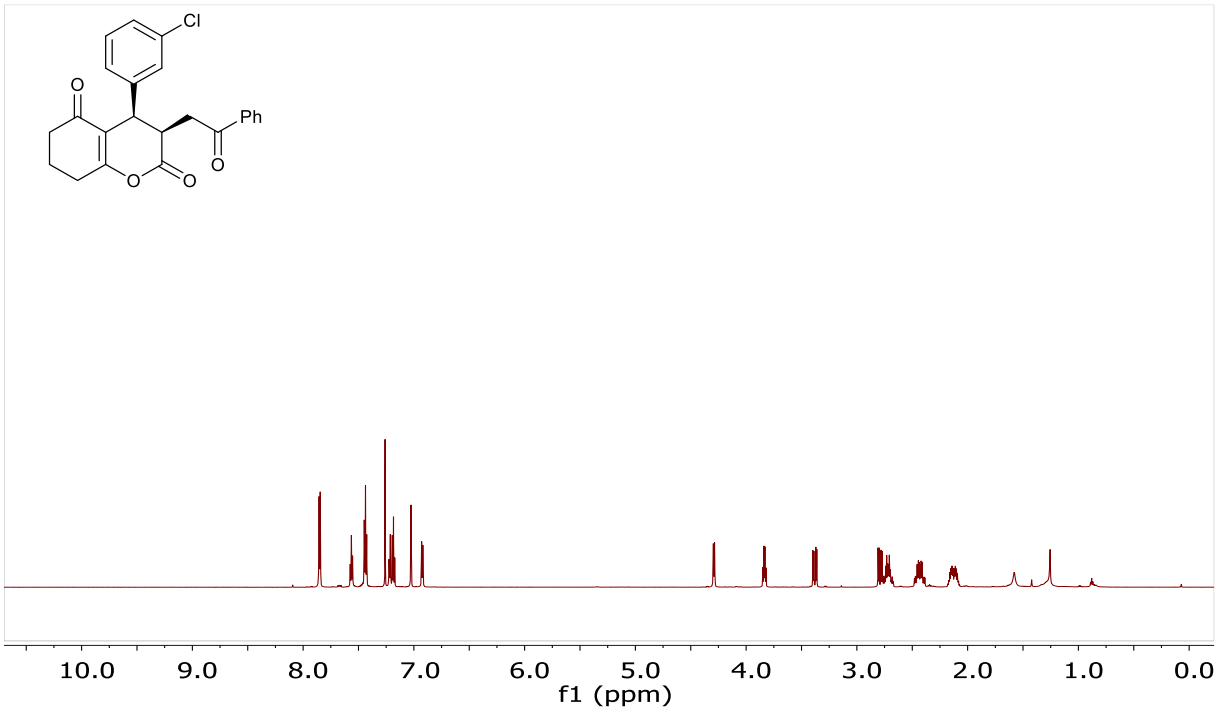


^{13}C NMR

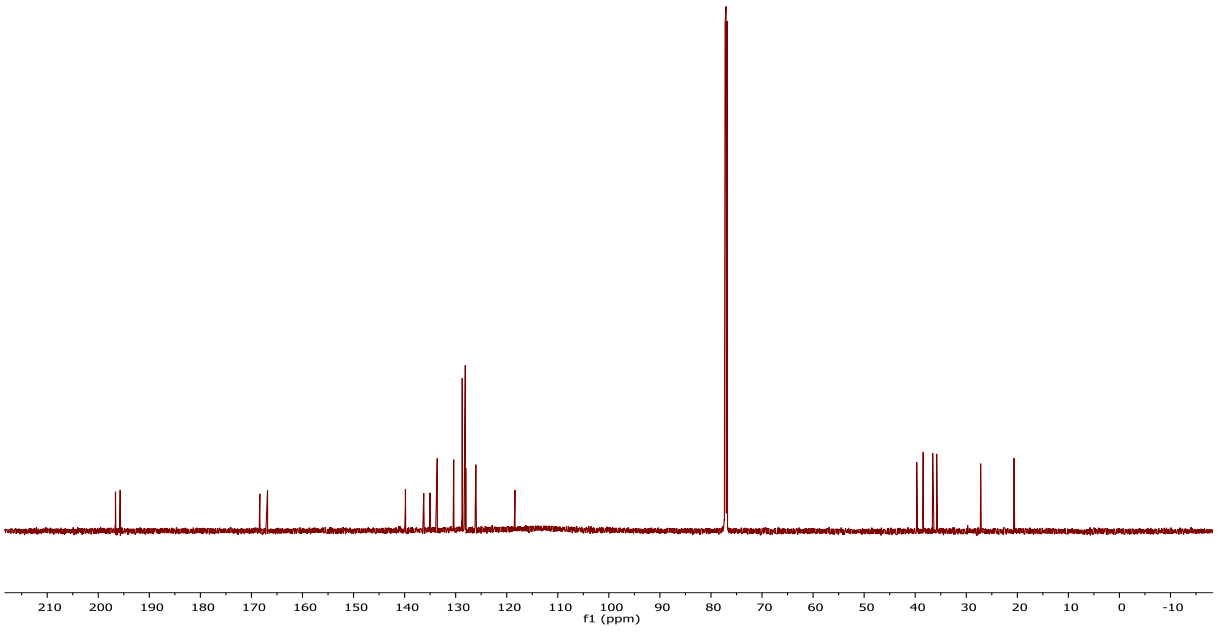


1e (3*R*,4*R*)-4-(3-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 5)

^{1}H NMR

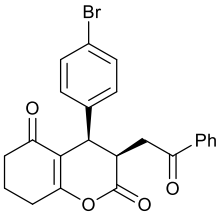


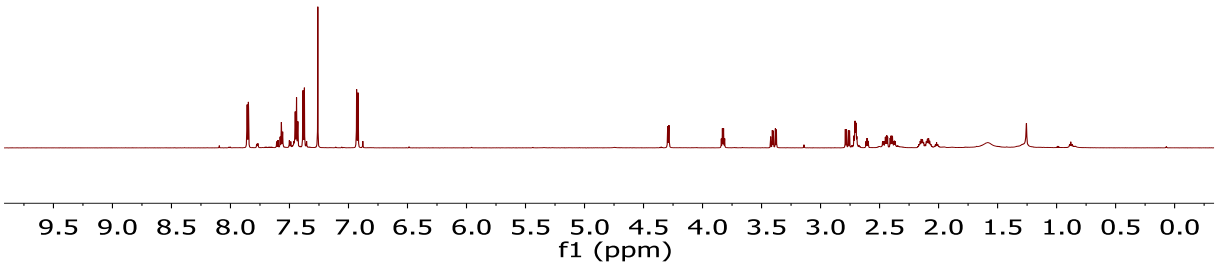
^{13}C NMR



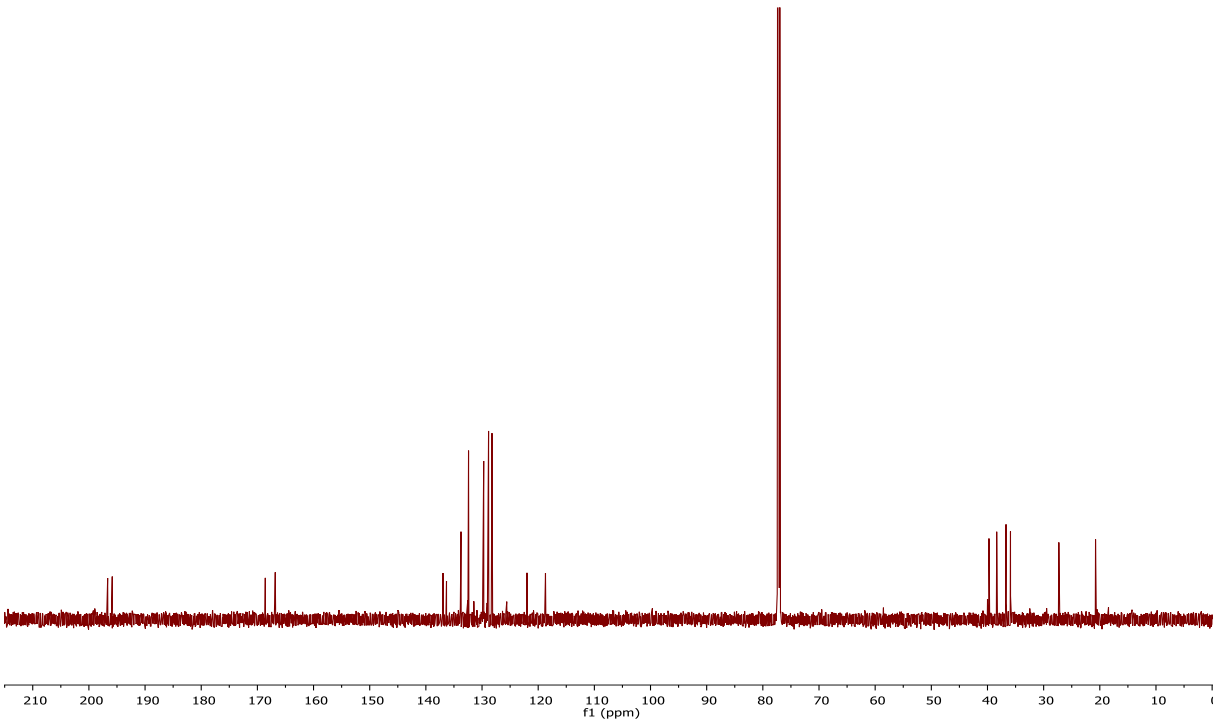
1f (3*R*,4*R*)-4-(4-Bromophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 6)

^{1}H NMR



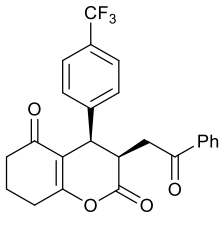


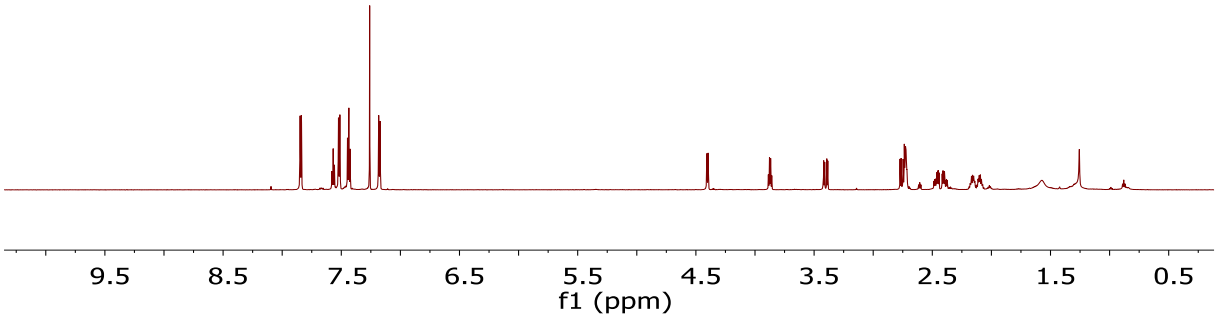
^{13}C NMR



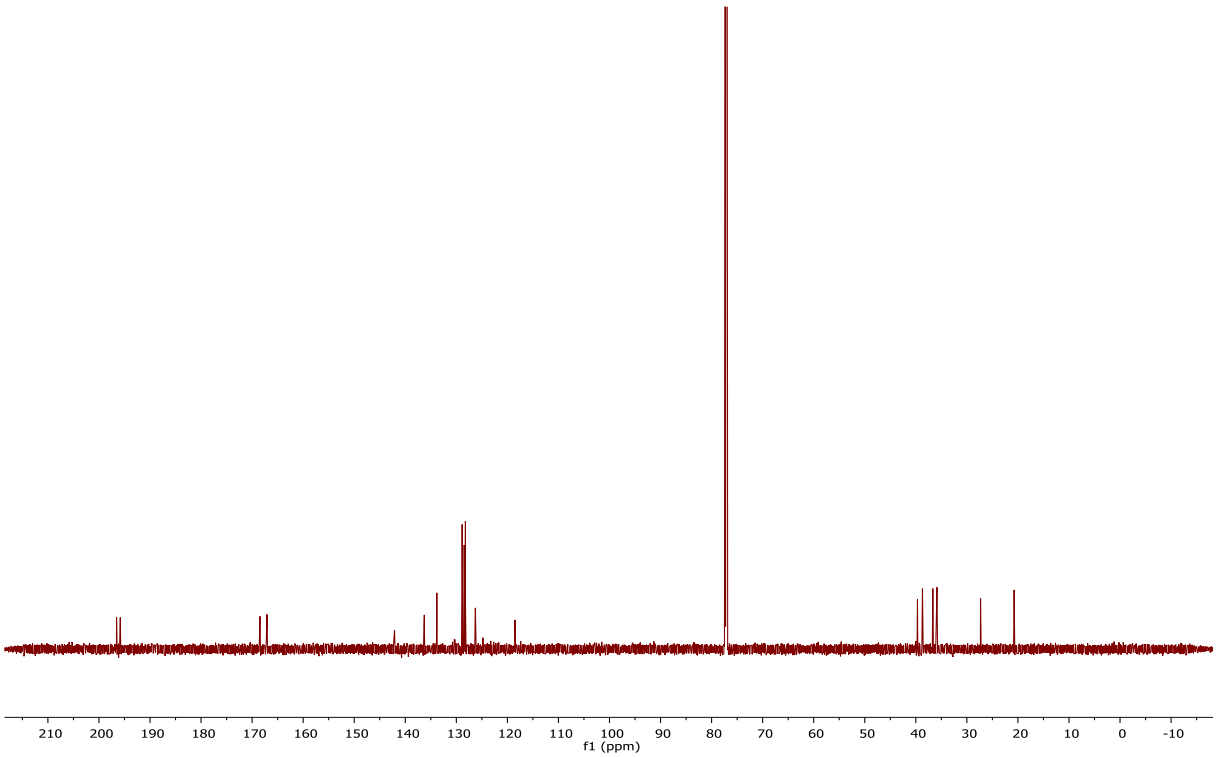
1g (3*R*,4*R*)-4-(4-Trifluoromethylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 7)

^{1}H NMR



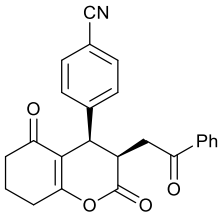


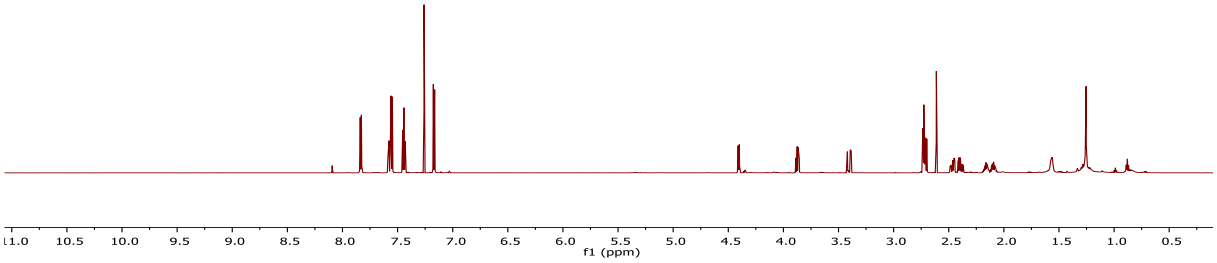
^{13}C NMR



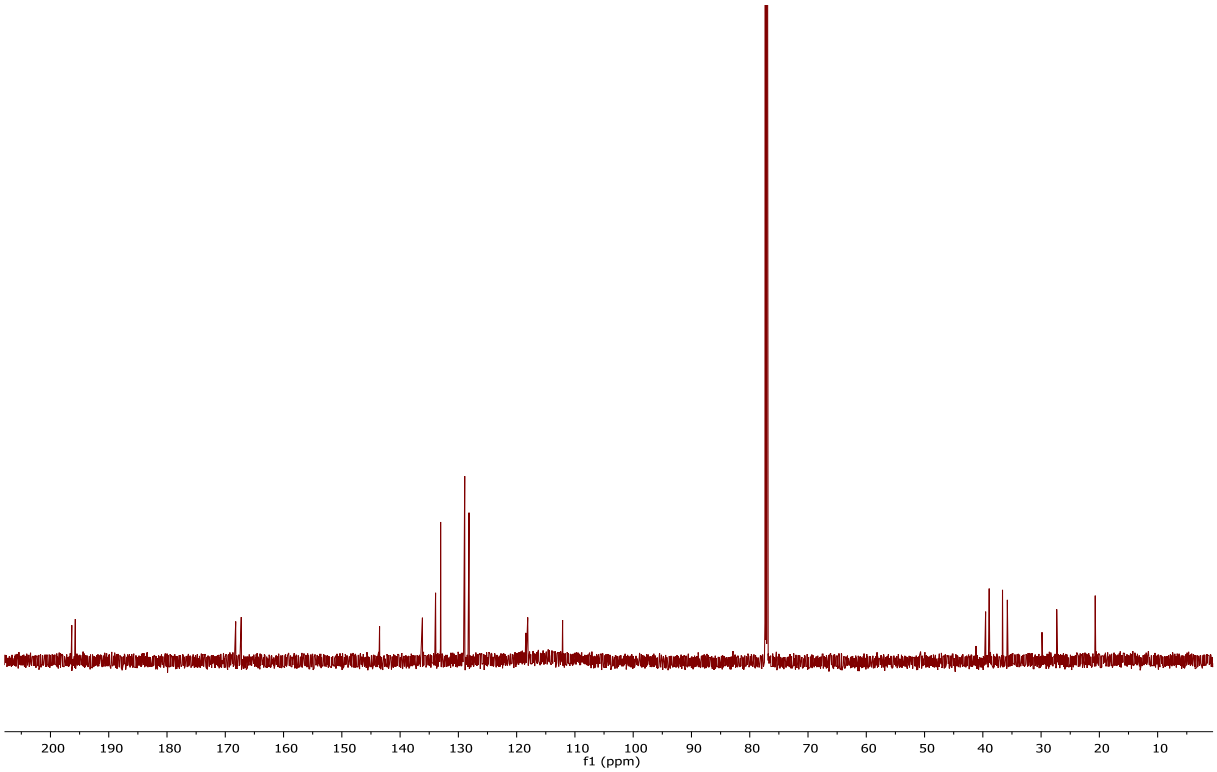
1h (3*R*,4*R*)-4-(4-Cyanophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 8)

