Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

NHC-mediated enantioselective formal [4+2] cycloadditions of alkylarylketenes and β,γ-unsaturated α-ketocarboxylic esters and amides

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SUPPORTING INFORMATION

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I General Information

Reactions involving moisture sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques in addition to dry solvents. All glassware used was flame dried and cooled under vacuum. Solvents (CH_2Cl_2, toluene, and Et_2O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40-60 °C. All other solvents were used as supplied without further purification unless stated otherwise. Unless stated chemicals were purchased from Acros-UK, Alfa Aeasar, Apollo Sientific, Fluorochem, Sigma-Aldrich, or TCI UK and used without further purification. Potassium bis(trimethylsilyl)amide (KHMDS) was used as a 0.5M solution in toluene as supplied (Aldrich). Triethylamine for ketene synthesis was distilled from CaH_2 before use. Where necessary, any requisite aldehydes were purified by Kugelrohr distillation under reduced pressure prior to use. Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C to −10 °C were obtained using ice/brine bath. Reflux conditions were obtained using either an oil bath equipped with a contact thermometer or a DrySyn heating plate equipped with a contact thermometer. *In vacuo* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller. Analytical thin layer chromatography (TLC) was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash silica chromatography was performed on Kieselgel 60 silica in the solvent system stated. ^{1}H, ^{13}C and ^{19}F nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz, ^{1}H, 75 MHz ^{13}C and 282 MHz ^{19}F), a Bruker Avance II 400 (400 MHz, ^{1}H, 100 MHz ^{13}C and 376 MHz ^{19}F) or a Bruker Ultrashield 500 (500 MHz, ^{1}H, 125 MHz ^{13}C and 470 MHz) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz and reported high to low. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets, dt (doublet of triplets), dq (doublet of quartets), td (triplet of doublets), dqt (doublet of quartets of triplets), dqd (doublet of quartets of doublets), qd (quartet of doublets), dquintet (doublet of quintets) and sept (septet). The abbreviation *Ph* is used to denote phenyl, br to denote broad and app to denote

apparent. Infrared spectra (μ_{max}) were recorded on either a Perkin-Elmer Spectrum GX FT-IR spectrometer using either thin films on NaCl plates, KBr discs or a Shimadzu IRAffinity-1 using a Pike attenuated total reflectance (ATR) accessory. Only characteristic absorbances are quoted. Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected. Dec refers to decomposition. HPLC analyses were obtained on a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector. Separation was achieved using the DACIEL CHIRALPAK or CHIRALCEL column stated. All chiral HPLC traces were compared to the authentic racemic spectrum prepared in analogous fashion. Mass spectrometric (m/z) data were acquired by electrospray ionisation (ESI), electron impact (EI), chemical ionisation (CI), atmospheric solids analysis probe (ASAP) or nanospray ionisation (NSI) either at the University of St Andrews Mass Spectrometry facility ([A] quoted) or at the EPSRC National Mass Spectrometry Service Centre, Swansea ([A]+ or [A]- quoted). At the University of St Andrews, high resolution ESI was carried out on a Micromass LCT spectrometer and low and high resolution EI and CI were carried out on a Micromass GCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, high resolution ESI and NSI were carried out on a Finnigan MAT 900 XLT or a Finnigan MAT 95 XP. Values are quoted as a ratio of mass to charge in Daltons. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at 20 °C.

All alkylarylketenes were prepared according to literature procedures.[1]

All γ-substituted-β,γ-unsaturated α-ketoesters and α-ketoamides were prepared according to procedure previously reported by our group.[2]

II General Experimental Procedures

General Procedure 1: NHC-Mediated formal [4+2] cycloaddition protocol

To a flame dried Schlenk flask under an atmosphere of argon was added azolium salt (0.0245 mmol), base (0.0221 mmol) and toluene (1.5 mL) and the resultant suspension was stirred at rt for 30 minutes. The requisite ketoester (0.245 mmol) was

added either as a solid with toluene (1.5 mL) added to wash any residual solid into the reaction mixture, or as a solution in toluene (1.5 mL). As soon as the addition of the ketoester was complete, a solution of the desired ketene (0.319 mmol or 0.588 mmol) in toluene (4 mL) was added over 2 h *via* syringe pump. Once the addition was complete the solution was left to stir at rt overnight before concentration *in vacuo* to give the crude product. Purification *via* column chromatography on silica gel gave the title compound.

III Experimental Procedures

Catalyst and Base Optimisation

Table 1 Entry 1: Following *general procedure* **1**, imidazolinium salt **2** (14.0 mg, 0.0245 mmol), KHMDS (0.05 mL, 0.5M in toluene, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (87:13 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*R*,4*R*)-8** and **(*anti*)-8** (46.4 mg, 54%) as a colourless solid; Chiral HPLC **(3*R*,4*R*)-8** Chiralpak AS-H (5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 14.1 min, t_R(3*R*,4*R*): 27.1 min, 10% ee; **(*anti*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 15.7 min, t_R(3*S*,4*R*): 29.1 min, <5% ee.

Table 1 Entry 2: Following *general procedure* **1**, triazolium salt **3** (14.0 mg, 0.0245 mmol), KHMDS (0.05 mL, 0.5M in toluene, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (87:13 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*S*,4*S*)-8** and **(3*R*,4*S*)-8** (29.1 mg. 34%) as a colourless solid; Chiral HPLC **(3*S*,4*S*)-8** Chiralpak AS-H (5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 14.2 min, t_R(3*R*,4*R*): 27.3 min, 16% ee; **(3*R*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 15.8 min, t_R(3*S*,4*R*): 30.3 min, 24% ee.

Table 1 Entry 3: Following *general procedure* **1**, triazolium salt **3** (14.0 mg, 0.0245 mmol), Cs_2CO_3 (7.2 mg, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319

mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (68:32 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*S*,4*S*)-8** and **(3*R*,4*S*)-8** (12.0 mg, 14%) as a colourless solid; Chiral HPLC **(3*S*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 17.9 min, t_R(3*R*,4*R*): 36.4 min, 89% ee; **(3*R*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 20.4 min, t_R(3*S*,4*R*): 41.5 min, 84% ee.

Table 1 Entry 4: Following *general procedure* **1**, triazolium salt **4** (14.0 mg, 0.0245 mmol), KHMDS (0.05 mL, 0.5M in toluene, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (98:2 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactone **(*syn*)-8** (36.8 mg, 47%) as a colourless solid; Chiral HPLC **(*syn*)-8** Chiralpak AS-H (5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 14.1 min, t_R(3*R*,4*R*): 26.9 min, <5% ee.

Table 1 Entry 8: Following *general procedure* **1**, triazolium salt **1** (14.0 mg, 0.0245 mmol), KHMDS (0.05 mL, 0.5M in toluene, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (61:39 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*R*,4*R*)-8** and **(3*R*,4*S*)-8** (44.5 mg. 52%) as a colourless solid; Chiral HPLC **(3R,4R)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 17.4 min, t_R(3*R*,4*R*): 32.7 min, 88% ee; **(3*R*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 19.1 min, t_R(3*S*,4*R*): 36.0 min, 17% ee.

Table 1 Entry 9: Following *general procedure* **1**, triazolium salt **1** (14.0 mg, 0.0245 mmol), Cs_2CO_3 (7.2 mg, 0.0221 mmol) with ethylphenylketene **7** (47.0 mg, 0.319 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (67:33 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*R*,4*R*)-8** and **(3*R*,4*S*)-8** (37.8 mg, 44%) as a colourless solid; **(3*R*,4*R*)-8** and **(3*R*,4*S*)-8** Chiral HPLC *syn* **(3*R*,4*R*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 17.4 min, t_R(3*R*,4*R*):

34.1 min, 96% ee; **(3*R*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 19.6 min, t_R(3*S*,4*R*): 38.5 min, 43% ee.

Table 1 Entry 10: Following *general procedure* **1**, triazolium salt **1** (14.0 mg, 0.0245 mmol), Cs_2CO_3 (7.2 mg, 0.0221 mmol) with ethylphenylketene **7** (86.0 mg, 0.588 mmol) and ketoester **6** (50.0 mg, 0.245 mmol) at rt overnight gave the crude product (66:34 dr *syn*:*anti*). Purification *via* column chromatography on silica gel (eluent petrol:EtOAc 90:10) gave lactones **(3*R*,4*R*)-8** and **(3*R*,4*S*)-8** (68.7 mg, 80%) as a colourless solid; Chiral HPLC **(3*R*,4*R*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*S*,4*S*): 16.2 min, t_R(3*R*,4*R*): 35.0 min, 96% ee; **(3*R*,4*S*)-8** Chiralpak AS-H (3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm) t_R(3*R*,4*S*): 18.5 min, t_R(3*S*,4*R*): 35.0 min, 19% ee.

IV nOe Studies on compounds 21 and 29

nOe Studies on isomeric dihydropyranone 21

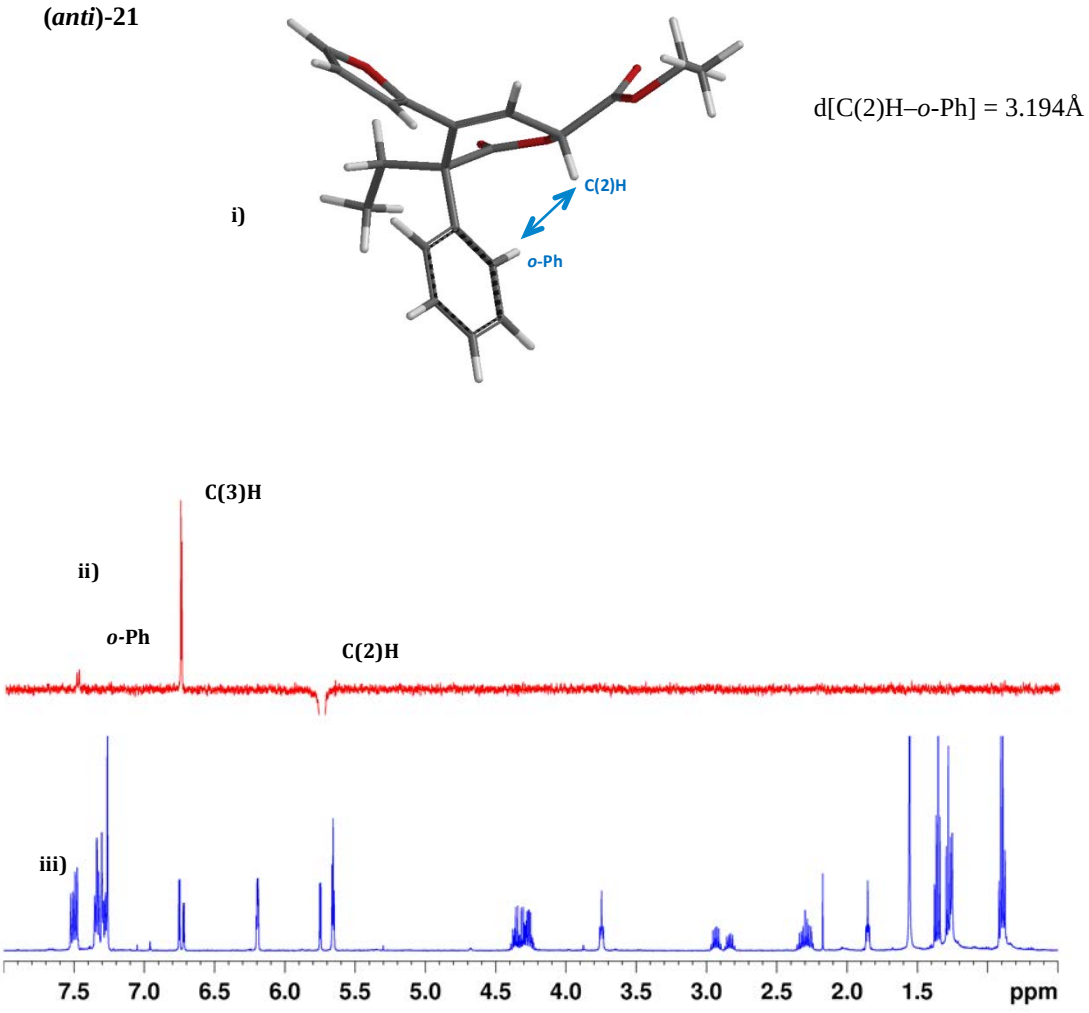


Figure 1: (i) MMFF optimised geometries of **(*anti*)-21** show the distance between C(2)H and *o*-Ph to be 3.194Å; (ii) 1D gradient NOESY shows strong reciprocal nOe between C(2)H and *o*-Ph (iii) ^{1}H NMR spectrum of **21** in $CDCl_3$.

nOe Studies on *anti*-dihydropyranone 29

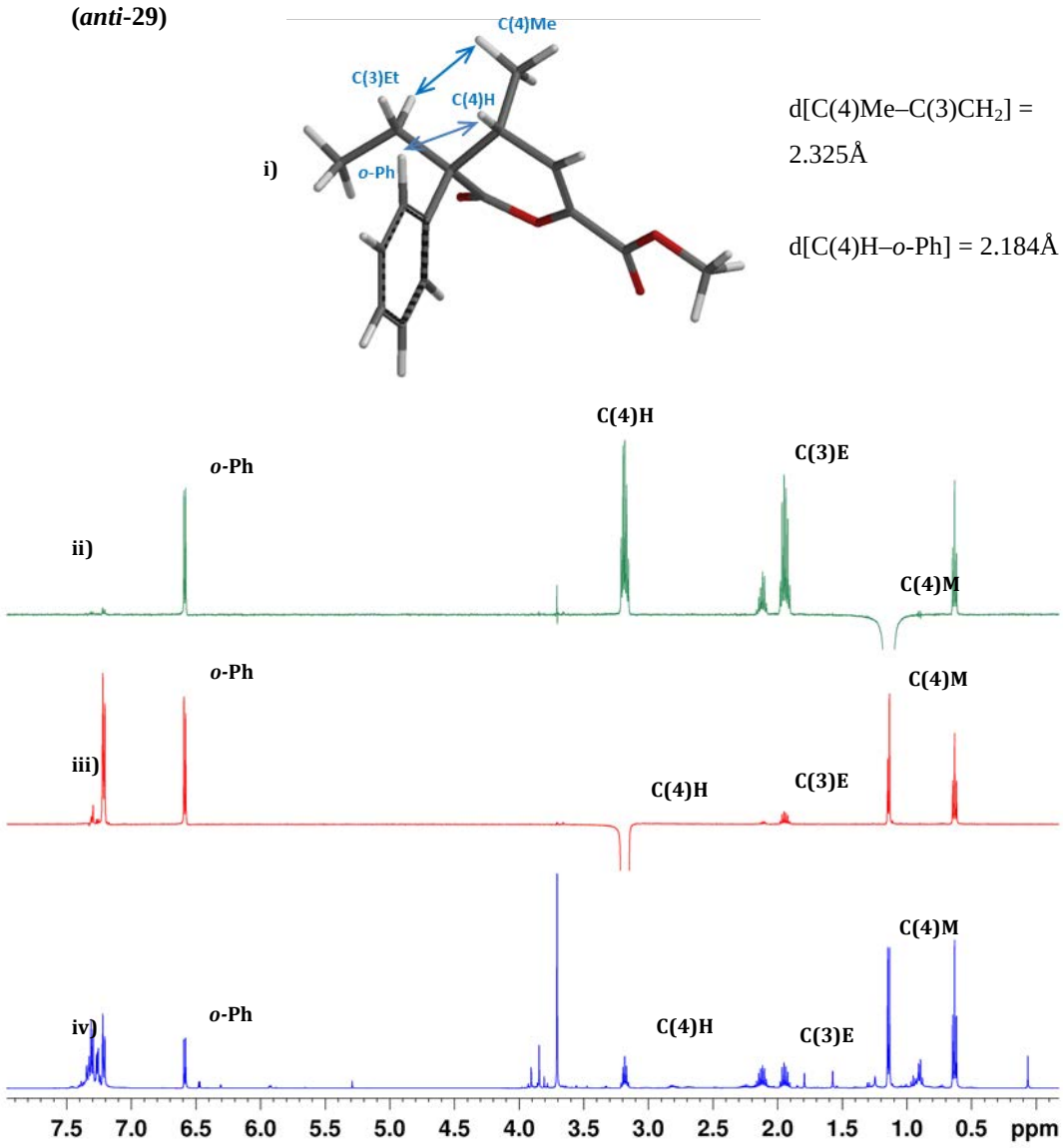
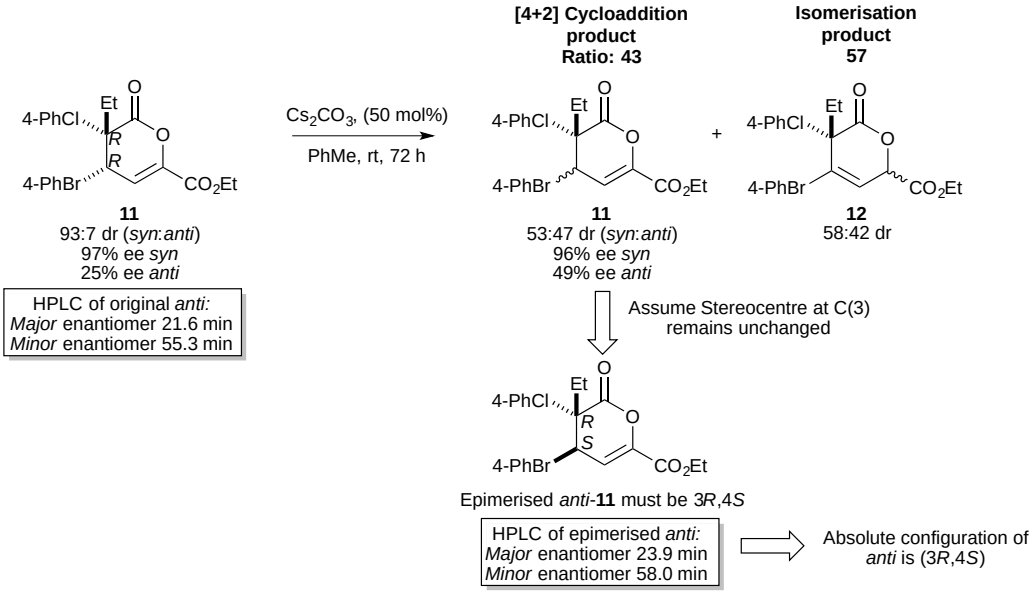


Figure 1: (i) MMFF optimised geometries of **(*anti*)-29** show the distances between C(4)Me and $C(3)CH_2$ and C(4)H and *o*-Ph to be 2.325Å and 2.184Å respectively; (ii) 1D gradient NOESY shows strong reciprocal NOE between C(4)Me and $C(3)CH_2$ (iii) 1D gradient NOESY shows strong reciprocal NOE between C(4)H and *o*-Ph (iv) ^{1}H NMR spectrum of **29** in $CDCl_3$.

V Absolute configuration of *anti*-dihydropyranone 11

The base catalysed isomerisation process allows the absolute configuration of the *anti*-dihydropyranone products to be deduced. From the known relative and absolute configuration of *syn*-dihydropyranone **11**, control experiments show that the ee of *syn*-dihydropyranone **11** remains unchanged after treatment with Cs_2CO_3 as presumably there is only epimerisation from the *syn* to the thermodynamically more stable *anti*-diastereoisomer and little or no epimerisation of the *anti* to the *syn*-diastereoisomer. Presumably in this base catalysed isomerisation process, the configuration of the all carbon quaternary stereocentre at C(3) remains unchanged (assuming that there is no retro Michael reaction). As a result any *anti*-dihydropyranone arising from the *syn*-dihydropyranone must have the (3*R*,4*S*) configuration (Scheme **1**).



Scheme 1: Utilisation of the base catalysed epimerisation to determine the absolute configuration of the *anti* dihydropyranone

HPLC analysis of *anti*-dihydropyranone **11** from this epimerisation process showed that the retention times of the major and minor enantiomer matched those of the synthesised *anti*-dihydropyranone **11** (Figure **2**). Based on the epimerisation mechanism shown above, the absolute configuration of *anti*-dihydropyranone **11** which was epimerised from *syn*-dihydropyranone **11** is (3*R*,4*S*). Therefore, synthesised *anti*-dihydropyranone **11** also has the (3*R*,4*S*) absolute configuration.

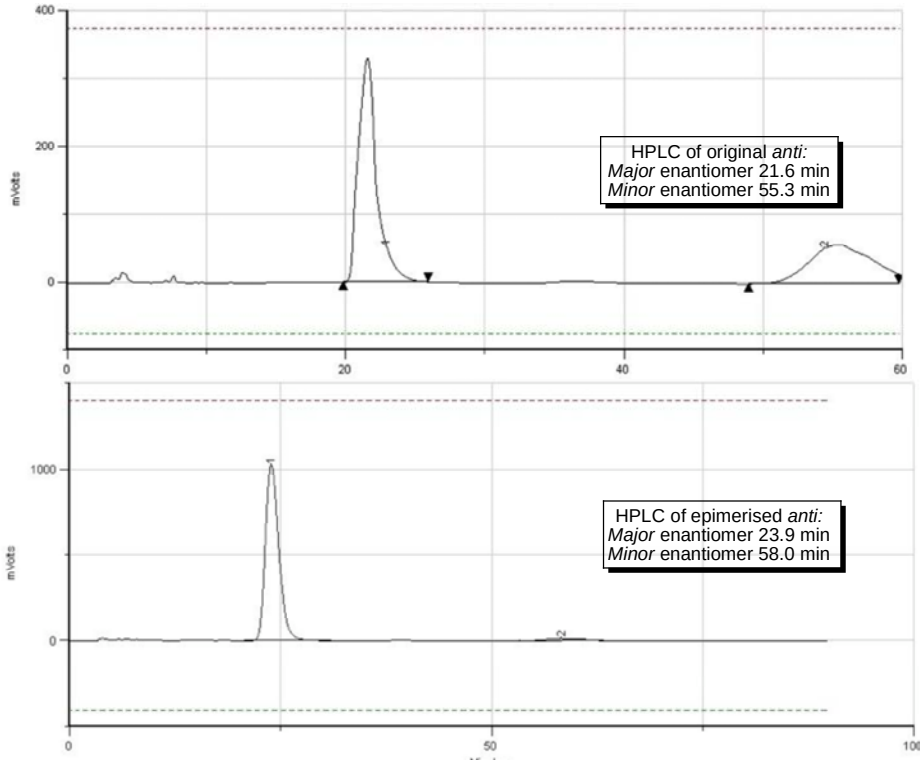


Figure 2: HPLC traces comparing synthesised *anti*-dihydropyranone with *anti*-dihydropyranone epimerised from *syn*-dihydropyranone

VI List of Unsuccessful Substrates

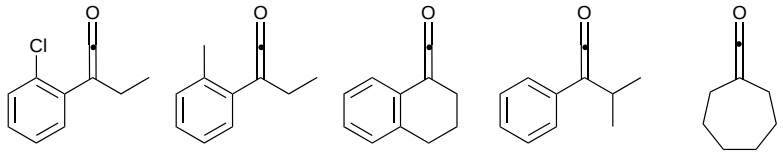


Figure 3: Ketenes that gave no conversion to cycloaddition products under optimised conditions

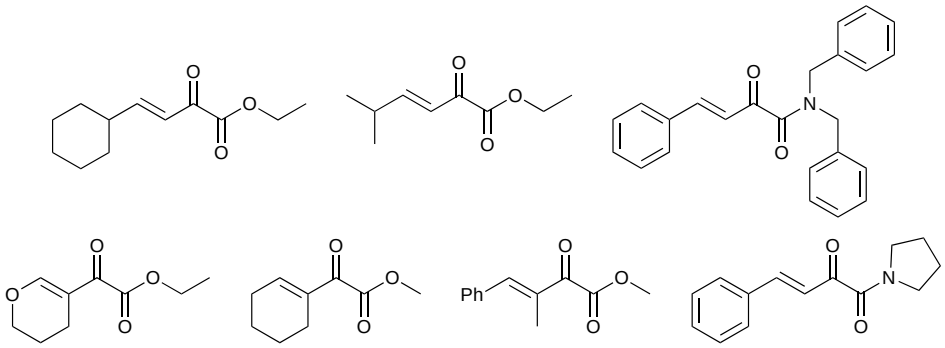


Figure 4: α-Ketocarboxylate substrates that gave no conversion to cycloaddition products under optimised conditions

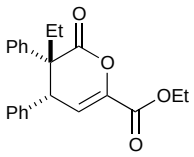
β-Methylene α-ketocarboxylate substrates were prepared according to literature procedures[3]

[1] a) B. L. Houdous and G. C. Fu, *J. Am. Chem. Soc*. 2002, **124**, 1578; b) L. M. Baigrie, H. R. Seiklay and T. T. Tidwell, *J. Am. Chem. Soc.* 1985, **107**, 5391; c) A. Sudo, S. Uchino and T. Endo, *J. Polym. Sci. Part A: Polym. Chem.* 2001, **39**, 2093; d) J. Douglas, J. E. Taylor, G. Churchill, A. M. Z. Slawin amd A. D. Smith, *J. Org. Chem.* 2013, *accepted*

[2] D. Belmessieri, L. C. Morrill, C. Simal, A. M. Z. Slawin and A. D. Smith, *J. Am. Chem. Soc.*, 2011, **133**, 2714

[3] a) S. C. M. Fell, M. J. Pearson, G. Burton and J. S. Elder, *J. Chem. Soc. Perkin. Trans. 1*, 1995, 1483; b) H. Stetter and G. Lorenz, *Chem. Ber.*, 1985, **118**, 1115

VII Crystal data and structure refinement for enantiopure (3*R*,4*R*)-8



(3*R*,4*R*)-8

A. Crystal Data

Empirical Formula	$C_{22}H_{22}O_4$
Formula Weight	350.41
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.200 X 0.100 X 0.050 mm
Crystal System	monoclinic
Lattice Type	Primitive
Lattice Parameters	a = 12.174(6) Å b = 6.293(3) Å c = 12.398(6) Å β = 98.90(2) ° V = 938.3(8) Å^3
Space Group	$P2_1$ (#4)
Z value	2
D_{calc}	1.240 g/cm^3
F_{000}	372.00
μ(CuKα)	6.853 cm^{-1}

B. Intensity Measurements

Diffractometer	Saturn70
Radiation	CuKα (λ = 1.54187 Å)
Voltage, Current	40kV, 20mA
Temperature	-100.0°C
Detector Aperture	70 x 70 mm
ω oscillation Range	1.0 - 0.0°
Pixel Size	0.034 mm
$2\theta_{max}$	137.0°
No. of Reflections Measured	Total: 9926 Unique: 3143 (R_{int} = 0.0642) Friedel pairs: 1387
Corrections	Lorentz-polarization Absorption (trans. factors: 0.688 - 0.966)

C. Structure Solution and Refinement

Structure Solution	Direct Methods
Refinement	Full-matrix least-squares on F^2

Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.0898 \cdot P)^2 + 0.1250 \cdot P]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	137.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3143
No. Variables	235
Reflection/Parameter Ratio	13.37
Residuals: R1 (I>2.00σ(I))	0.0508
Residuals: R (All reflections)	0.0548
Residuals: wR2 (All reflections)	0.1471
Goodness of Fit Indicator	1.045
Flack Parameter (Friedel pairs = 1387)	0.1(3)
Max Shift/Error in Final Cycle	0.003
Maximum peak in Final Diff. Map	0.28 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.19 $e^-/Å^3$

Table **1**. Atomic coordinates and B_{iso}/B_{eq} for **8**

atom	x	y	z	B_{eq}
O1	0.3233(2)	0.5315(3)	0.1670(2)	3.77(4)
O22	0.3534(2)	0.2975(4)	-0.0842(2)	4.69(5)
O2	0.3216(2)	0.6344(3)	0.3349(2)	4.31(4)
O21	0.4087(2)	0.6151(4)	-0.0130(2)	5.80(6)
C2	0.3083(2)	0.4878(4)	0.2723(2)	3.29(5)
C3	0.2875(2)	0.2583(4)	0.3013(2)	2.84(4)
C4	0.2185(2)	0.1407(4)	0.2023(2)	3.06(4)
C5	0.2680(2)	0.1861(4)	0.1009(3)	3.51(5)
C6	0.3149(2)	0.3736(5)	0.0886(2)	3.51(5)
C7	0.4072(2)	0.1590(4)	0.3224(2)	3.16(5)
C8	0.4840(3)	0.2481(4)	0.4204(3)	4.03(6)
C9	0.2297(2)	0.2372(4)	0.4018(2)	3.07(5)
C10	0.2340(2)	0.0412(4)	0.4556(2)	3.40(5)
C11	0.1781(3)	0.0081(4)	0.5437(3)	3.81(5)
C12	0.1178(2)	0.1702(5)	0.5809(3)	3.96(5)
C13	0.1113(2)	0.3637(5)	0.5285(3)	4.16(6)
C14	0.1660(2)	0.3976(5)	0.4395(3)	3.67(5)
C15	0.0944(2)	0.1938(4)	0.1835(2)	3.20(5)
C16	0.0547(3)	0.3871(5)	0.1395(3)	4.25(6)
C17	-0.0588(3)	0.4323(6)	0.1233(3)	5.02(7)
C18	-0.1327(3)	0.2837(7)	0.1501(3)	5.22(7)
C19	-0.0949(3)	0.0896(7)	0.1915(3)	5.54(8)
C20	0.0186(3)	0.0458(5)	0.2090(3)	4.34(6)
C21	0.3649(3)	0.4451(5)	-0.0061(3)	4.22(6)
C23	0.4115(3)	0.3378(8)	-0.1756(3)	5.84(9)
C24	0.4002(3)	0.1513(11)	-0.2435(4)	7.93(12)

Table **2**. Atomic coordinates and Biso involving hydrogen atoms for **8**

atom	x	y	z	Biso
H4	0.2259	-0.0153	0.2168	3.67
H5	0.2658	0.0809	0.0457	4.21
H7A	0.4001	0.0039	0.3326	3.80
H7B	0.4425	0.1810	0.2565	3.80
H8A	0.4959	0.4001	0.4094	4.83
H8B	0.5555	0.1736	0.4286	4.83
H8C	0.4501	0.2279	0.4864	4.83
H10	0.2760	-0.0715	0.4313	4.08
H11	0.1815	-0.1268	0.5784	4.57
H12	0.0809	0.1487	0.6422	4.76
H13	0.0690	0.4752	0.5534	5.00
H14	0.1600	0.5317	0.4039	4.40
H16	0.1055	0.4898	0.1202	5.10
H17	-0.0849	0.5656	0.0938	6.02
H18	-0.2100	0.3149	0.1400	6.27
H19	-0.1462	-0.0146	0.2082	6.65
H20	0.0442	-0.0875	0.2389	5.20
H23A	0.3790	0.4626	-0.2175	7.00
H23B	0.4910	0.3671	-0.1492	7.00
H24A	0.4363	0.0306	-0.2024	9.51
H24B	0.4356	0.1765	-0.3082	9.51
H24C	0.3212	0.1199	-0.2662	9.51

Table **3**. Bond lengths (Å) for **8**

atom	atom	distance	atom	atom	distance
O1	C2	1.373(4)	O1	C6	1.383(4)
O22	C21	1.334(4)	O22	C23	1.448(5)
O2	C2	1.200(3)	O21	C21	1.204(4)
C2	C3	1.519(4)	C3	C4	1.562(4)
C3	C7	1.570(4)	C3	C9	1.529(4)
C4	C5	1.502(4)	C4	C15	1.530(4)
C5	C6	1.330(4)	C6	C21	1.474(5)
C7	C8	1.521(4)	C9	C10	1.399(4)
C9	C14	1.397(4)	C10	C11	1.389(4)
C11	C12	1.378(4)	C12	C13	1.376(5)
C13	C14	1.390(5)	C15	C16	1.389(4)
C15	C20	1.382(4)	C16	C17	1.394(4)
C17	C18	1.374(5)	C18	C19	1.377(6)
C19	C20	1.392(4)	C23	C24	1.439(8)

Table **4**. Bond lengths involving hydrogens (Å) for **8**

atom	atom	distance	atom	atom	distance
C4	H4	1.000	C5	H5	0.950
C7	H7A	0.990	C7	H7B	0.990

C8	H8A	0.980	C8	H8B	0.980
C8	H8C	0.980	C10	H10	0.950
C11	H11	0.950	C12	H12	0.950
C13	H13	0.950	C14	H14	0.950
C16	H16	0.950	C17	H17	0.950
C18	H18	0.950	C19	H19	0.950
C20	H20	0.950	C23	H23A	0.990
C23	H23B	0.990	C24	H24A	0.980
C24	H24B	0.980	C24	H24C	0.980

Table **5**. Bond angles (°) for **8**

atom	atom	atom	angle	atom	atom	atom	angle
C2	O1	C6	121.19(19)	C21	O22	C23	115.9(3)
O1	C2	O2	115.9(3)	O1	C2	C3	117.8(2)
O2	C2	C3	126.0(3)	C2	C3	C4	110.70(19)
C2	C3	C7	103.47(18)	C2	C3	C9	113.0(2)
C4	C3	C7	108.36(19)	C4	C3	C9	109.91(19)
C7	C3	C9	111.21(19)	C3	C4	C5	109.3(2)
C3	C4	C15	114.5(2)	C5	C4	C15	110.23(19)
C4	C5	C6	119.9(3)	O1	C6	C5	122.9(3)
O1	C6	C21	110.2(3)	C5	C6	C21	126.9(3)
C3	C7	C8	115.3(2)	C3	C9	C10	118.5(2)
C3	C9	C14	124.0(3)	C10	C9	C14	117.4(3)
C9	C10	C11	121.3(3)	C10	C11	C12	120.2(3)
C11	C12	C13	119.5(3)	C12	C13	C14	120.7(3)
C9	C14	C13	120.9(3)	C4	C15	C16	121.7(3)
C4	C15	C20	119.8(3)	C16	C15	C20	118.4(3)
C15	C16	C17	120.8(3)	C16	C17	C18	119.9(3)
C17	C18	C19	120.0(3)	C18	C19	C20	120.1(3)
C15	C20	C19	120.8(3)	O22	C21	O21	124.4(3)
O22	C21	C6	110.8(3)	O21	C21	C6	124.7(3)
O22	C23	C24	107.5(4)				

Table **6**. Bond angles involving hydrogens (°) for **8**

atom	atom	atom	angle	atom	atom	atom	angle
C3	C4	H4	107.5	C5	C4	H4	107.5
C15	C4	H4	107.5	C4	C5	H5	120.0
C6	C5	H5	120.0	C3	C7	H7A	108.5
C3	C7	H7B	108.5	C8	C7	H7A	108.5
C8	C7	H7B	108.5	H7A	C7	H7B	107.5
C7	C8	H8A	109.5	C7	C8	H8B	109.5
C7	C8	H8C	109.5	H8A	C8	H8B	109.5
H8A	C8	H8C	109.5	H8B	C8	H8C	109.5
C9	C10	H10	119.3	C11	C10	H10	119.3
C10	C11	H11	119.9	C12	C11	H11	119.9
C11	C12	H12	120.3	C13	C12	H12	120.3
C12	C13	H13	119.6	C14	C13	H13	119.6
C9	C14	H14	119.6	C13	C14	H14	119.6

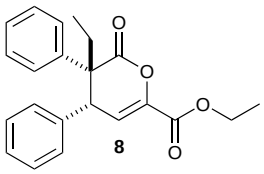
C15	C16	H16	119.6	C17	C16	H16	119.6
C16	C17	H17	120.1	C18	C17	H17	120.1
C17	C18	H18	120.0	C19	C18	H18	120.0
C18	C19	H19	120.0	C20	C19	H19	120.0
C15	C20	H20	119.6	C19	C20	H20	119.6
O22	C23	H23A	110.2	O22	C23	H23B	110.2
C24	C23	H23A	110.2	C24	C23	H23B	110.2
H23A	C23	H23B	108.5	C23	C24	H24A	109.5
C23	C24	H24B	109.5	C23	C24	H24C	109.5
H24A	C24	H24B	109.5	H24A	C24	H24C	109.5
H24B	C24	H24C	109.5				

Table **7**. Torsion Angles(O) for **8**
(Those having bond angles > 160 or < 20 degrees are excluded.)