^{1}H NMR



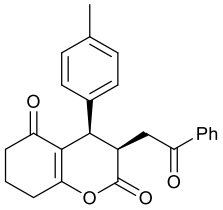


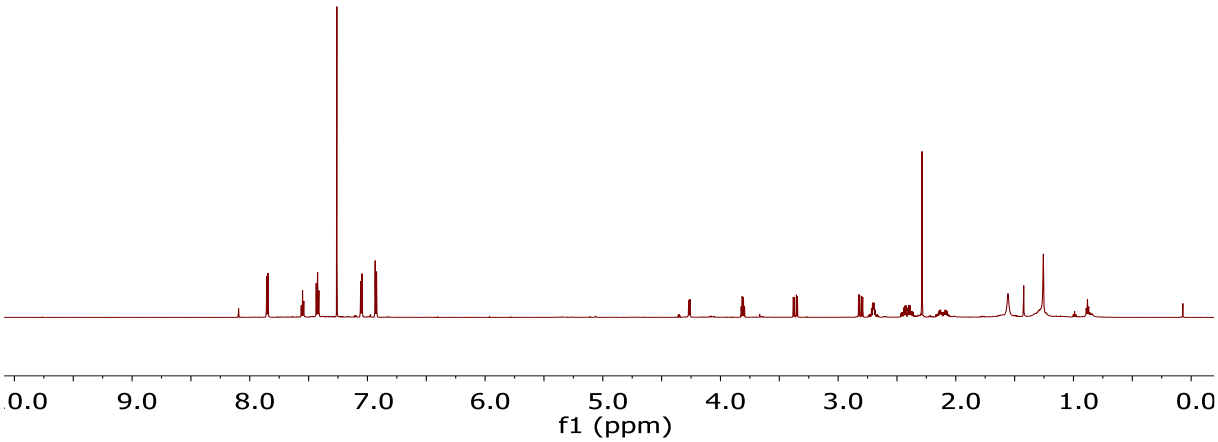
^{13}C NMR



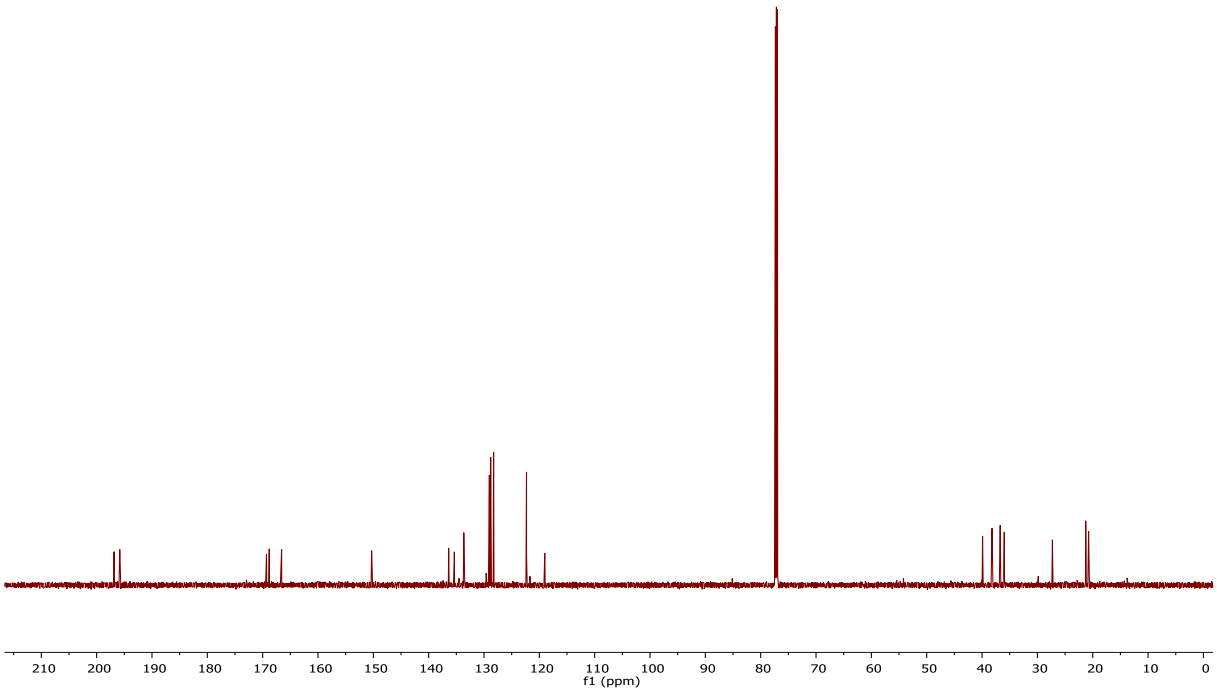
1i (3*R*,4*R*)-4-(4-Methylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 9)

^{1}H NMR



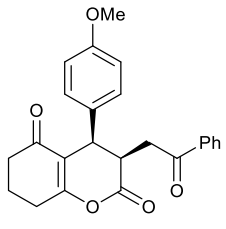


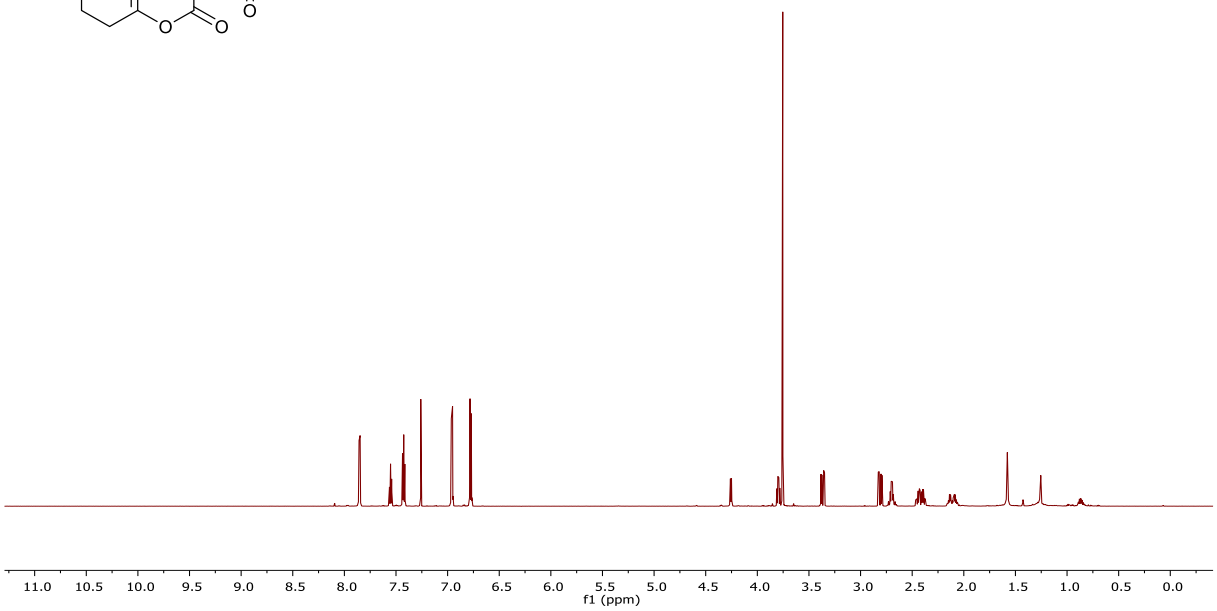
^{13}C NMR



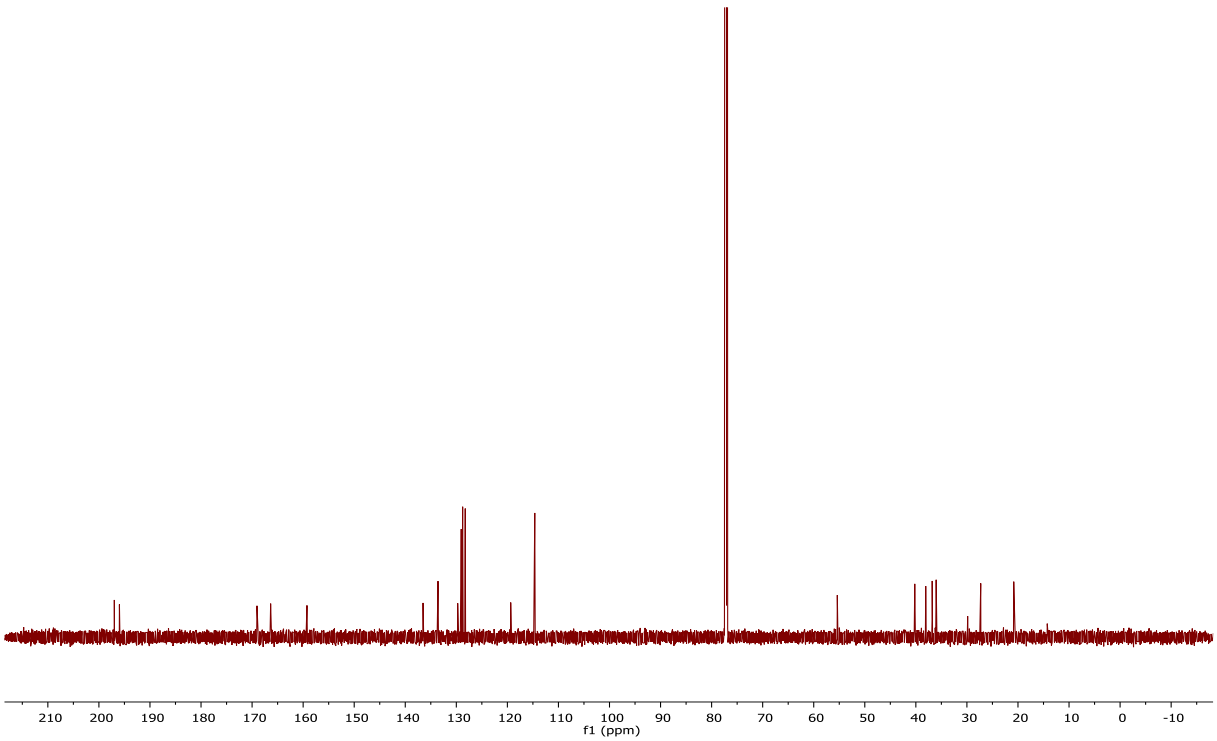
1j (3*R*,4*R*)-4-(4-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 10)

^{1}H NMR

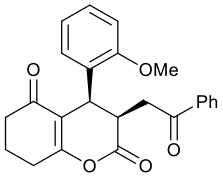




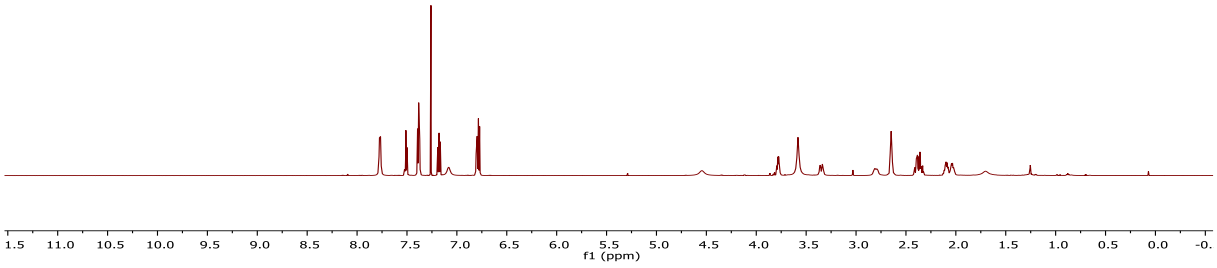
^{13}C NMR



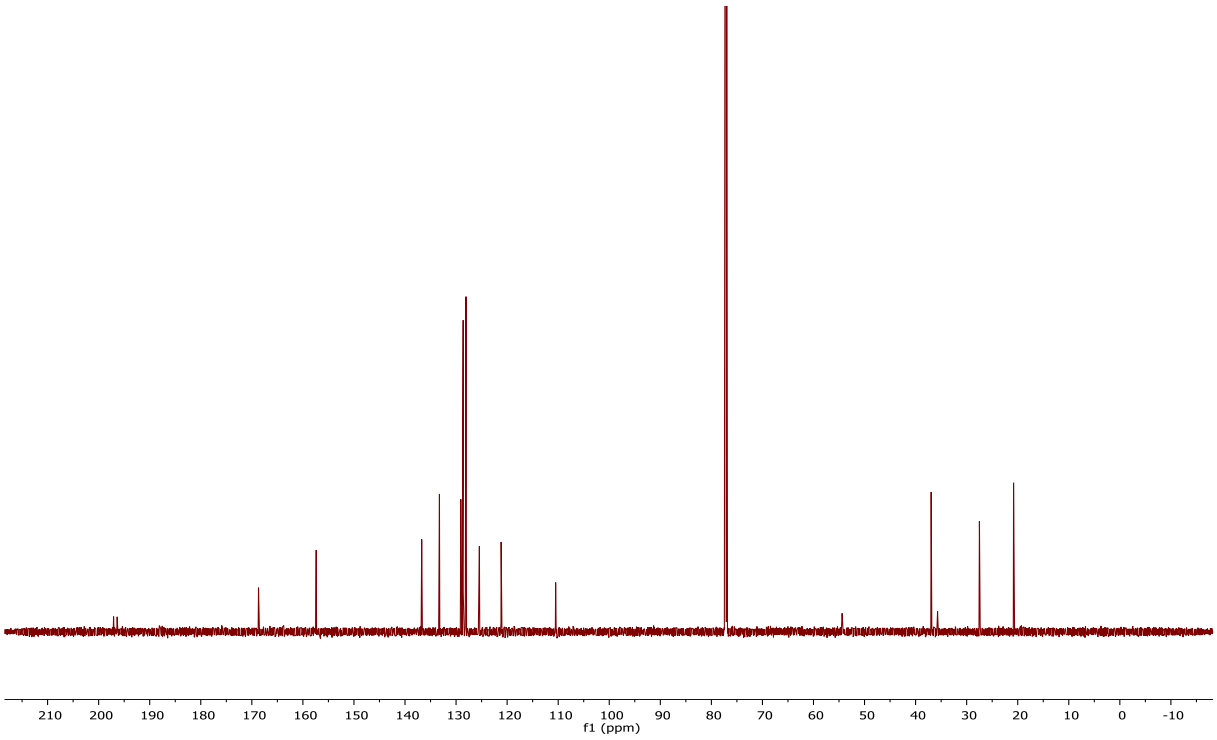
1k (3*R*,4*R*)-4-(2-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 11)



^{1}H NMR

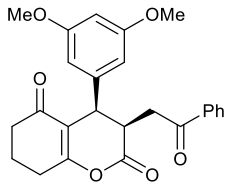


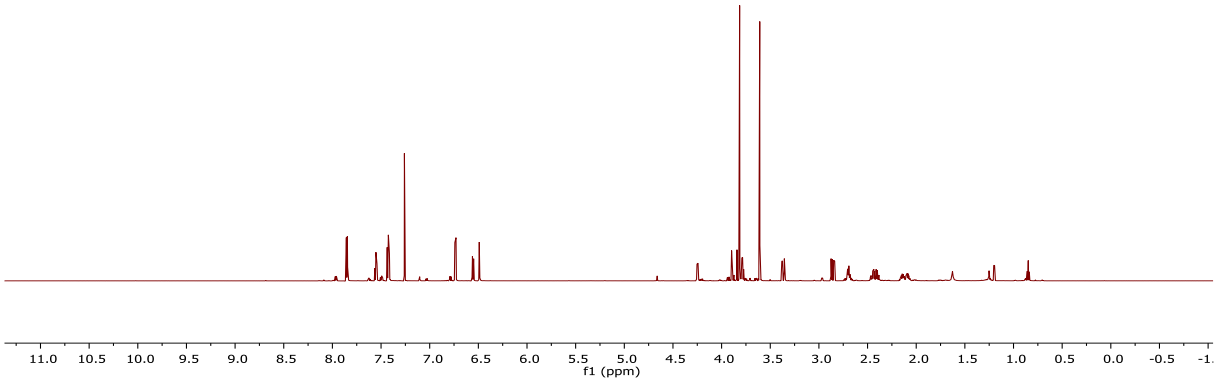
^{13}C NMR



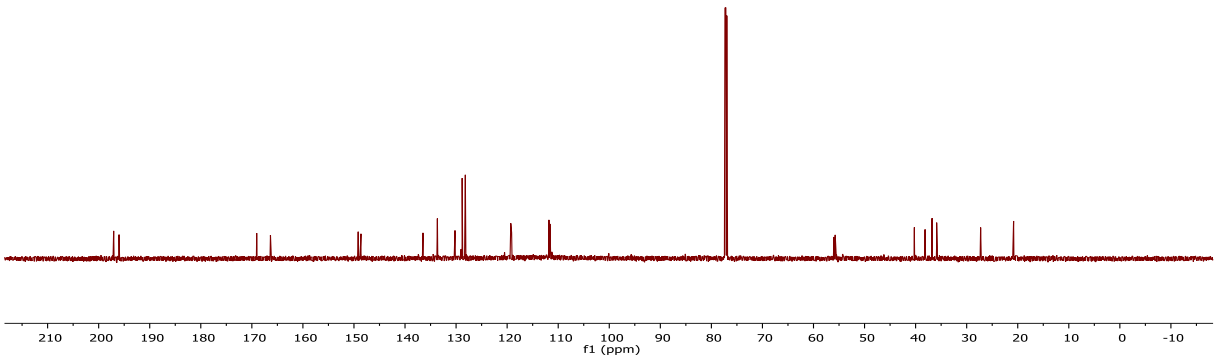
1l (3*R*,4*R*)-4-(3,5-Dimethoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 12)

^{1}H NMR

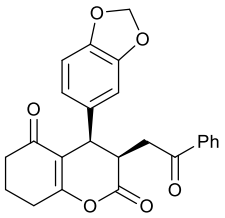




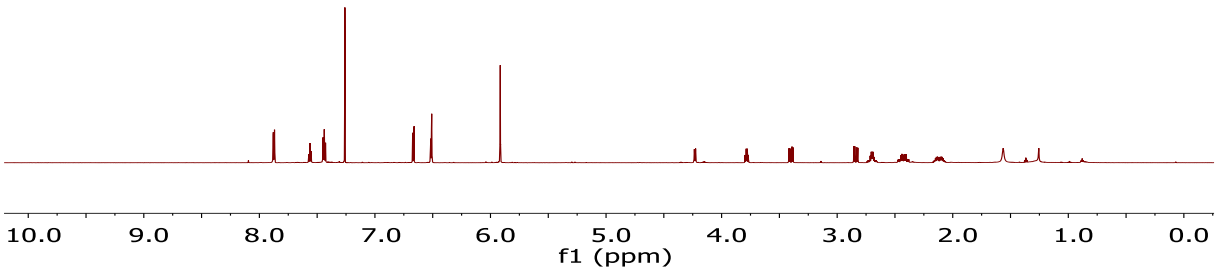
^{13}C NMR



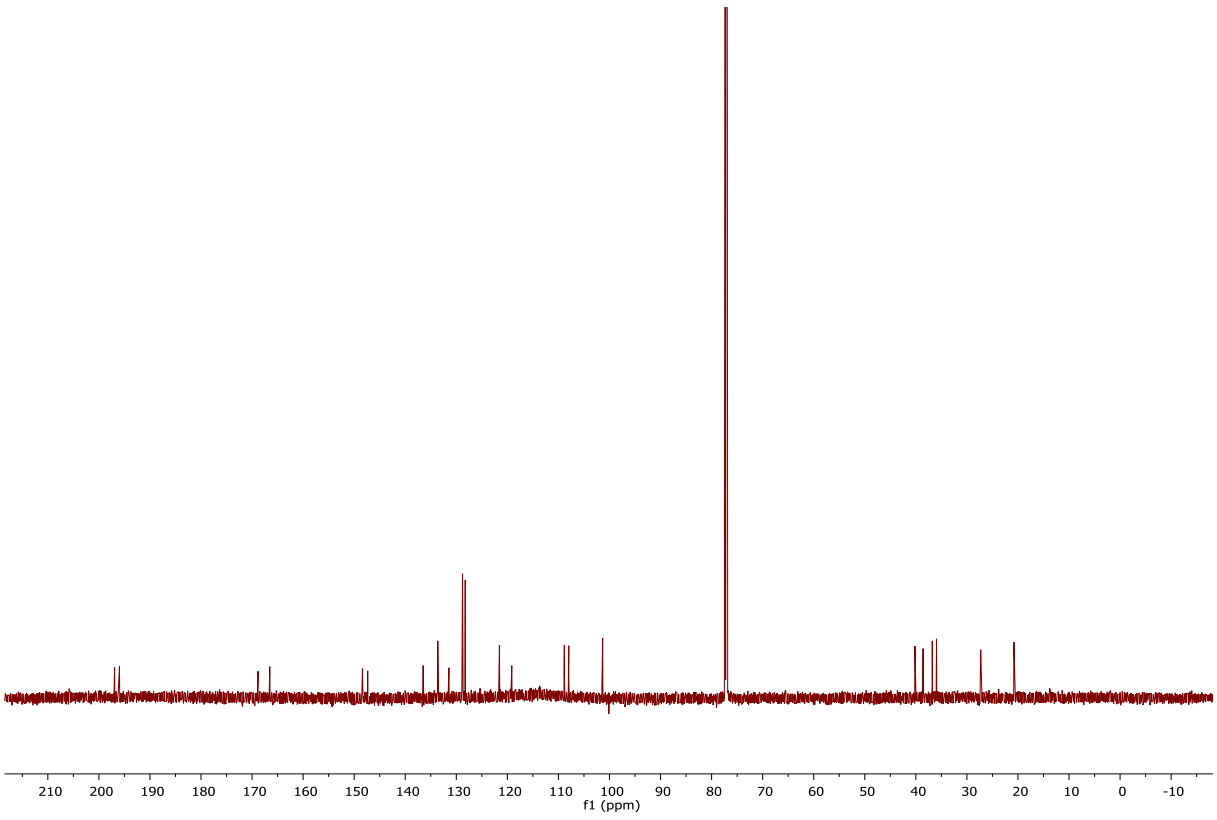
1m (3*R*,4*R*)-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 13)



^{1}H NMR

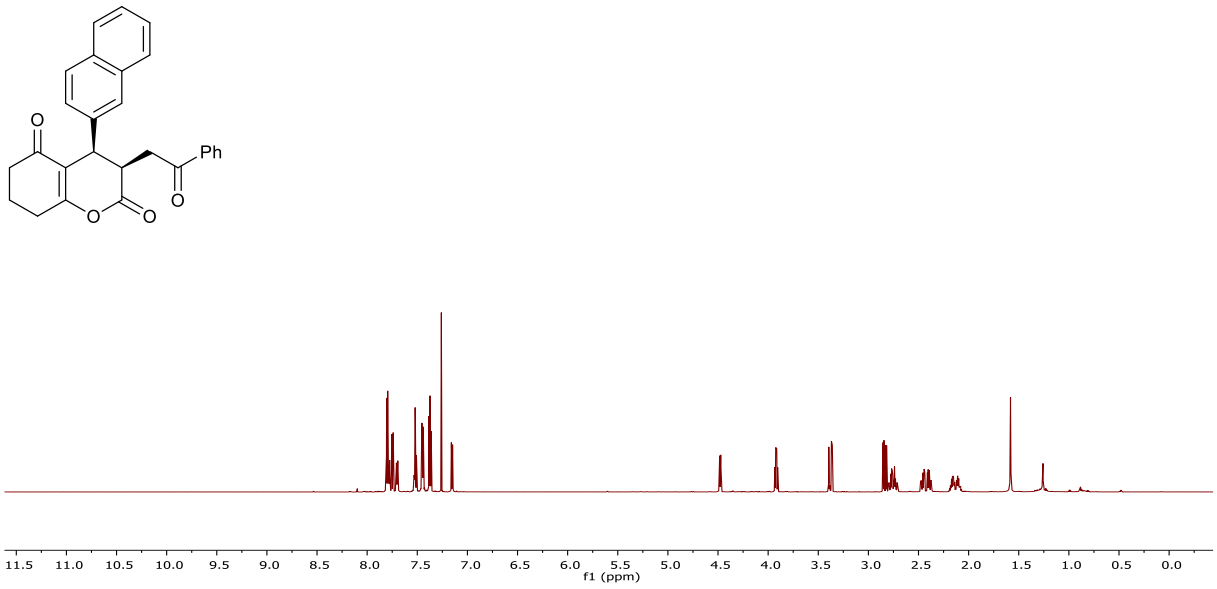


^{13}C NMR

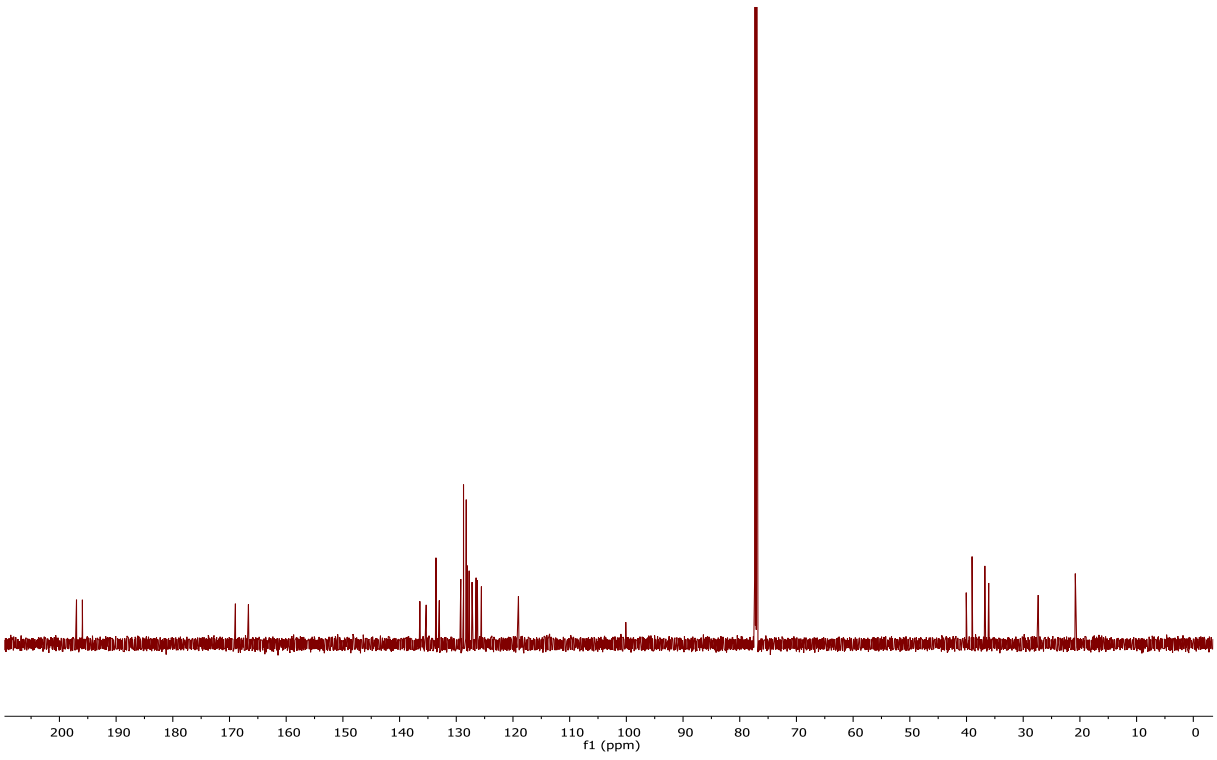


1n (3*R*,4*R*)-4-(Naphthalen-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 14)

^{1}H NMR

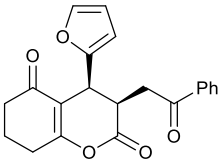


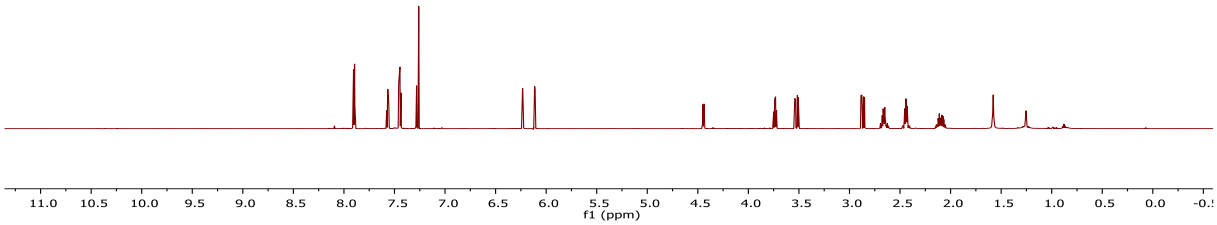
^{13}C NMR



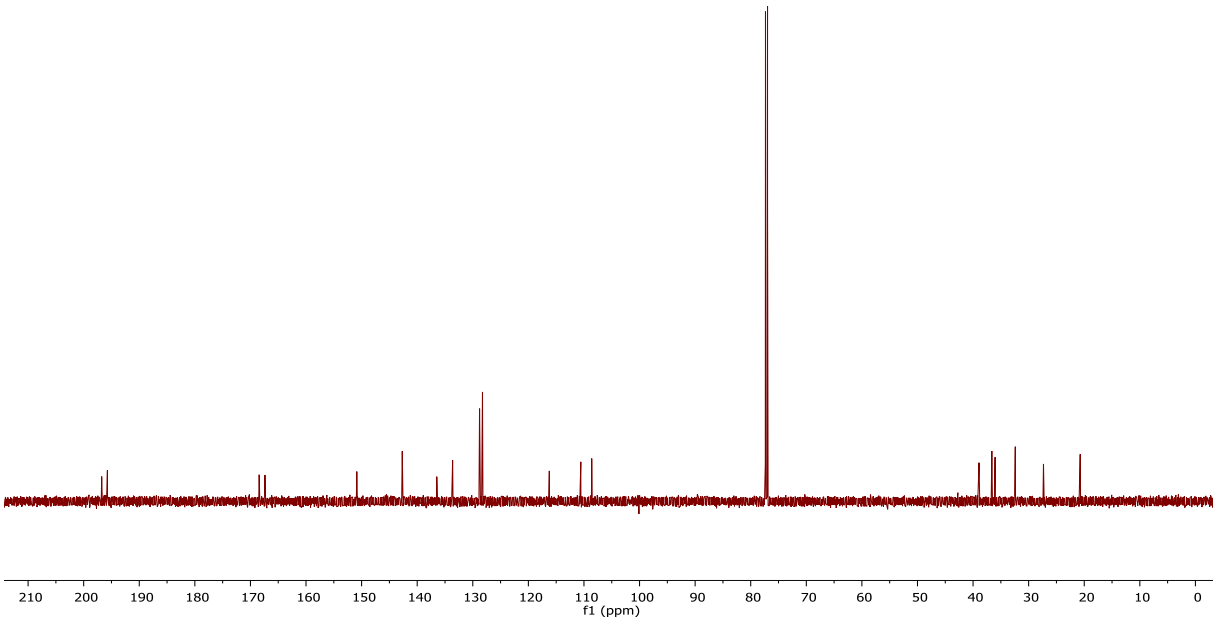
1o (3*R*,4*S*)-4-(Furan-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 15)

^{1}H NMR



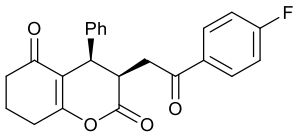


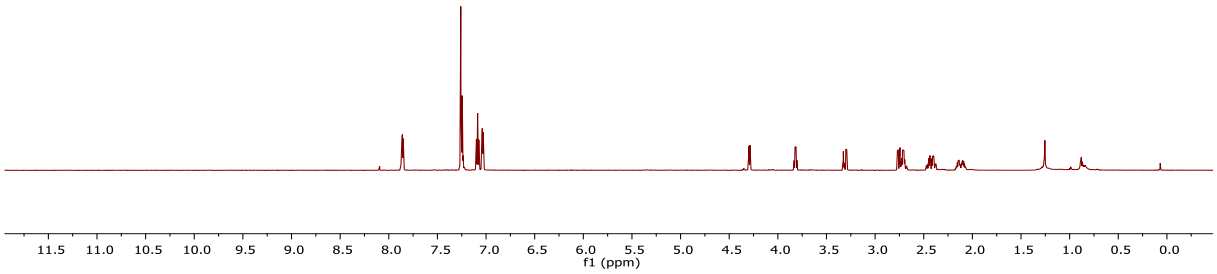
^{13}C NMR



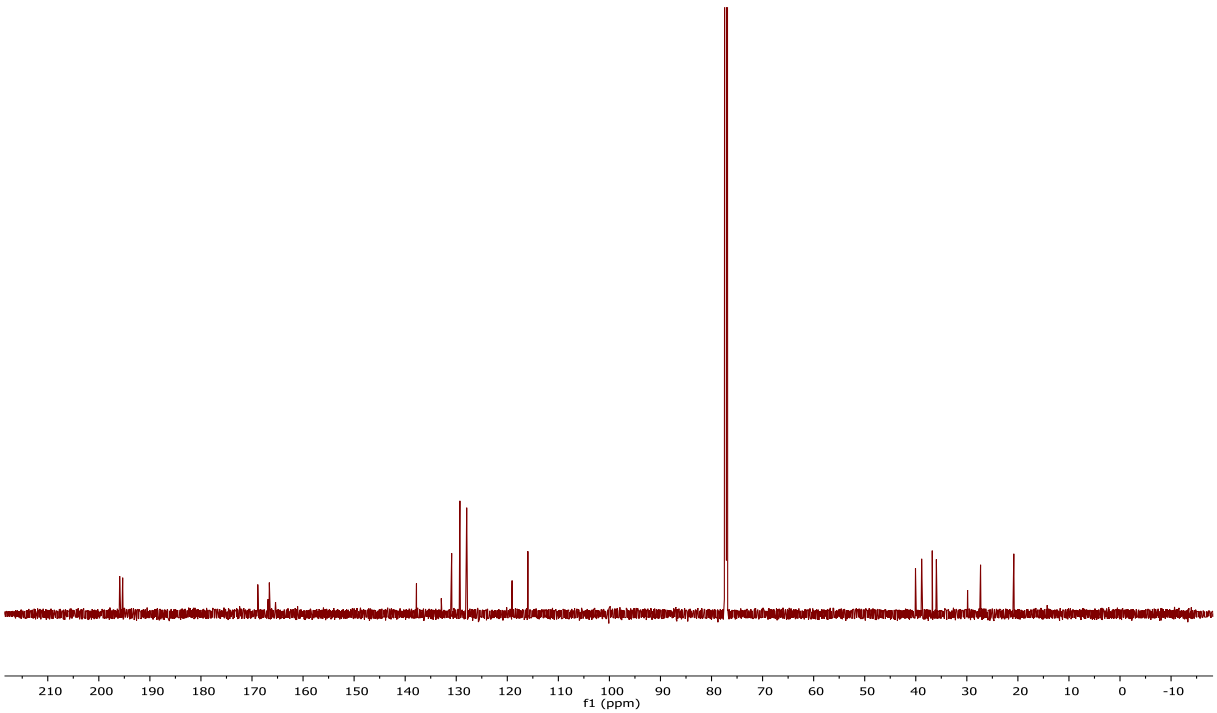
1p (3*R*,4*R*)-3-(2-(4-Fluorophenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