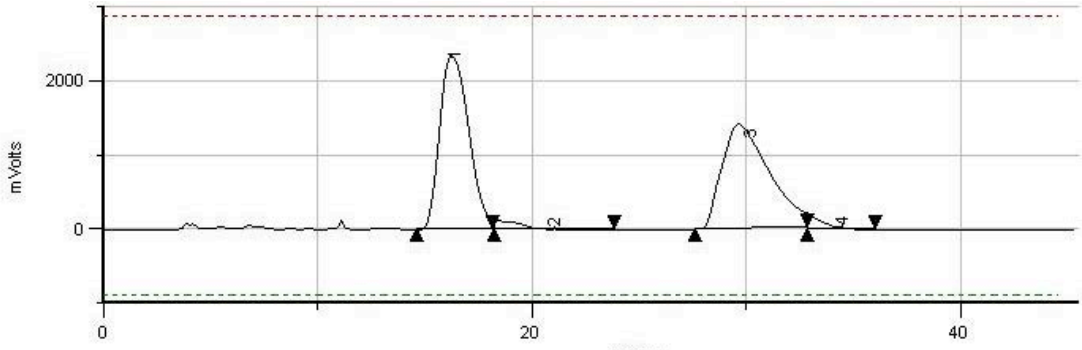
atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C2	O1	C6	C5	15.9(4)	C2	O1	C6	C21	-163.82(18)
C6	O1	C2	O2	177.27(19)	C6	O1	C2	C3	2.7(3)
C21	O22	C23	C24	173.1(2)	C23	O22	C21	O21	8.7(4)
C23	O22	C21	C6	-172.4(2)	O1	C2	C3	C4	-34.3(3)
O1	C2	C3	C7	81.6(3)	O1	C2	C3	C9	-158.08(17)
O2	C2	C3	C4	151.7(3)	O2	C2	C3	C7	-92.4(3)
O2	C2	C3	C9	28.0(3)	C2	C3	C4	C5	47.3(3)
C2	C3	C4	C15	-76.9(3)	C2	C3	C7	C8	65.5(3)
C2	C3	C9	C10	-161.92(17)	C2	C3	C9	C14	22.6(3)
C4	C3	C7	C8	-177.00(17)	C7	C3	C4	C5	-65.5(3)
C7	C3	C4	C15	170.26(17)	C4	C3	C9	C10	73.9(3)
C4	C3	C9	C14	-101.6(3)	C9	C3	C4	C5	172.78(16)
C9	C3	C4	C15	48.6(3)	C7	C3	C9	C10	-46.1(3)
C7	C3	C9	C14	138.43(19)	C9	C3	C7	C8	-56.1(3)
C3	C4	C5	C6	-33.3(3)	C3	C4	C15	C16	74.1(3)
C3	C4	C15	C20	-106.9(3)	C5	C4	C15	C16	-49.7(3)
C5	C4	C15	C20	129.3(2)	C15	C4	C5	C6	93.4(3)
C4	C5	C6	O1	1.6(4)	C4	C5	C6	C21	178.64(19)
O1	C6	C21	O22	-177.49(18)	O1	C6	C21	O21	1.4(4)
C5	C6	C21	O22	2.8(4)	C5	C6	C21	O21	-178.3(3)
C3	C9	C10	C11	-176.41(18)	C3	C9	C14	C13	176.83(18)
C10	C9	C14	C13	1.3(4)	C14	C9	C10	C11	-0.6(4)
C9	C10	C11	C12	-0.7(4)	C10	C11	C12	C13	1.4(4)
C11	C12	C13	C14	-0.8(4)	C12	C13	C14	C9	-0.6(4)
C4	C15	C16	C17	-179.8(2)	C4	C15	C20	C19	-179.3(2)
C16	C15	C20	C19	-0.3(4)	C20	C15	C16	C17	1.1(4)
C15	C16	C17	C18	-0.6(5)	C16	C17	C18	C19	-0.8(5)
C17	C18	C19	C20	1.7(5)	C18	C19	C20	C15	-1.2(5)

VIII HPLC and NMR Spectra

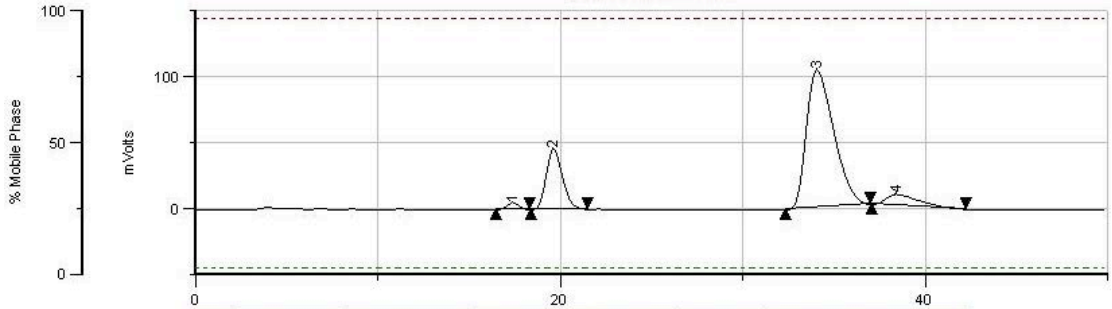
HPLC data compound **8**: *syn* Chiralpak AS-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 96% ee; *anti* Chiralpak AS-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 19% ee.



8

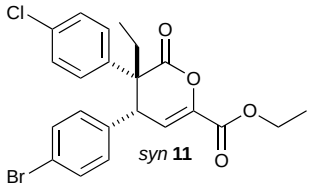


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	16.25	372784992.00	47.93	SL-320-RAC
2	1.00	*2	18.25	21901464.00	2.82	SL-320-RAC
3	1.00	*3	29.65	366004928.00	47.06	SL-320-RAC
4	1.00	*4	32.90	17004398.00	2.19	SL-320-RAC

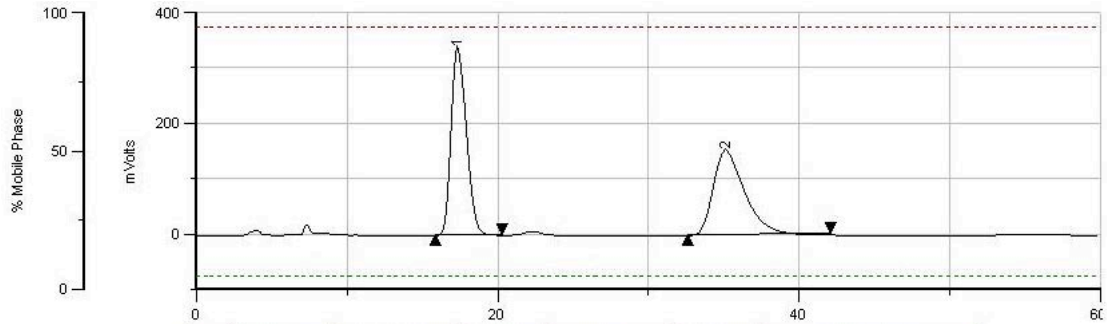


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	17.37	419793.41	1.65	SL-321-PC1-AS-H-3%ipoh
2	1.00	2	19.62	4782405.50	18.83	SL-321-PC1-AS-H-3%ipoh
3	1.00	3	34.07	18291760.00	72.03	SL-321-PC1-AS-H-3%ipoh
4	1.00	4	38.45	1901403.00	7.49	SL-321-PC1-AS-H-3%ipoh

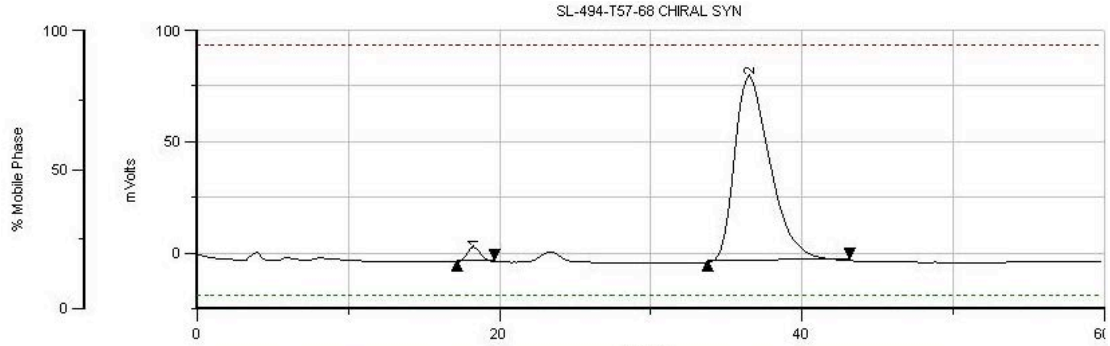
HPLC data compound **11**: *syn* Chiralpak AS-H 5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 95% ee.



syn **11**

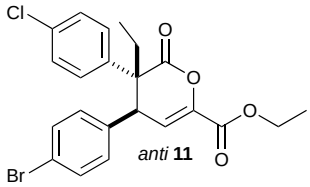


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	17.32	39890080.00	51.39	SL-493-T43-59 "SYN" AS-H
2	1.00	*2	35.14	37734220.00	48.61	SL-493-T43-59 "SYN" AS-H

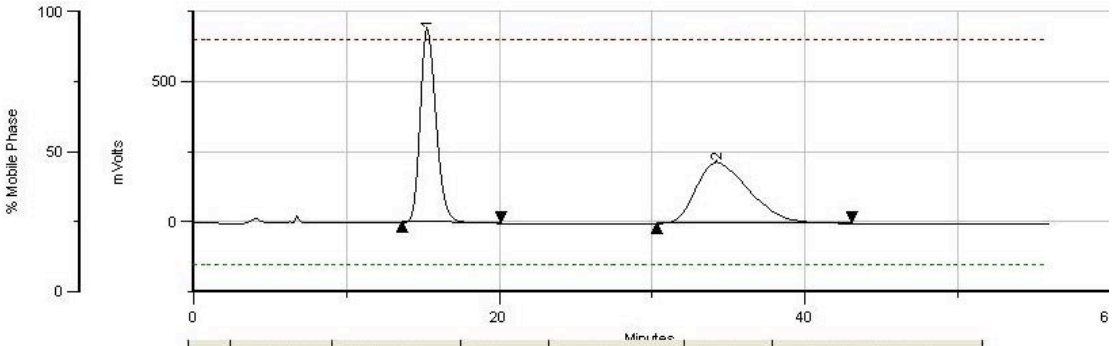


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	2.00	*1	18.28	672361.50	2.85	SL-494-T57-68 CHIRAL SYN
2	2.00	2	36.51	22909914.00	97.15	SL-494-T57-68 CHIRAL SYN

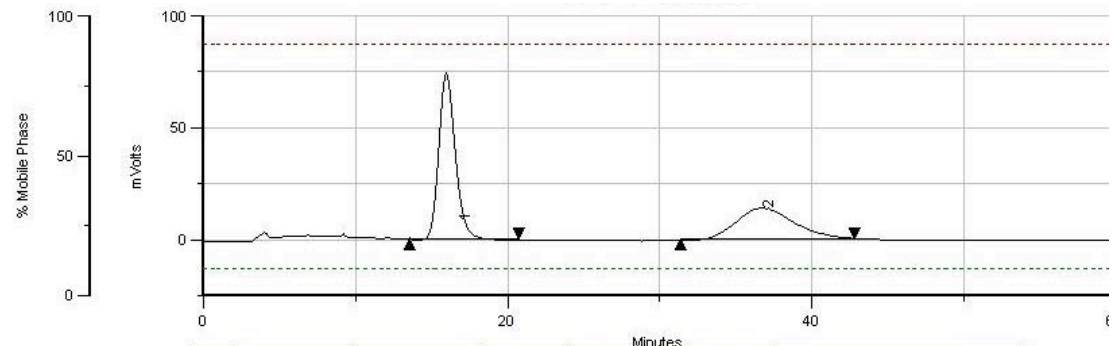
anti Chiralpak AS-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 18% ee.



anti **11**

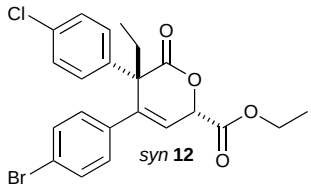


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	15.27	83632488.00	48.99	SL-493-T31-42 AS-H RAC
2	1.00	2	34.22	87093648.00	51.01	SL-493-T31-42 AS-H RAC

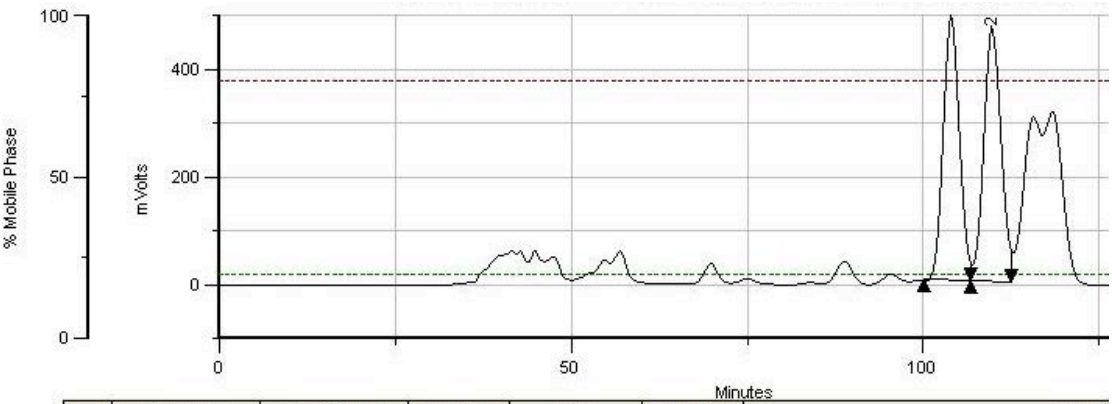


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	3.00	*1	15.96	9544399.00	58.60	SL-464-T37-48 CHIRAL ANTI
2	3.00	*2	36.65	6741832.50	41.40	SL-464-T37-48 CHIRAL ANTI

HPLC data compound **12**: *syn* Chiralpak AD-H 20% IPA:hexane, flowrate 0.1 mL min^{-1}, 254 nm, 88% ee.



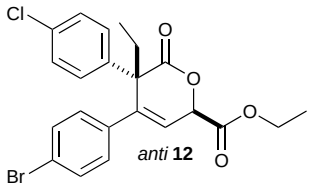
syn **12**



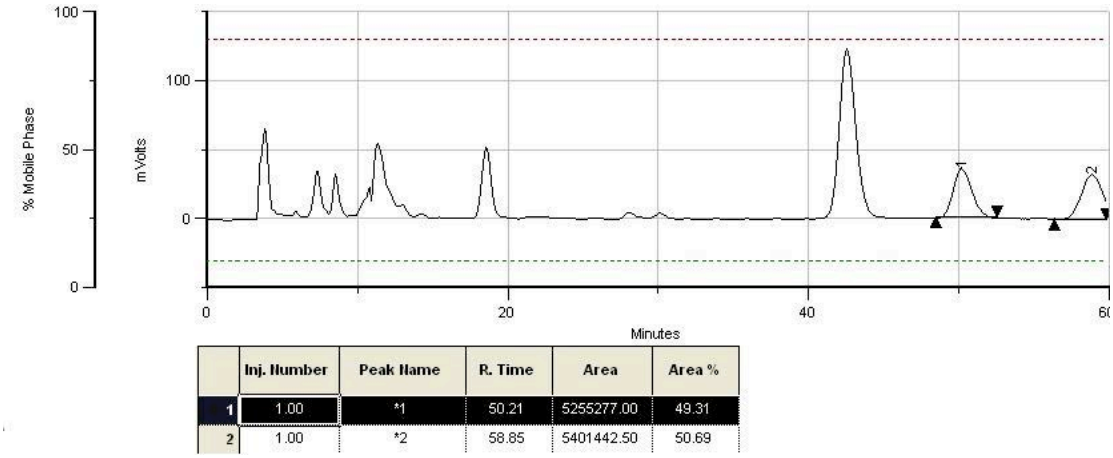
	Inj. Number	Peak Name	R. Time	Area	Area %	Sampl
1	1.00	*1	103.98	131752704.00	49.27	SL-801-T88-100 pClPhEtket+pBr Acc isomer p
2	1.00	2	109.79	135636928.00	50.73	SL-801-T88-100 pClPhEtket+pBr Acc isomer p

	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	103.19	517451168.00	93.89
2	1.00	2	109.25	33696660.00	6.11

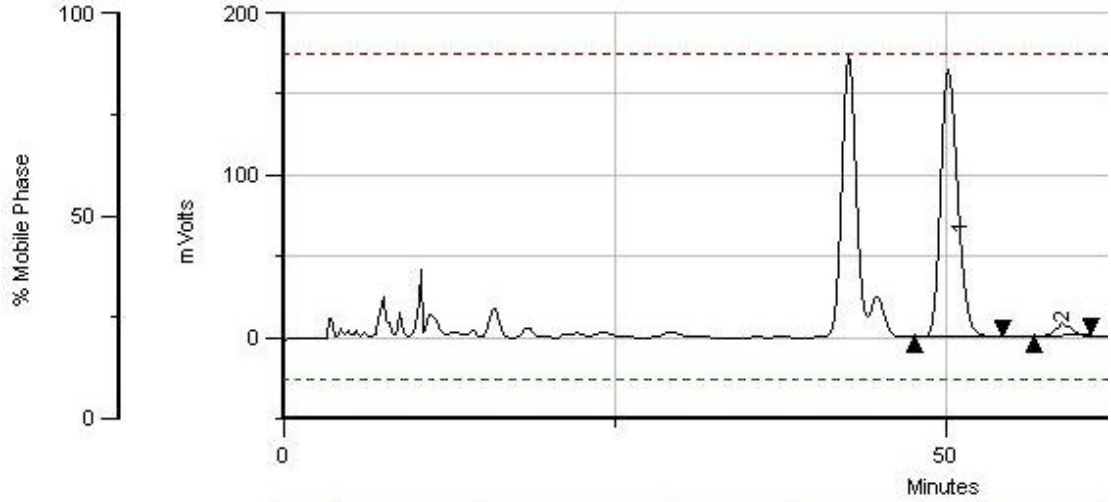
anti Chiralpak IC 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 86% ee.



anti **12**

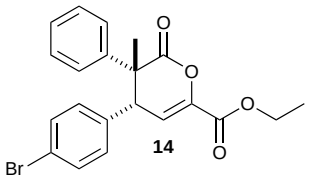


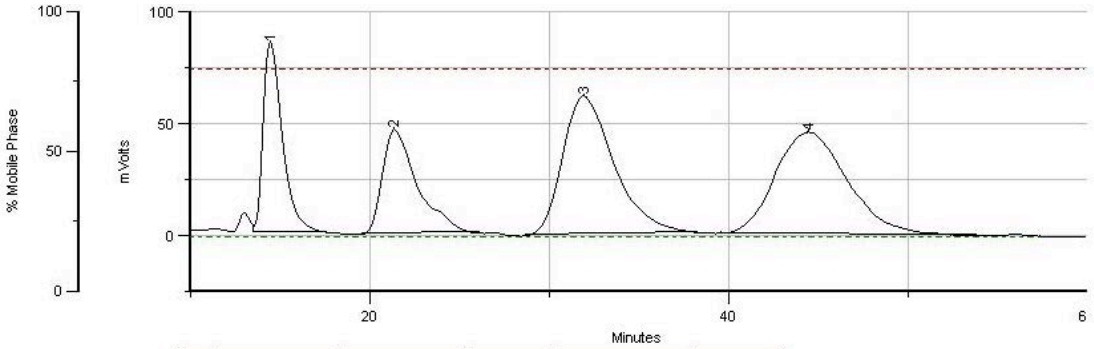
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	50.21	5255277.00	49.31
2	1.00	*2	58.85	5401442.50	50.69



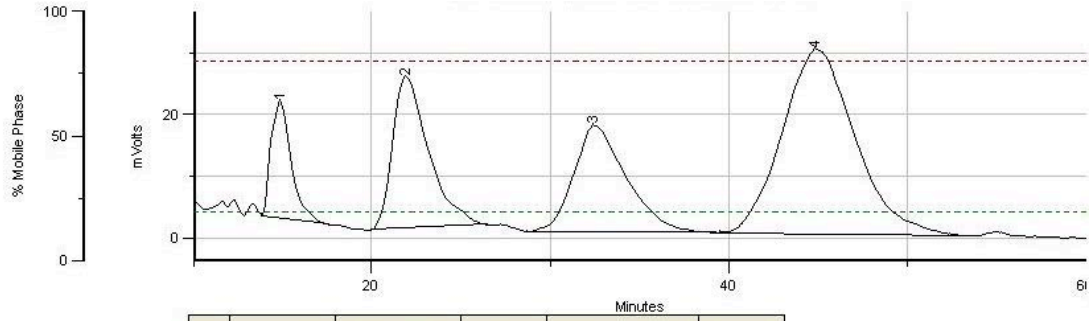
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	50.07	24787268.00	95.22
2	1.00	*2	58.82	1244072.38	4.78

HPLC data compound **14**: *syn* + *anti* Chiralcel OJ-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 41% ee, *anti* 39% ee.



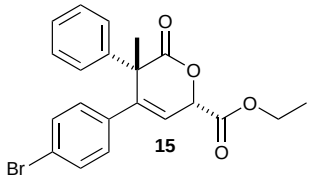


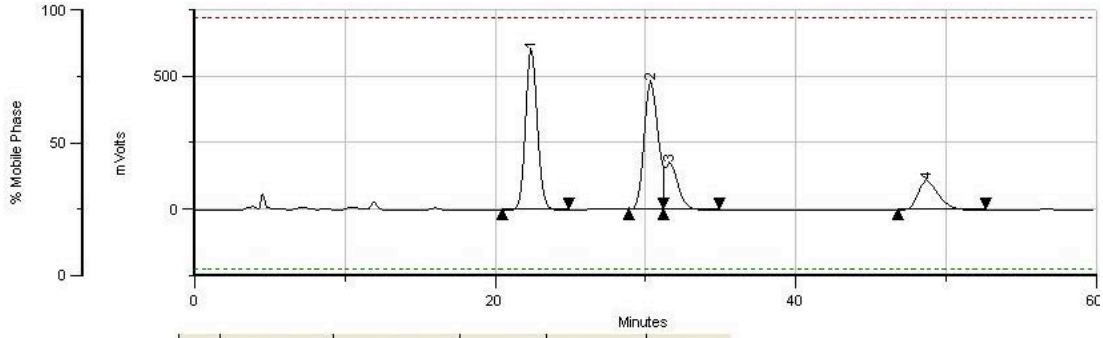
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	14.45	10560910.00	16.61
2	1.00	2	21.37	10552473.00	16.60
3	1.00	3	31.93	20625664.00	32.44
4	1.00	*4	44.58	21843560.00	34.35



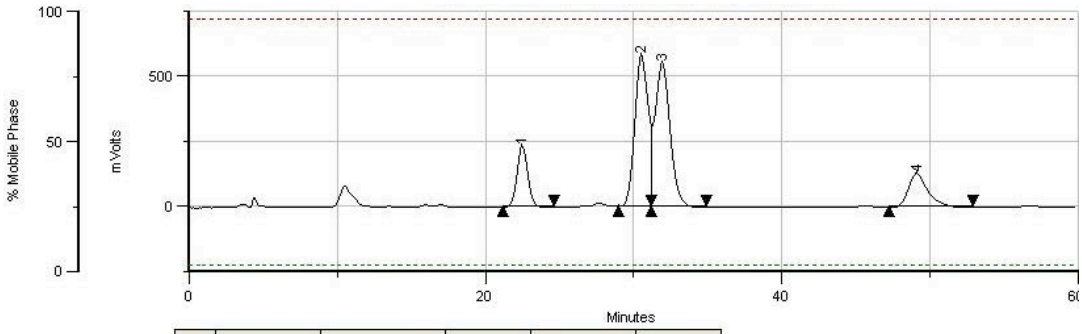
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	14.89	2539473.25	8.80
2	1.00	2	21.93	5826409.50	20.19
3	1.00	*3	32.44	6048971.00	20.97
4	1.00	*4	44.93	14437118.00	50.04

HPLC data compound **15**: *syn* + *anti* Chiralpak AD-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 52% ee, *anti* 52% ee.



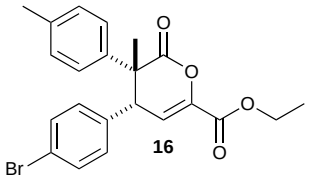


	Inj. Number	Peak Name	R. Time	Area	Area %
1	2.00	*1	22.37	55074500.00	38.35
2	2.00	*2	30.32	53498180.00	37.25
3	2.00	3	31.63	17237800.00	12.00
4	2.00	4	48.70	17802506.00	12.40

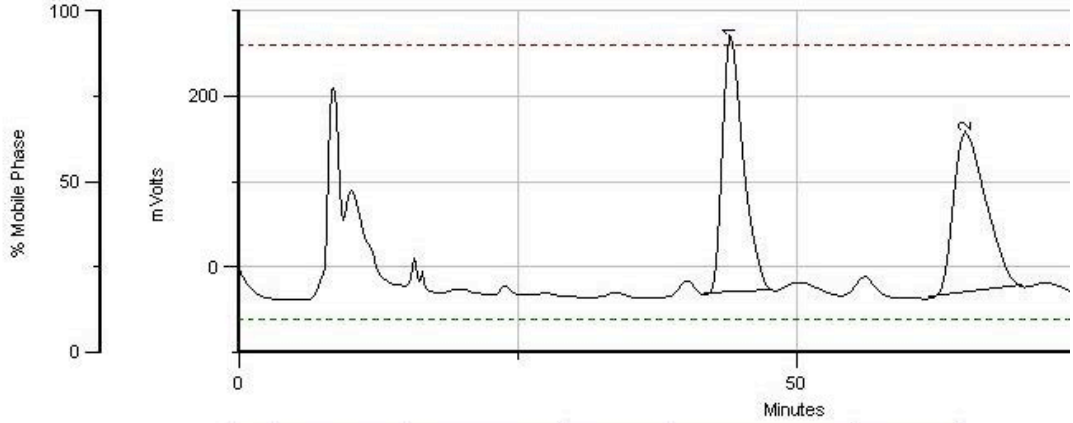


	Inj. Number	Peak Name	R. Time	Area	Area %
1	3.00	*1	22.48	20061992.00	11.95
2	3.00	*2	30.51	62626996.00	37.30
3	3.00	3	31.92	64766428.00	38.58
4	3.00	*4	49.10	20439076.00	12.17

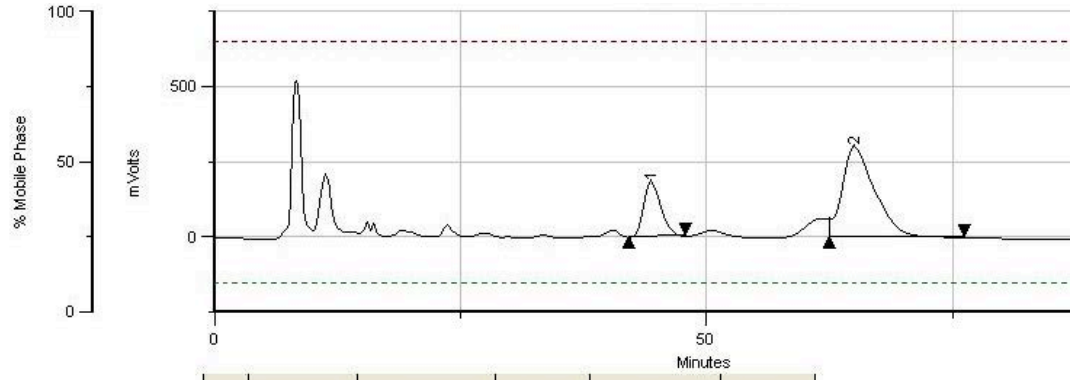
HPLC data compound *syn* **16**: Chiralpak AS-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 52% ee.



16

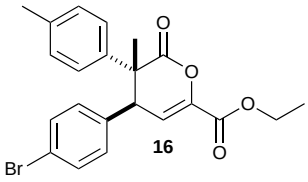


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	43.99	65892804.00	50.61
2	1.00	*2	65.01	64308512.00	49.39



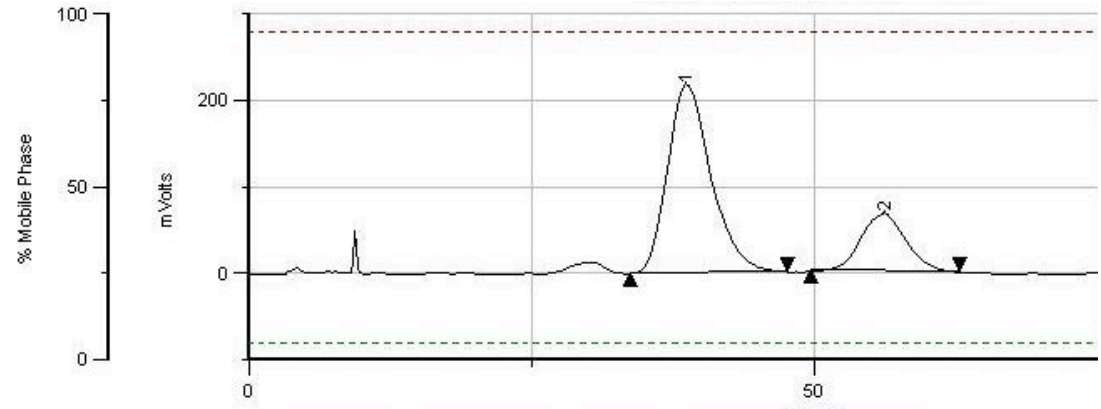
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	44.34	37327600.00	23.91
2	1.00	*2	65.03	118784968.00	76.09

HPLC data compound *anti* **16**: Chiral HPLC Chiralpak AS-H 5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 51% ee.



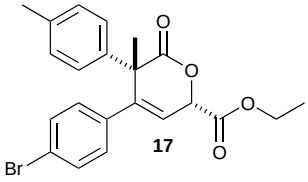
16

	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	37.59	28516508.00	49.69
2	1.00	*2	51.56	28875462.00	50.31

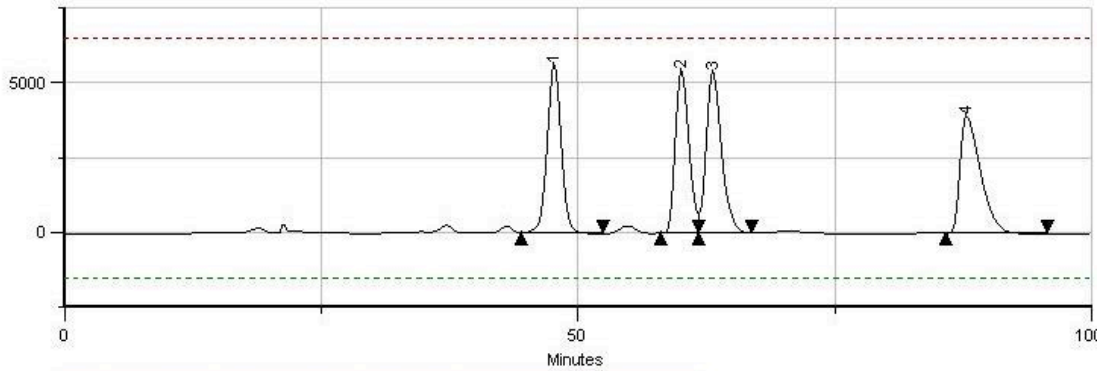


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	38.66	97272832.00	75.55
2	1.00	2	56.14	31488014.00	24.45

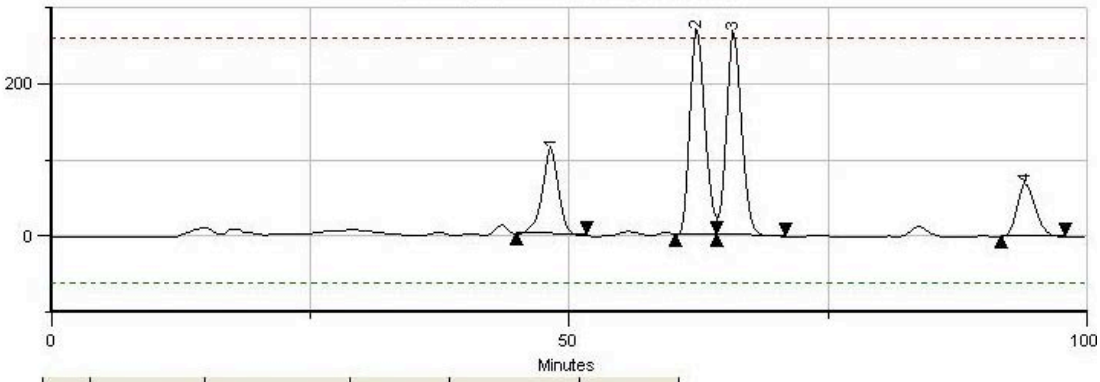
HPLC data compound **17**: Chiralpak AD-H 10% IPA:hexane, flowrate 0.25 mL min^{-1}, 254 nm, *syn* 52% ee *anti* 37% ee.