^{1}H NMR



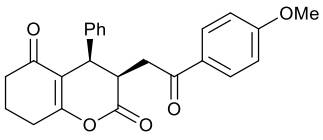


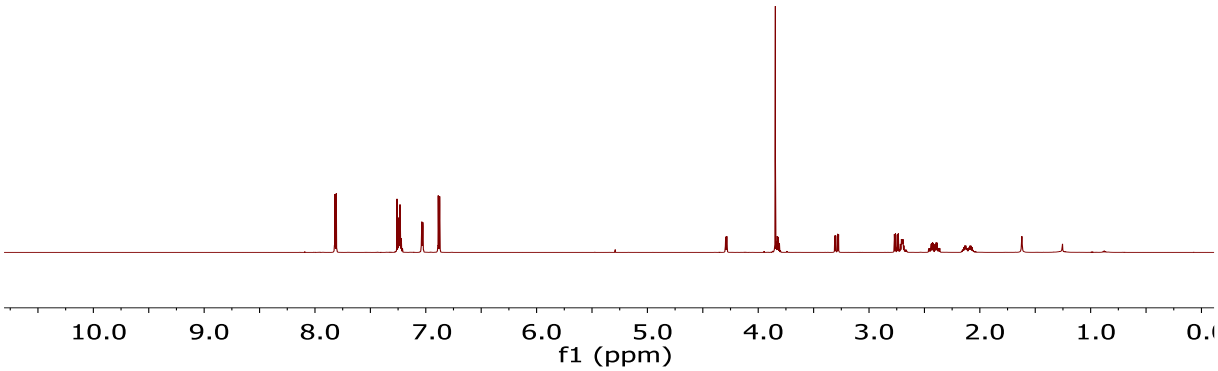
^{13}C NMR



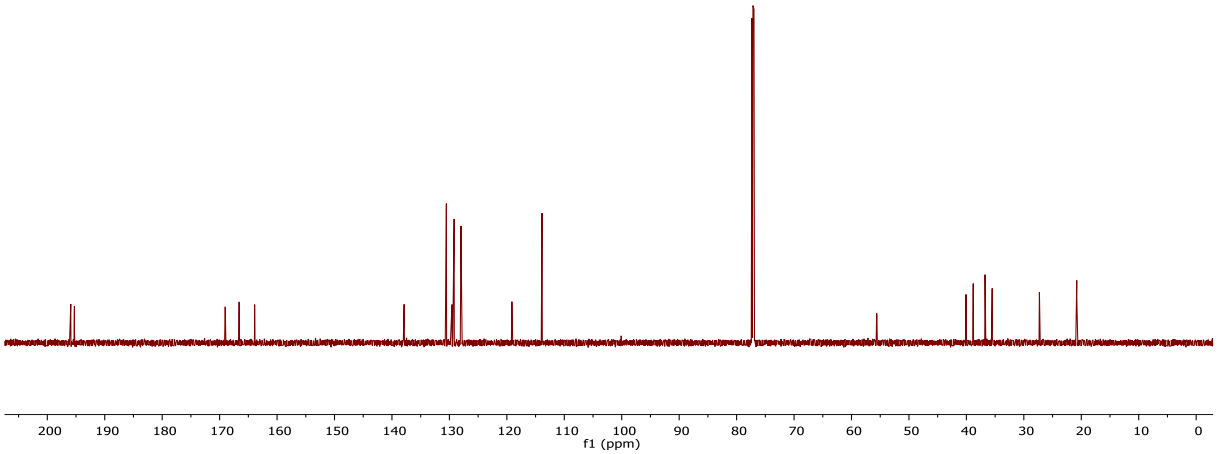
1q (3*R*,4*R*)-3-(2-(4-Methoxyphenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

^{1}H NMR



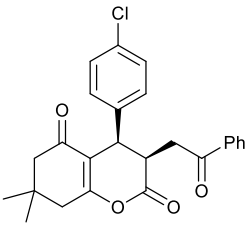


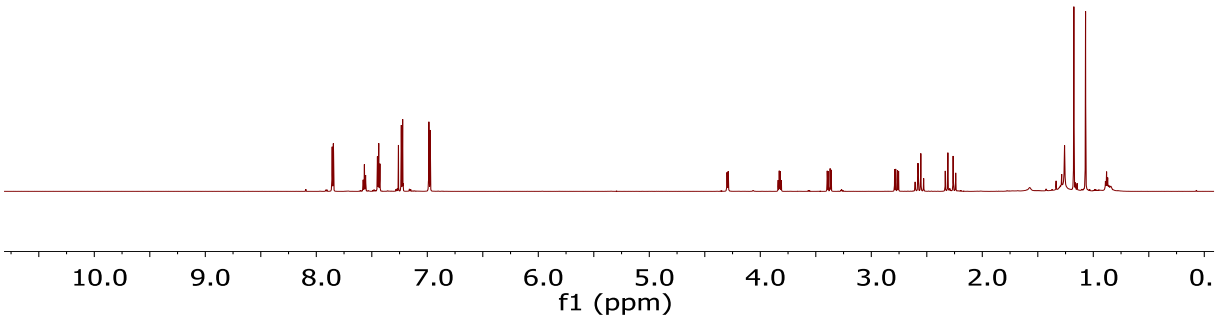
^{13}C NMR



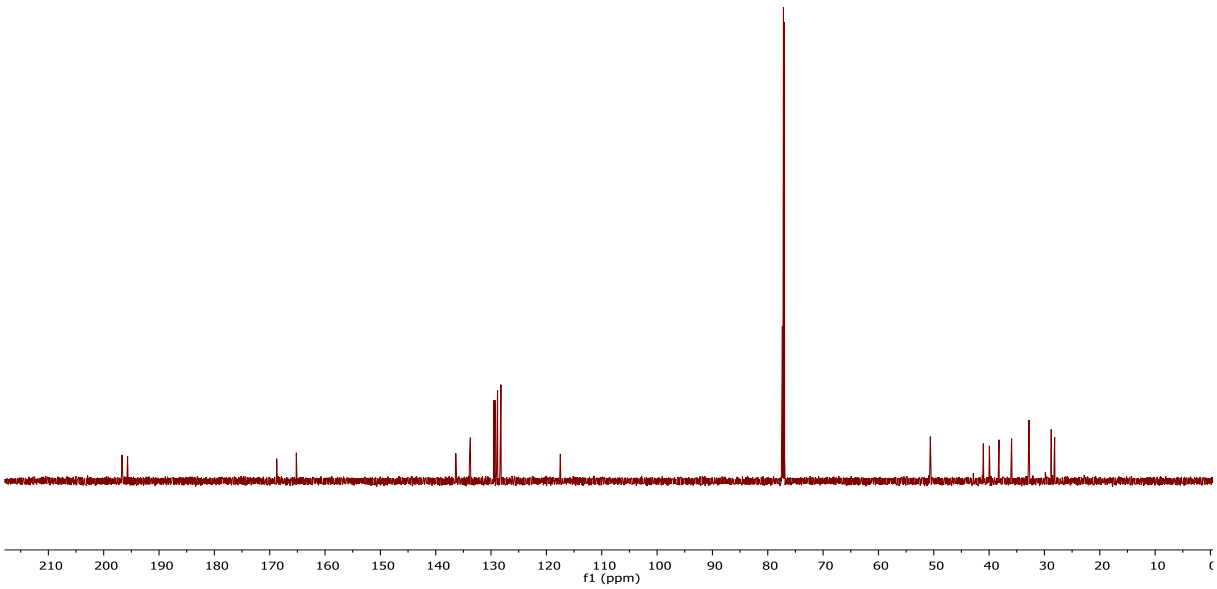
1r (3*R*,4*R*)-4-(4-Chlorophenyl)-7,7-dimethyl-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

^{1}H NMR



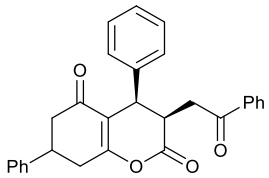


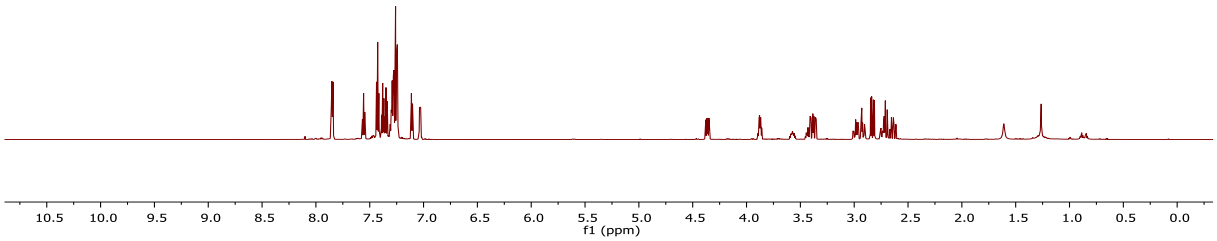
^{13}C NMR



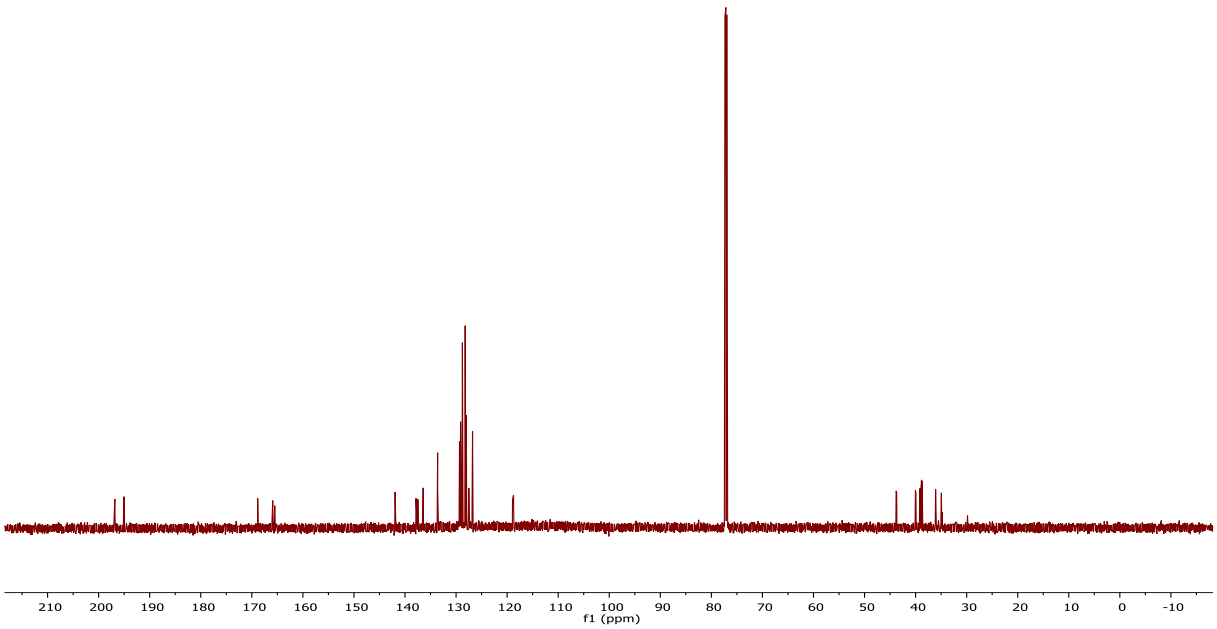
1s (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4,7-diphenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

^{1}H NMR





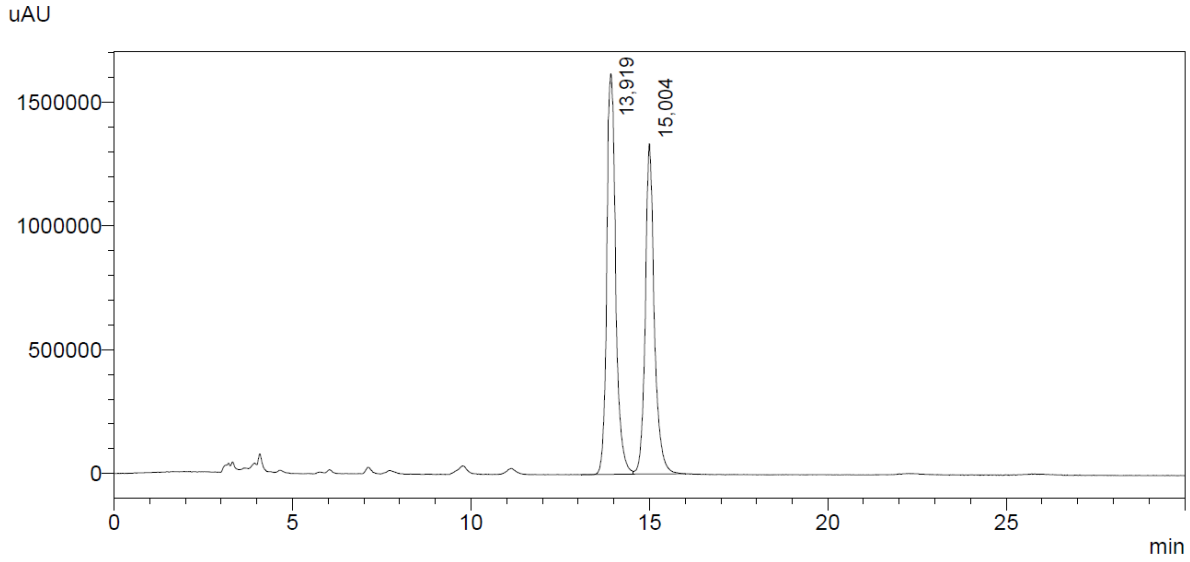
^{13}C NMR



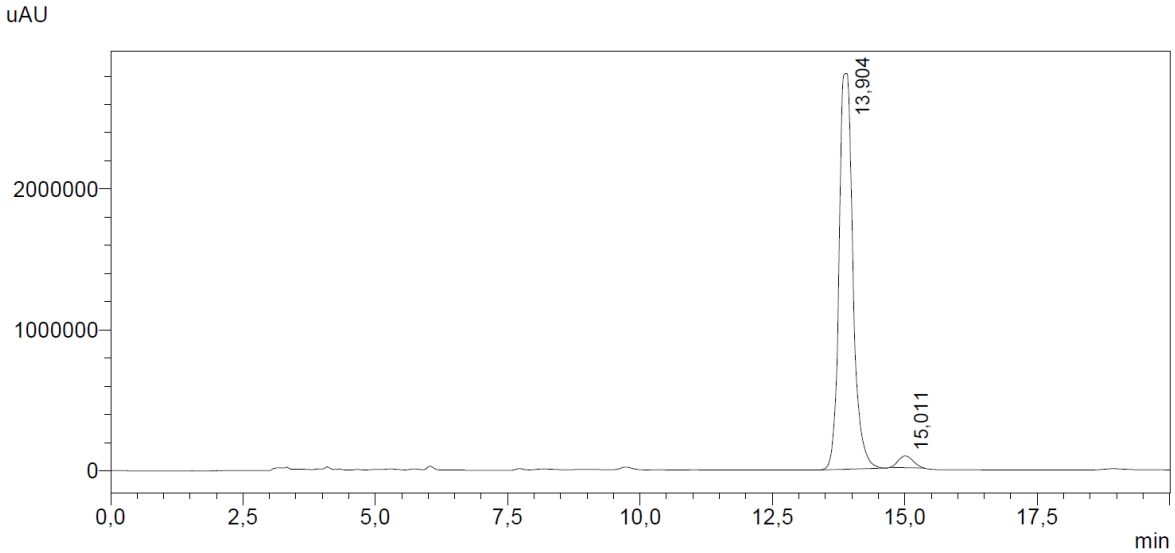
6. HPLC traces

1a (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 1)

Racemic mixture



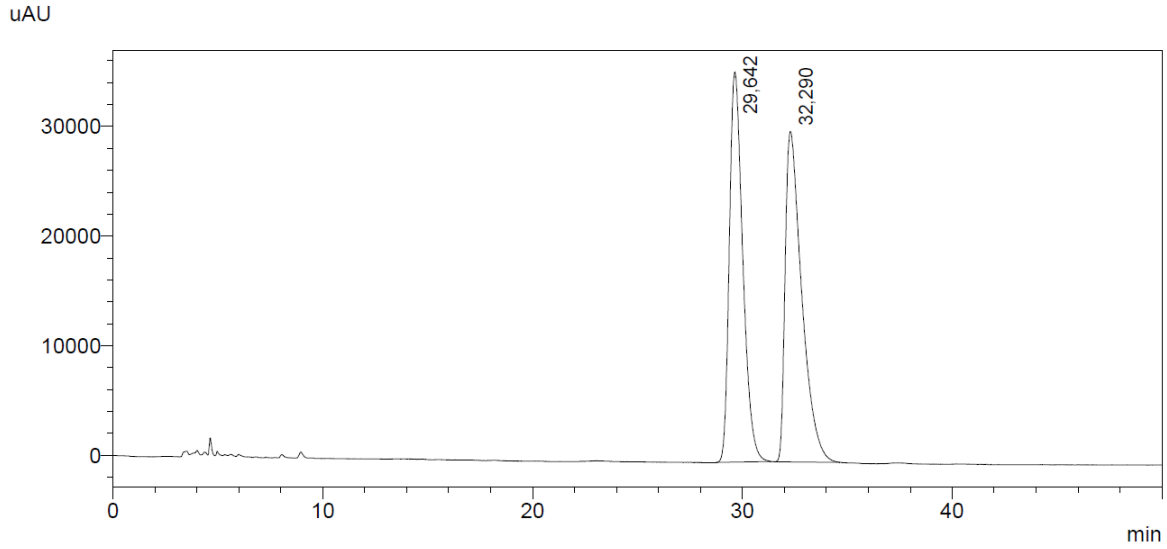
Enantiomerically enriched mixture



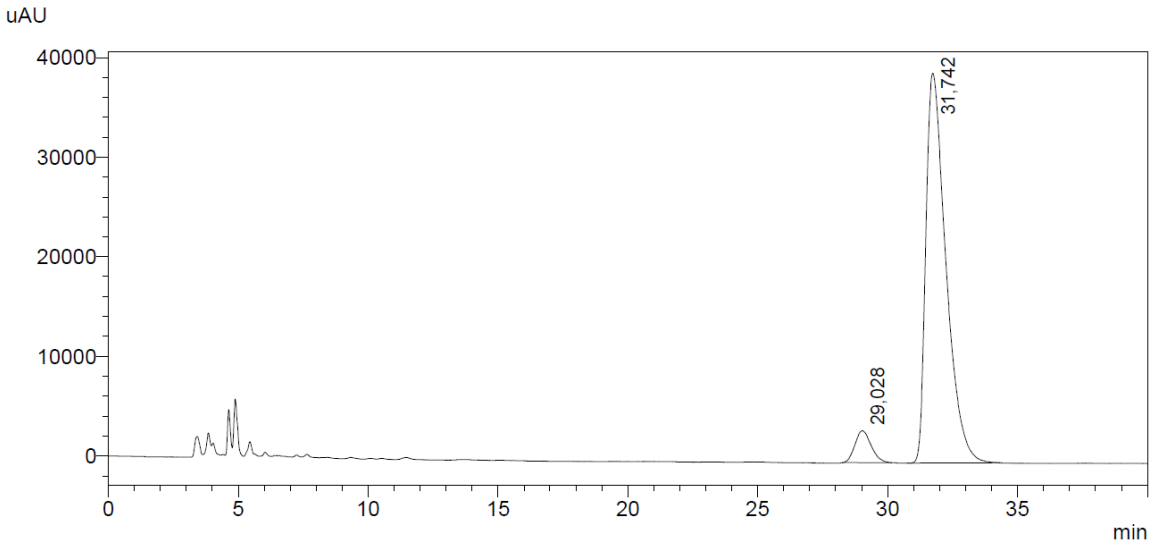
Peak#	Ret. Time	Area%
1	13,904	96,921
2	15,011	3,079
Total		100,000

1b 4-(3-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-3,4,7,8-tetrahydro-2*H*-chromene-2,5(6*H*)-dione (Table 2, entry 2)