17

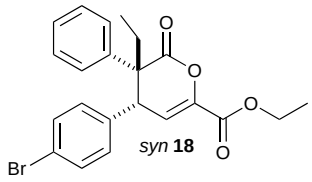


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	47.67	902889664.00	25.08
2	1.00	*2	60.05	842021056.00	23.39
3	1.00	3	63.10	944136064.00	26.22
4	1.00	*4	87.85	911560192.00	25.32

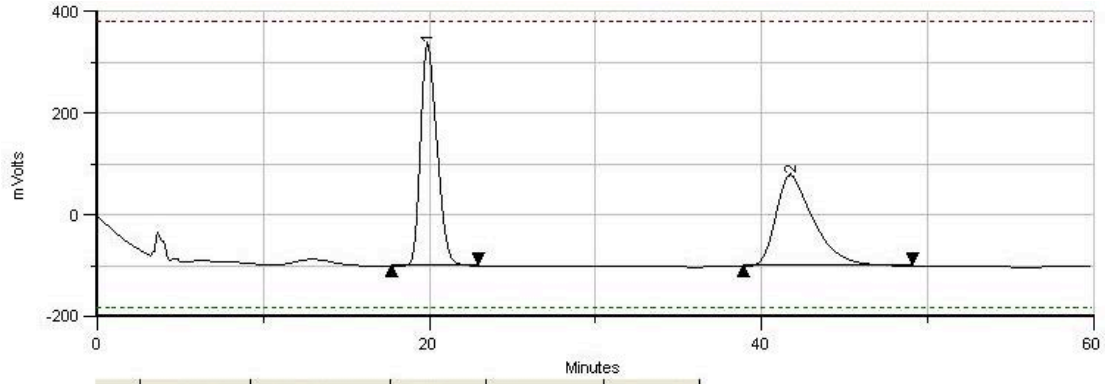


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	48.18	21023230.00	16.59
2	1.00	2	62.29	45824908.00	36.15
3	1.00	3	65.86	45567536.00	35.95
4	1.00	*4	94.08	14336293.00	11.31

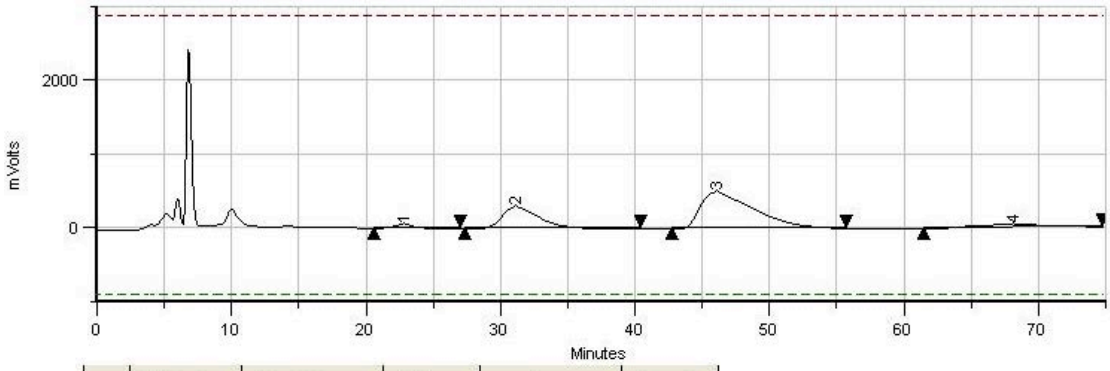
HPLC data compound *syn* **18**: Chiralpak AS-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 92% ee.



syn **18**

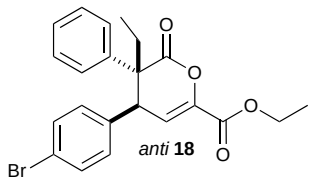


	Inj. Number	Peak Name	R. Time	Area	Area %
1	2.00	*1	19.87	50478828.00	51.09
2	2.00	2	41.74	48332988.00	48.91

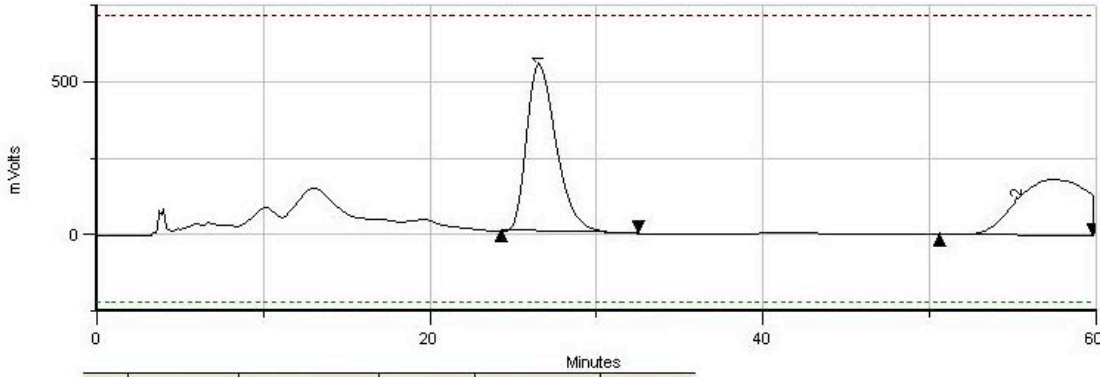


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	22.90	9439306.00	2.48
2	1.00	2	31.16	96543624.00	25.32
3	1.00	3	46.08	229110944.00	60.10
4	1.00	*4	67.65	46153936.00	12.11

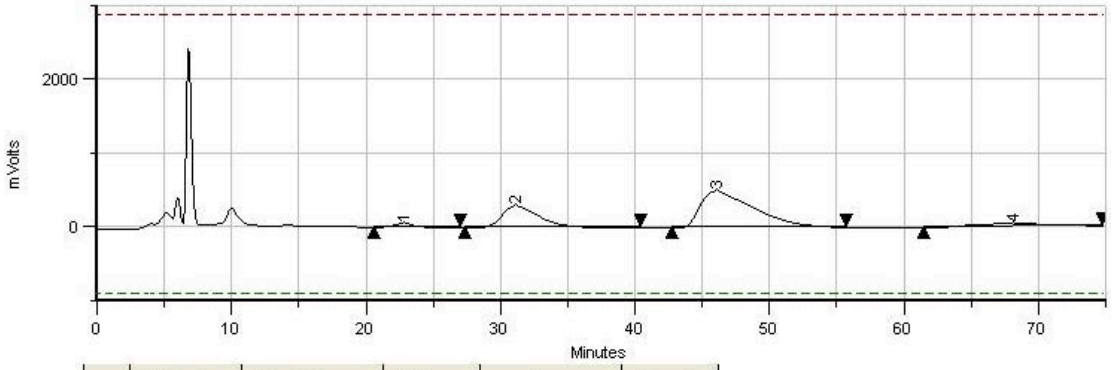
HPLC data compound *anti* **18**: Chiralpak AS-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 36% ee.



anti **18**

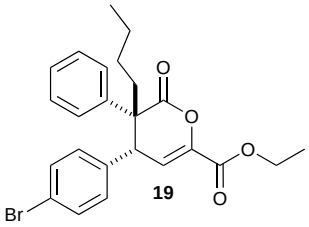


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	26.53	114386792.00	55.74
2	1.00	*2	57.50	90817064.00	44.26

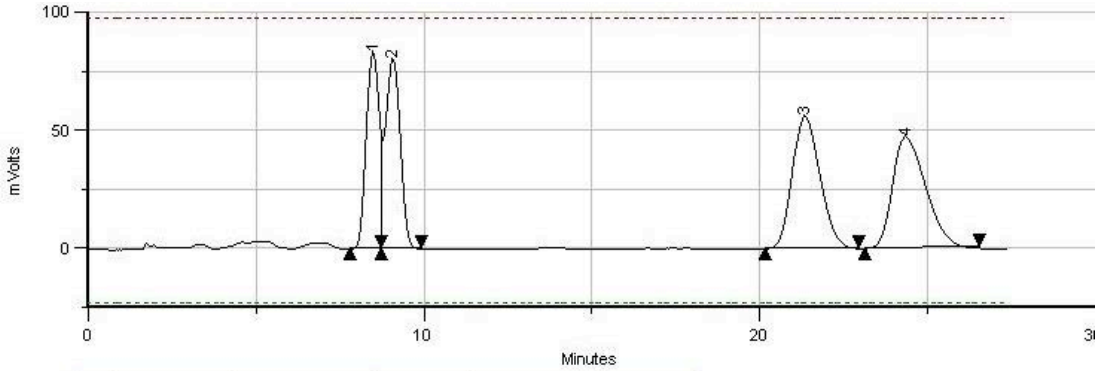


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	22.90	9439306.00	2.48
2	1.00	2	31.16	96543624.00	25.32
3	1.00	3	46.08	229110944.00	60.10
4	1.00	*4	67.65	46153936.00	12.11

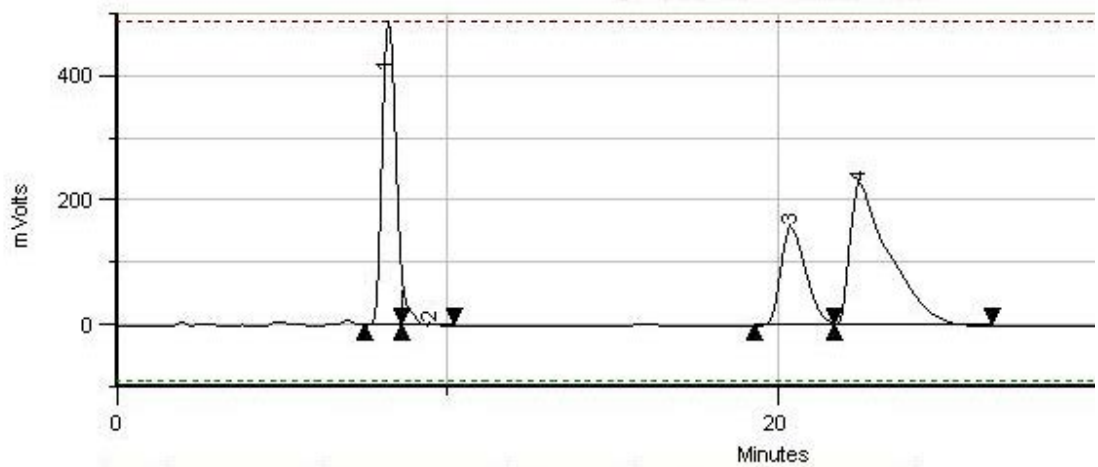
HPLC data compound **19**: Chiralpak AD-H 2% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 88% ee, *anti*, 38% ee.



19

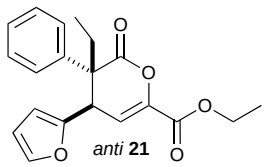


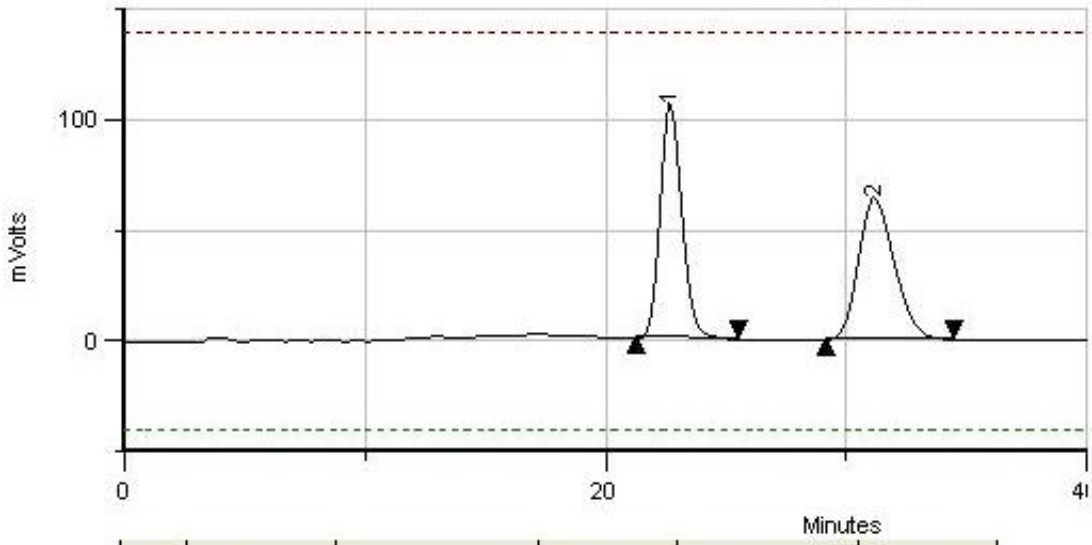
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.48	3843689.50	20.53
2	1.00	2	9.08	4030851.00	21.53
3	1.00	*3	21.35	5386112.00	28.77
4	1.00	4	24.33	5461570.50	29.17



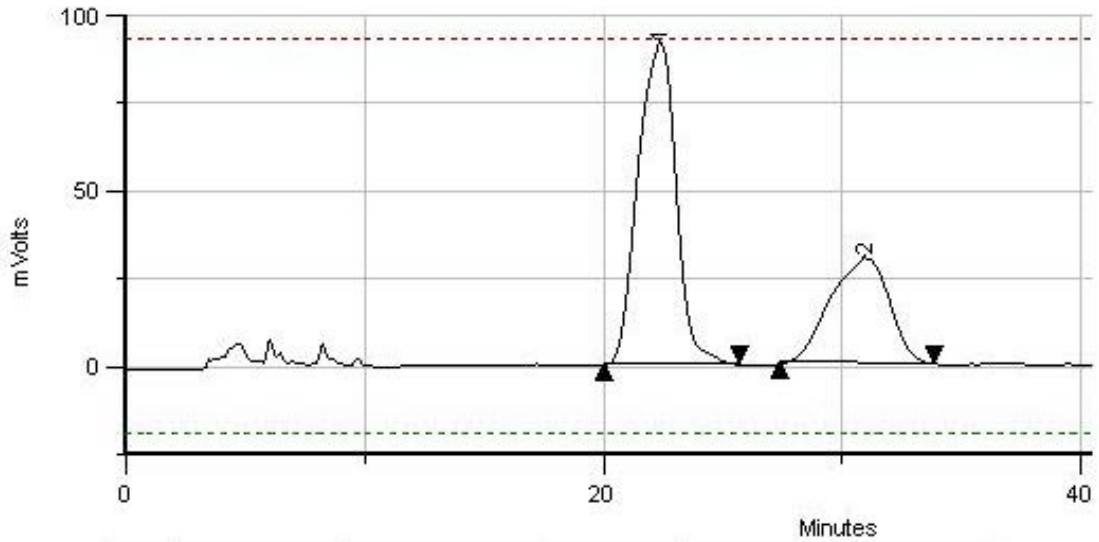
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.22	23488572.00	32.95
2	1.00	*2	8.68	1378288.62	1.93
3	1.00	*3	20.42	14315124.00	20.08
4	1.00	4	22.51	32107300.00	45.04

HPLC data compound *anti* **20**: Chiralpak AS-H 5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 32% ee.



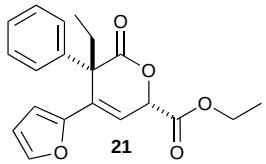


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	22.67	11291442.00	50.35
2	1.00	2	31.14	11133028.00	49.65

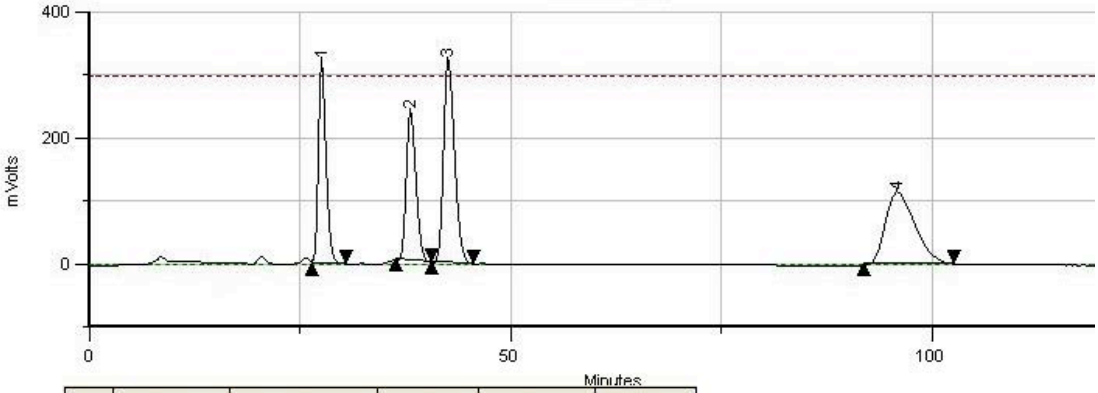


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	22.41	16960220.00	66.15
2	1.00	2	31.02	8677331.00	33.85

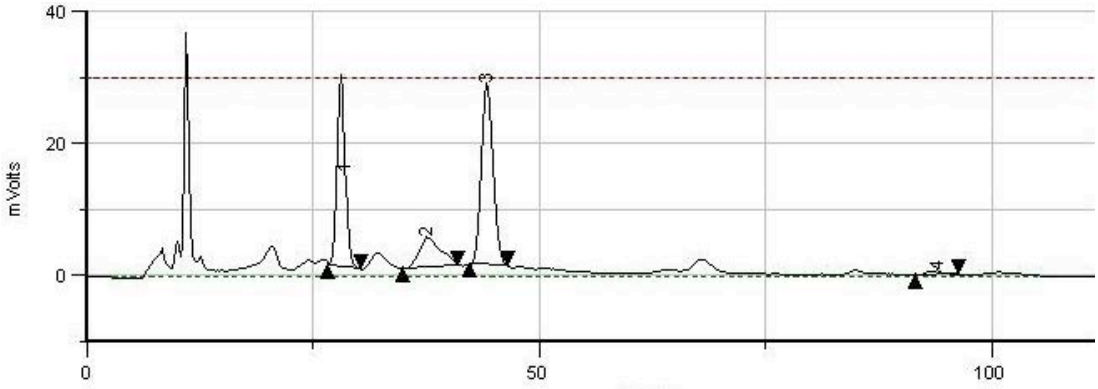
HPLC data compound *syn* + *anti* **21**:



Chiralpak AS-H 20% IPA:hexane, flowrate 0.25 mL min^{-1}, 254 nm, *anti* 41% ee, *syn* 91% ee.

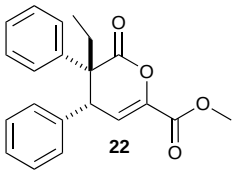


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	27.52	33892688.00	20.90
2	1.00	2	38.09	31887752.00	19.67
3	1.00	3	42.57	49200484.00	30.35
	1.00	4	95.98	47151036.00	29.08

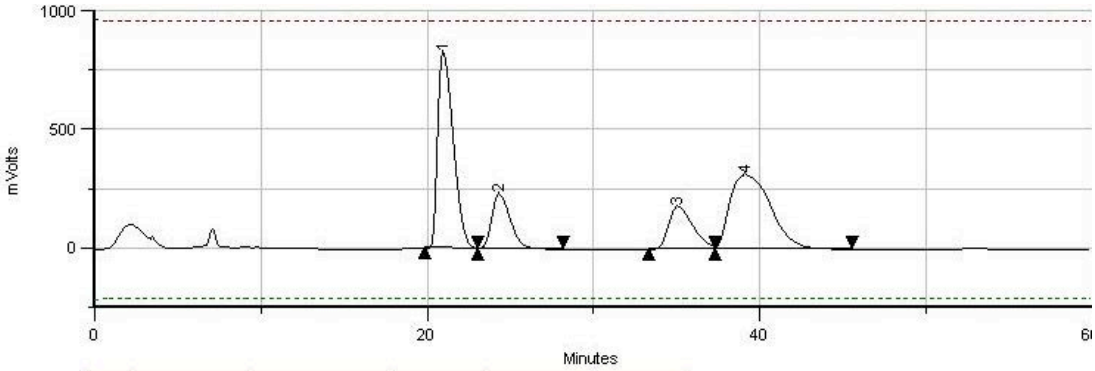


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	28.07	3203212.25	35.91
2	1.00	*2	37.75	1345597.88	15.08
3	1.00	3	44.19	4187559.00	46.94
4	1.00	*4	93.42	184847.50	2.07

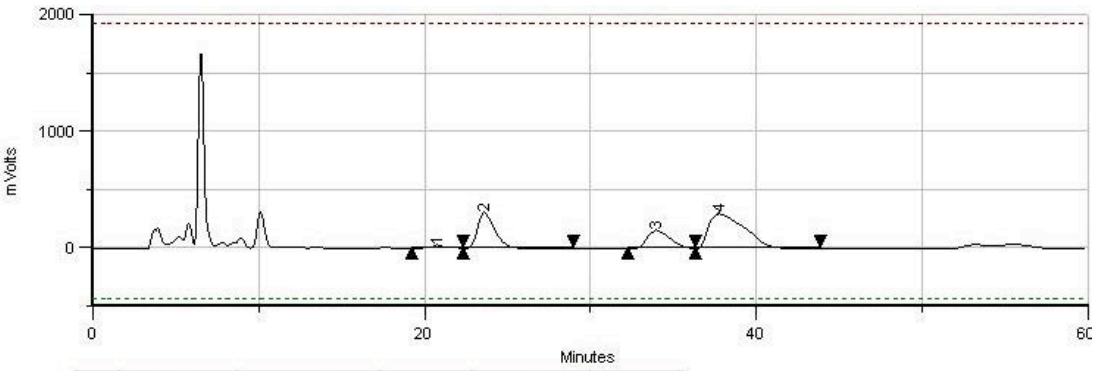
HPLC data compound *syn* + *anti* **22**: Chiralpak AS-H 3% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 94% ee, *anti* 18% ee.



22

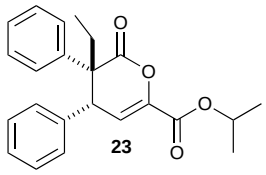


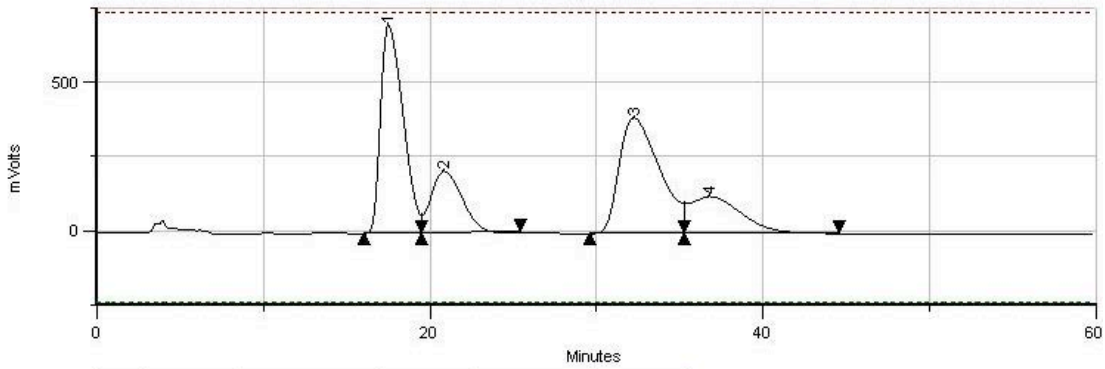
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	20.95	90357072.00	37.60
2	1.00	2	24.33	30075472.00	12.51
3	1.00	3	35.07	30465382.00	12.68
	1.00	4	39.14	89430304.00	37.21



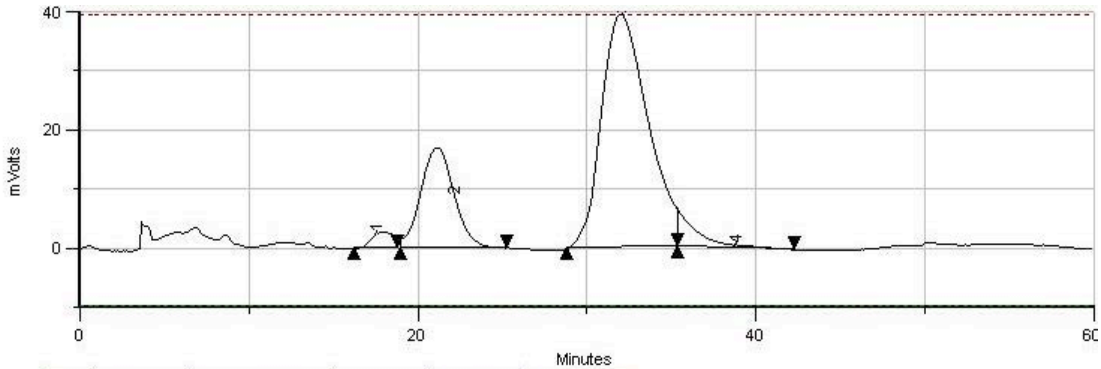
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	20.78	2189037.50	1.56
2	1.00	2	23.60	36879452.00	26.20
3	1.00	3	34.00	25583216.00	18.17
4	1.00	4	37.76	76110632.00	54.07

HPLC data compound *syn* + *anti* **23**: Chiralpak AS-H 1% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 93% ee, *anti* 93% ee.



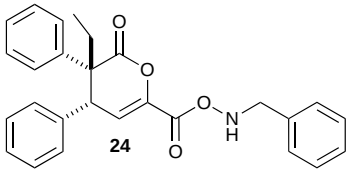


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	17.51	109674072.00	35.33
2	1.00	2	20.86	45621724.00	14.69
3	1.00	3	32.26	110757744.00	35.68
	1.00	4	36.79	44405224.00	14.30

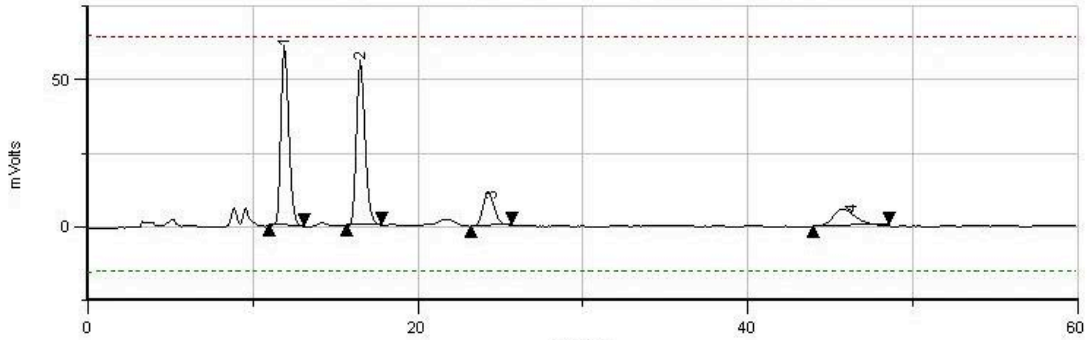


	Inj. Number	Peak Name	R. Time	Area	Area %
1	3.00	*1	17.89	444345.72	2.48
2	3.00	*2	21.14	3920294.00	21.92
3	3.00	*3	31.99	12642461.00	70.70
4	3.00	*4	35.41	874766.94	4.89

HPLC data compound *syn* + *anti* **24**: Chiralpak AD-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 98% ee, *anti* 57% ee.



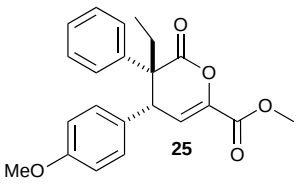
24



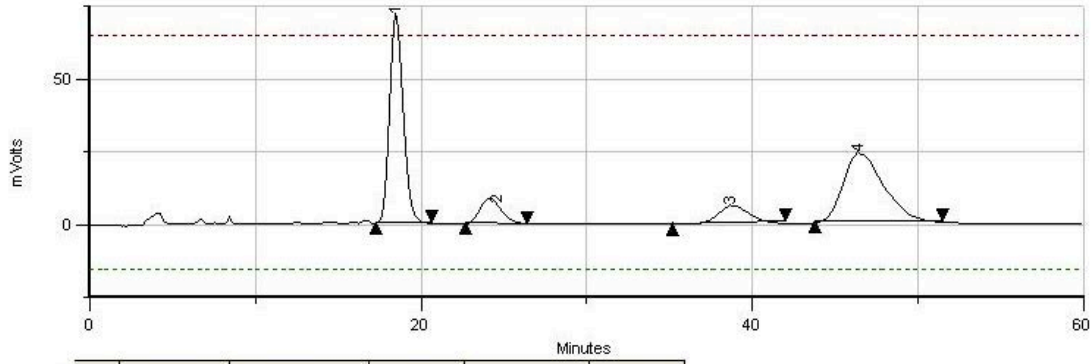
1	1.00	*1	11.90	3409963.00	38.84
2	1.00	2	16.50	3395998.50	38.68
3	1.00	*3	24.26	975948.38	11.12
	1.00	*4	45.74	996892.12	11.36

	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.92	19961978.00	65.69
2	1.00	*2	16.75	250462.41	0.82
3	1.00	*3	24.68	2192788.50	7.22
4	1.00	4	46.73	7985136.50	26.28

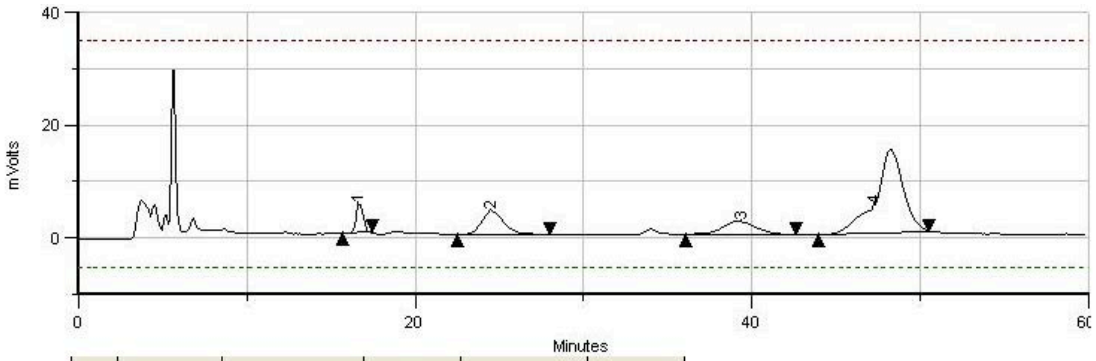
HPLC data compound *syn* + *anti* **25**: Chiralpak AS-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, *syn* 80% ee, *anti* 4% ee.



25

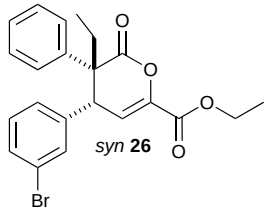


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	18.47	6855863.50	41.36
2	1.00	*2	24.13	1416403.25	8.55
3	1.00	*3	38.77	1453188.62	8.77
4	1.00	4	46.41	6849227.50	41.32

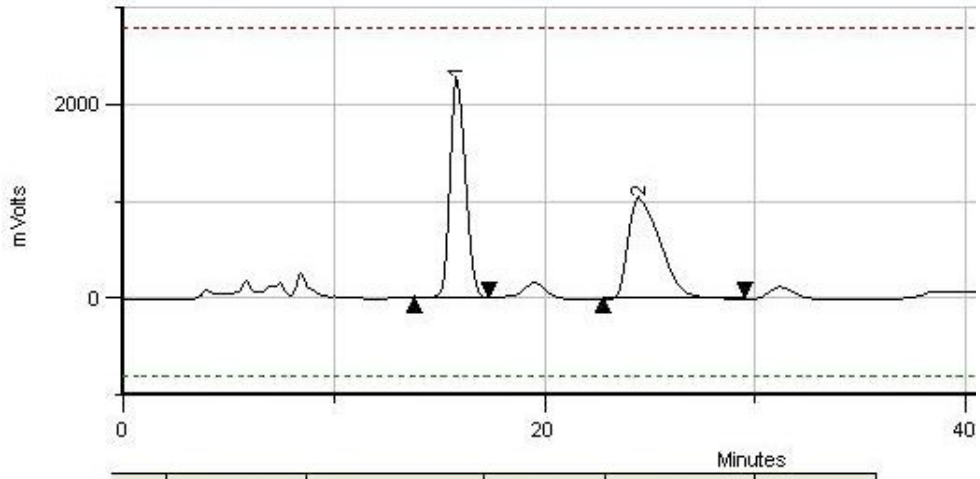


	Inj. Number	Peak Name	R. Time	Area	Area %
1	2.00	*1	16.69	277259.81	5.86
2	2.00	*2	24.56	763190.38	16.13
3	2.00	*3	39.09	701265.69	14.82
4	2.00	*4	48.23	2988992.25	63.18

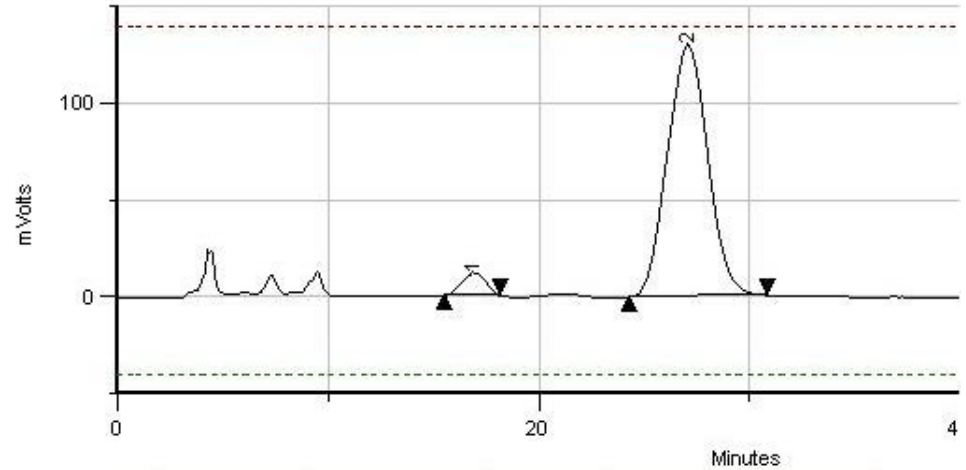
HPLC data compound *syn* **26**: Chiralpak AS-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 89% ee.



syn **26**

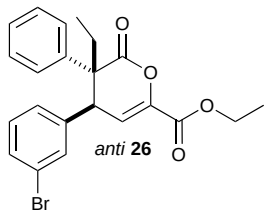


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	15.83	193908480.00	51.09
2	1.00	*2	24.47	185610624.00	48.91

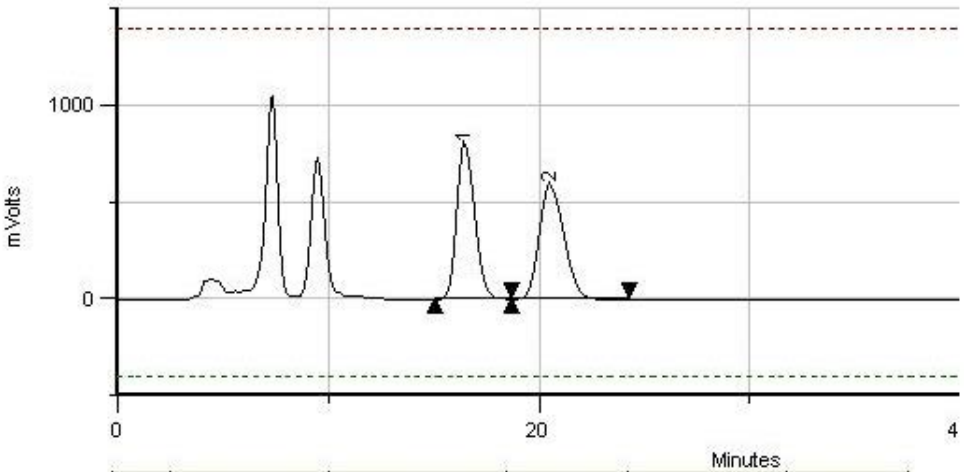


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	16.96	1657459.88	5.44
2	1.00	2	27.08	28838184.00	94.56

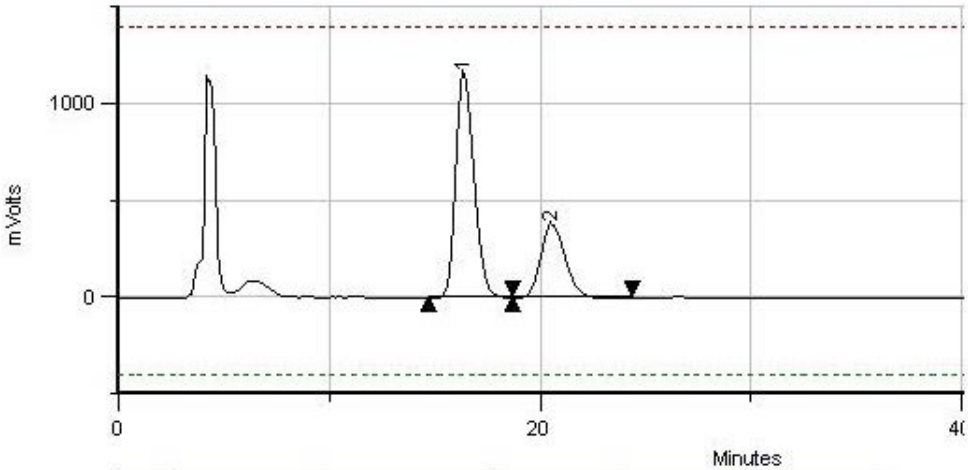
HPLC data compound *anti* **26**: Chiralpak AS-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 39% ee.



anti **26**

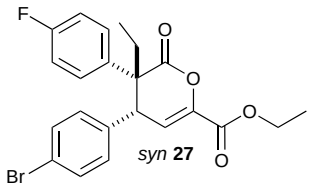


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	16.46	80513512.00	49.76
2	1.00	2	20.51	81276480.00	50.24