Racemic mixture



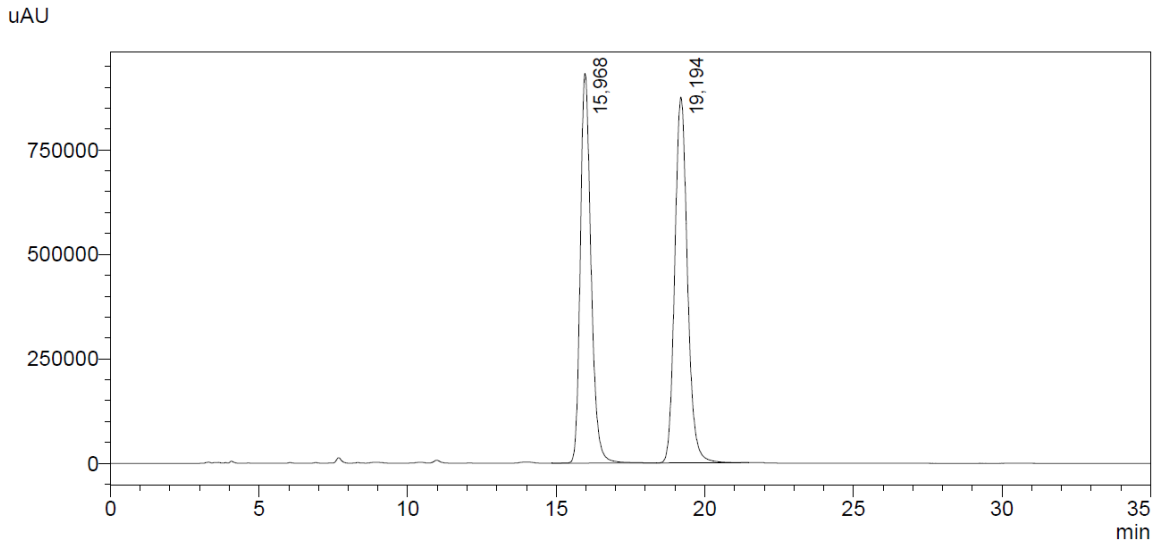
Enantiomerically enriched mixture



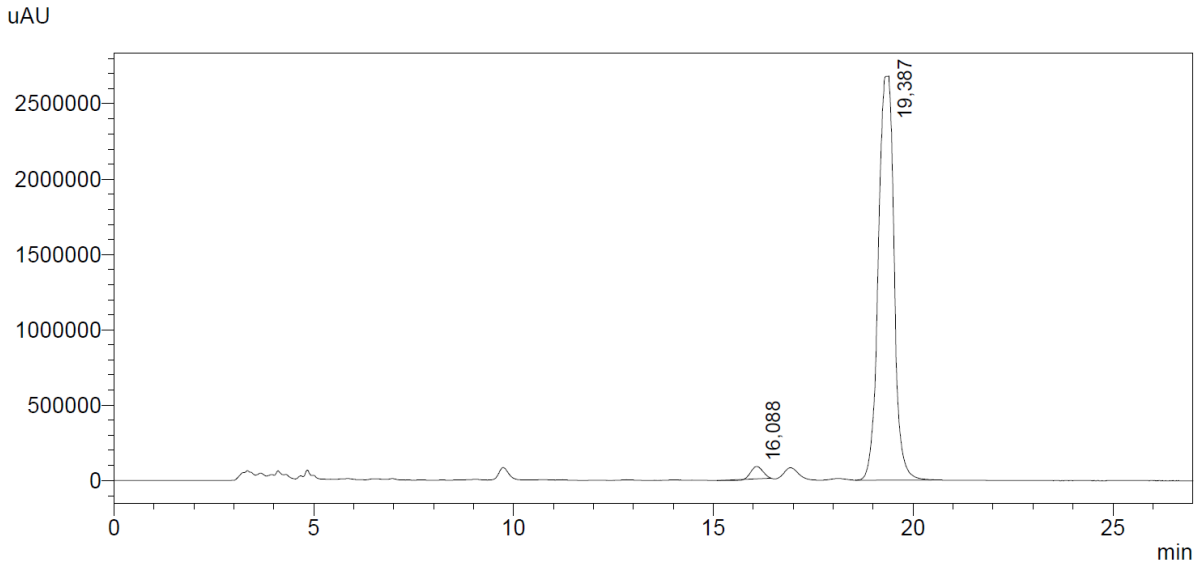
Peak#	Ret. Time	Area%
1	29,028	6,209
2	31,742	93,791
Total		100,000

1c (3*R*,4*R*)-4-(2-Fluorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 3)

Racemic mixture



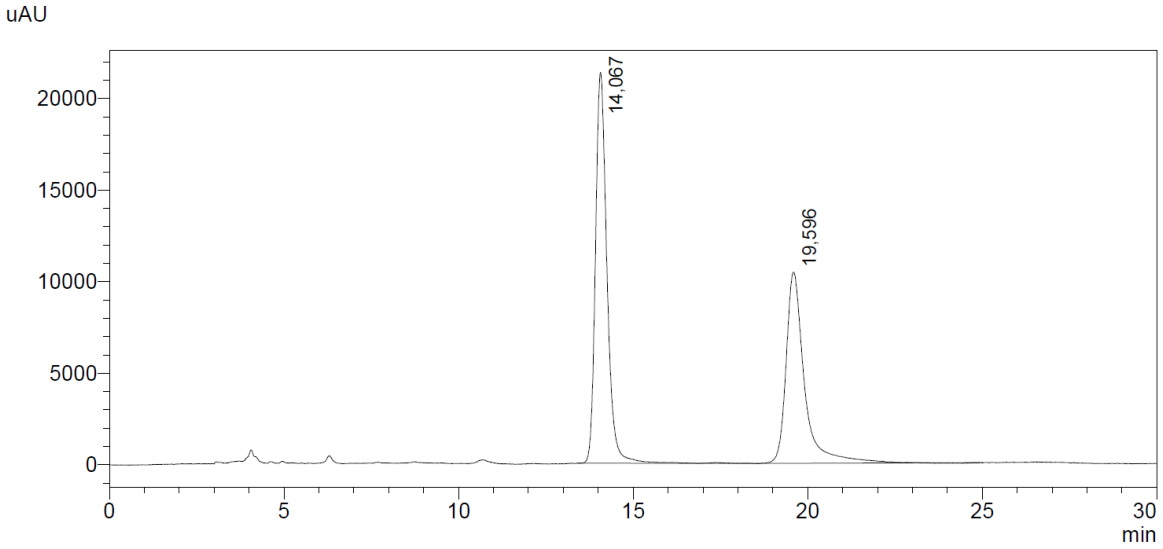
Enantiomerically enriched mixture



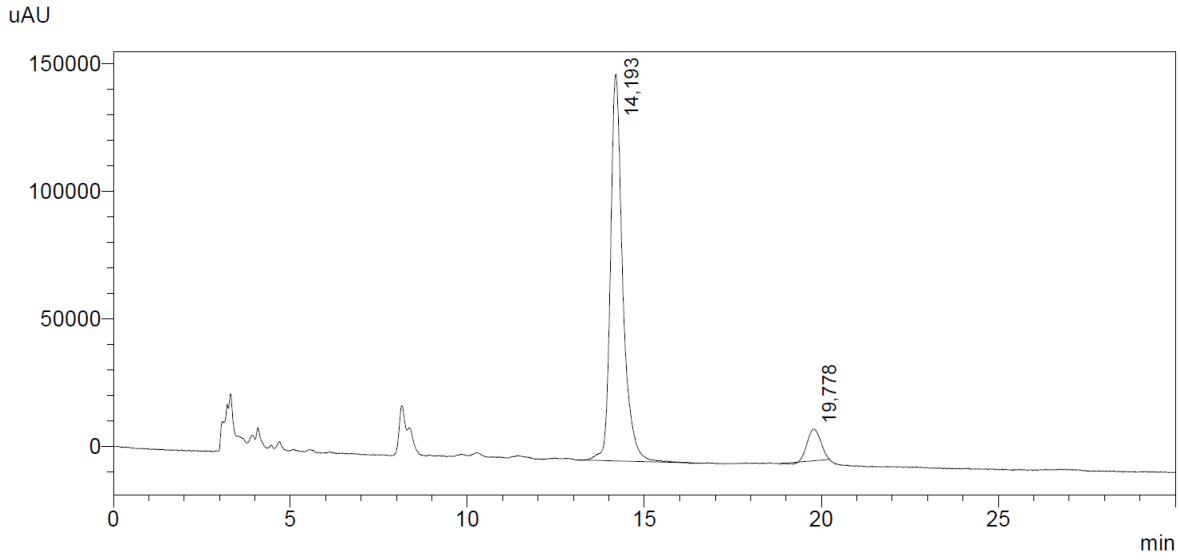
Peak#	Ret. Time	Area%
1	16,088	2,130
2	19,387	97,870
Total		100,000

1d (3*R*,4*R*)-4-(4-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 4)

Racemic mixture



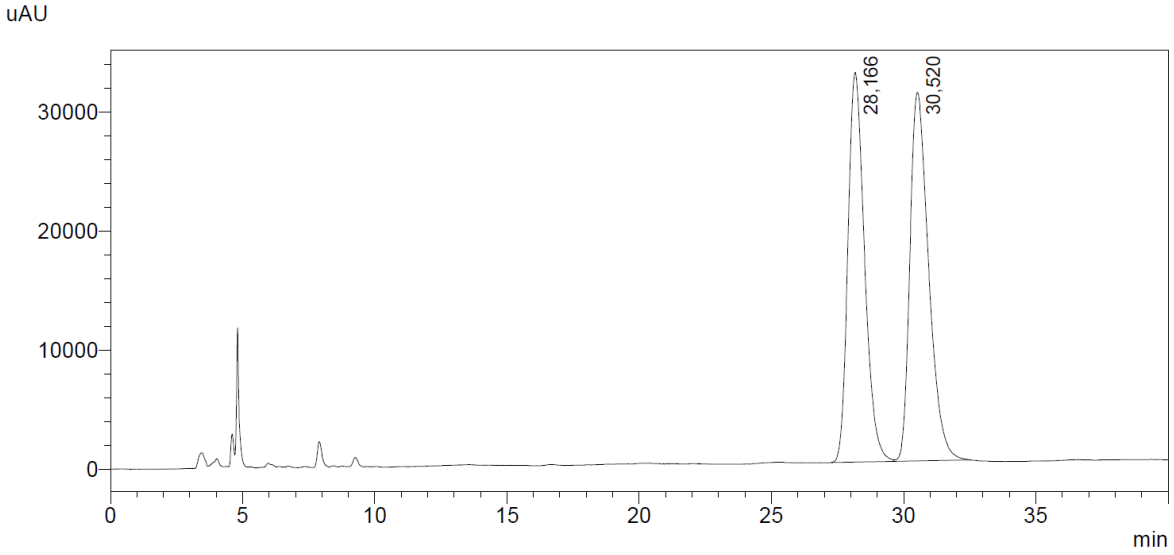
Enantiomerically enriched mixture



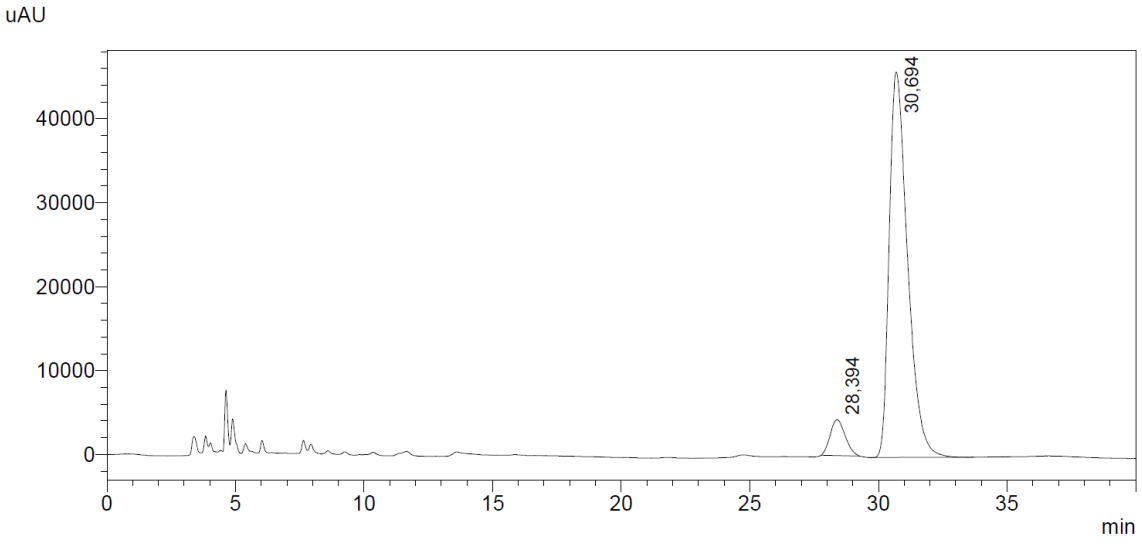
Peak#	Ret. Time	Area%
1	14,193	91,903
2	19,778	8,097
Total		100,000

1e (3*R*,4*R*)-4-(3-Chlorophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 5)

Racemic mixture



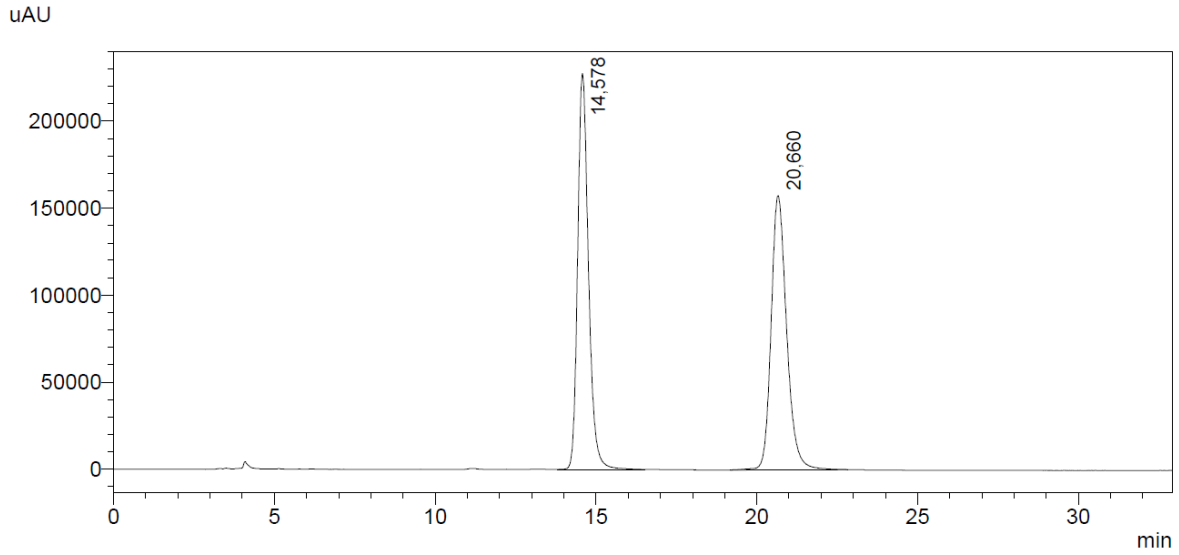
Enantiomerically enriched mixture



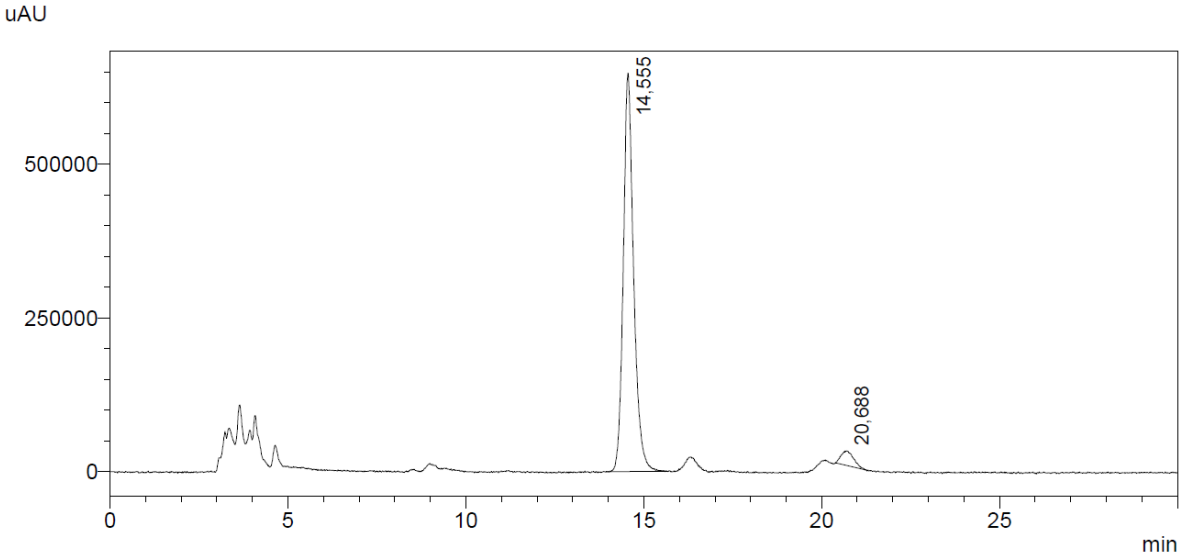
Peak#	Ret. Time	Area%
1	28,394	7,053
2	30,694	92,947
Total		100,000

1f (3*R*,4*R*)-4-(4-Bromophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 6)

Racemic mixture



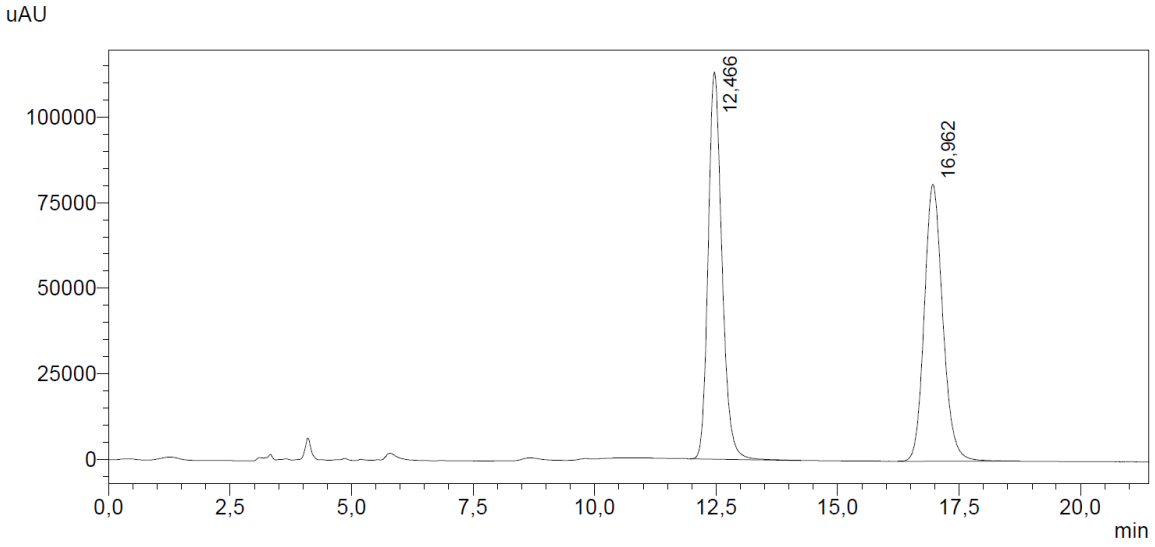
Enantiomerically enriched mixture



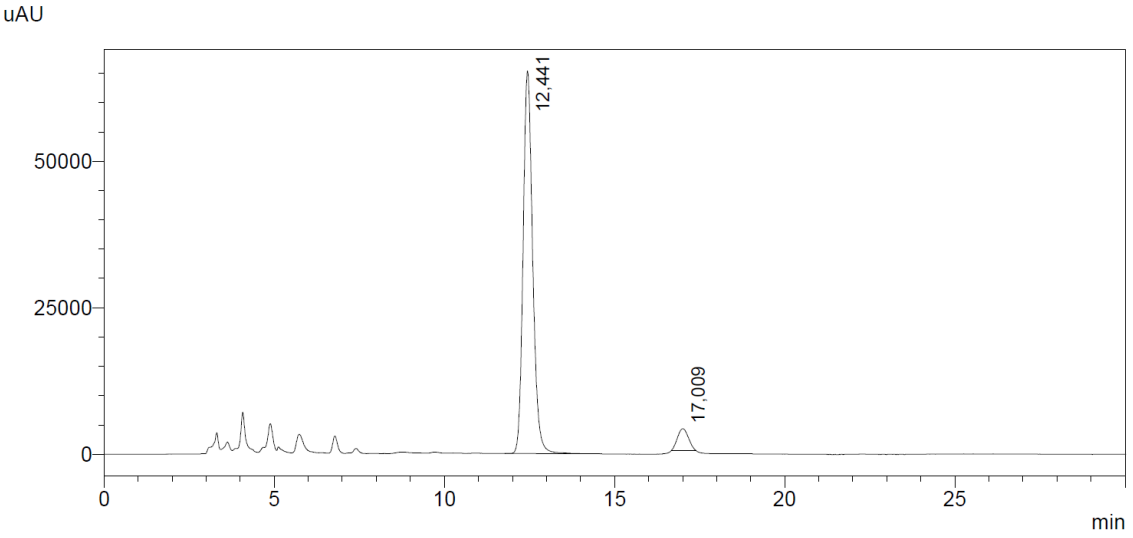
Peak#	Ret. Time	Area%
1	14,555	95,710
2	20,688	4,290
Total		100,000

1g (3*R*,4*R*)-4-(4-Trifluoromethylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 7)

Racemic mixture



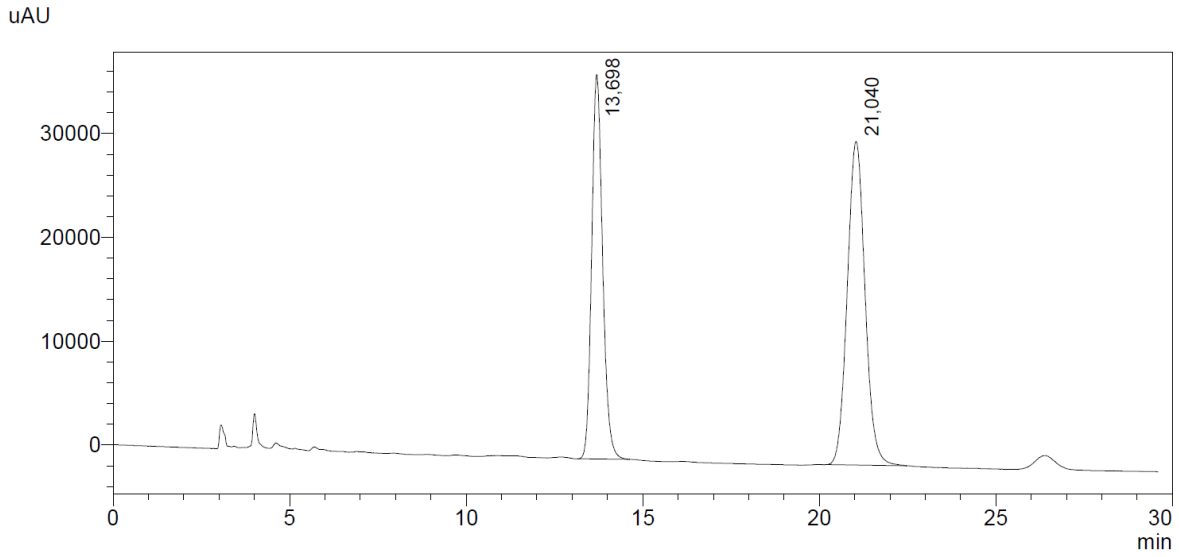
Enantiomerically enriched mixture



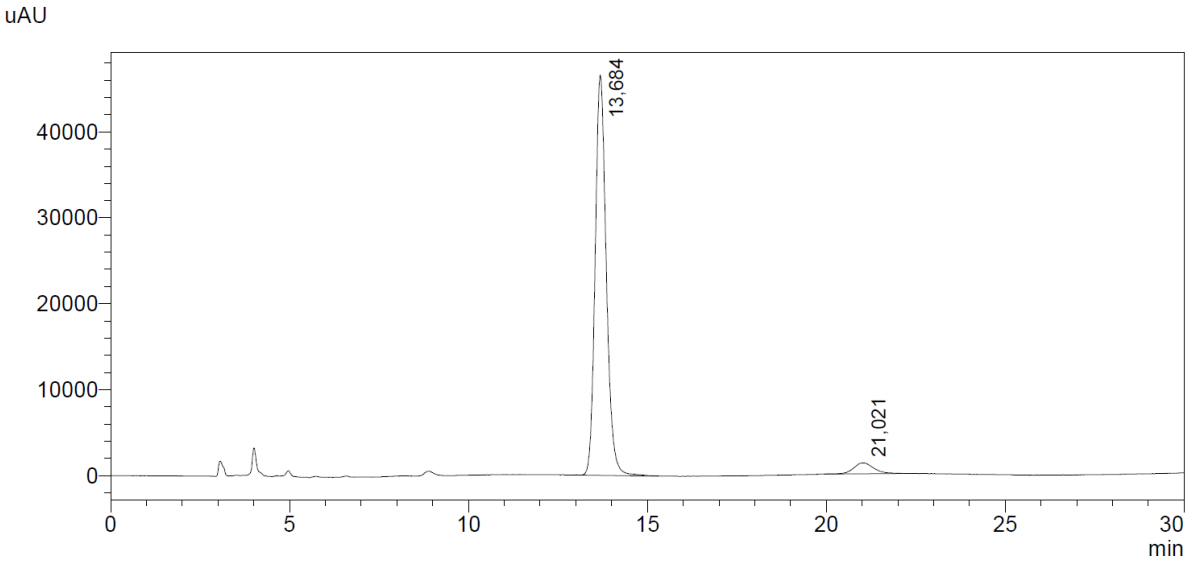
Peak#	Ret. Time	Area%
1	12,441	93,956
2	17,009	6,044
Total		100,000

1h (3*R*,4*R*)-4-(4-Cyanophenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 8)

Racemic mixture



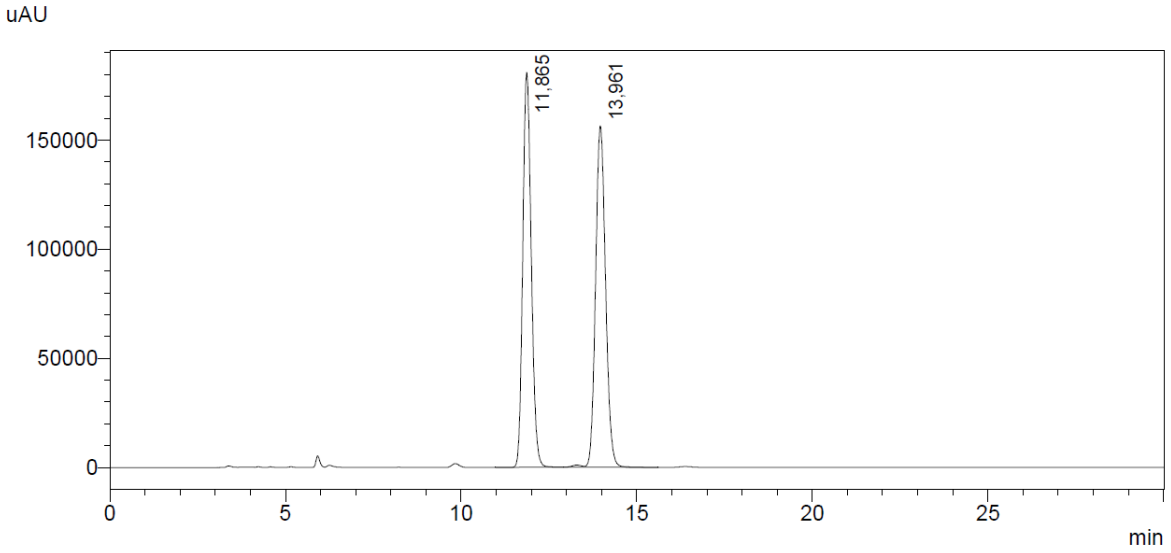
Enantiomerically enriched mixture



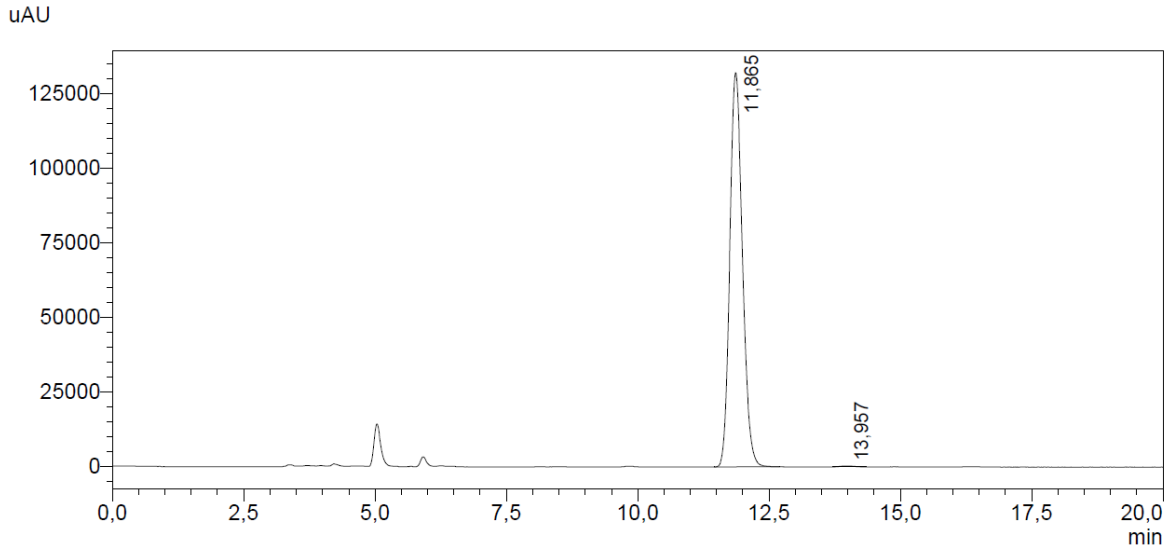
Peak#	Ret. Time	Area%
1	13,684	95,411
2	21,021	4,589
Total		100,000

1i (3*R*,4*R*)-4-(4-Methylphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 10)

Racemic mixture



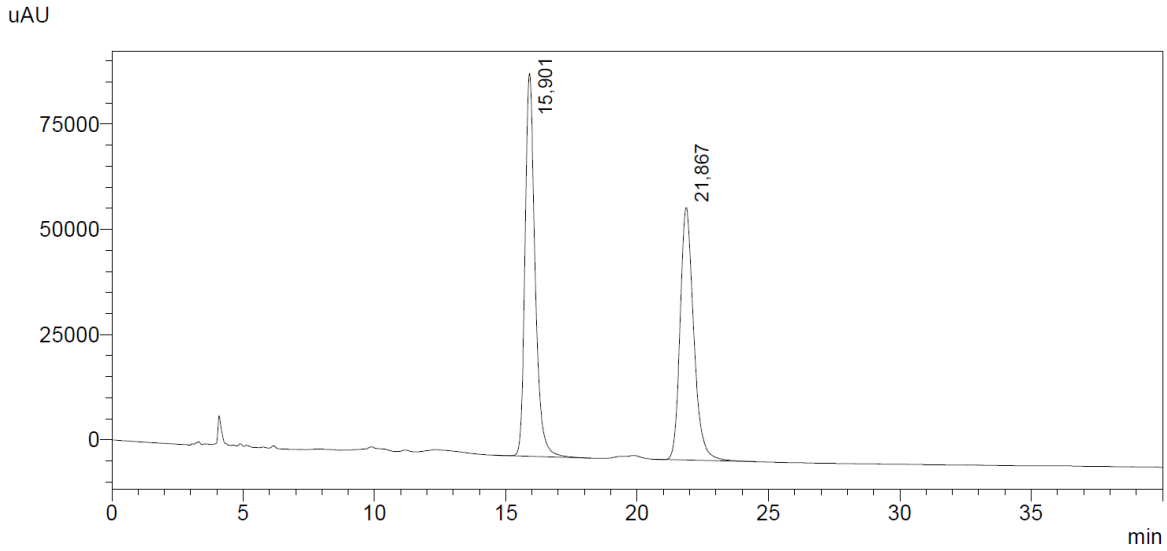
Enantiomerically enriched mixture



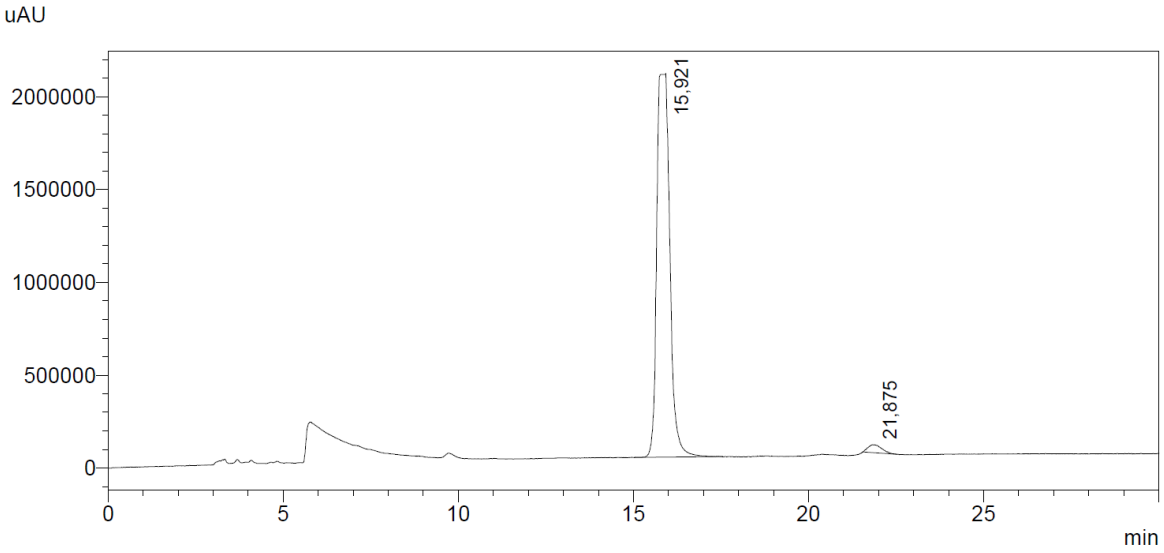
Peak#	Ret. Time	Area%
1	11,865	99,729
2	13,957	0,271
Total		100,000

1j (3*R*,4*R*)-4-(4-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 11)