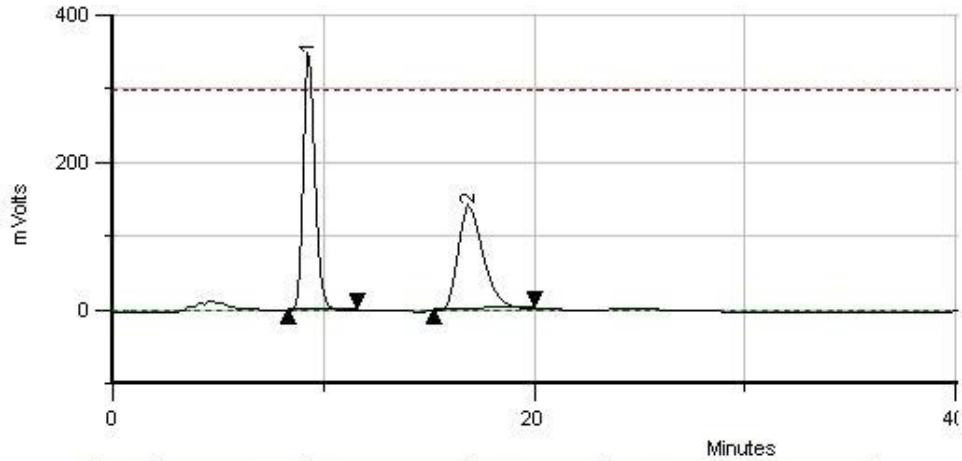


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	16.36	117437432.00	69.28
2	1.00	2	20.55	52066484.00	30.72

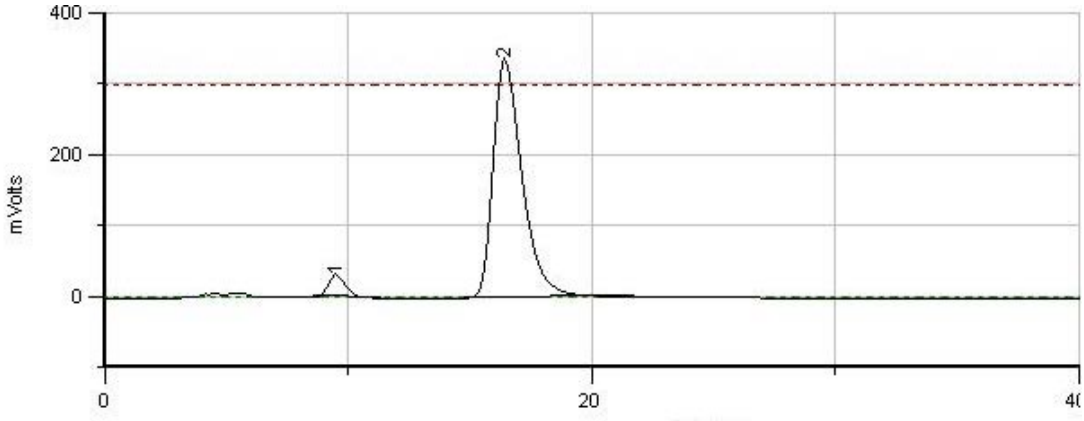
HPLC data compound *syn* **27**: Chiralpak AS-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 89% ee.



syn **27**

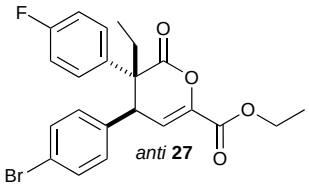


	Inj. Number	Peak Name	R. Time	Area	Area %
1	2.00	*1	9.29	22367058.00	52.79
2	2.00	2	16.89	19999764.00	47.21

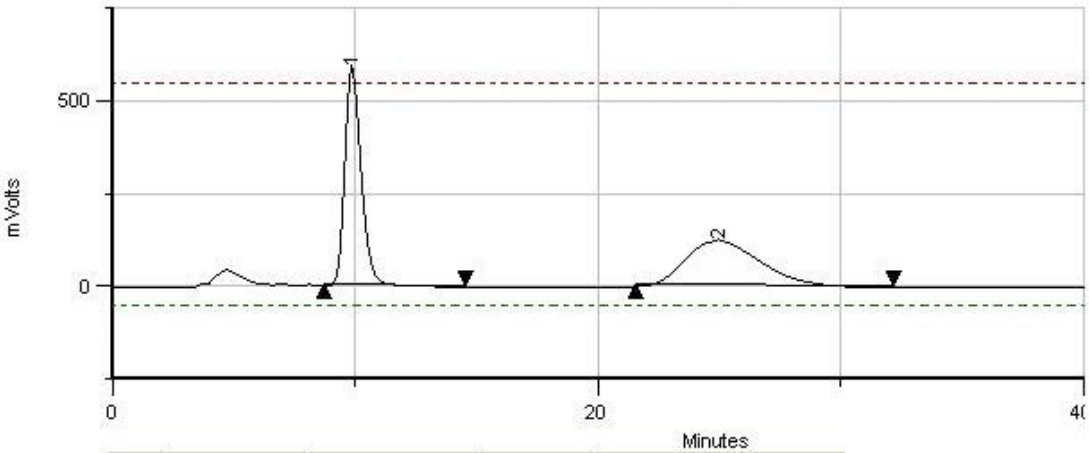


	Inj. Number	Peak Name	R. Time	Area	Area %
1	3.00	*1	9.48	2621179.25	5.29
2	3.00	2	16.42	46967720.00	94.71

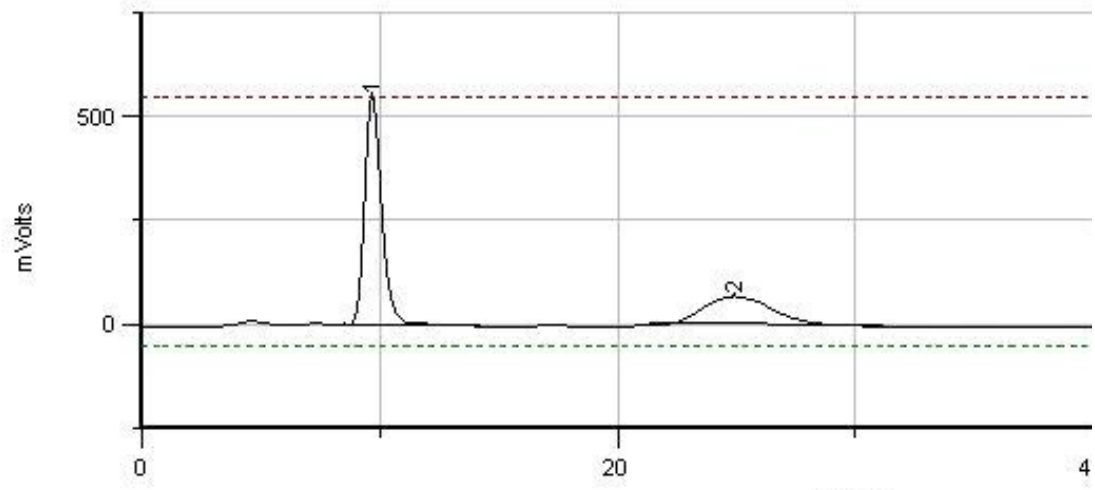
HPLC data compound *anti* **27**: Chiralpak AS-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 31% ee.



anti **27**

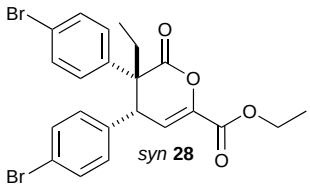


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.85	46327616.00	50.79
2	1.00	2	24.97	44881024.00	49.21

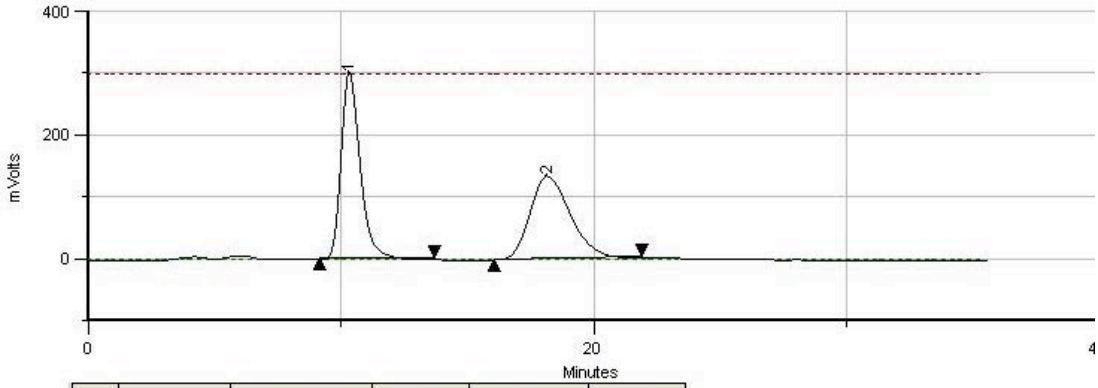


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.67	46800176.00	65.48
2	1.00	2	24.93	24667168.00	34.52

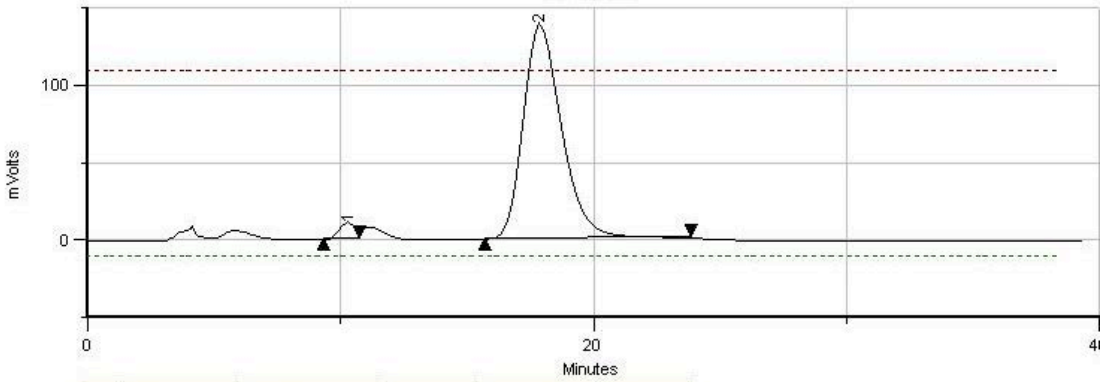
HPLC data compound *syn* **28**: Chiralpak AS-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 93% ee.



syn **28**

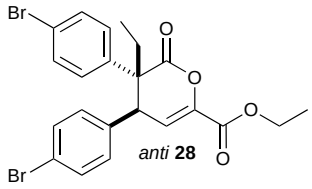


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.32	26615608.00	51.51
2	1.00	2	18.16	25055226.00	48.49

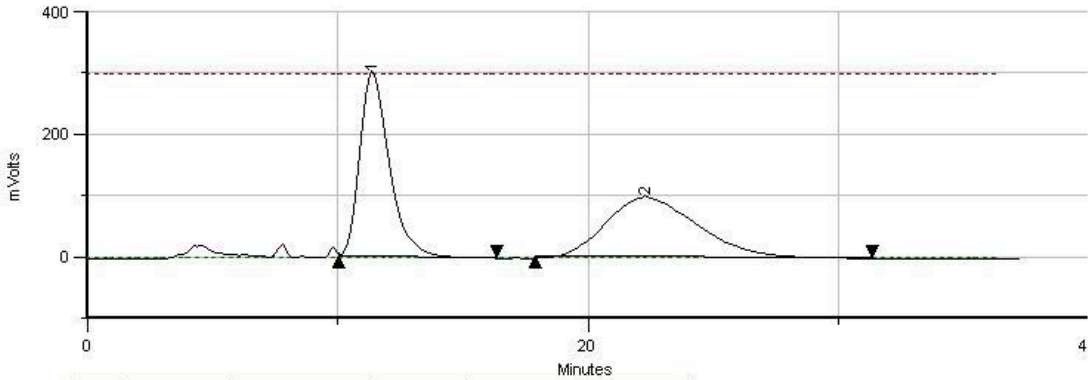


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.27	883686.69	3.47
2	1.00	*2	17.89	24558024.00	96.53

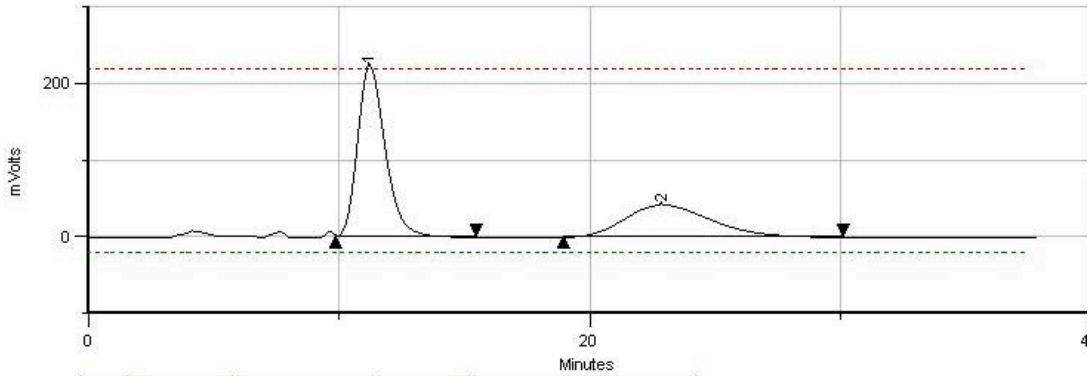
HPLC data compound *anti* **28**: Chiralpak AS-H 20% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 26% ee.



anti **28**

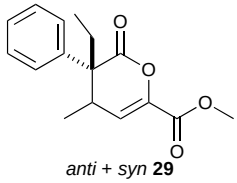


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.37	41977924.00	49.55
2	1.00	2	22.27	42746244.00	50.45

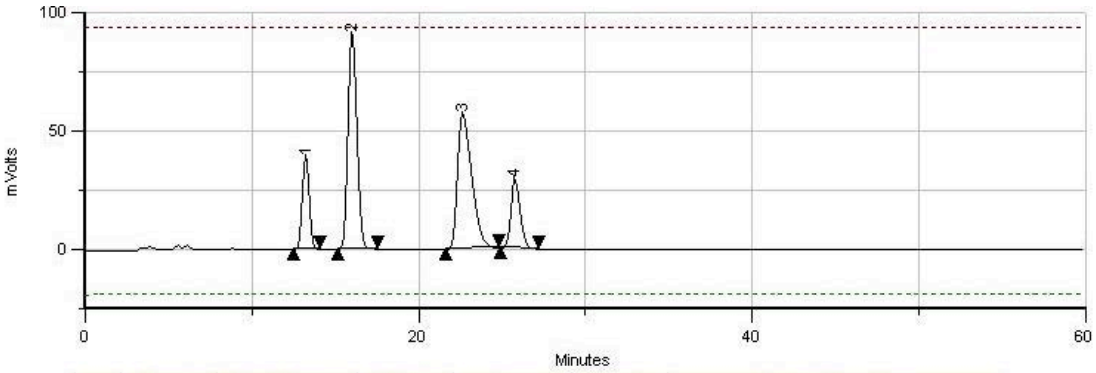


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.22	28924644.00	62.96
2	1.00	2	22.87	17015566.00	37.04

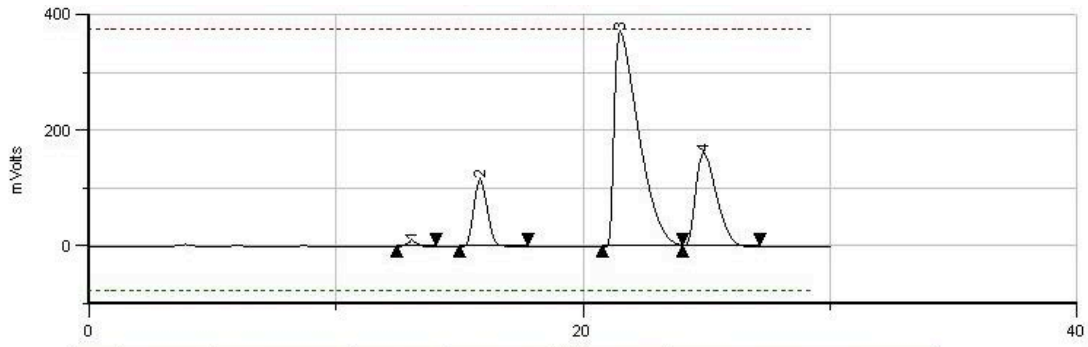
HPLC data compound *anti* + *syn* **29**: Chiralpak AS-H 5% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 70% ee *anti*, 94% ee *syn*.



anti + *syn* **29**

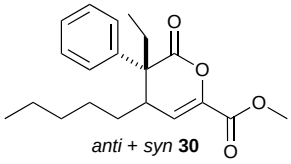


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	13.22	1906282.38	12.58	SL-488-T9-15 me AKE recemic AS-H
2	1.00	2	16.00	5670063.50	37.43	SL-488-T9-15 me AKE recemic AS-H
3	1.00	3	22.64	5688156.00	37.55	SL-488-T9-15 me AKE recemic AS-H
4	1.00	4	25.77	1884110.88	12.44	SL-488-T9-15 me AKE recemic AS-H

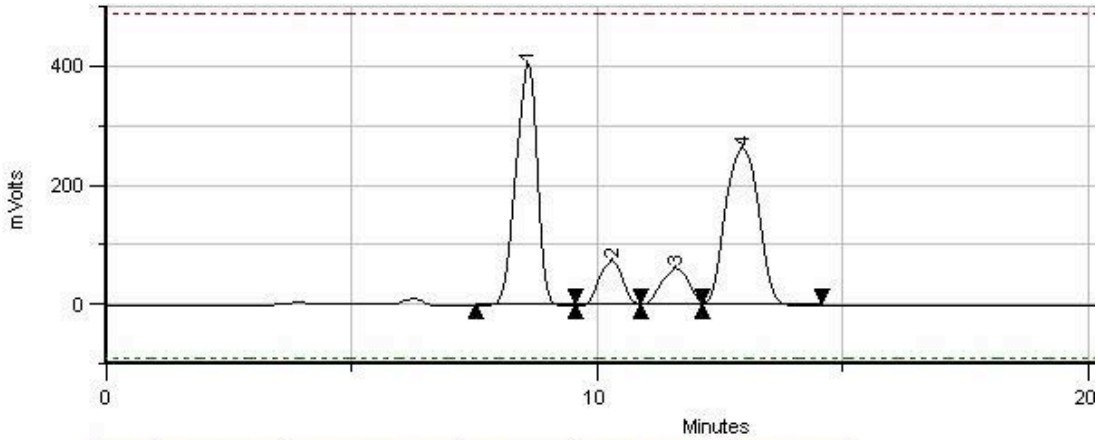


	Inj. Number	Peak Name	R. Time	Area	Area %	Sample Descrip.
1	1.00	*1	13.08	499043.41	0.75	SL-489-T10-15 Me AKE CHIRAL
2	1.00	2	15.83	7444804.50	11.12	SL-489-T10-15 Me AKE CHIRAL
3	1.00	3	21.52	42907416.00	64.07	SL-489-T10-15 Me AKE CHIRAL
4	1.00	4	24.90	16114334.00	24.06	SL-489-T10-15 Me AKE CHIRAL

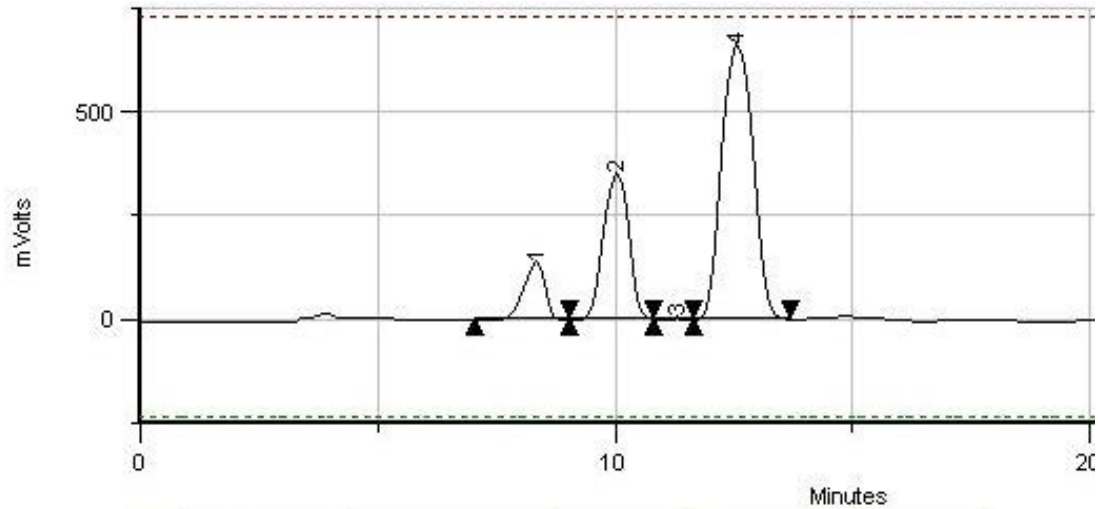
HPLC data compound *anti* + *syn* **30**: Chiralpak AD-H 2% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 75% ee *anti*, 97% ee *syn*.



anti + *syn* **30**

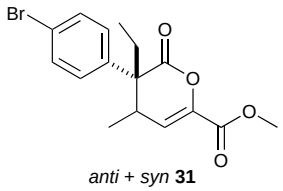


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.60	20462718.00	41.09
2	1.00	2	10.30	4229034.50	8.49
3	1.00	3	11.63	4218453.50	8.47
4	1.00	4	12.97	20891370.00	41.95

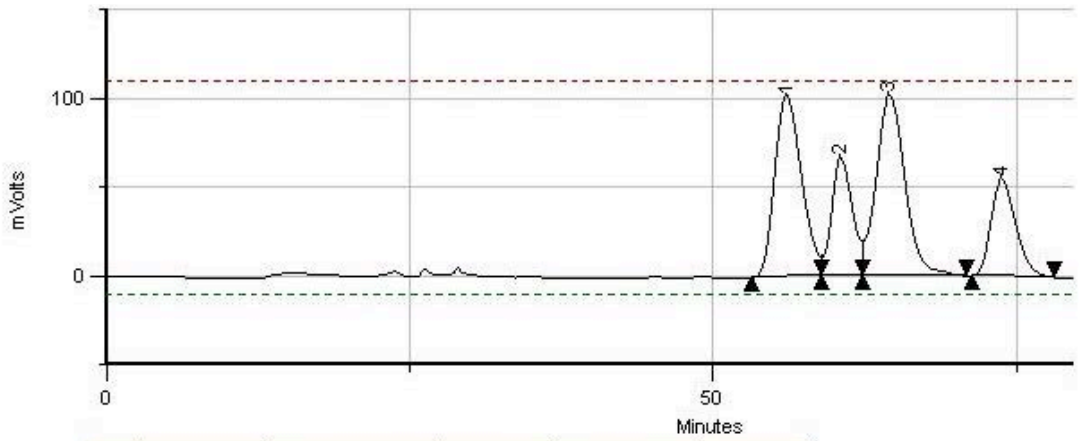


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.35	7468898.50	9.18
2	1.00	2	10.04	22131552.00	27.21
3	1.00	3	11.31	314056.69	0.39
4	1.00	4	12.57	51432356.00	63.23

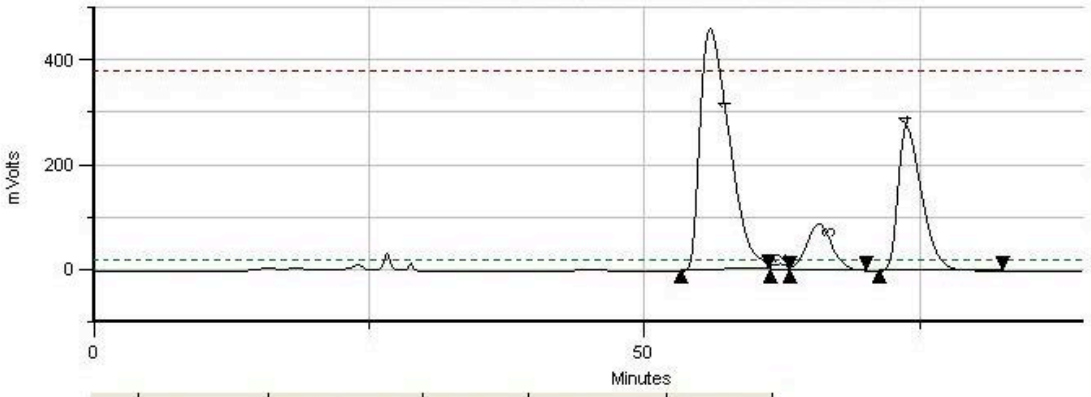
HPLC data compound *anti* + *syn* **31**: Chiralpak OJ-H 20% IPA:hexane, flowrate 0.25 mL min^{-1}, 254 nm, 71% ee *anti*, 94% ee *syn*.



anti + *syn* **31**

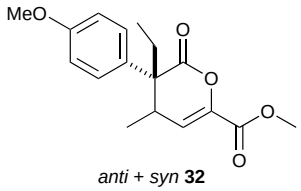


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	56.03	26461130.00	32.55
2	1.00	2	60.52	13469162.00	16.57
3	1.00	3	64.55	28336278.00	34.86
4	1.00	4	73.78	13026560.00	16.02

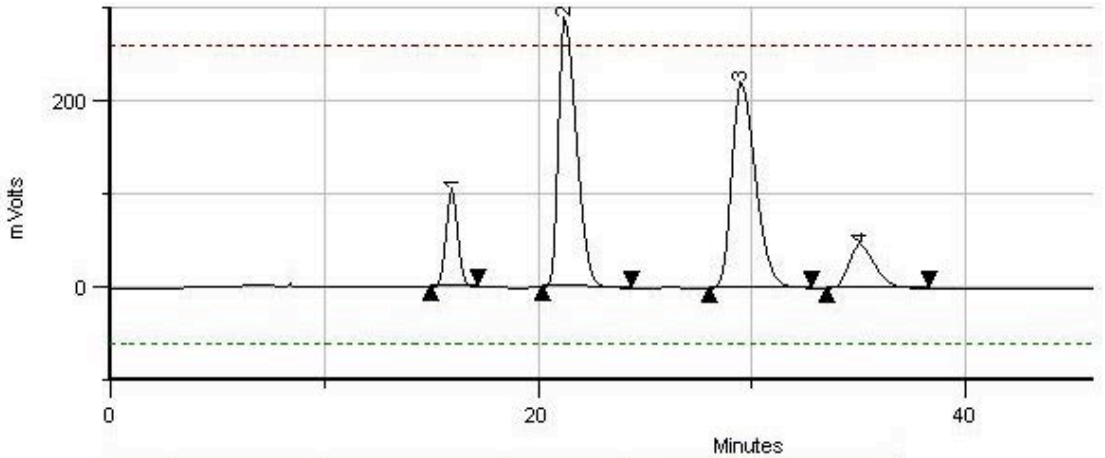


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	55.98	142038960.00	59.71
2	1.00	*2	61.59	2063177.00	0.87
3	1.00	*3	65.83	24183428.00	10.17
4	1.00	4	73.84	69611048.00	29.26

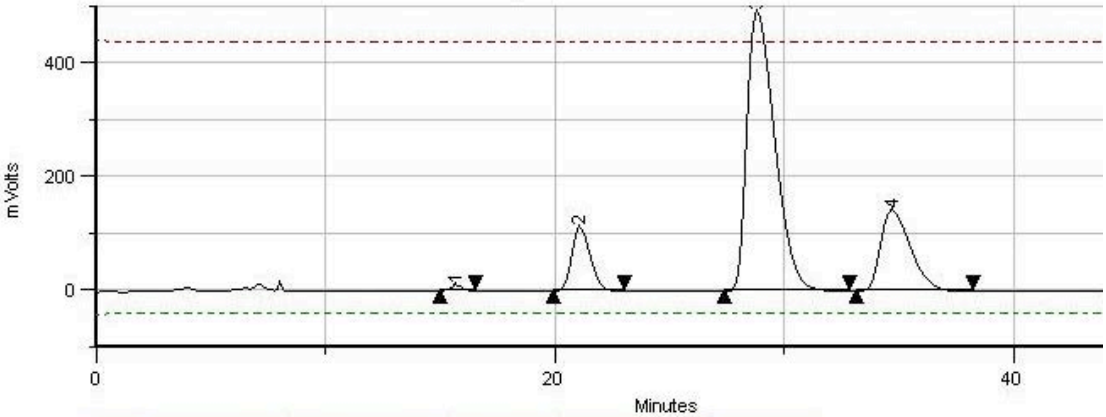
HPLC data compound *anti* + *syn* **32**: Chiralpak AS-H 10% IPA:hexane, flowrate 1 mL min^{-1}, 254 nm, 74% ee *anti*, 95% ee *syn*.



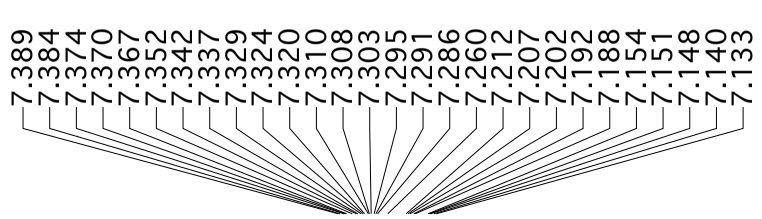
anti + *syn* **32**

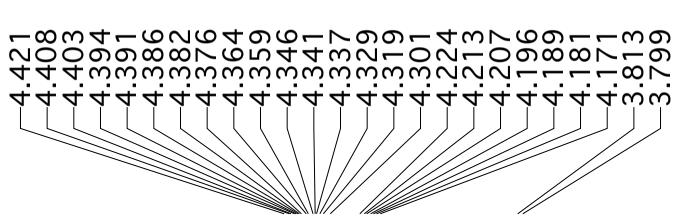


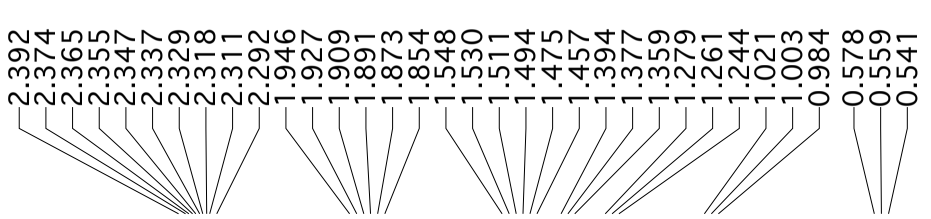
	Inj. Number	Peak Name	R. Time	Area	Area %
1	2.00	*1	15.95	6672695.50	9.52
2	2.00	*2	21.27	28391958.00	40.51
3	2.00	3	29.51	28440238.00	40.57
4	2.00	4	35.06	6588995.50	9.40

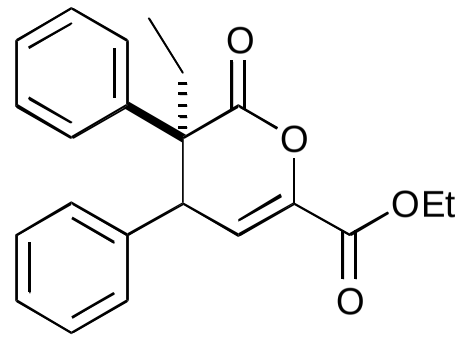


	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	15.73	573919.06	0.56
2	1.00	*2	21.09	10711823.00	10.40
3	1.00	3	28.82	69911080.00	67.85
	1.00	4	34.72	21840910.00	21.20

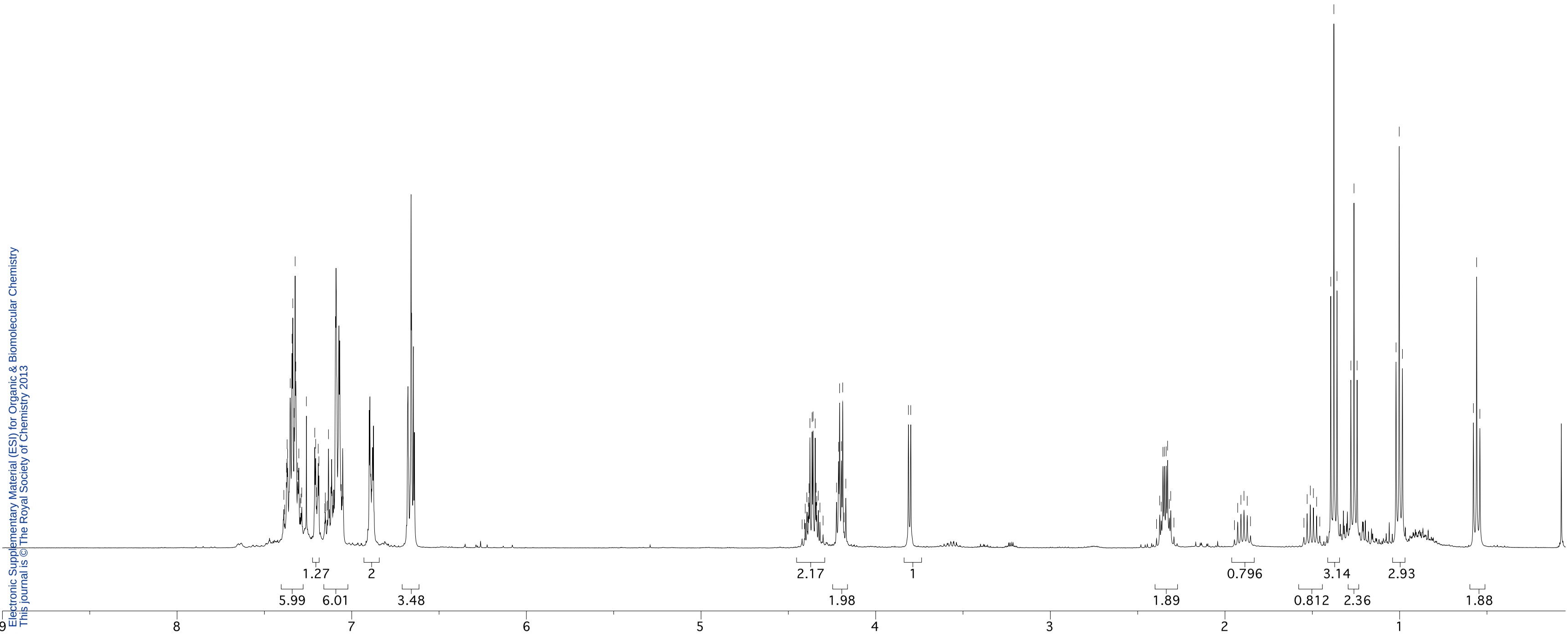


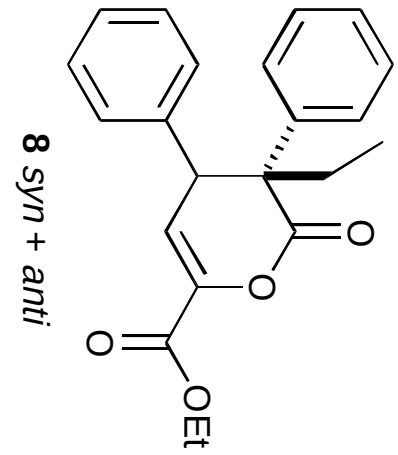






8 *syn* + *anti*





8 *syn* + *anti*

170.126
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141.222
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136.349
136.122
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128.855
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128.190
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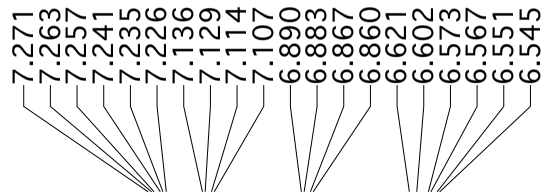
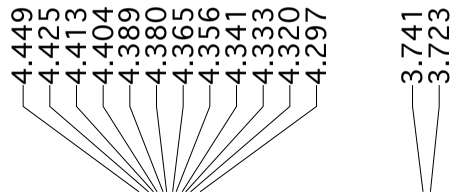
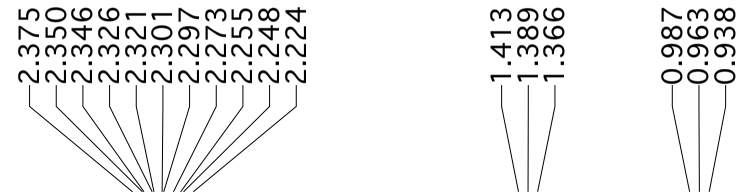
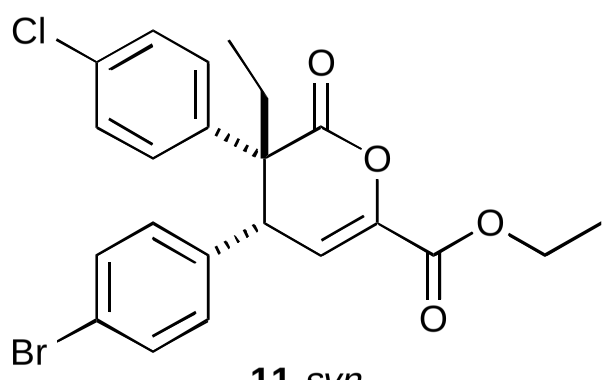
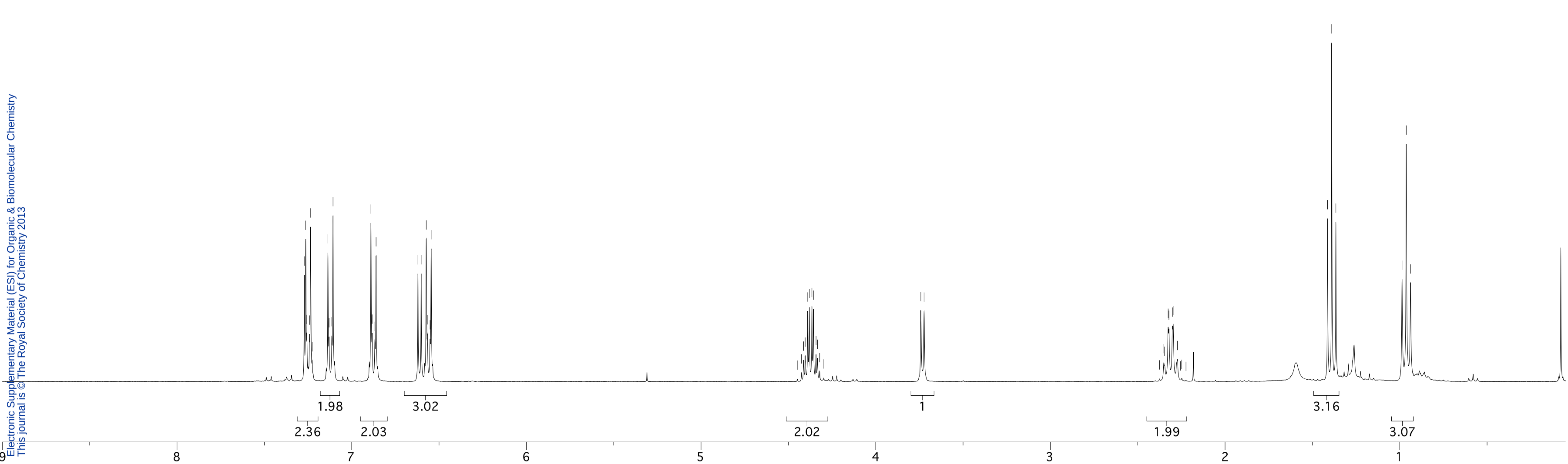


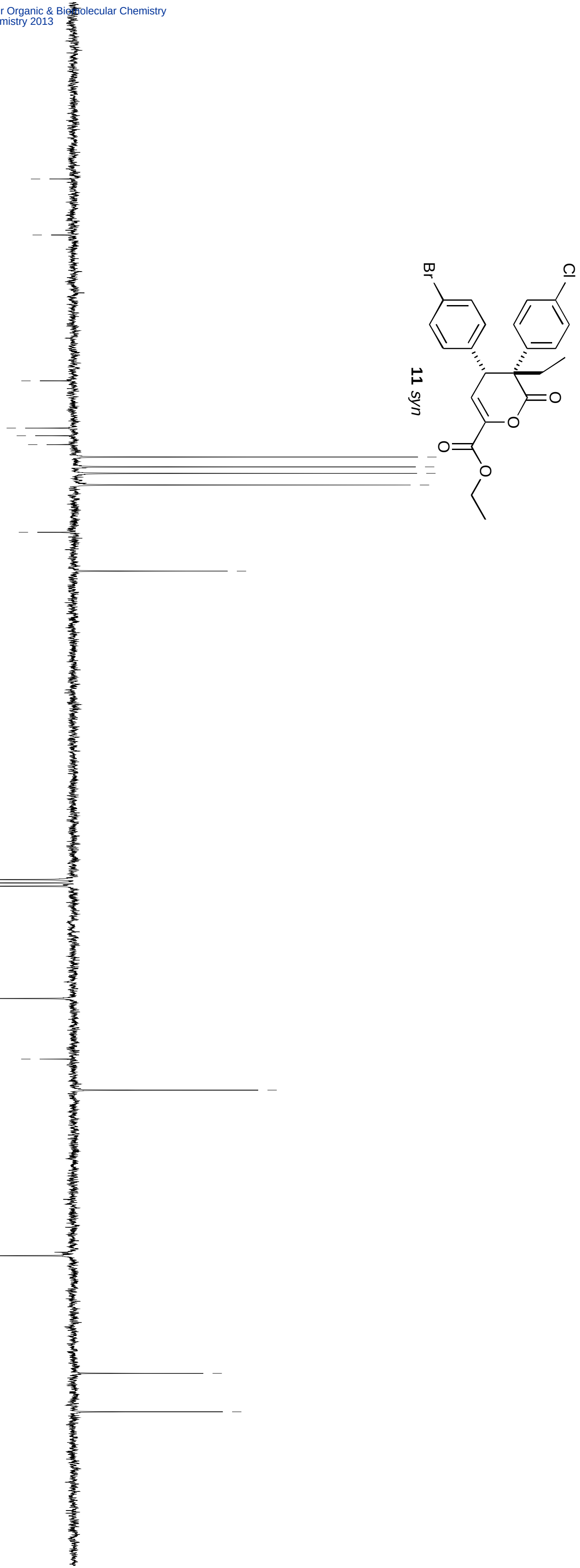






11 *syn*





167.363
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54.587
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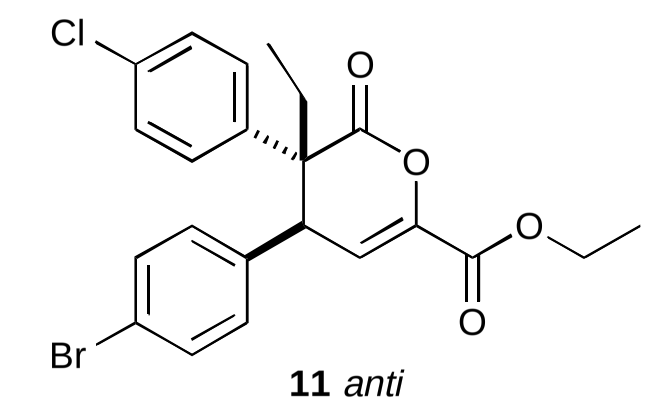
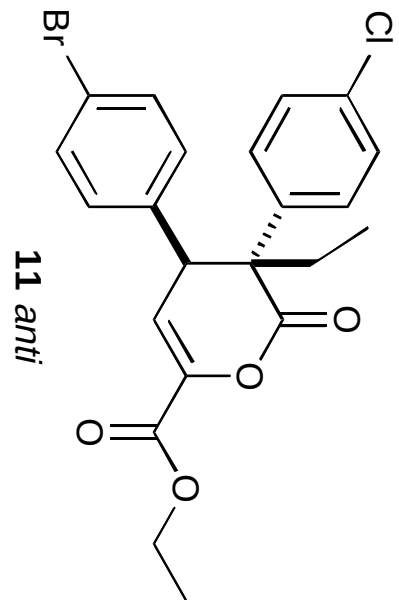
29.386
14.310
9.386



11 *anti*



11 *anti*

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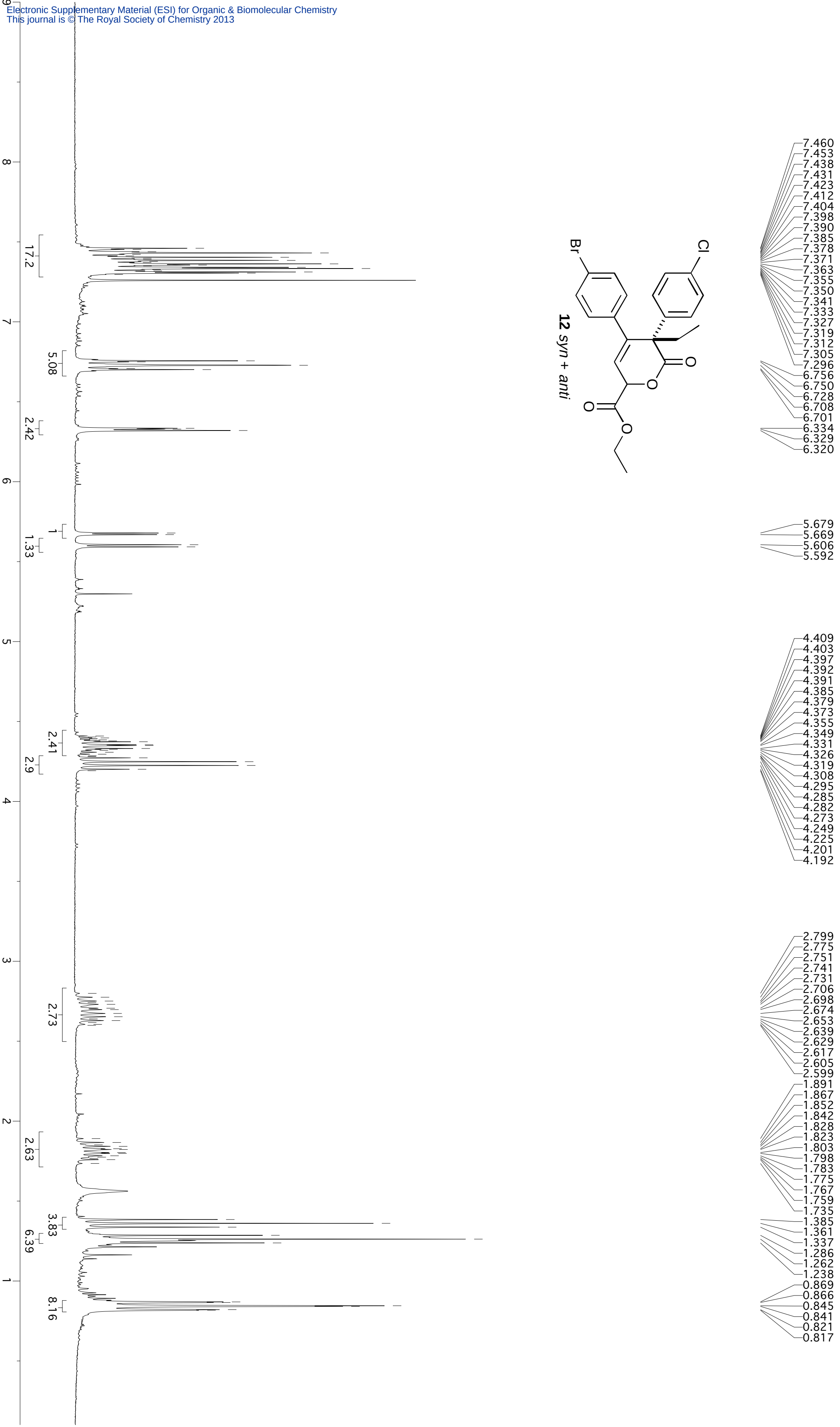
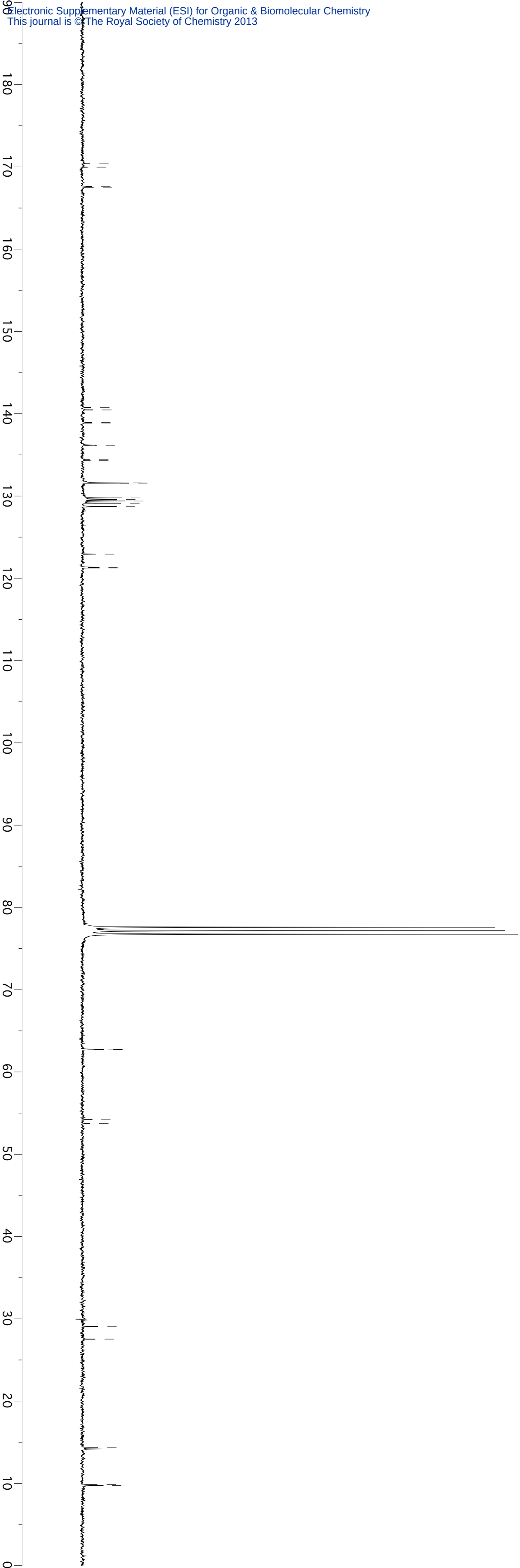
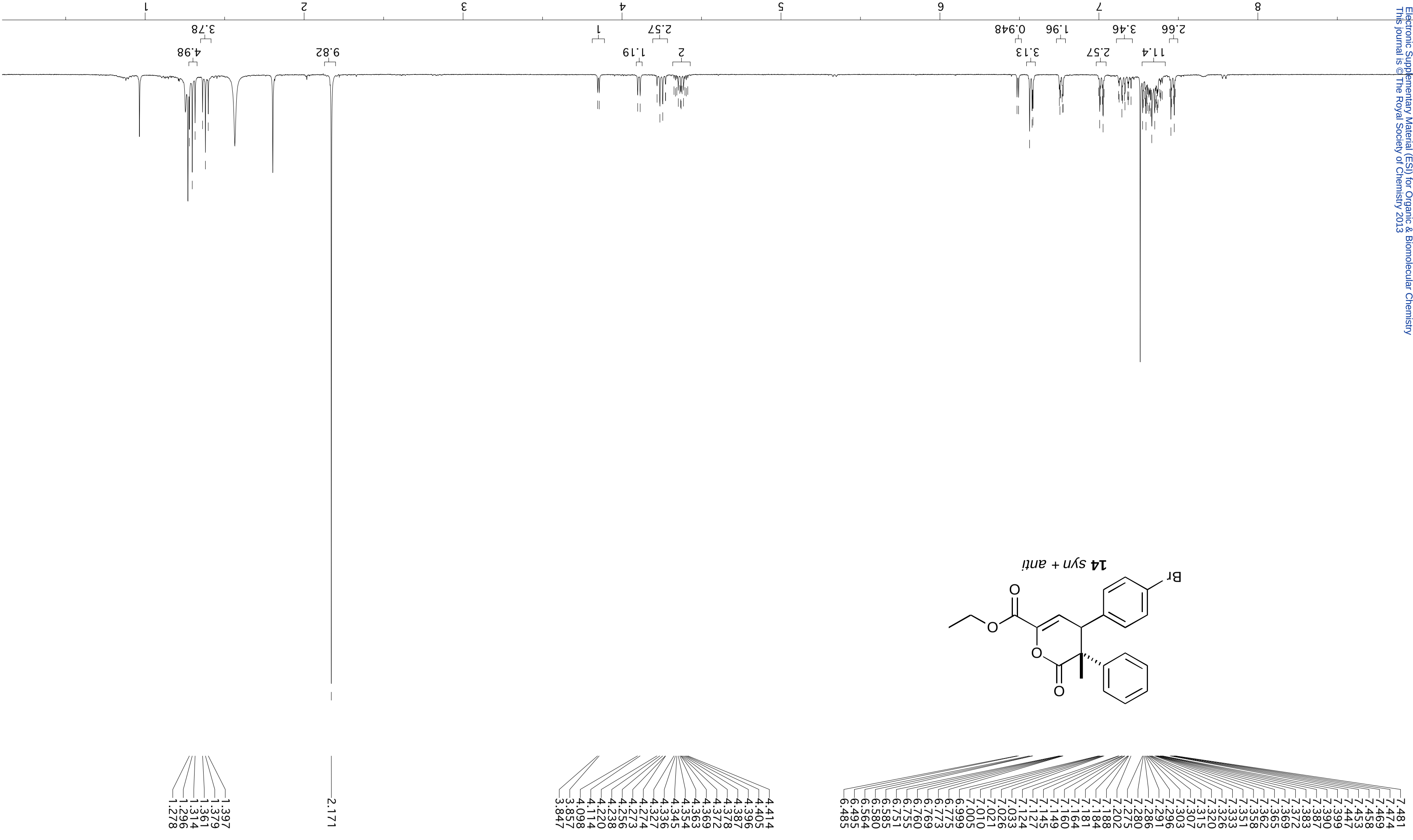
117.045
62.185
53.533
45.936
28.086
14.191
8.385



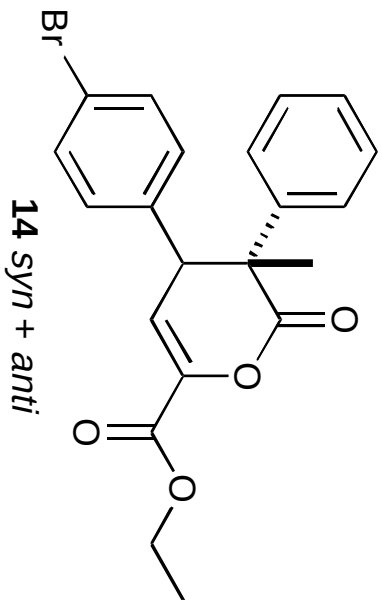


12 *syn* + *anti*

170.382
169.970
167.597
167.534
140.764
140.459
138.960
138.872
136.193
136.175
134.472
134.292
131.597
131.568
129.761
129.574
129.525
129.390
129.129
128.721
122.934
121.342
121.258
62.775
62.735
54.193
53.757
29.067
27.536
14.326
14.185
9.850
9.749

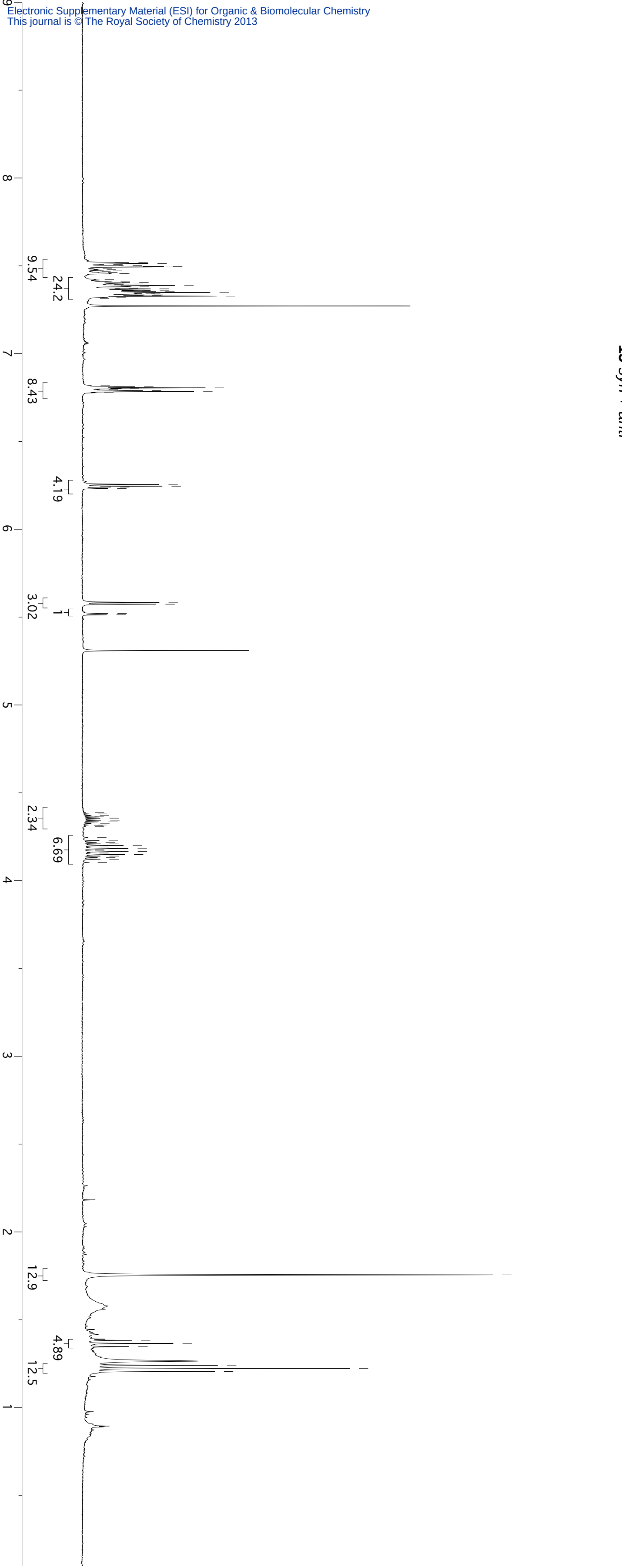


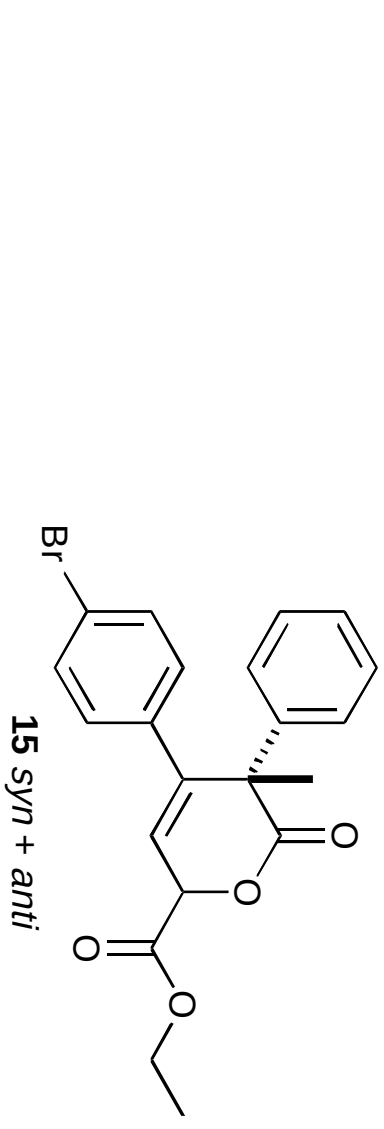
14 *syn* + *anti*



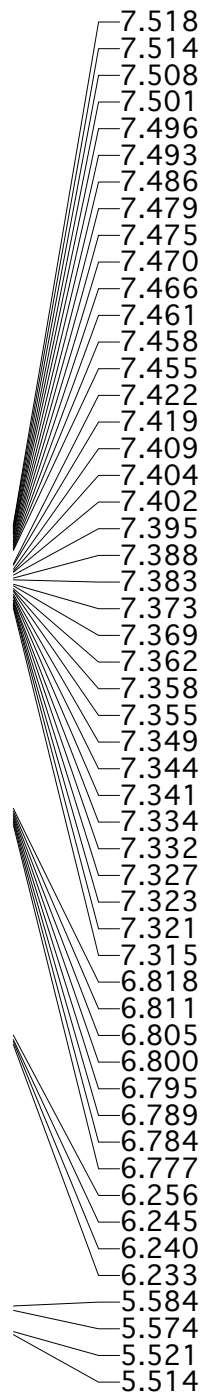
14 *syn* + *anti*

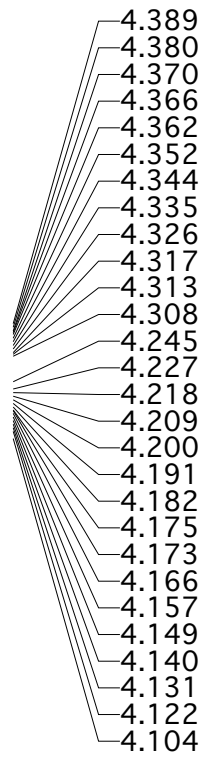
170.133
169.860
160.297
160.147
142.203
142.173
140.840
136.553
135.493
135.242
132.353
131.492
131.312
130.489
129.157
128.086
127.603
125.803
122.506
122.174
118.126
117.106
62.281
62.133
50.602
50.467
49.248
48.524
24.421
24.109
14.332
14.211

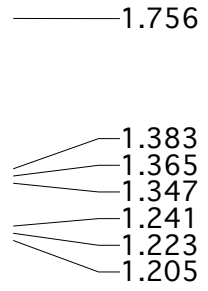


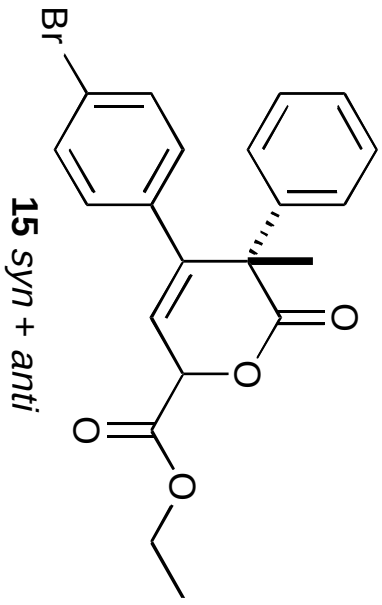


15 *syn* + *anti*



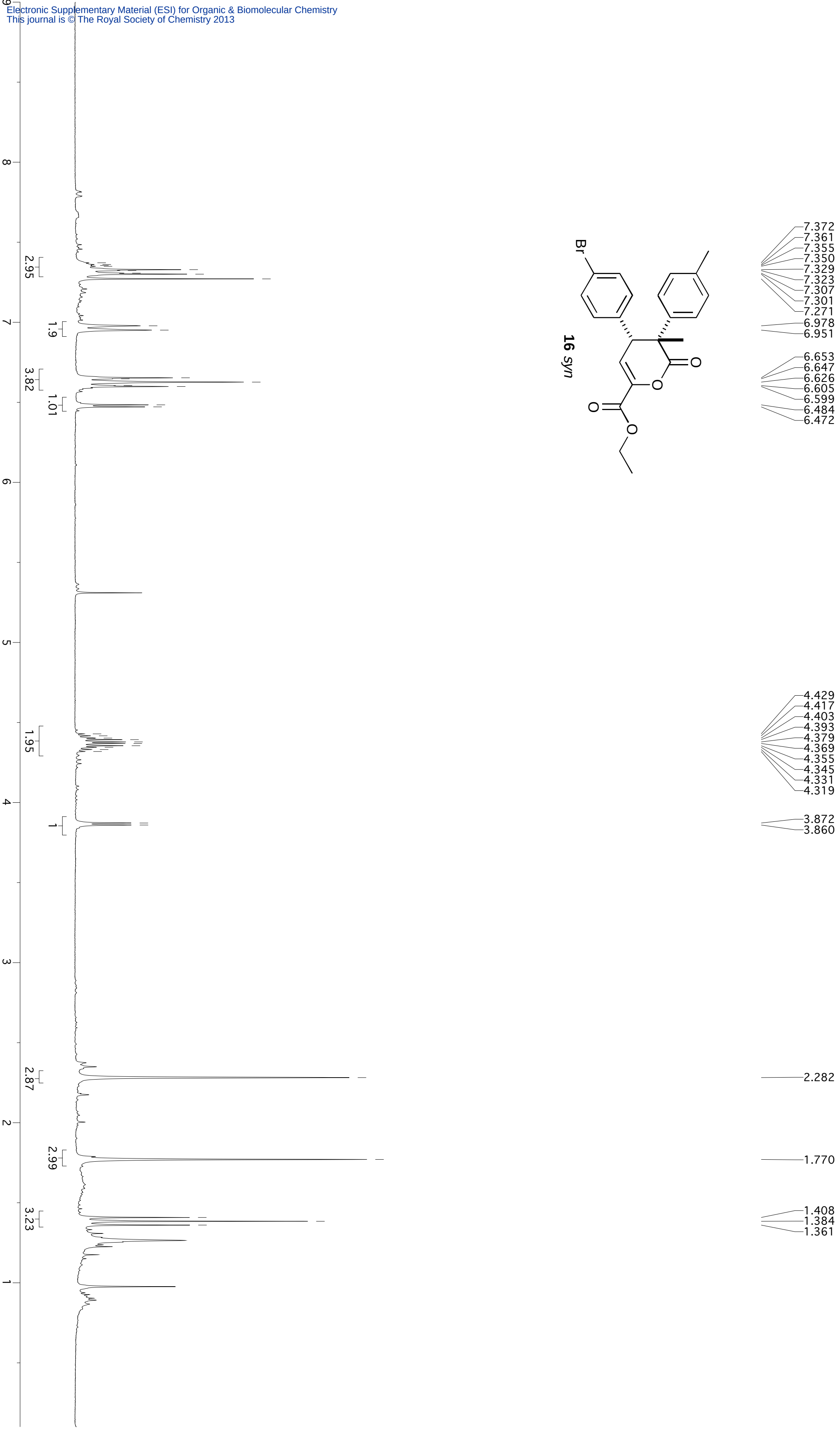


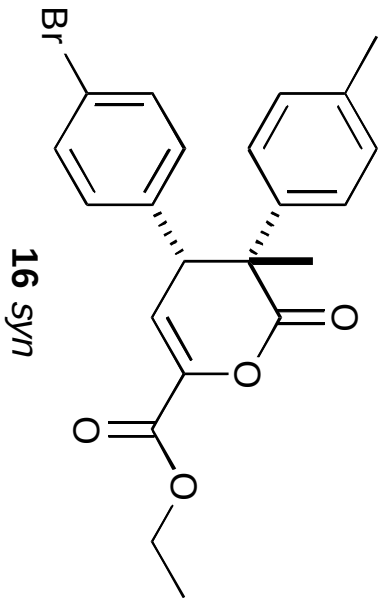




15 *syn* + *anti*

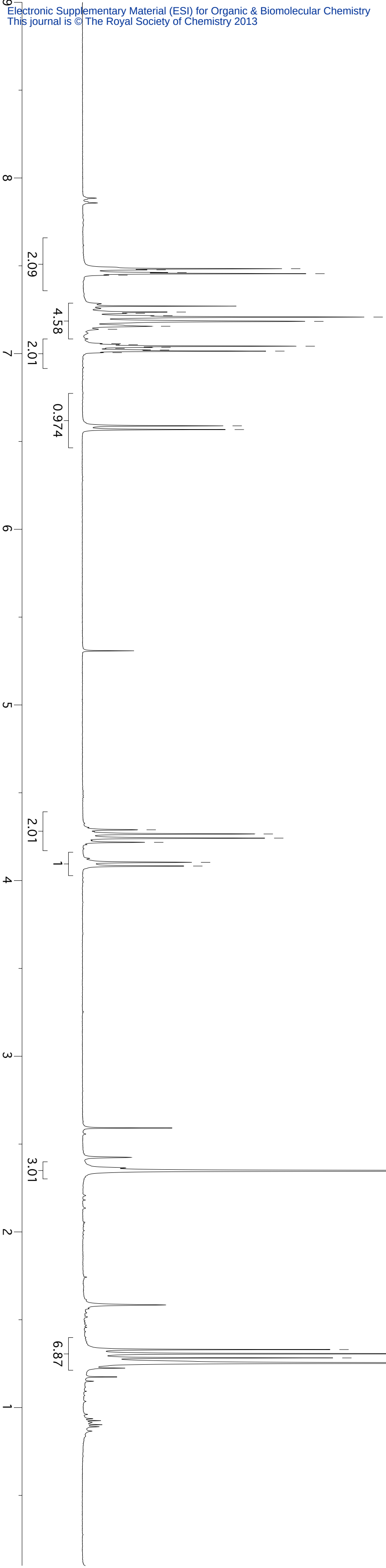
171.375
171.341
167.761
167.442
144.164
142.843
140.064
139.529
136.783
131.462
130.029
129.944
129.316
128.957
128.307
128.168
127.614
127.051
122.711
120.490
119.471
76.439
76.005
62.716
62.556
49.722
49.380
24.727
23.762
14.312
14.120

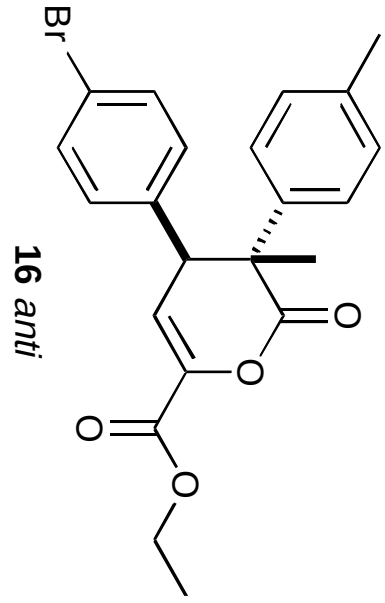




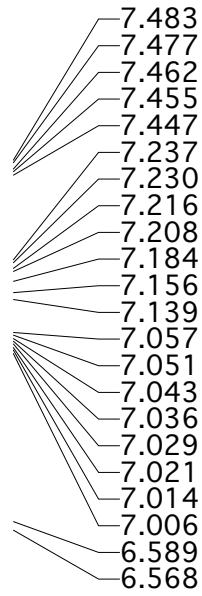
16 *syn*

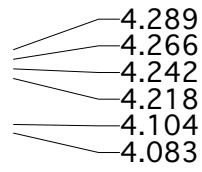
170.053
160.328
142.183
137.666
135.604
133.361
131.662
131.263
128.753
127.500
122.136
118.364
62.225
50.251
48.874
24.397
21.042
14.331