Racemic mixture



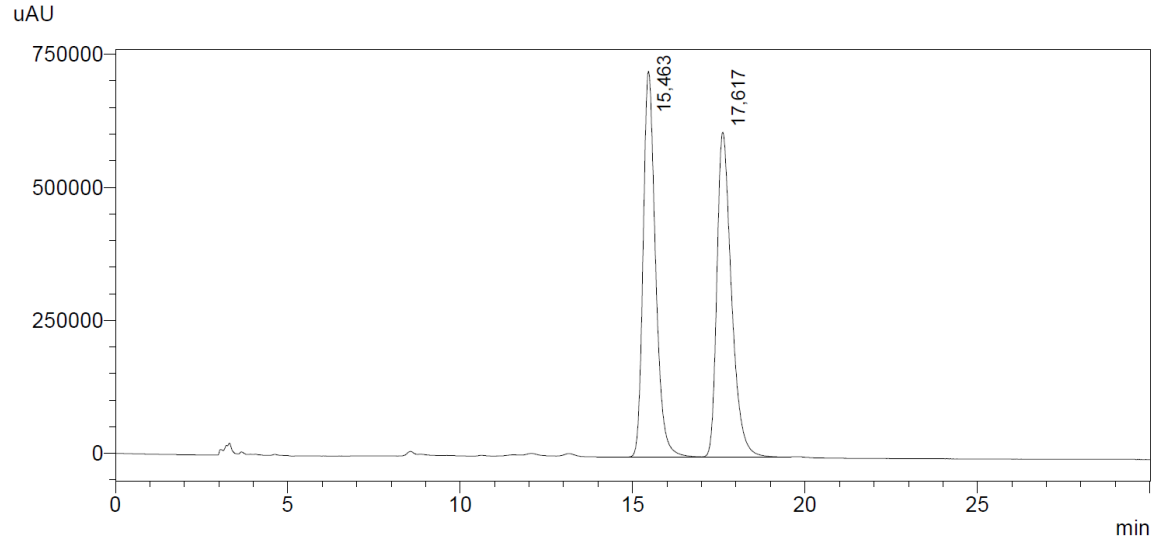
Enantiomerically enriched mixture



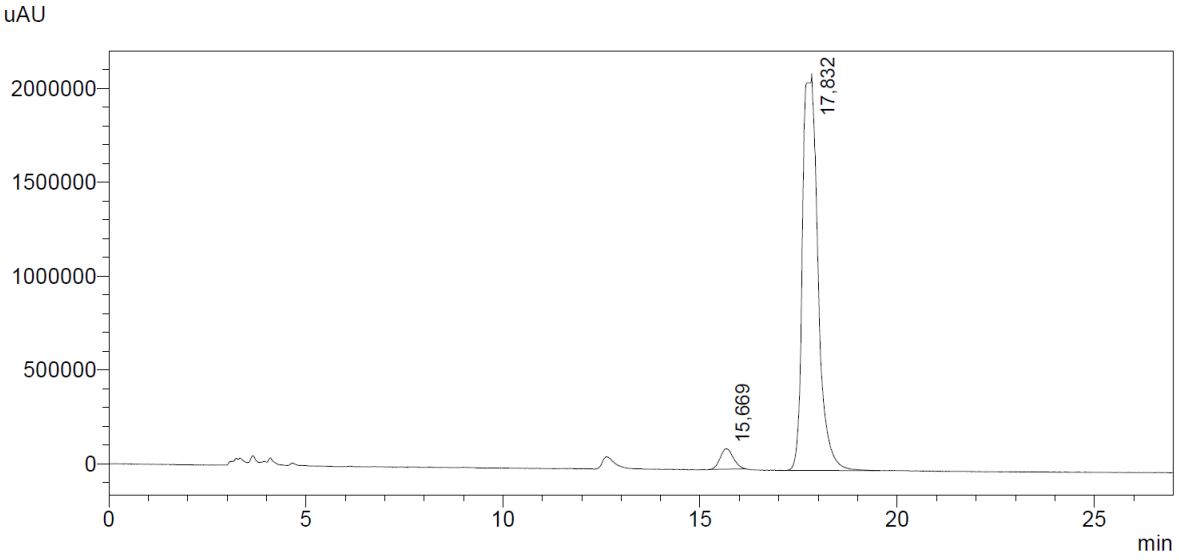
Peak#	Ret. Time	Area%
1	15,921	97,834
2	21,875	2,166
Total		100,000

1k (3*R*,4*R*)-4-(2-Methoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 11)

Racemic mixture



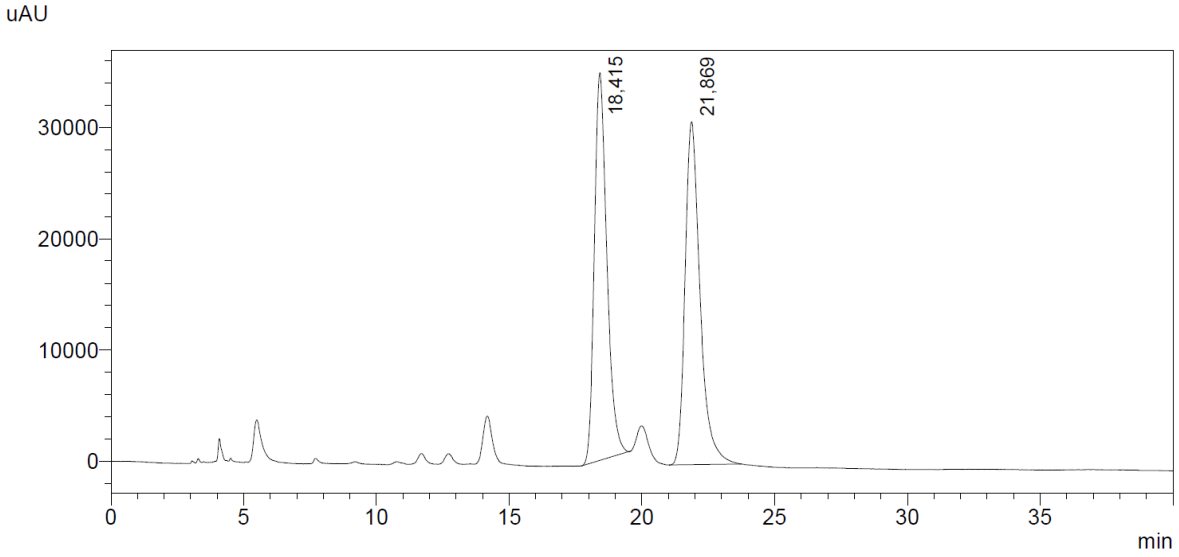
Enantiomerically enriched mixture



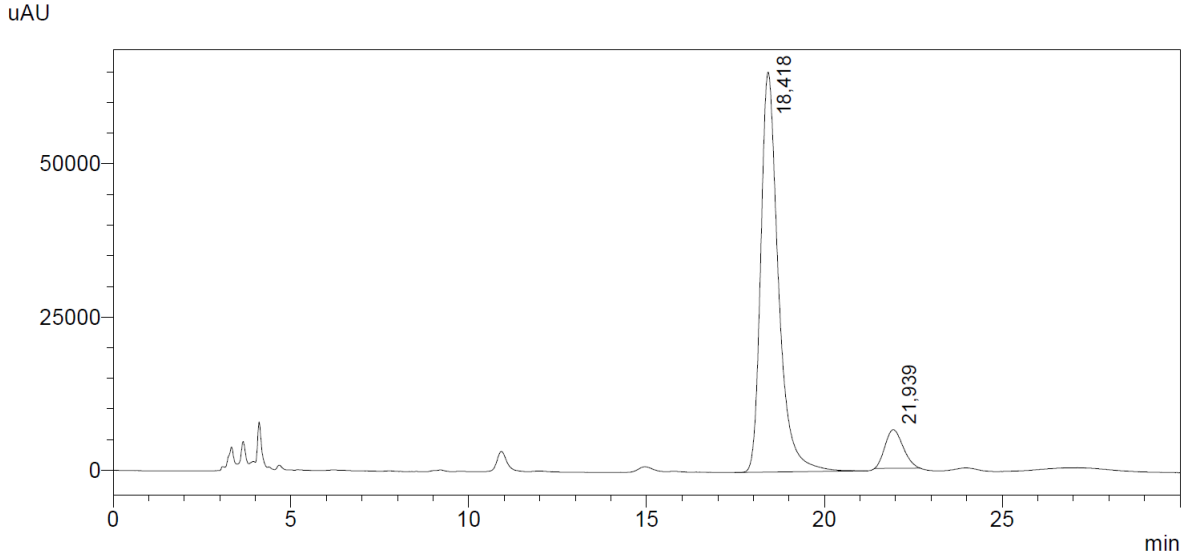
Peak#	Ret. Time	Area%
1	15,669	4,205
2	17,832	95,795
Total		100,000

1l (3*R*,4*R*)-4-(3,5-Dimethoxyphenyl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 12)

Racemic mixture



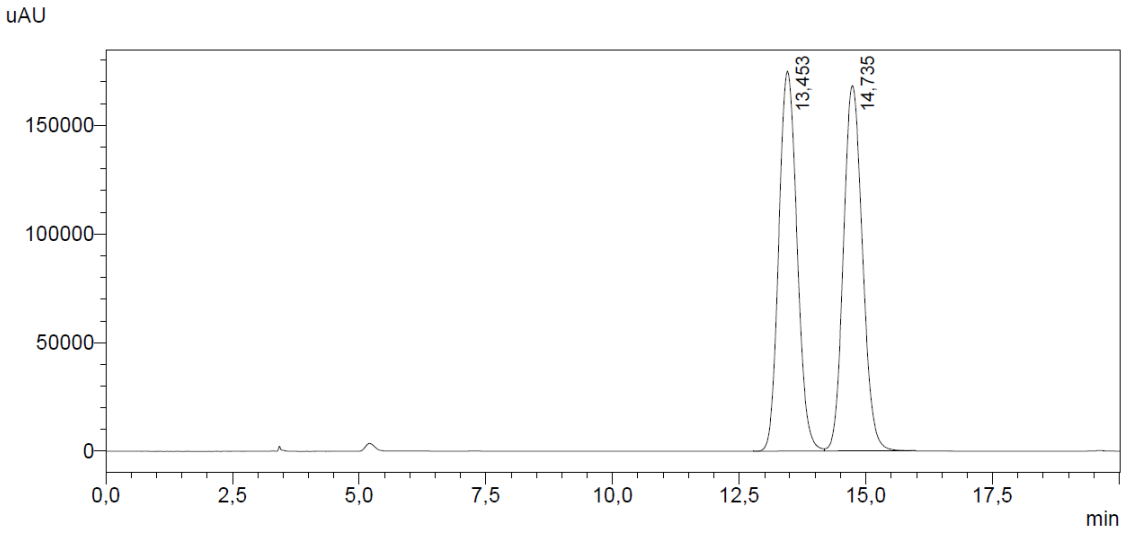
Enantiomerically enriched mixture



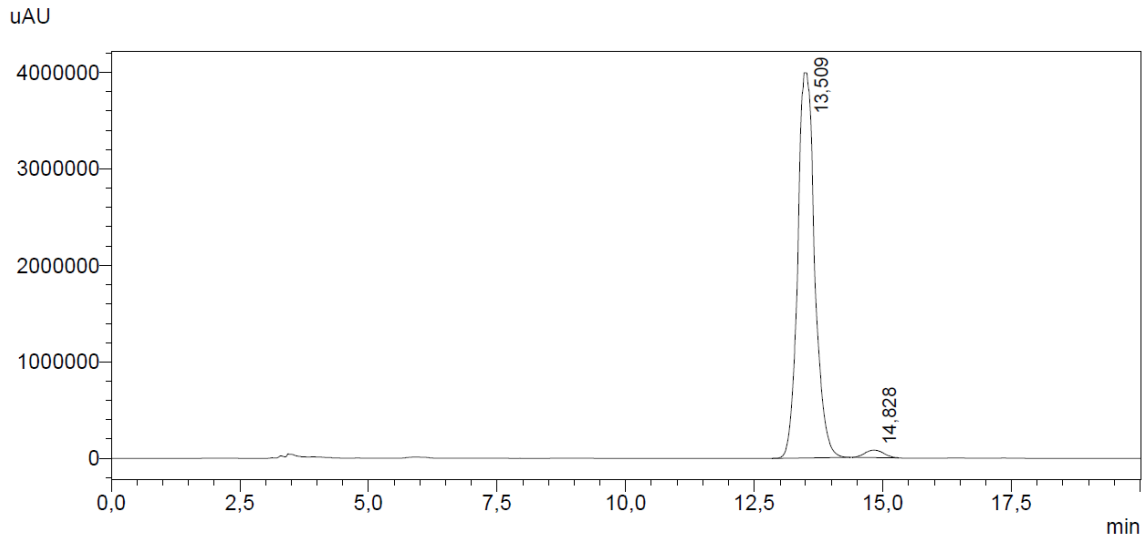
Peak#	Ret. Time	Area%
1	18,418	90,997
2	21,939	9,003
Total		100,000

1m (3*R*,4*R*)-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 13)

Racemic mixture



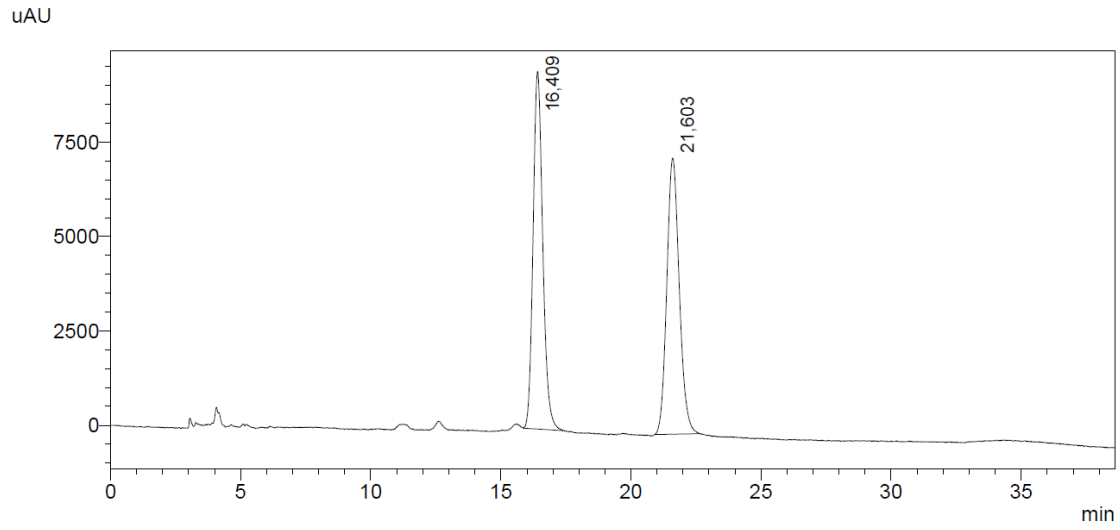
Enantiomerically enriched mixture



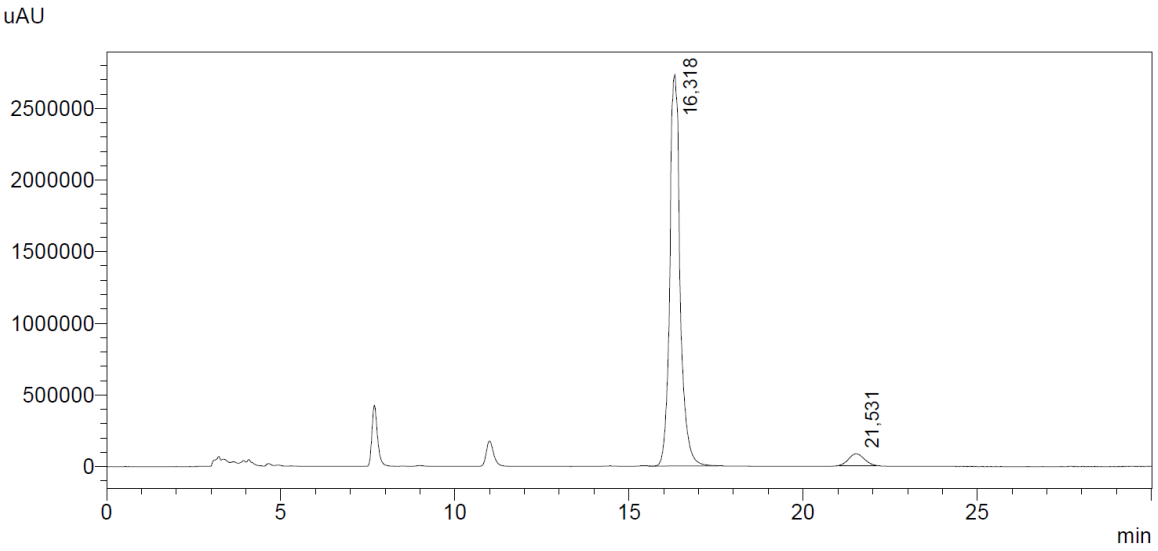
Peak#	Ret. Time	Area%
1	13,509	97,912
2	14,828	2,088
Total		100,000

1n (3*R*,4*R*)-4-(Naphthalen-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 14)

Racemic mixture



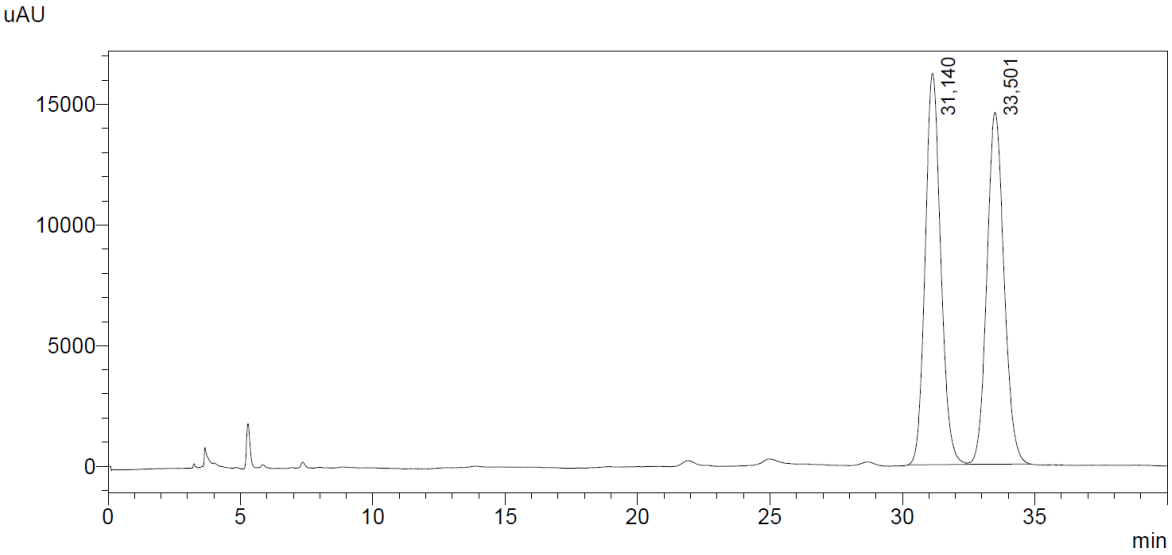
Enantiomerically enriched mixture



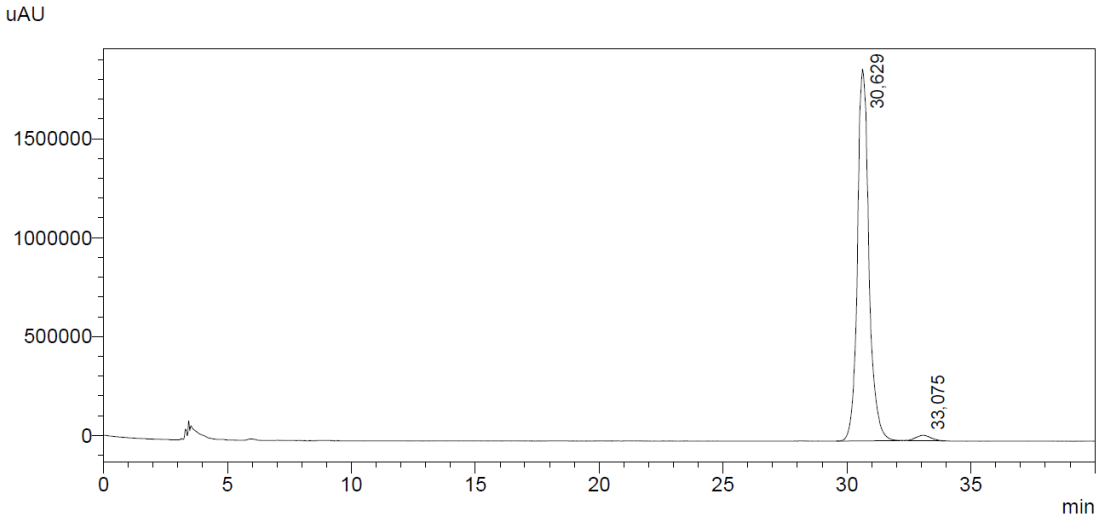
Peak#	Ret. Time	Area%
1	16,318	95,808
2	21,531	4,192
Total		100,000

1o (3*R*,4*S*)-4-(Furan-2-yl)-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Table 2, entry 15)

Racemic mixture



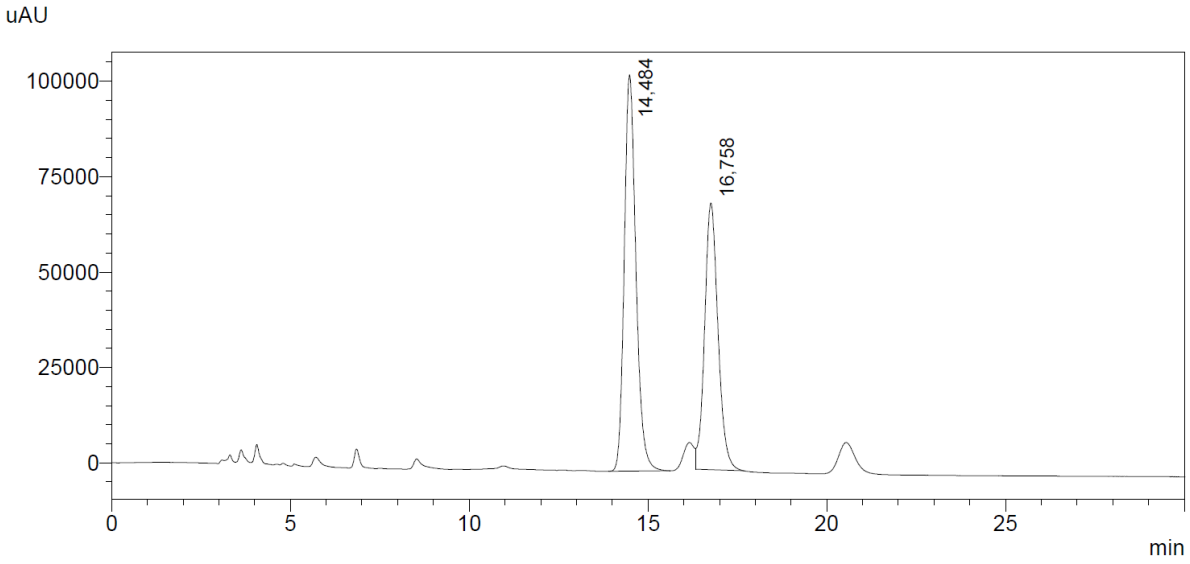
Enantiomerically enriched mixture



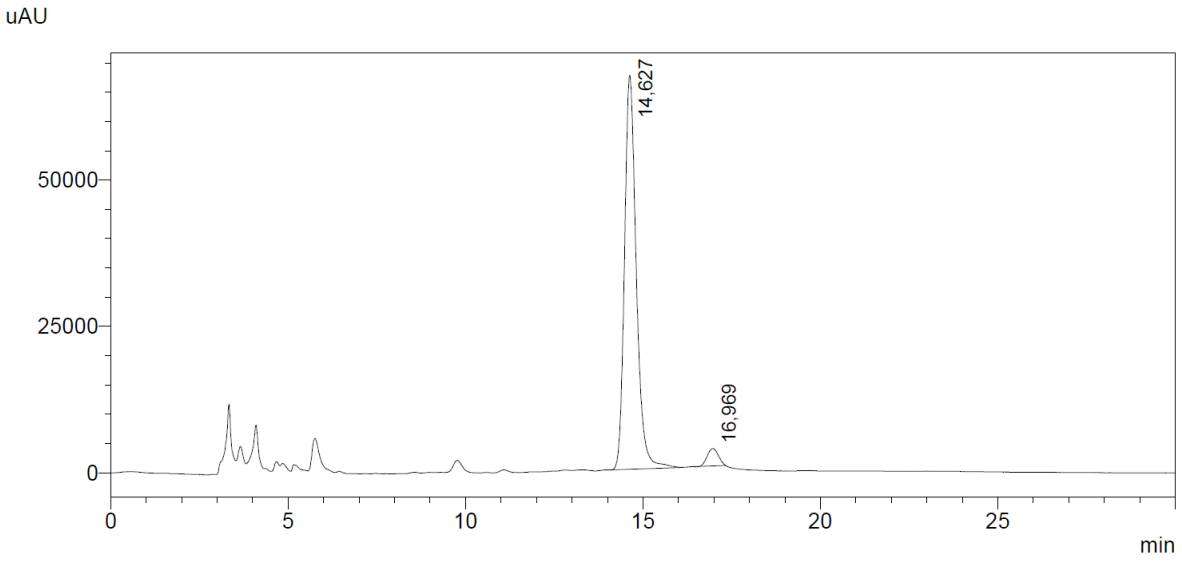
Peak#	Ret. Time	Area%
1	30,629	98,125
2	33,075	1,875
Total		100,000

1p (3*R*,4*R*)-3-(2-(4-Fluorophenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Racemic mixture



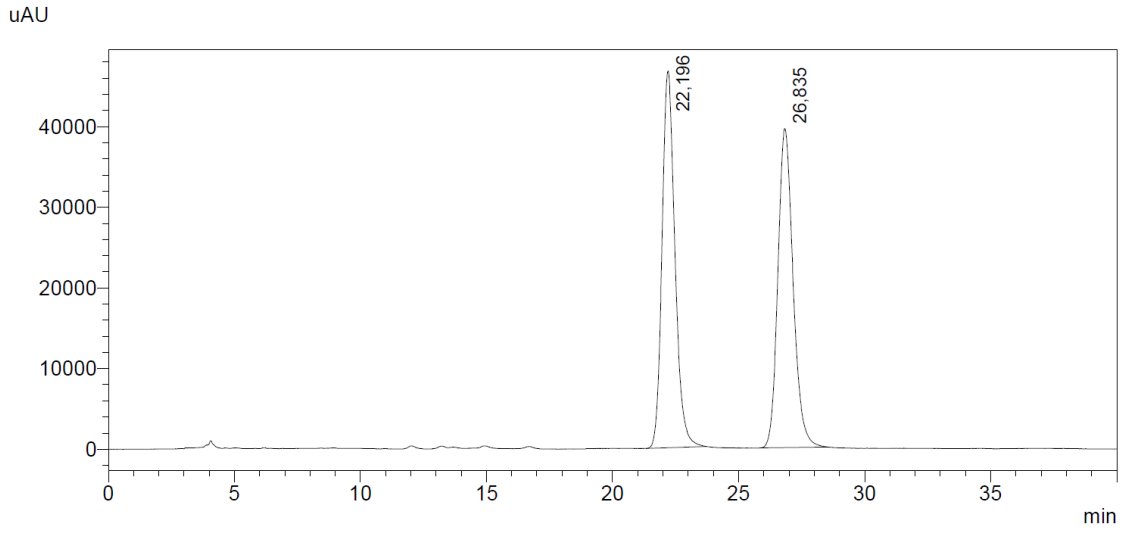
Enantiomerically enriched mixture



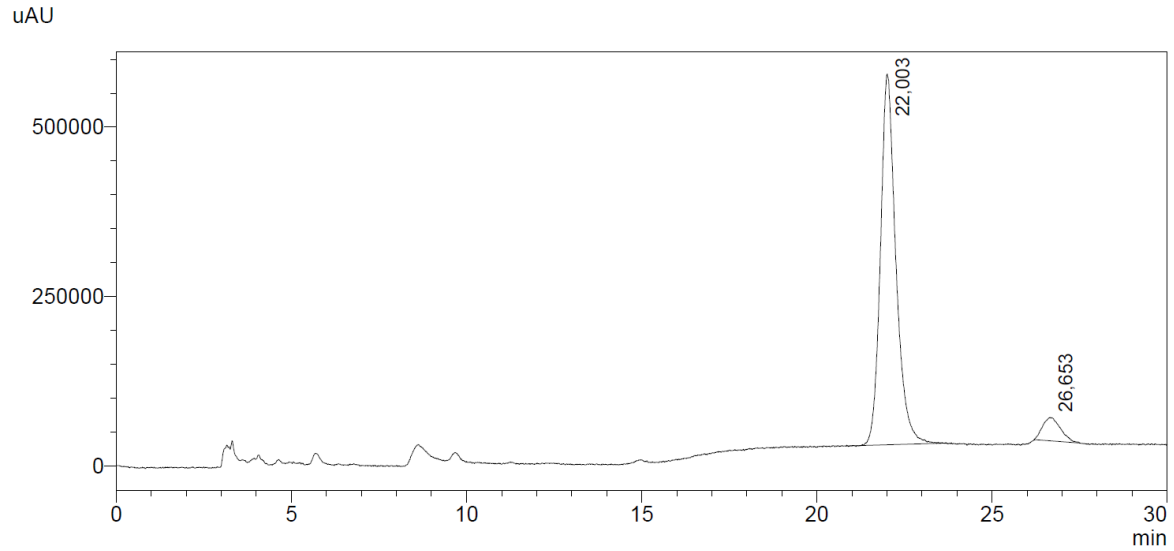
Peak#	Ret. Time	Area%
1	14,627	96,060
2	16,969	3,940
Total		100,000

1q (3*R*,4*R*)-3-(2-(4-Methoxyphenyl)-2-oxoethyl)-4-phenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Racemic mixture



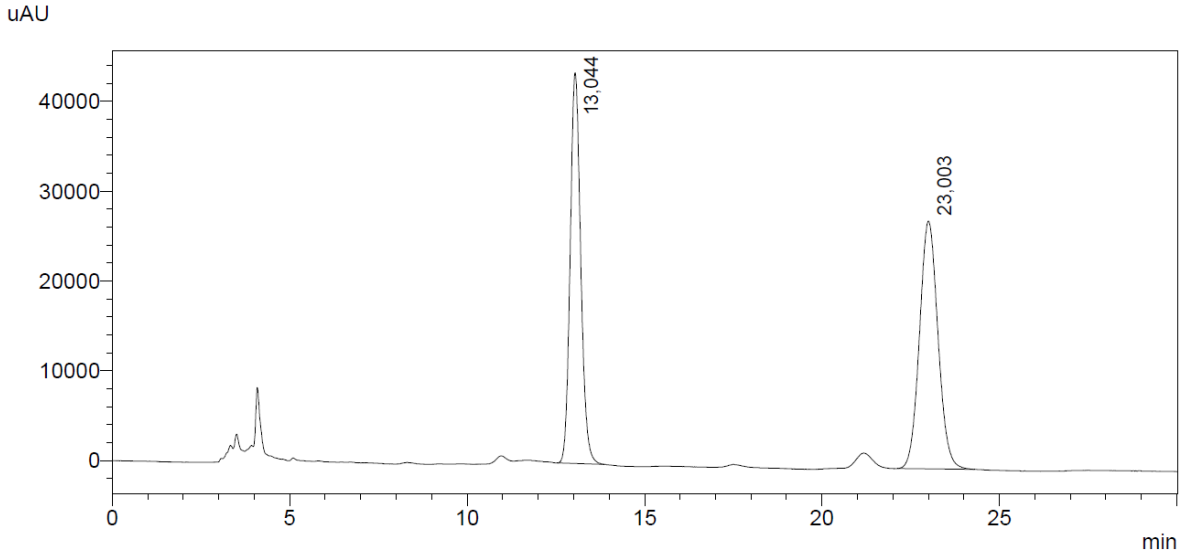
Enantiomerically enriched mixture



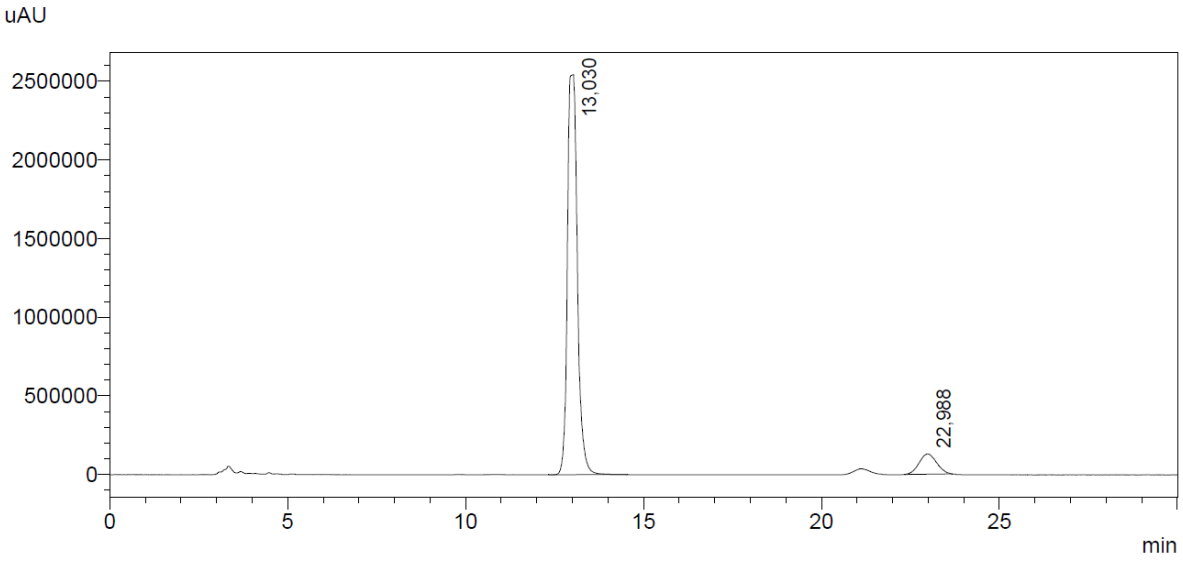
Peak#	Ret. Time	Area%
1	22,003	93,095
2	26,653	6,905
Total		100,000

1r (3*R*,4*R*)-4-(4-Chlorophenyl)-7,7-dimethyl-3-(2-oxo-2-phenylethyl)-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Racemic mixture



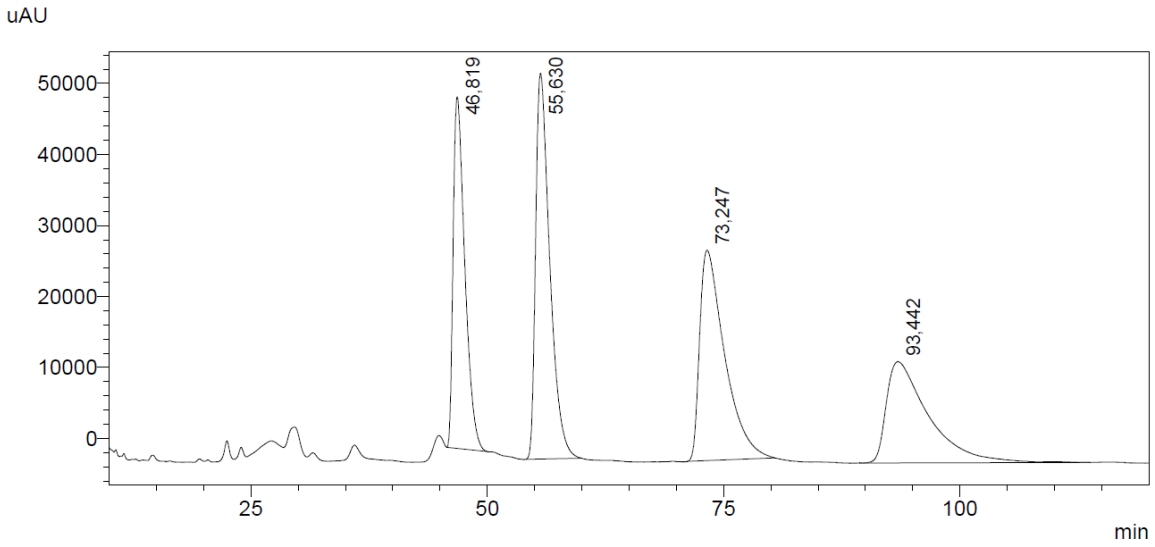
Enantiomerically enriched mixture



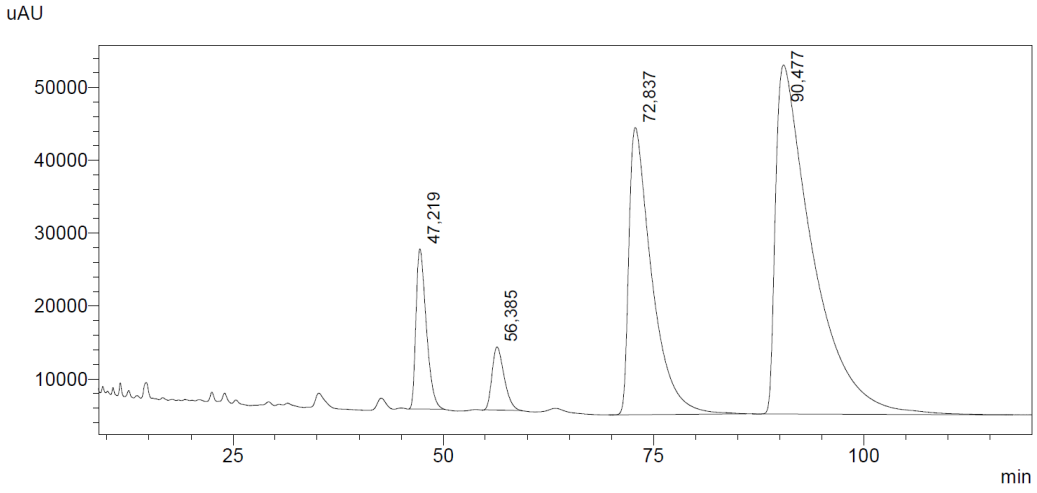
Peak#	Ret. Time	Area%
1	13,030	91,869
2	22,988	8,131
Total		100,000

1s (3*R*,4*R*)-3-(2-Oxo-2-phenylethyl)-4,7-diphenyl-4,6,7,8-tetrahydro-2*H*-chromene-2,5(3*H*)-dione (Scheme 3)

Racemic mixture



Enantiomerically enriched mixture



Peak#	Ret. Time	Area%
1	47,219	7,547
2	56,385	3,507
3	72,837	30,185
4	90,477	58,761
Total		100,000