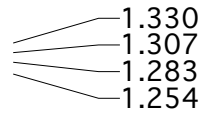


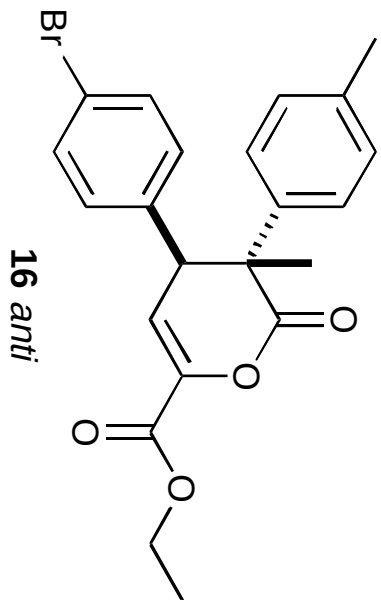


16 *anti*



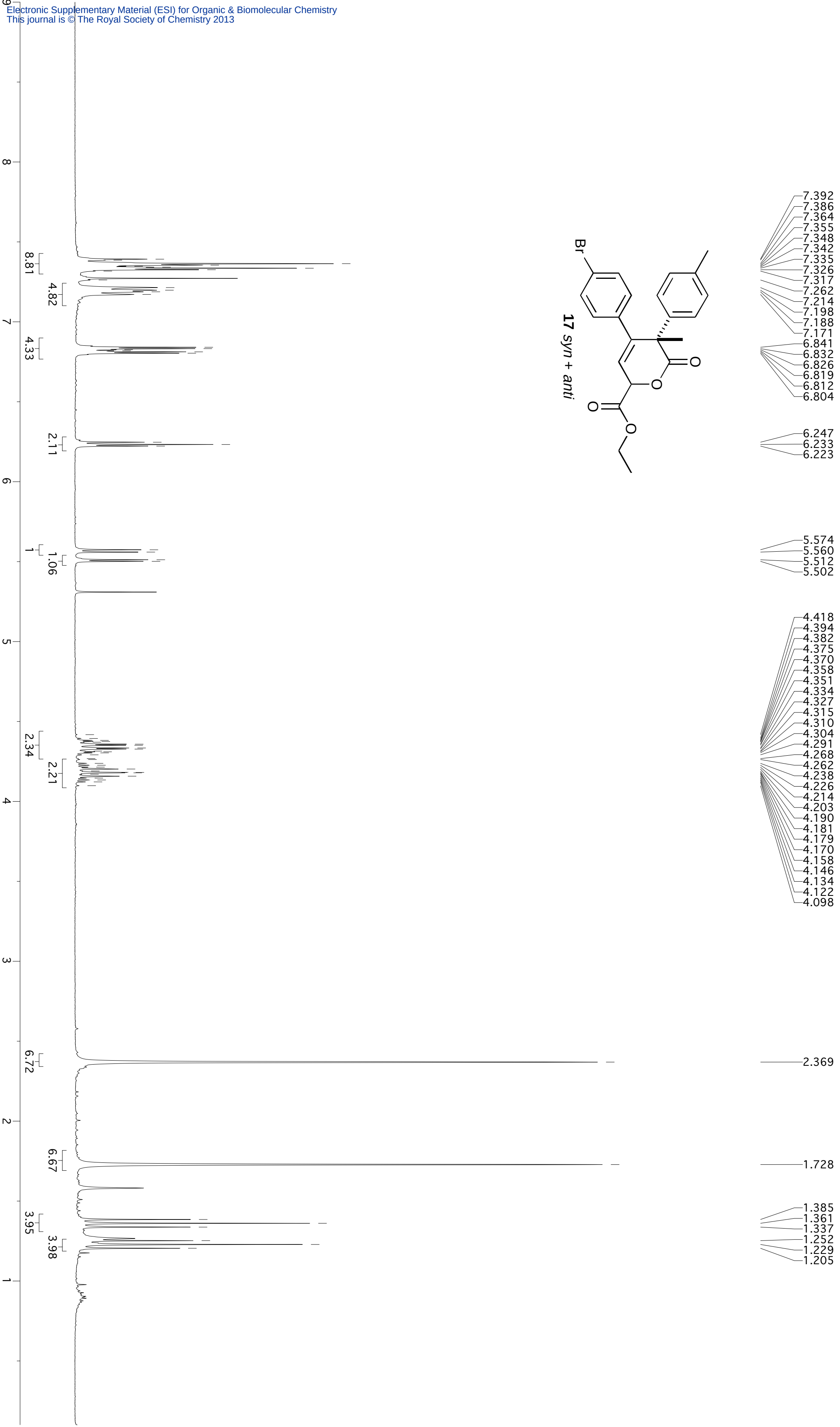


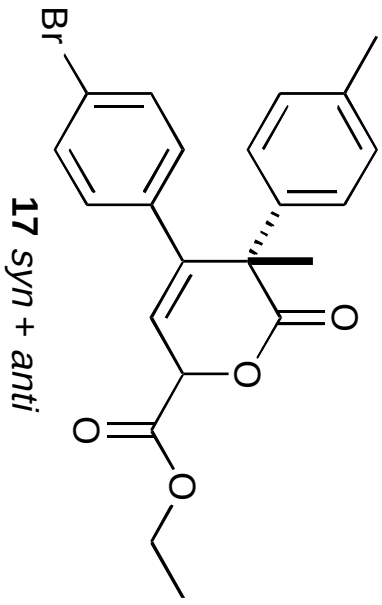




16 *anti*

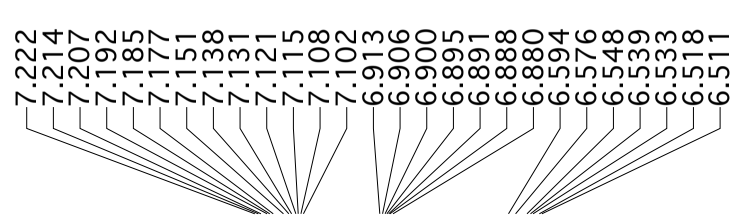
170.271
160.189
142.152
137.884
137.856
135.421
132.334
130.482
129.806
125.655
122.442
117.140
62.085
50.259
48.520
24.232
21.084
14.210

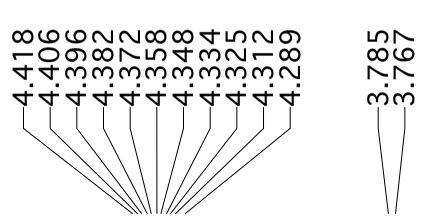


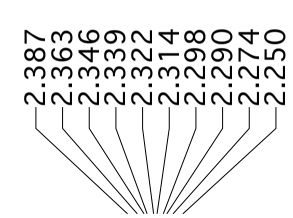


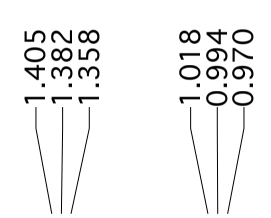
17 *syn* + *anti*

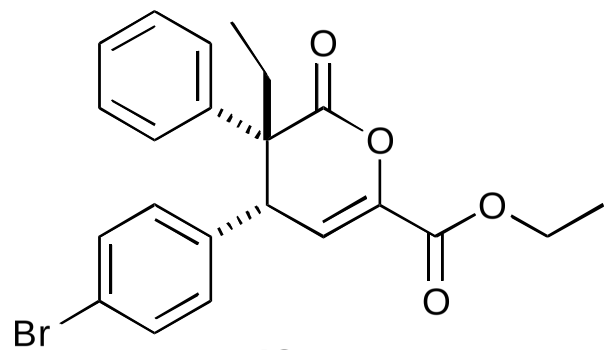
171.508
171.466
167.792
167.467
144.204
142.864
136.882
131.428
130.014
129.928
129.648
127.449
126.889
122.633
120.419
119.299
76.742
76.397
75.944
62.675
62.518
49.369
48.985
24.669
23.762
21.176
14.301
14.094



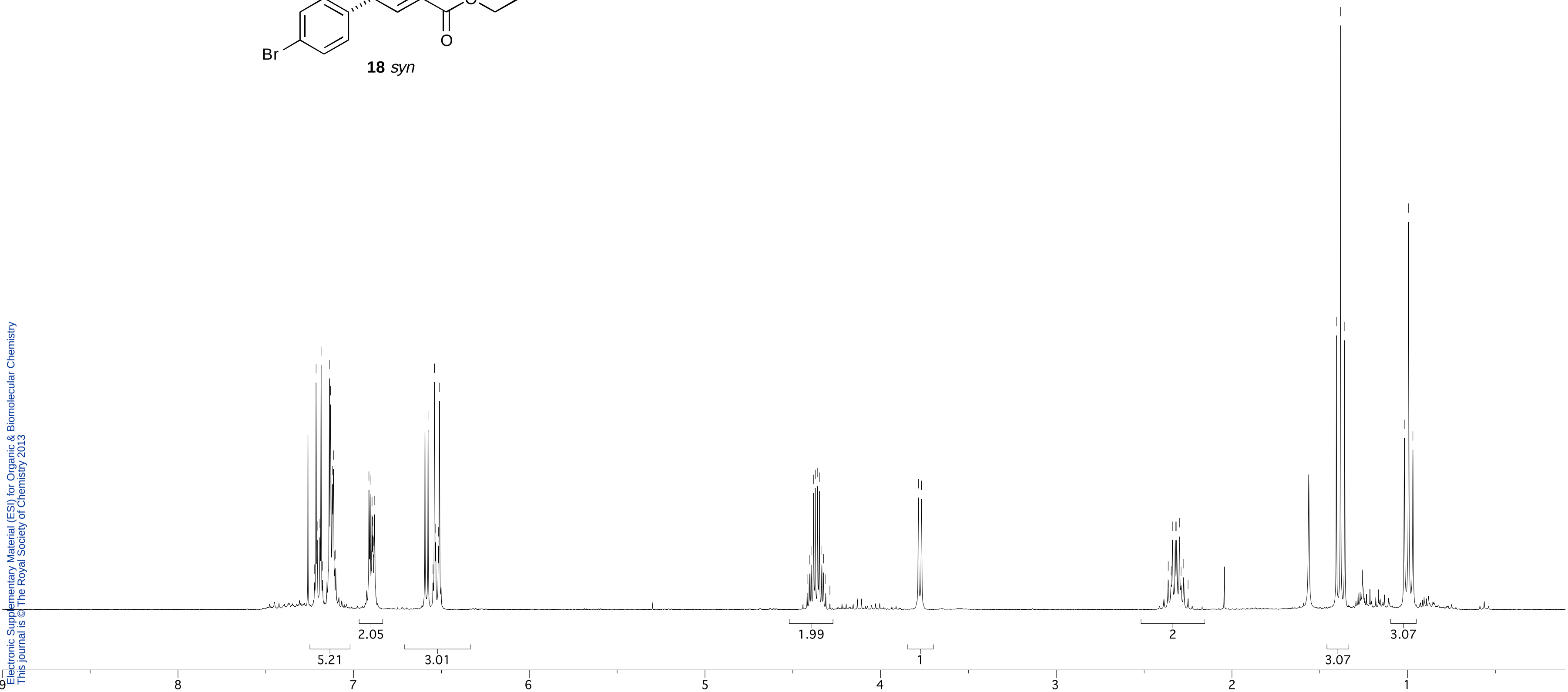


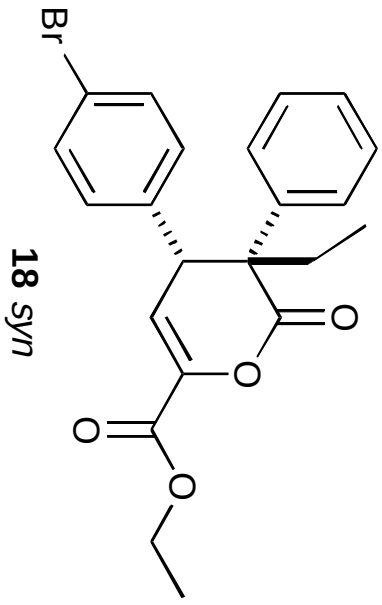






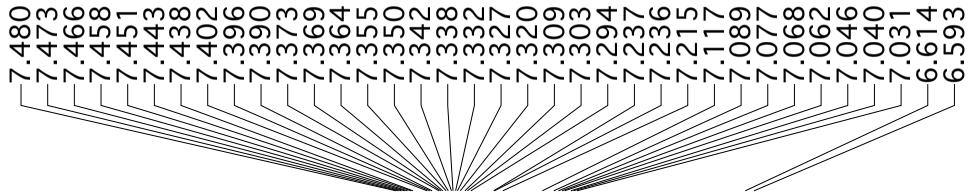
18 *syn*

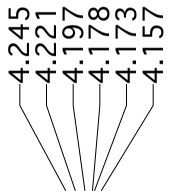


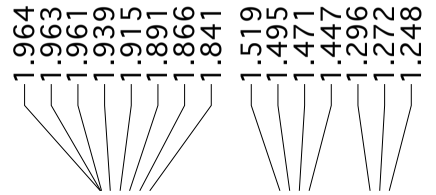


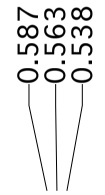
18 *syn*

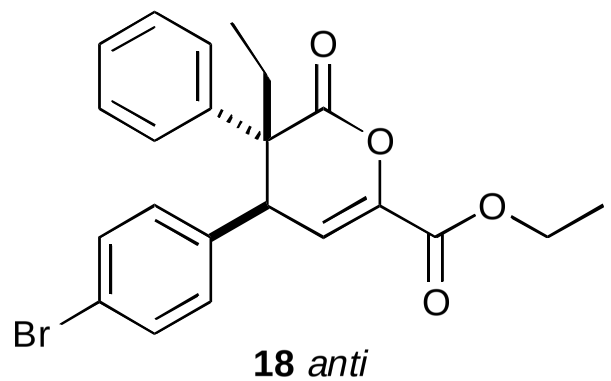
167.778
160.362
141.561
135.889
135.828
131.478
130.641
128.149
128.036
127.391
121.852
117.466
62.277
54.905
50.291
29.228
14.336
9.476



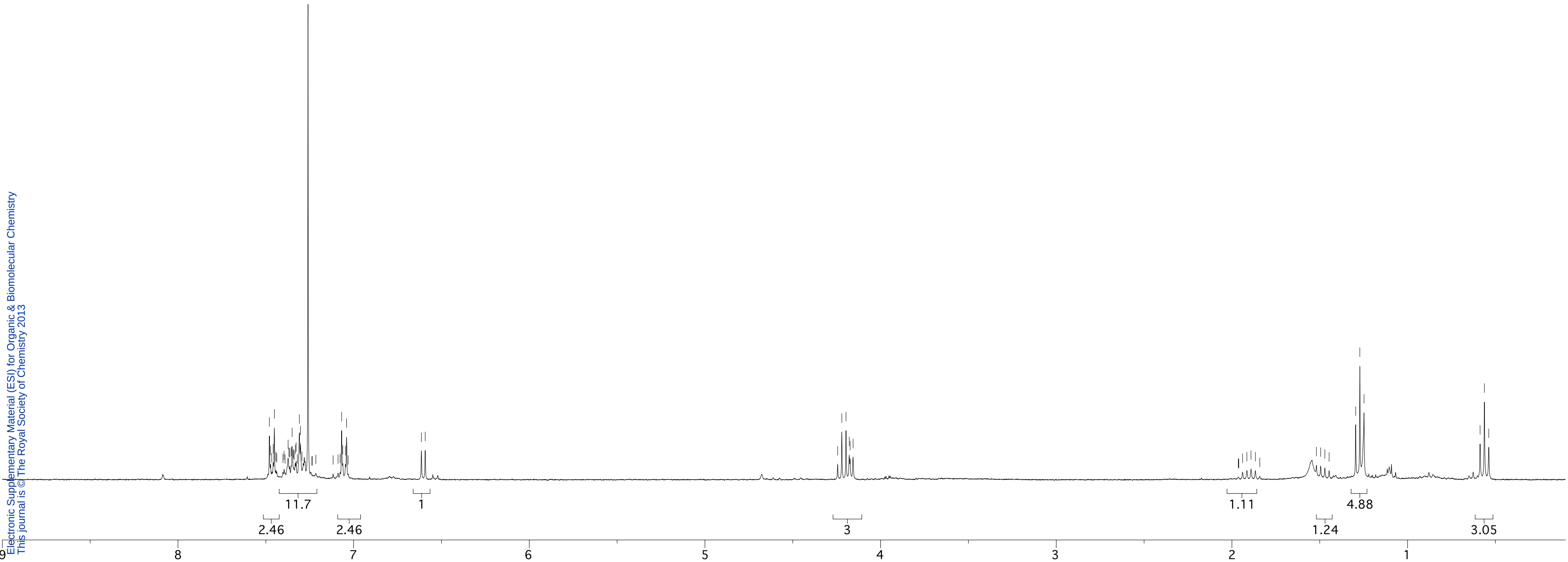


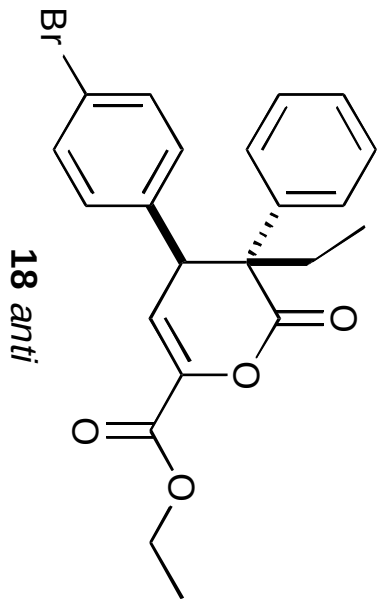






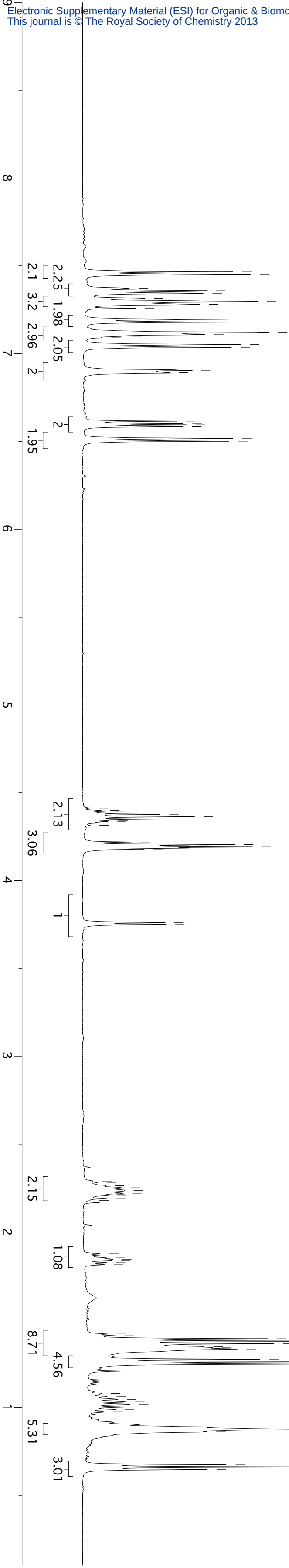
18 *anti*

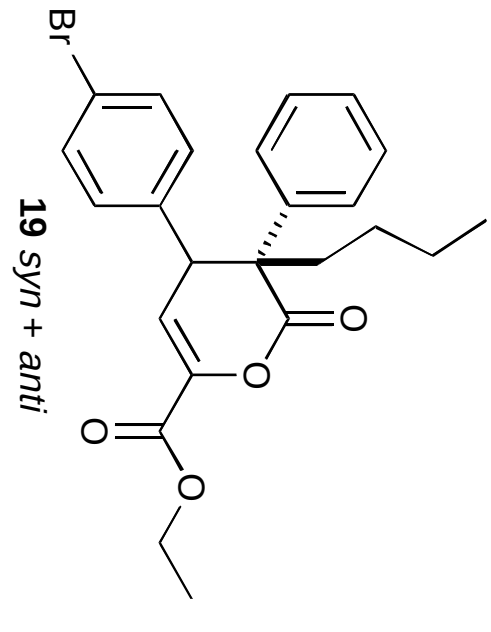




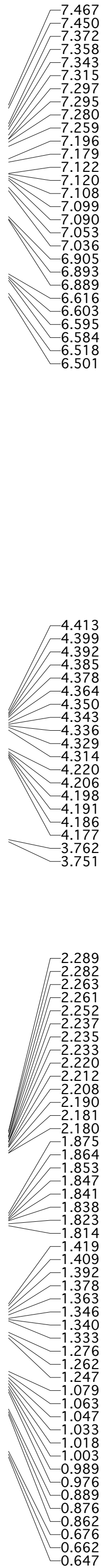
18 *anti*

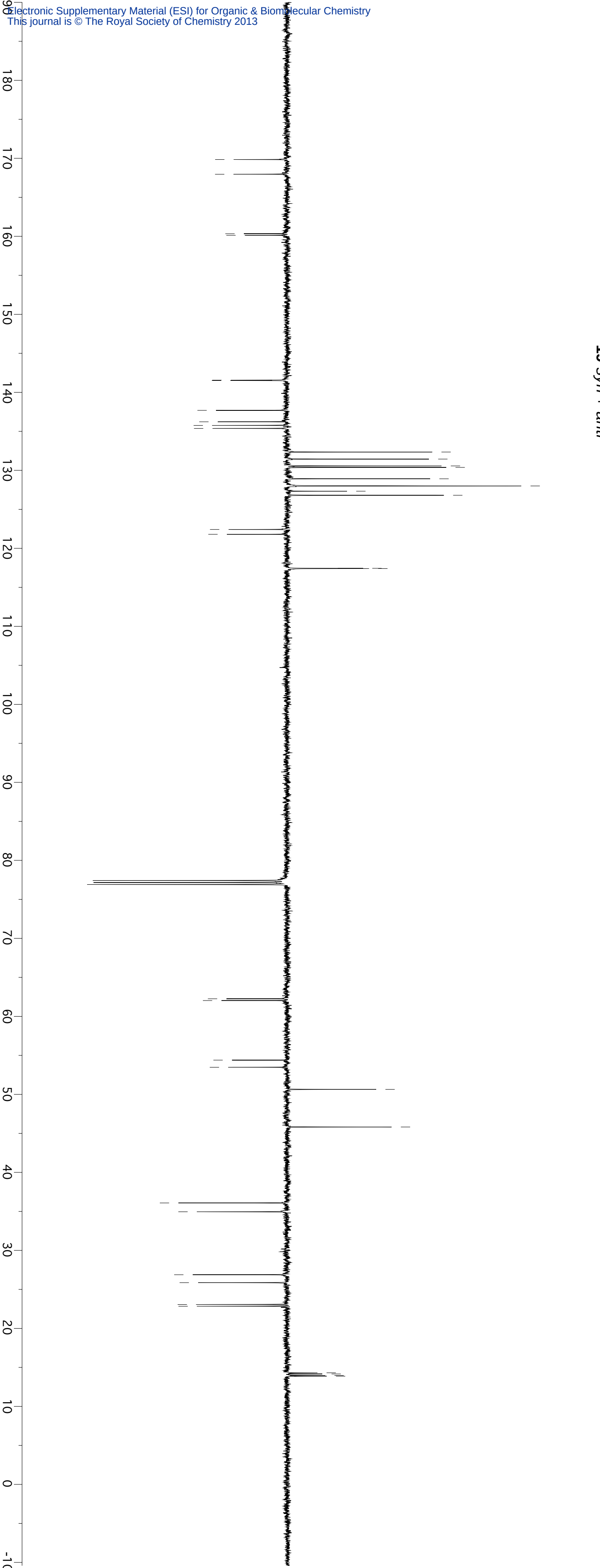
169.826
160.176
141.676
137.378
135.403
132.402
132.063
130.417
128.959
128.088
126.933
122.457
117.353
62.061
53.867
45.951
28.373
14.188
8.474





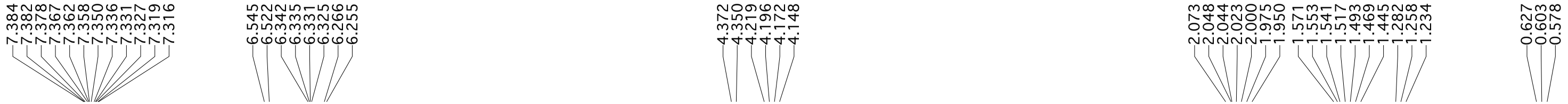
19 *syn* + *anti*

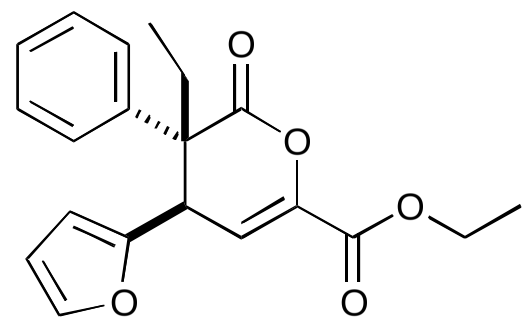




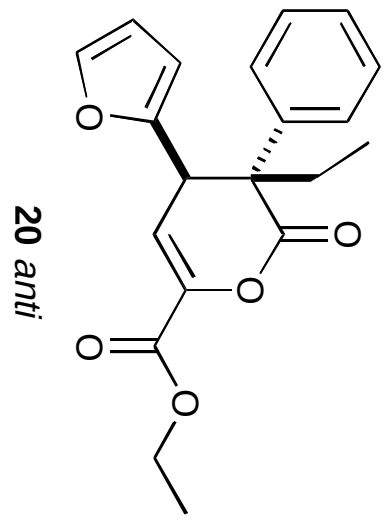
19 *syn* + *anti*

169.847
167.960
160.337
160.128
141.565
141.512
137.686
136.225
135.761
135.374
132.346
131.443
130.566
130.376
128.919
127.998
127.326
126.803
122.421
121.798
117.440
117.408
62.260
62.030
54.392
53.477
50.639
45.818
36.084
34.950
26.882
25.864
23.065
22.843
14.308
14.161
13.973
13.873



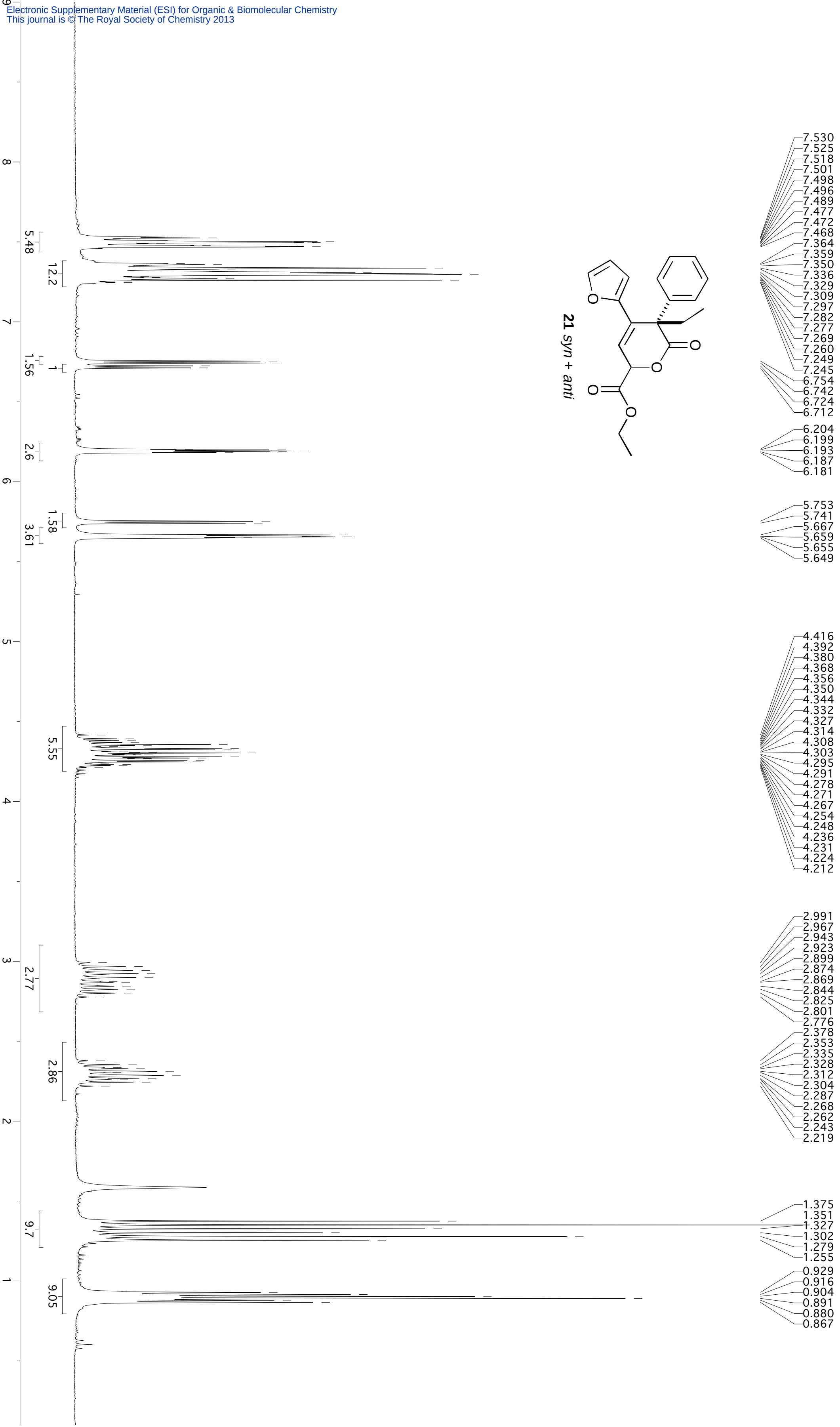


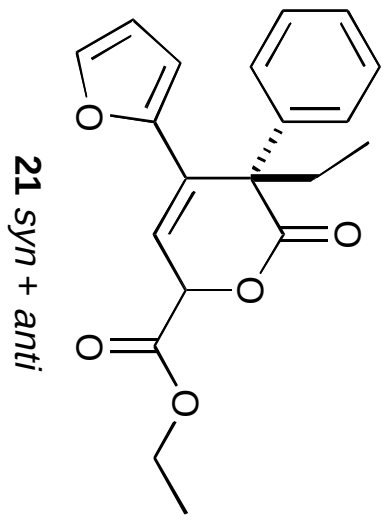
20 *anti*



20 *anti*

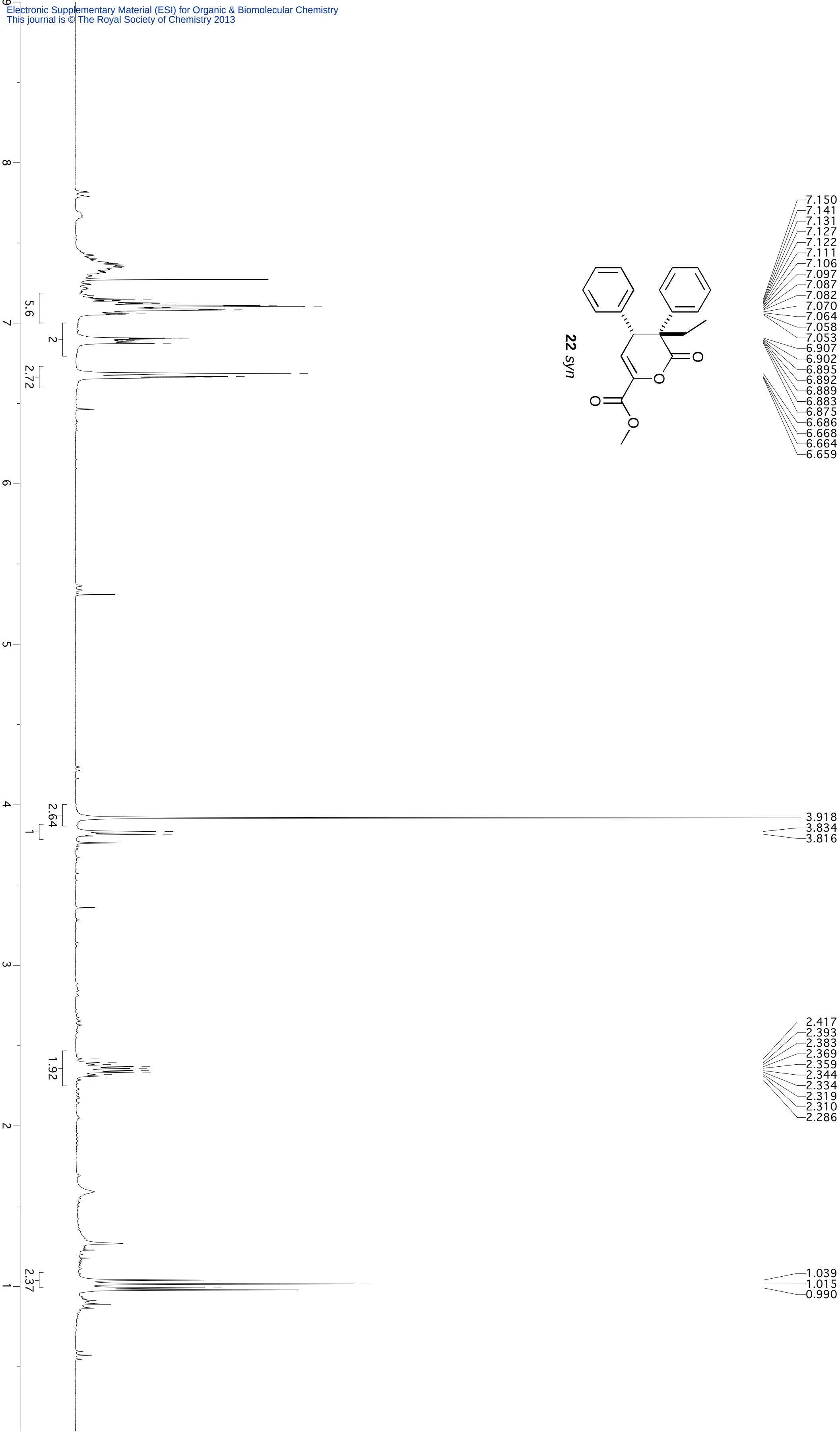
169.718
160.220
149.379
143.164
142.029
136.646
128.908
128.043
126.839
114.530
110.631
109.041
61.934
53.367
38.123
29.105
14.143
8.066

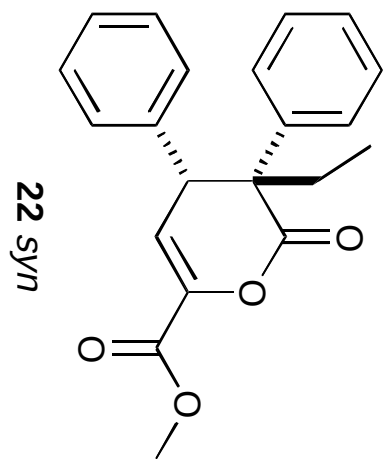




21 *syn* + *anti*

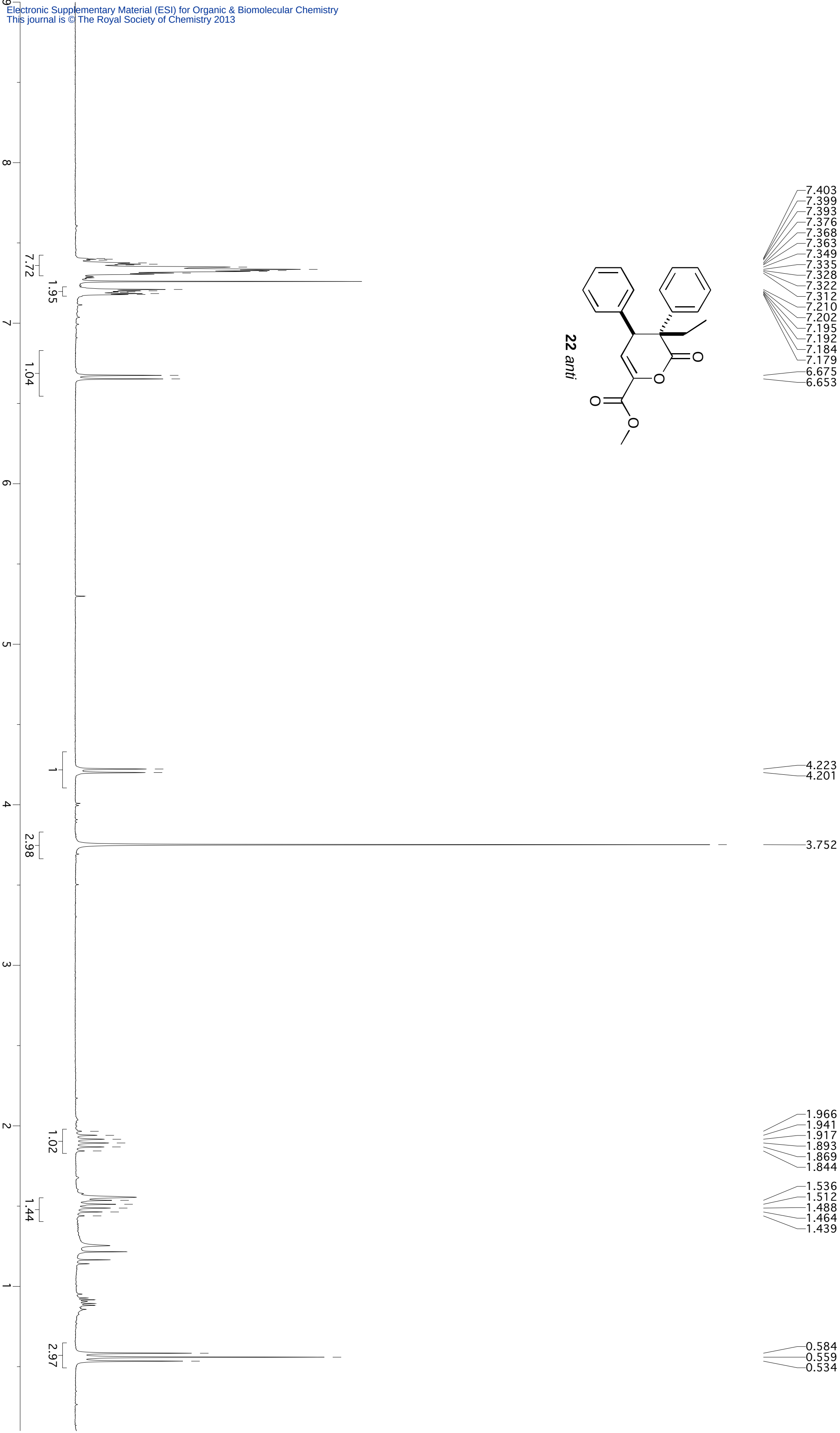
170.828
170.729
167.876
167.761
149.264
142.306
141.072
140.694
130.855
130.682
128.933
128.719
127.965
127.876
127.578
127.108
116.482
116.290
111.341
110.129
77.059
62.620
52.805
52.487
30.109
28.779
14.273
14.166
10.080
9.900

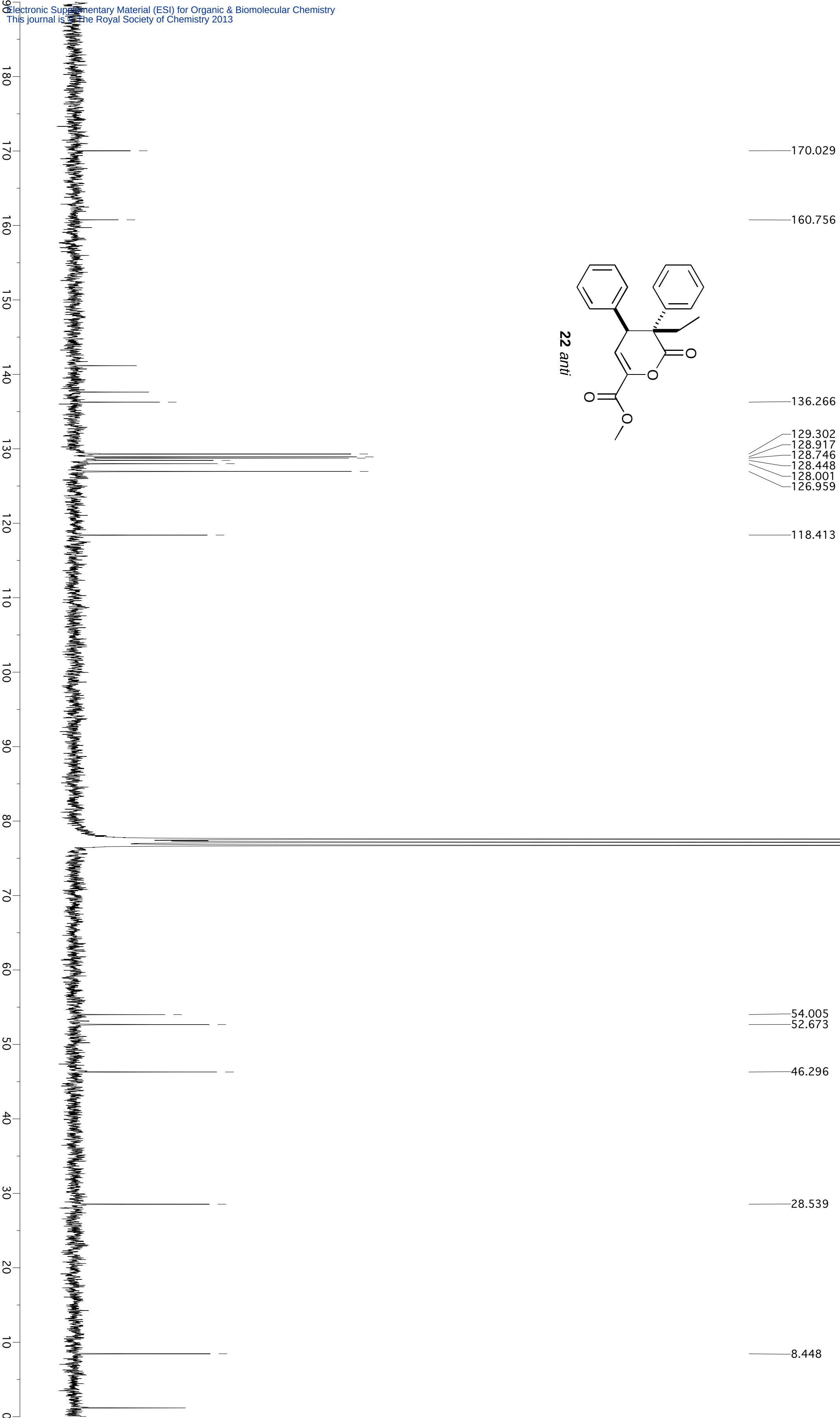


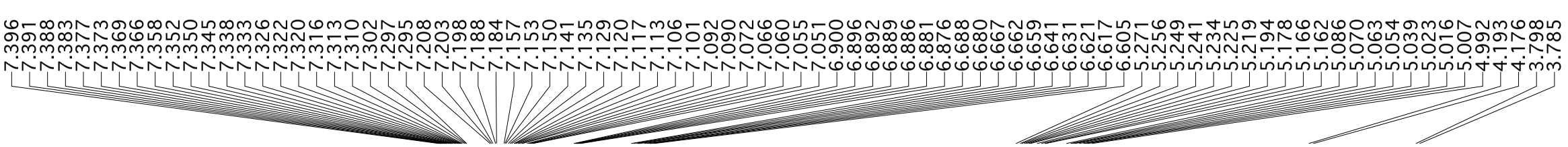


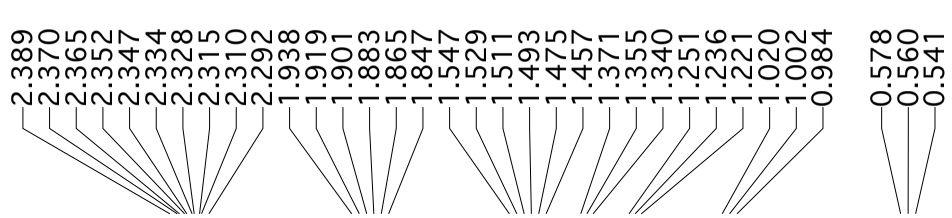
22 *syn*

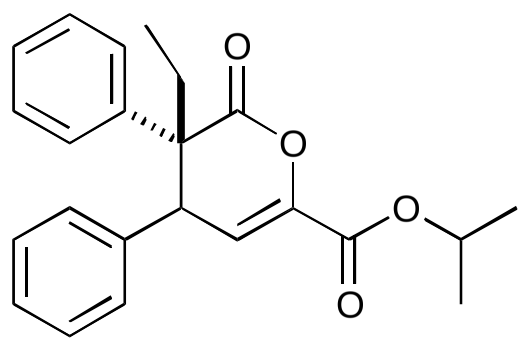
168.017
160.924
141.065
136.620
136.071
129.012
128.363
128.196
127.795
127.137
118.562
55.114
52.867
50.865
29.195
9.497



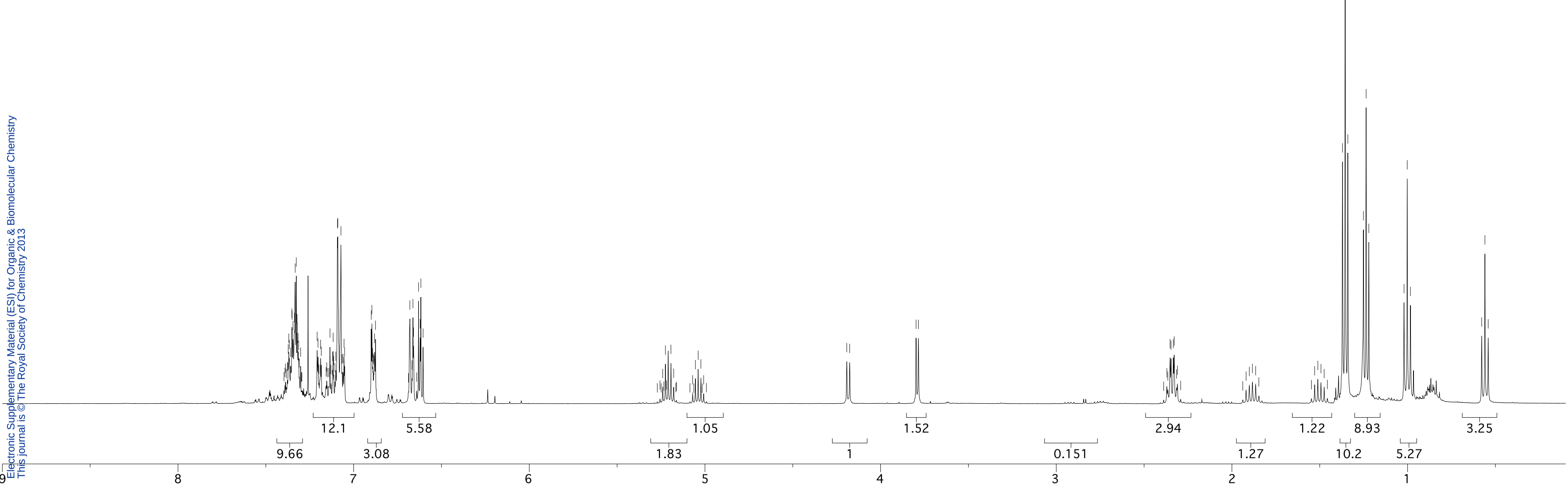


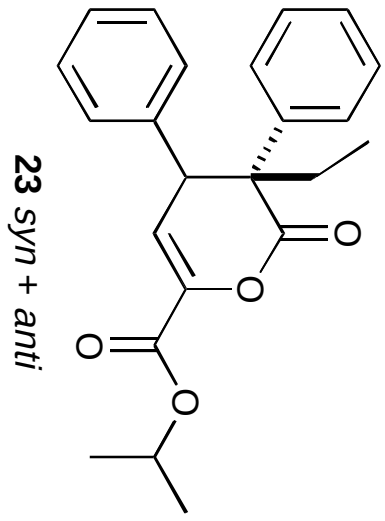






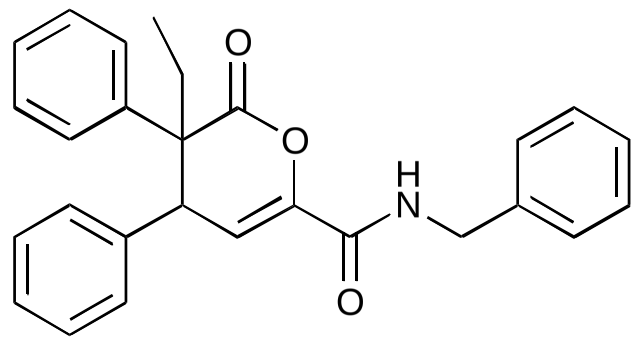
23 *syn + anti*



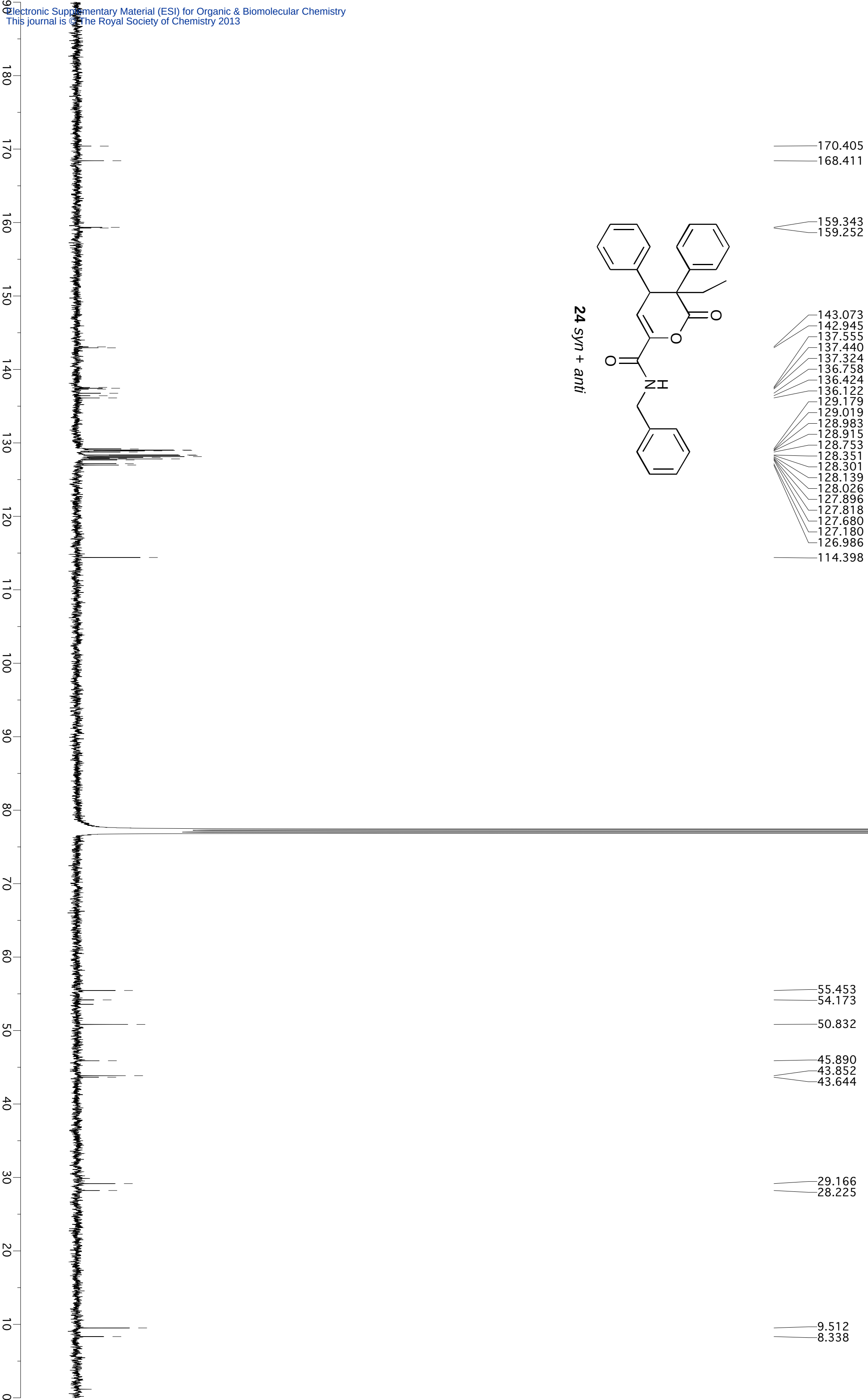


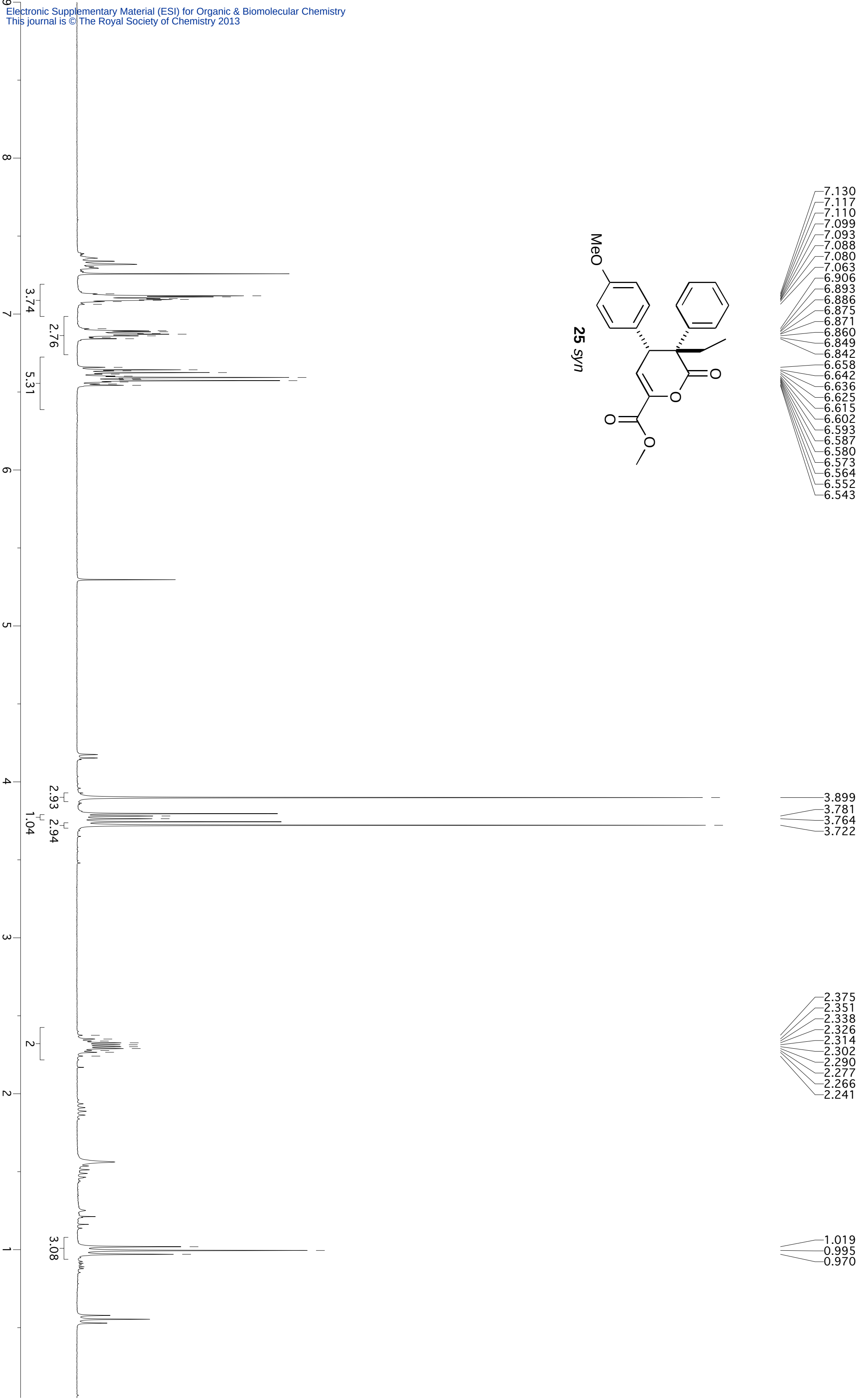
23 *syn* + *anti*

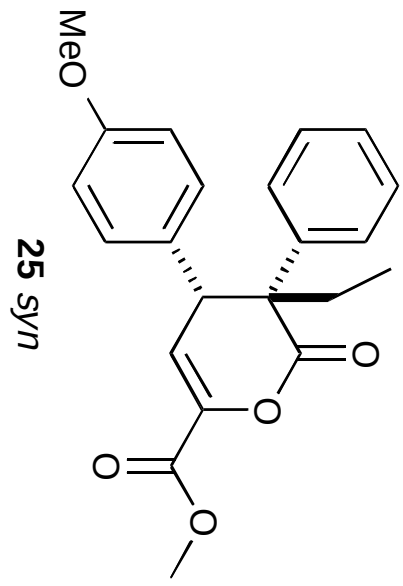
170.246
168.192
159.993
159.838
141.623
141.459
137.741
136.820
136.457
136.190
129.234
129.016
128.833
128.790
128.338
128.213
127.903
127.757
127.723
127.061
126.964
117.885
117.731
70.051
69.823
55.096
53.949
50.934
46.533
29.206
28.512
21.954
21.936
21.818
9.507
8.506



24 *syn + anti*

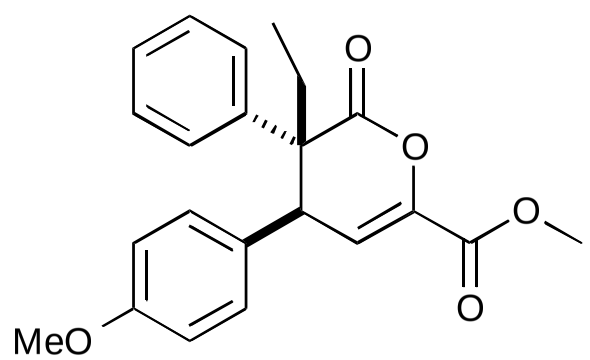




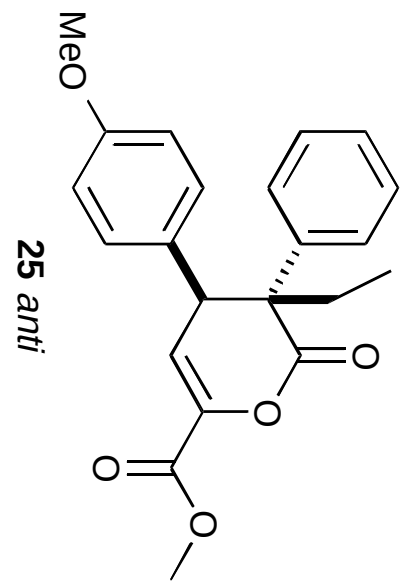


25 *syn*

168.212
160.963
159.137
140.867
136.170
130.119
128.251
127.819
127.127
119.003
113.701
55.357
55.258
52.845
49.928
29.082
9.526

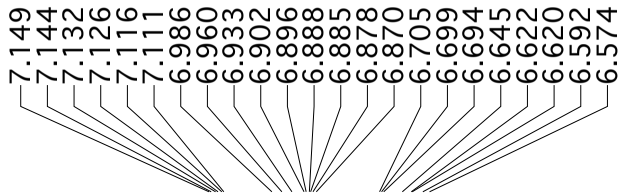


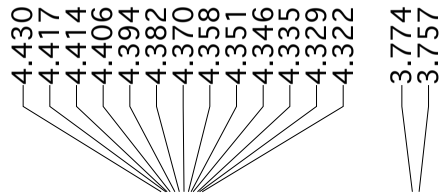
25 *anti*

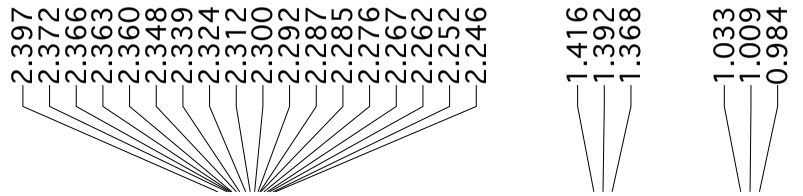


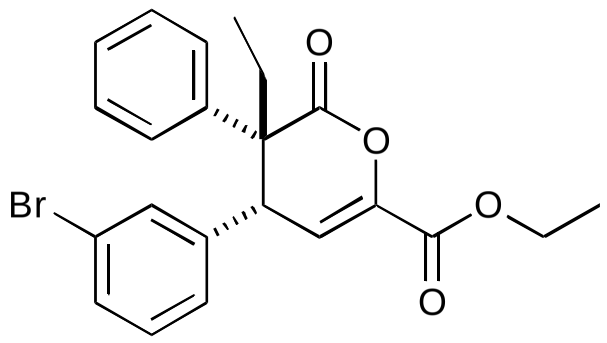
25 *anti*

170.150
160.798
159.622
140.918
137.711
132.243
129.821
128.885
127.945
126.963
118.743
114.633
55.456
52.646
45.403
28.505
8.440

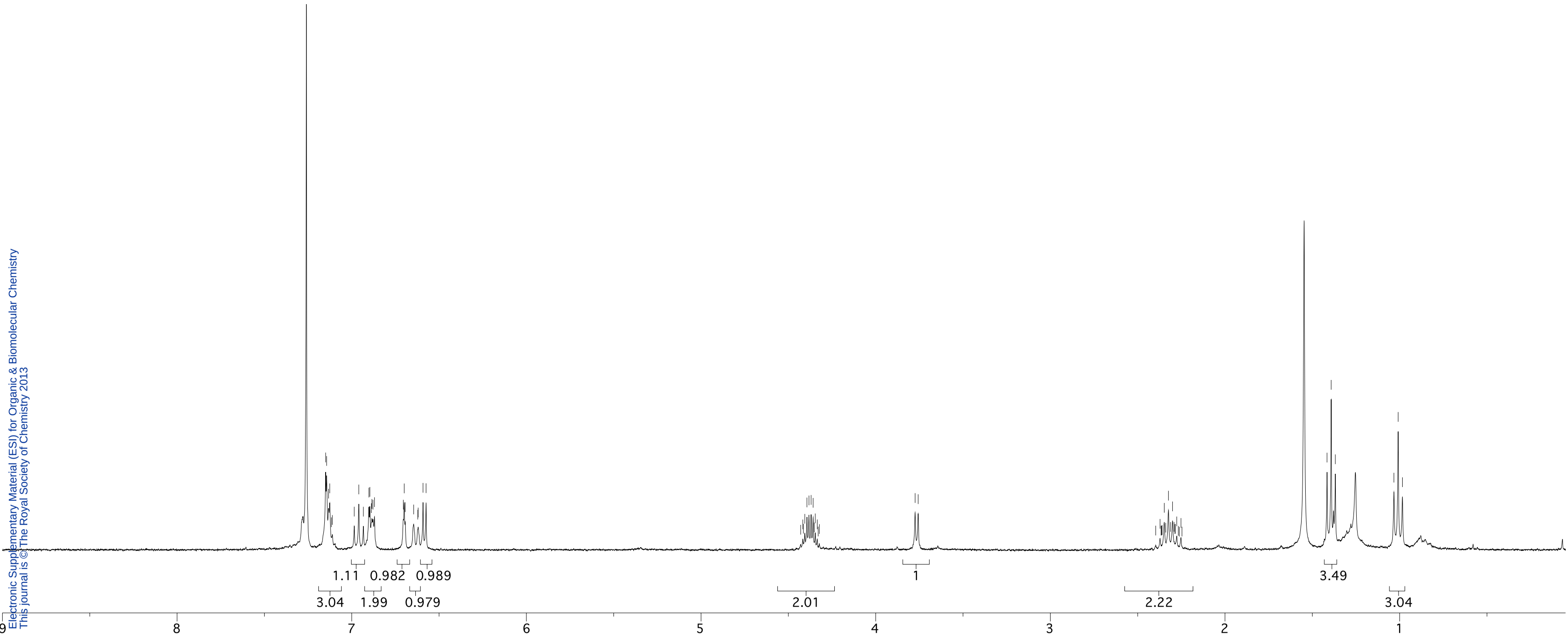


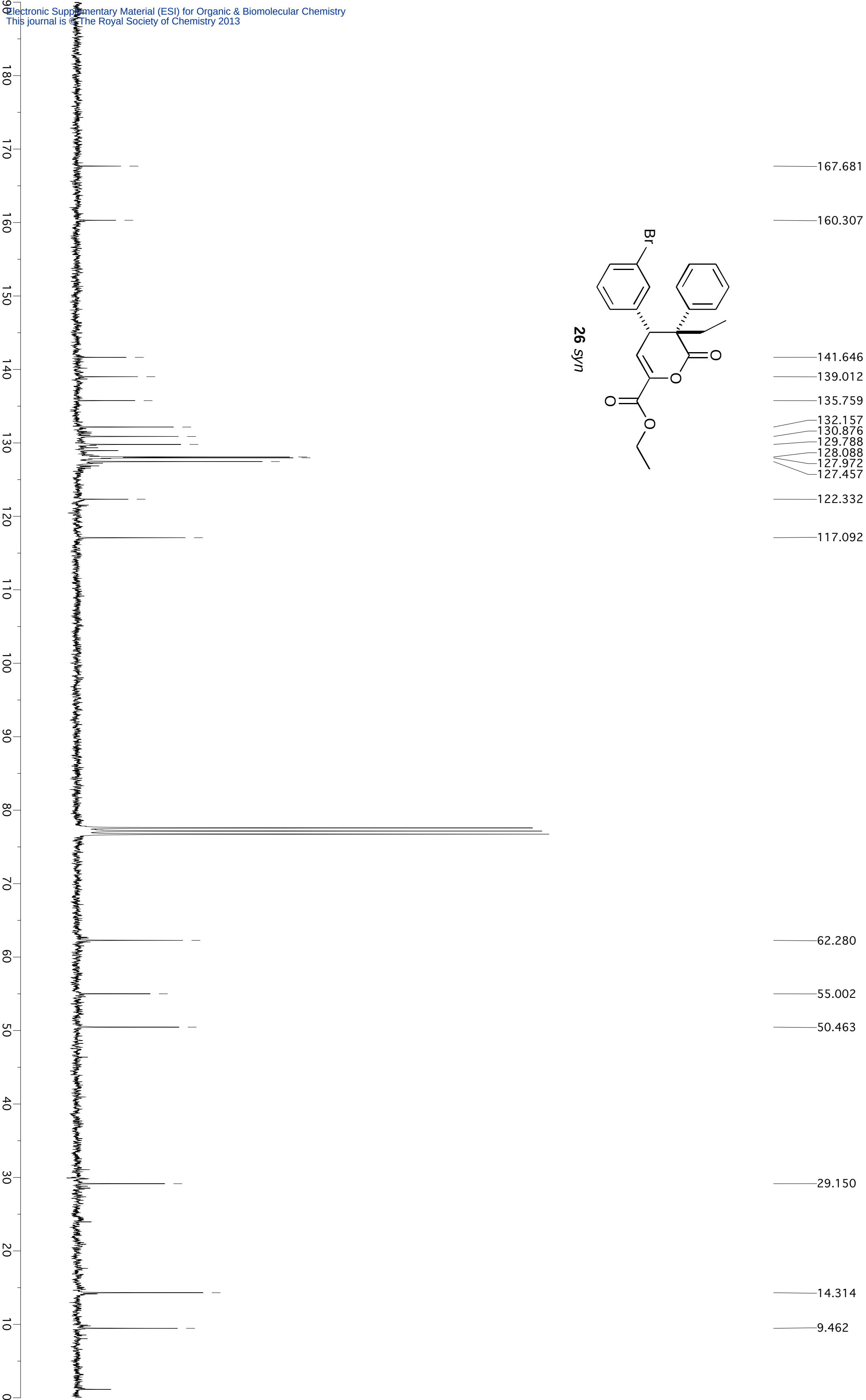


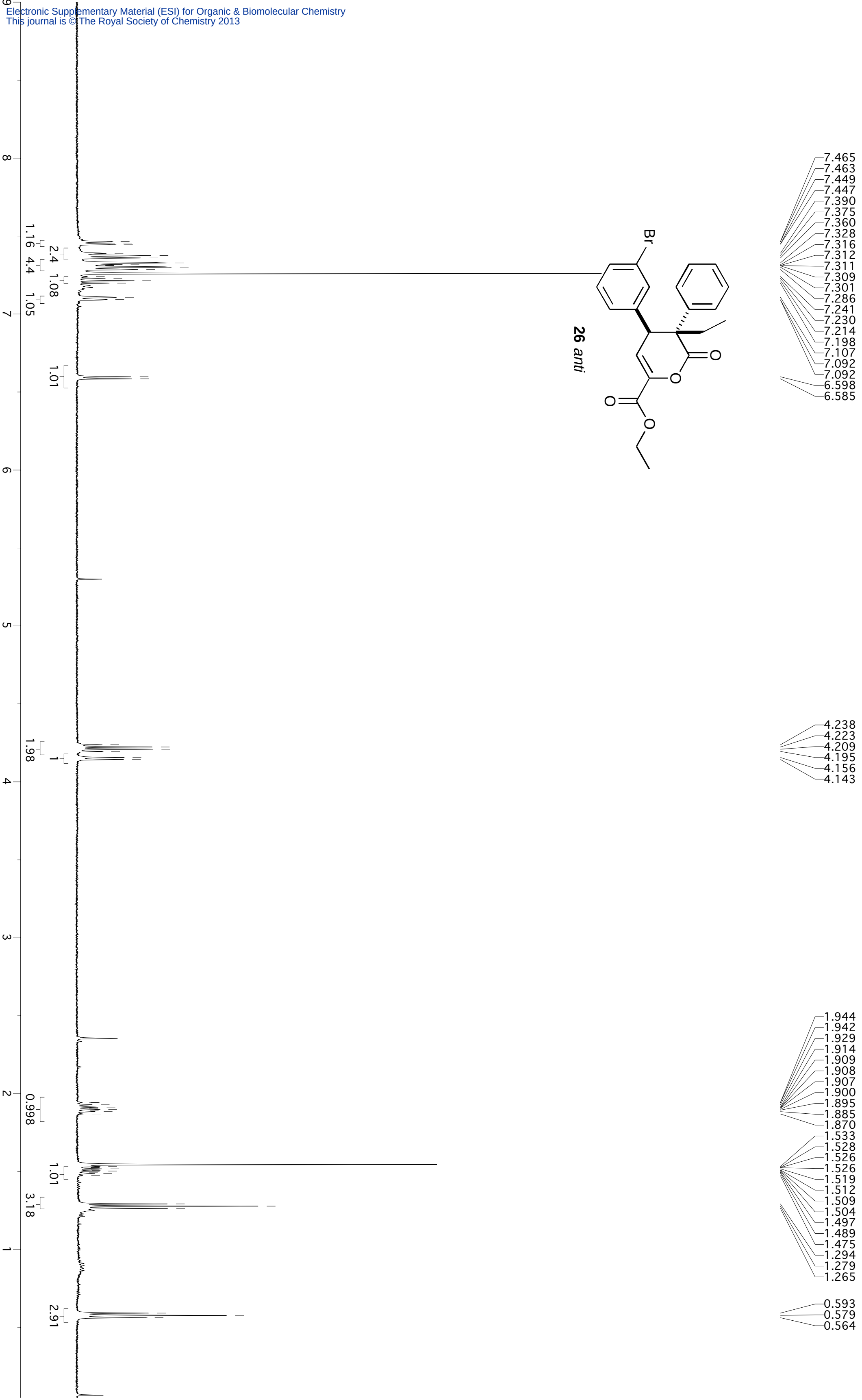


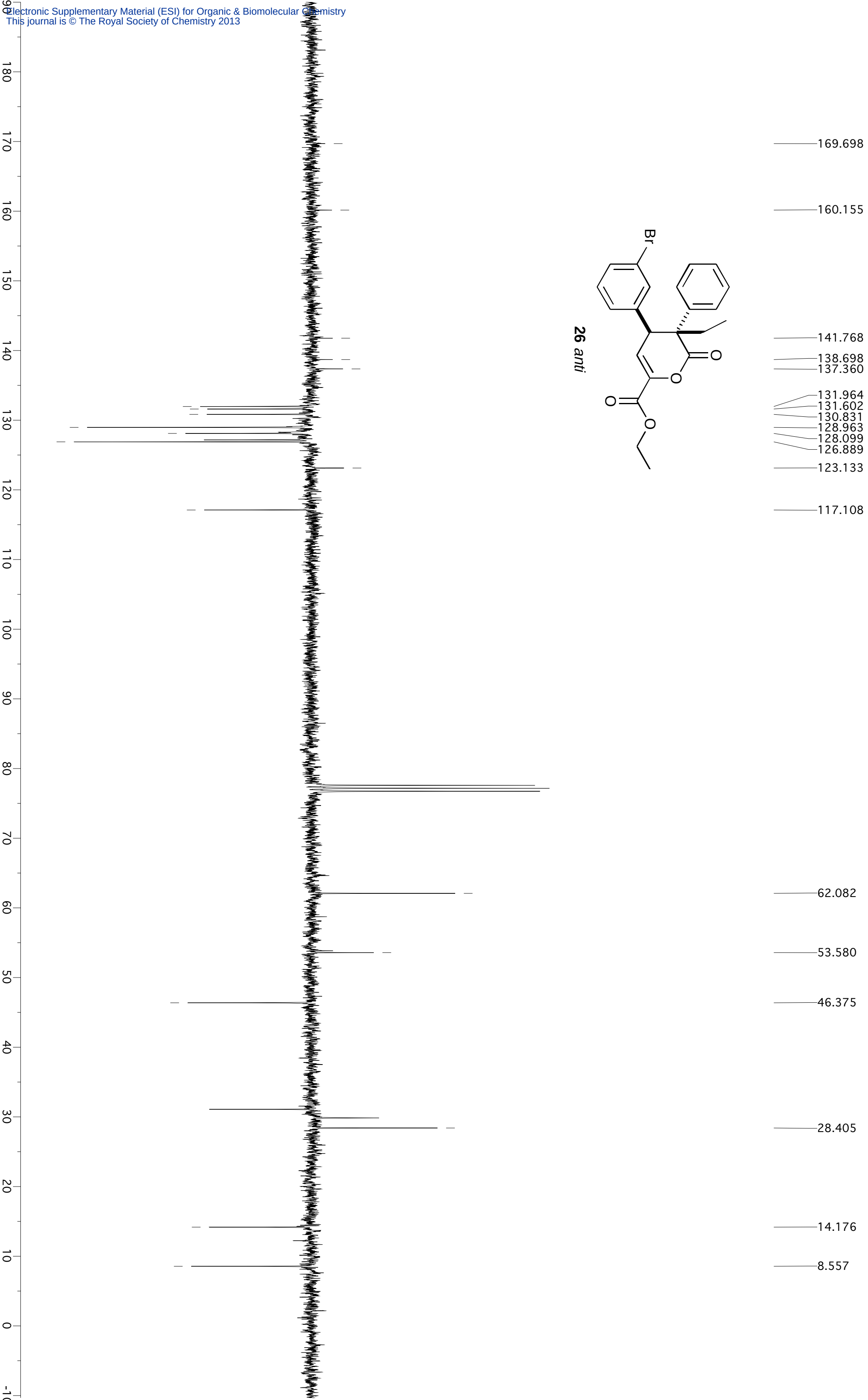


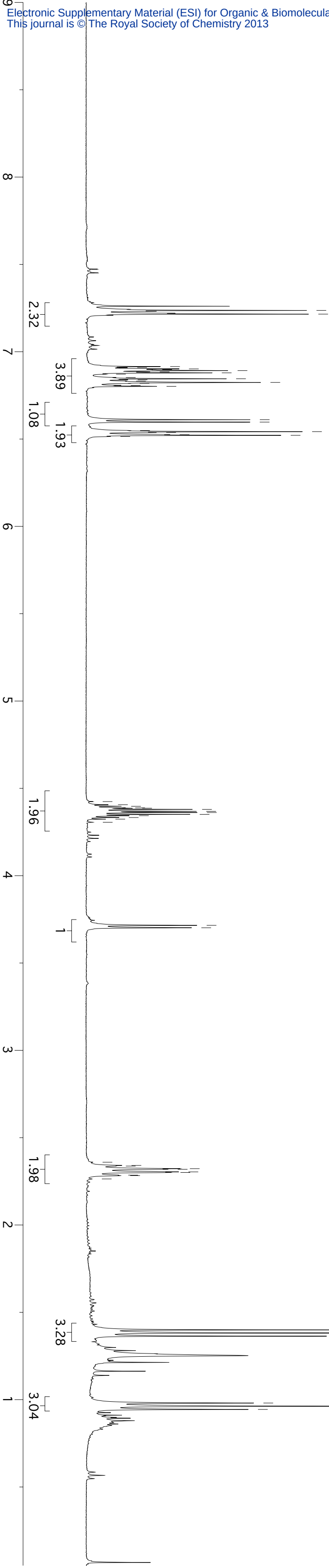
26 *syn*



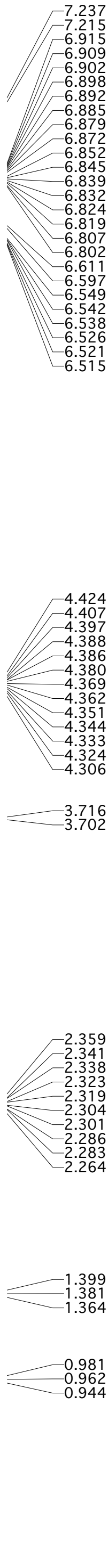


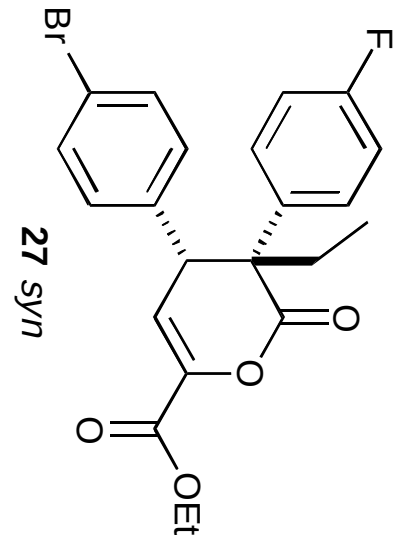






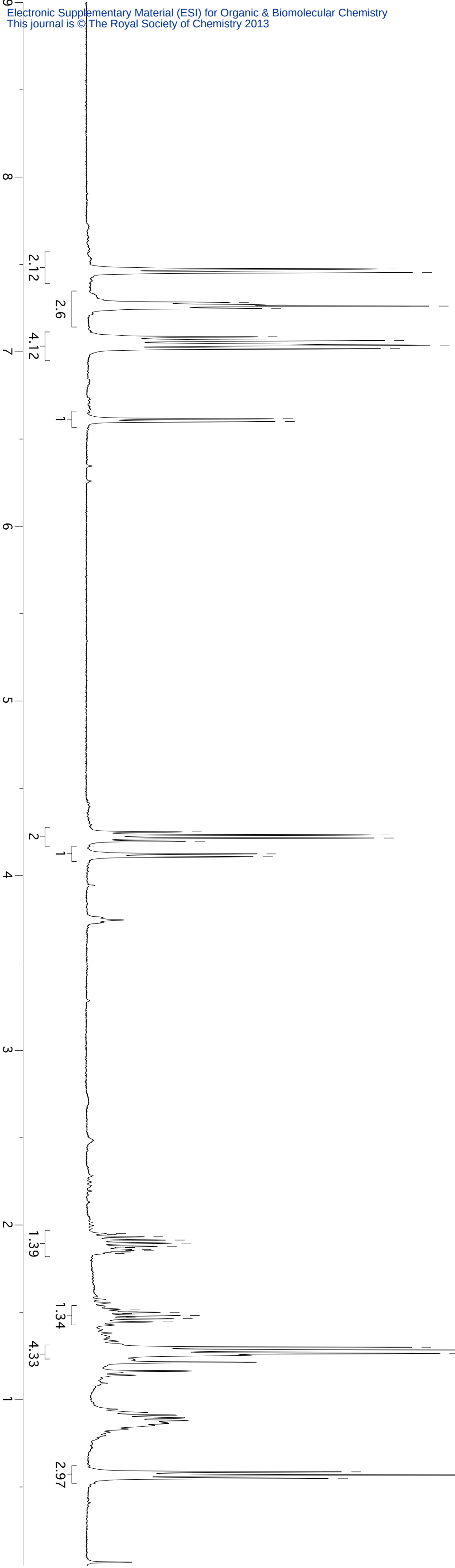
27 *syn*



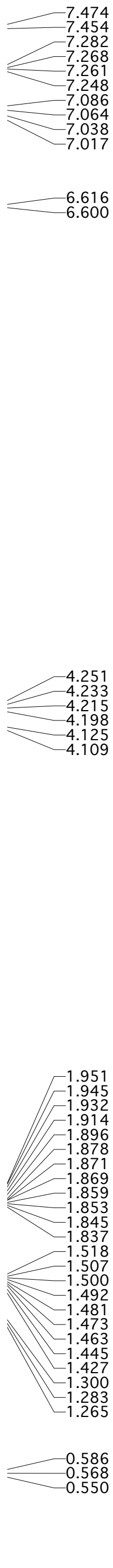


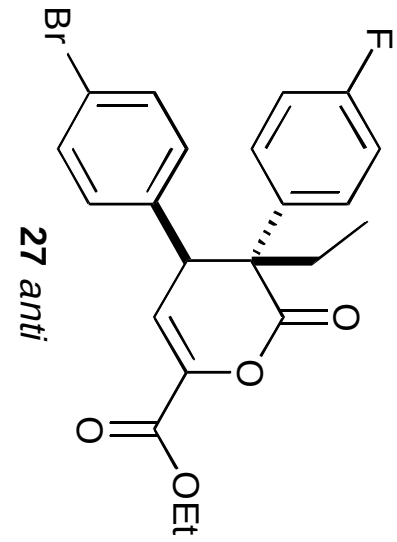
27 *syn*

167.551
163.335
160.217
160.057
141.501
135.592
131.664
130.435
129.989
129.884
121.989
117.131
115.026
114.745
62.314
54.533
50.810
29.476
14.299
9.381



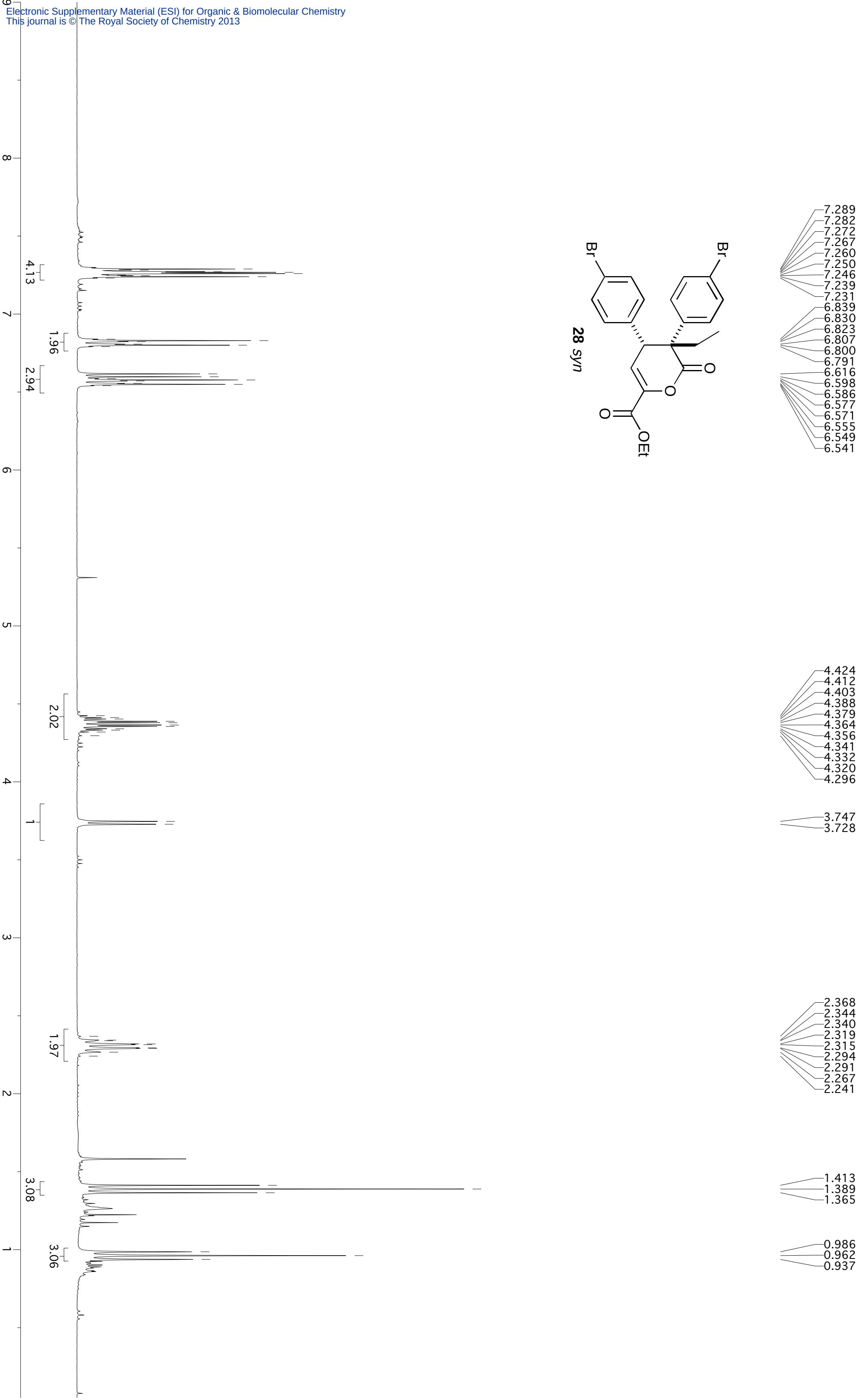
27 *anti*

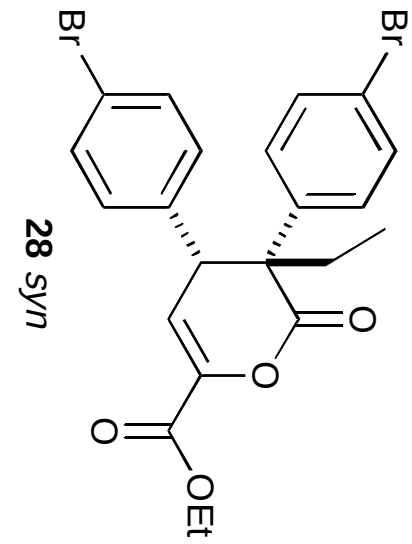




27 *anti*

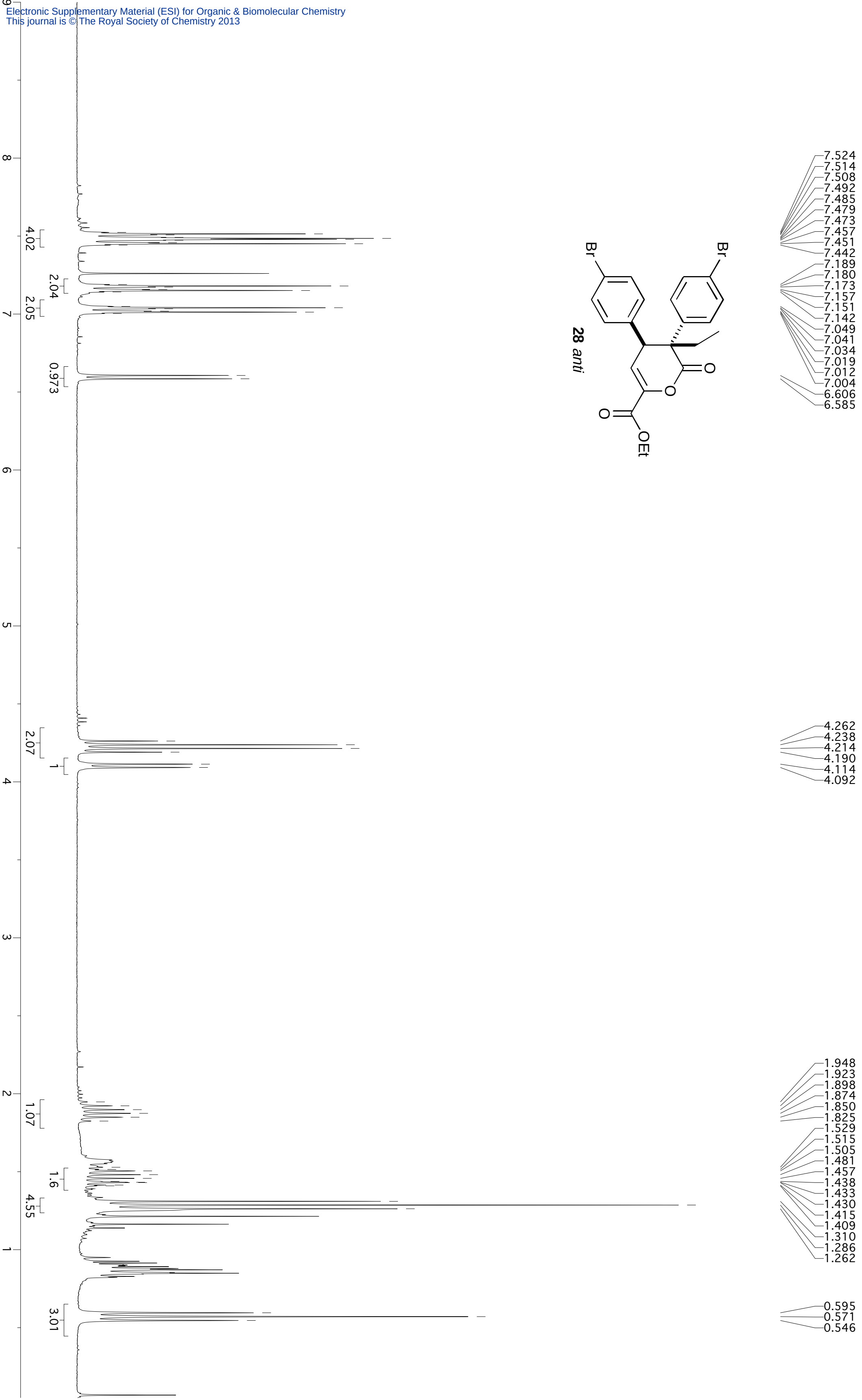
169.593
163.904
160.618
160.055
141.691
135.126
133.137
133.092
132.434
130.364
128.791
128.683
122.563
117.096
116.080
115.795
62.154
53.352
46.033
28.118
14.193
8.344

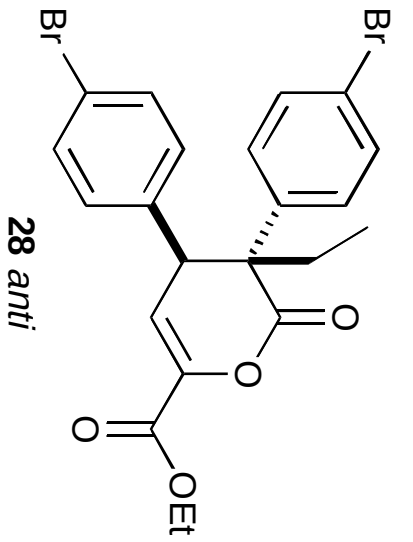




28 *syn*

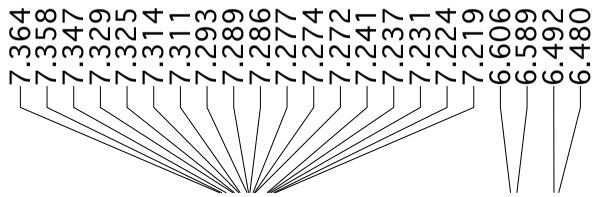
167.313
160.181
141.517
135.424
135.011
131.752
131.116
130.493
129.984
122.123
121.555
117.111
62.348
54.644
50.500
29.354
14.314
9.392

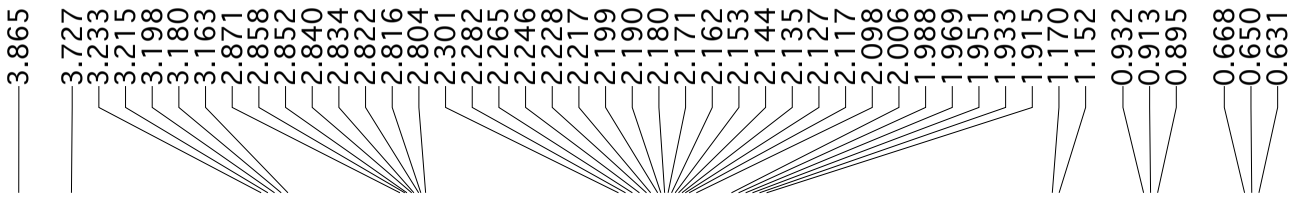


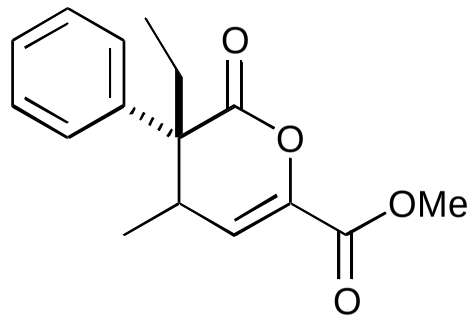


28 *anti*

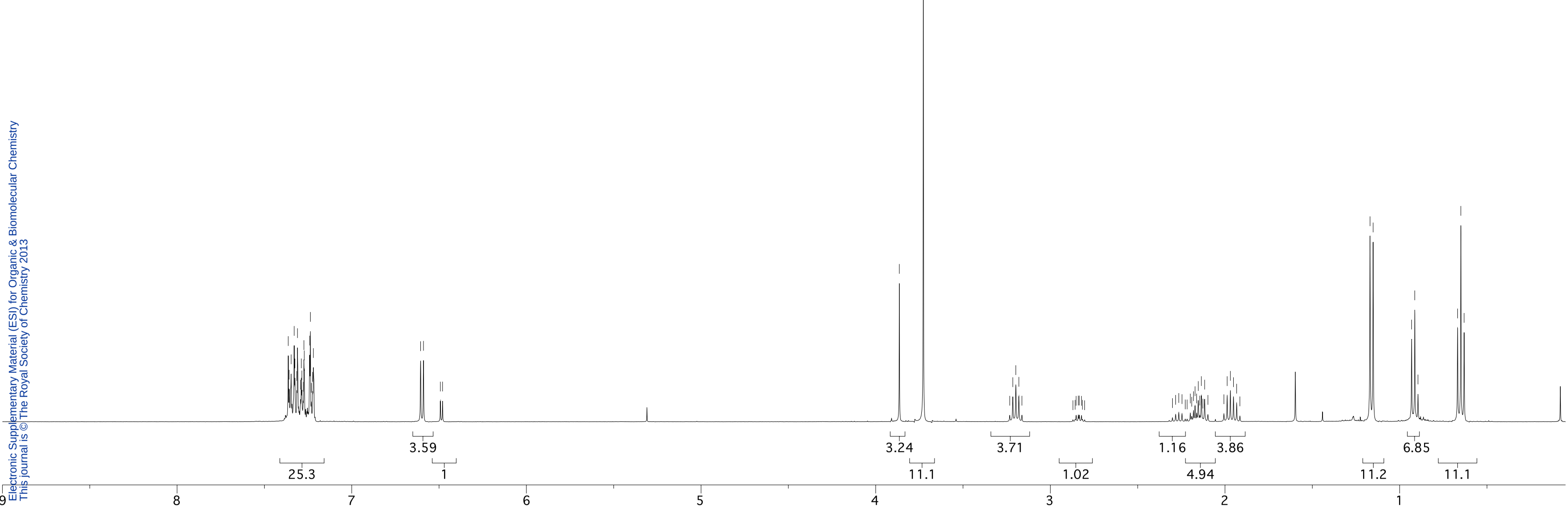
169.325
159.998
141.774
136.567
134.968
132.469
132.121
130.359
128.716
122.625
122.199
117.026
62.192
53.620
45.898
28.067
14.193
8.399



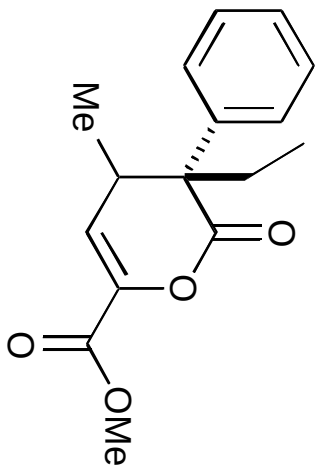




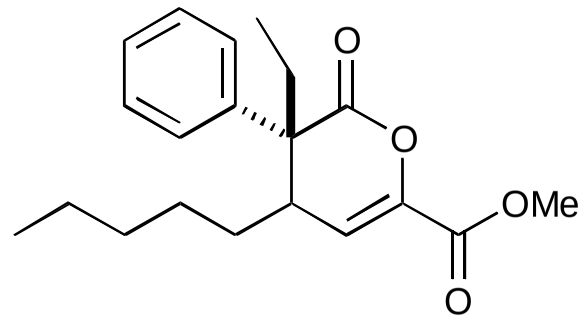
29 *anti* + *syn*



29 *anti* + syn

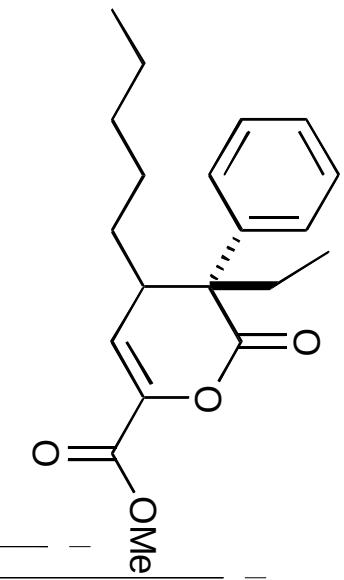


170.540
168.654
160.884
160.696
140.583
140.019
137.632
136.851
128.750
128.451
127.964
127.807
127.468
127.060
121.171
120.694
53.646
53.511
52.718
52.544
36.924
32.000
28.884
27.833
16.136
14.427
9.302
7.753

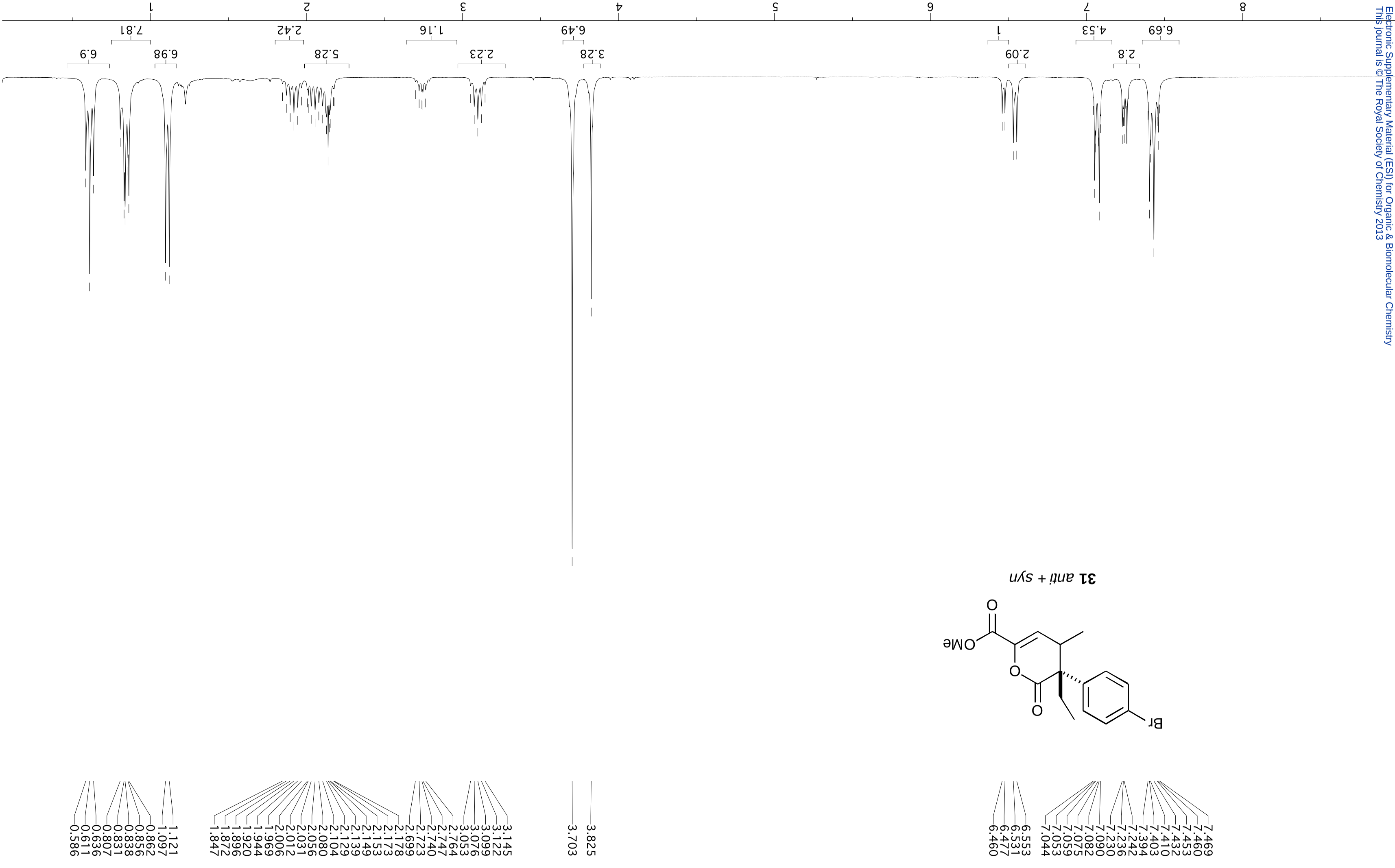


30 *anti +* syn

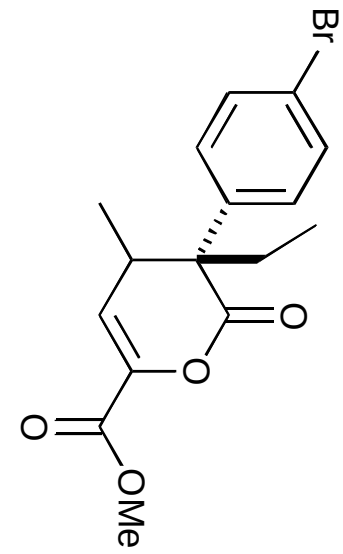
30 *anti* + *syn*



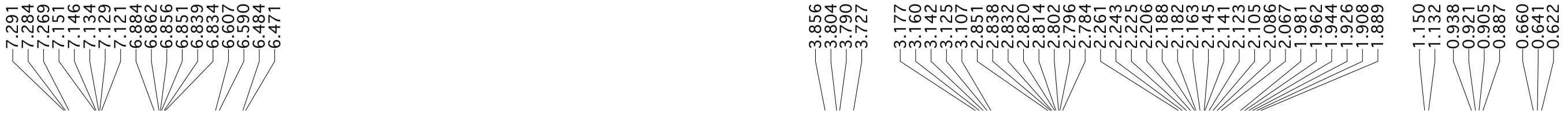
170.872
168.731
160.869
160.620
140.512
140.298
137.873
137.227
128.703
128.428
127.840
127.718
127.369
126.981
120.078
119.908
53.192
53.043
52.697
52.524
42.132
36.971
32.001
31.727
30.453
29.711
29.389
27.815
26.972
26.818
22.598
22.540
14.142
14.077
9.226
7.809

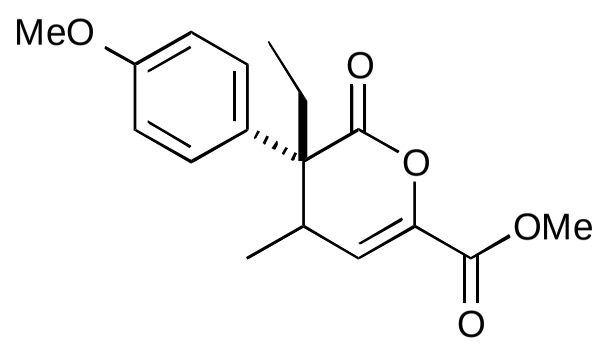


31 *anti* + *syn*

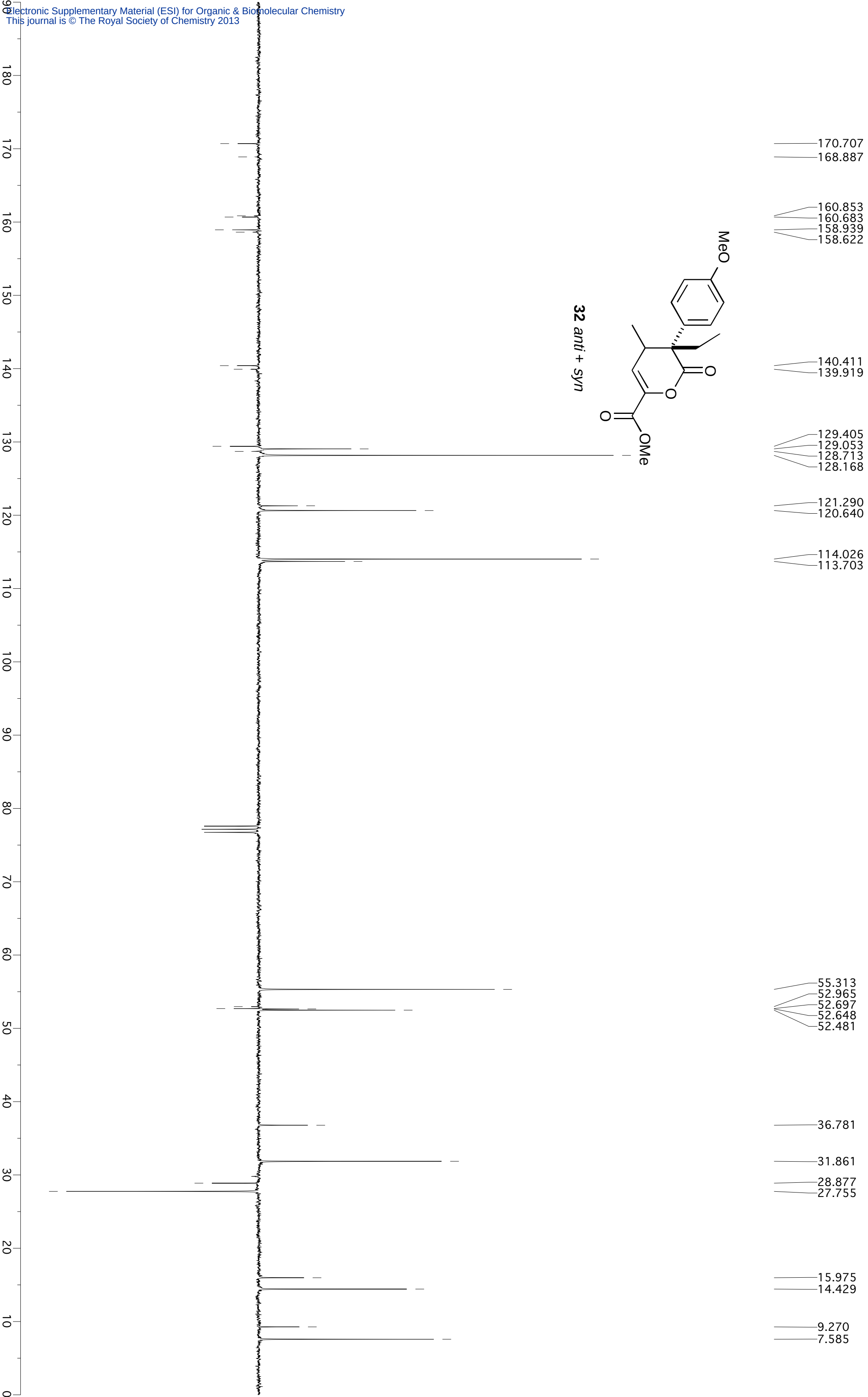


170.010
168.066
160.690
160.478
140.663
140.042
136.812
136.001
131.891
131.546
129.793
128.795
121.878
121.531
120.645
120.286
53.432
53.218
52.741
52.593
37.345
32.018
29.012
27.566
16.226
14.326
9.172
7.657





32 *anti* + *syn*



32 *anti* + *syn*