Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2012

Catalytic, enantio- and diastereoselective synthesis of γ-butyrolactones incorporating quaternary stereocentres

Francesco Manoni, Claudio Cornaggia, James Murray, Sean Tallon and Stephen J. Connon*

Centre for Synthesis and Chemical Biology, Trinity Biomedical Sciences Institute, School of Chemistry, University of Dublin, Trinity College, Dublin 2, Ireland

Table of Contents

This journal is © The Royal Society of Chemistry 2012

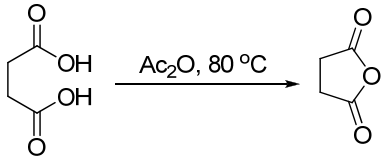
1.0 General

Proton Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker DPX 400 MHz and Bruker Avance II 600MHz spectrometers, using as solvent $CDCl_3$ or DMSO-d_6 and referenced relative to residual $CHCl_3$ (δ = 7.26 ppm) or DMSO (δ = 2.50 ppm). Chemical shifts are reported in ppm and coupling constants (*J*) in Hertz. Carbon NMR spectra were recorded on the same instruments (100.6 MHz and 150.9 MHz respectively) with total proton decoupling. HSQC, HMBC, NOESY and TOCSY NMR experiments were used to aid assignment of NMR peaks when required. All melting points are uncorrected. Infrared spectra were obtained on a Perkin Elmer Spectrum 100 FT-IR spectrometer equipped with a universal ATR sampling accessory. A Waters micromass LCT-tof mass spectrometer was used in ESI positive and ESI negative modes for electrospray ionization mass spectrometry. Flash chromatography was carried out using silica gel, particle size 0.04-0.063 mm. TLC analysis was performed on precoated $60F_{254}$ slides, and visualised by UV irradiation and $KMnO_4$ staining. Optical rotation measurements are quoted in units of 10^{-1} deg cm^2 g^{-1}. Tetrahydrofuran (THF) was distilled over sodium-benzophenone and stored under argon. Methanol (MeOH) and isopropyl alcohol (^{i}PrOH) were dried over activated 3Å molecular sieves. Commercially available anhydrous *t*-butyl methyl ether (MTBE) was used. Analytical CSP-HPLC was performed on Daicel Chiralcel OD-H or OD (4.6 mm x 25 cm) columns. The X-ray crystallography data for crystal sample ***cis*-23** were collected on a Rigaku Saturn 724 CCD diffractometer. A suitable crystal was selected and mounted on a glass fibre tip and placed on the goniometer head in a 150K N_2 gas stream. The data sets were collected using Crystalclear-SM 1.4.0 software and, for each crystal, 1246 diffraction images, of 0.5^o per image, were recorded. Data integration, reduction and correction for absorption and polarisation effects were all performed using Crystalclear-SM 1.4.0 software. Space group determination, structure solution and refinement were obtained using Crystalstructure ver. 3.8 and Bruker Shelxtl Ver. 6.14 software. The absolute configuration of product ***trans*-23** was unequivocally assigned as (2*R*,3*S*). From this configurational assignment, and from the assumption that all the herein reported reactions follow the same stereochemical pathway under the described conditions, the absolute configuration has been assigned to **17a-d**, **18**-**26**, obtained as major diastereoisomers.

This journal is © The Royal Society of Chemistry 2012

2.0 Synthesis of anhydrides

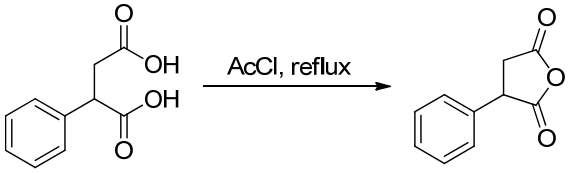
Dihydrofuran-2,5-dione (Succinic anhydride) (**9**)



A 50 mL round-bottomed flask containinig a stirring bar was charged with succinic acid (2.0 g, 16.94 mmol). Acetic anhydride (25.0 mL) was added, the flask was fitted with a condenser and the reaction mixture was heated at 80 °C for 2 h. The excess acetic anhydride was removed *in vacuo* to obtain **9** as a white solid (1.69 g, 100%).

M.p. 118-120 °C (lit.[1] m.p. 117-119 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.89 (s, 4H).

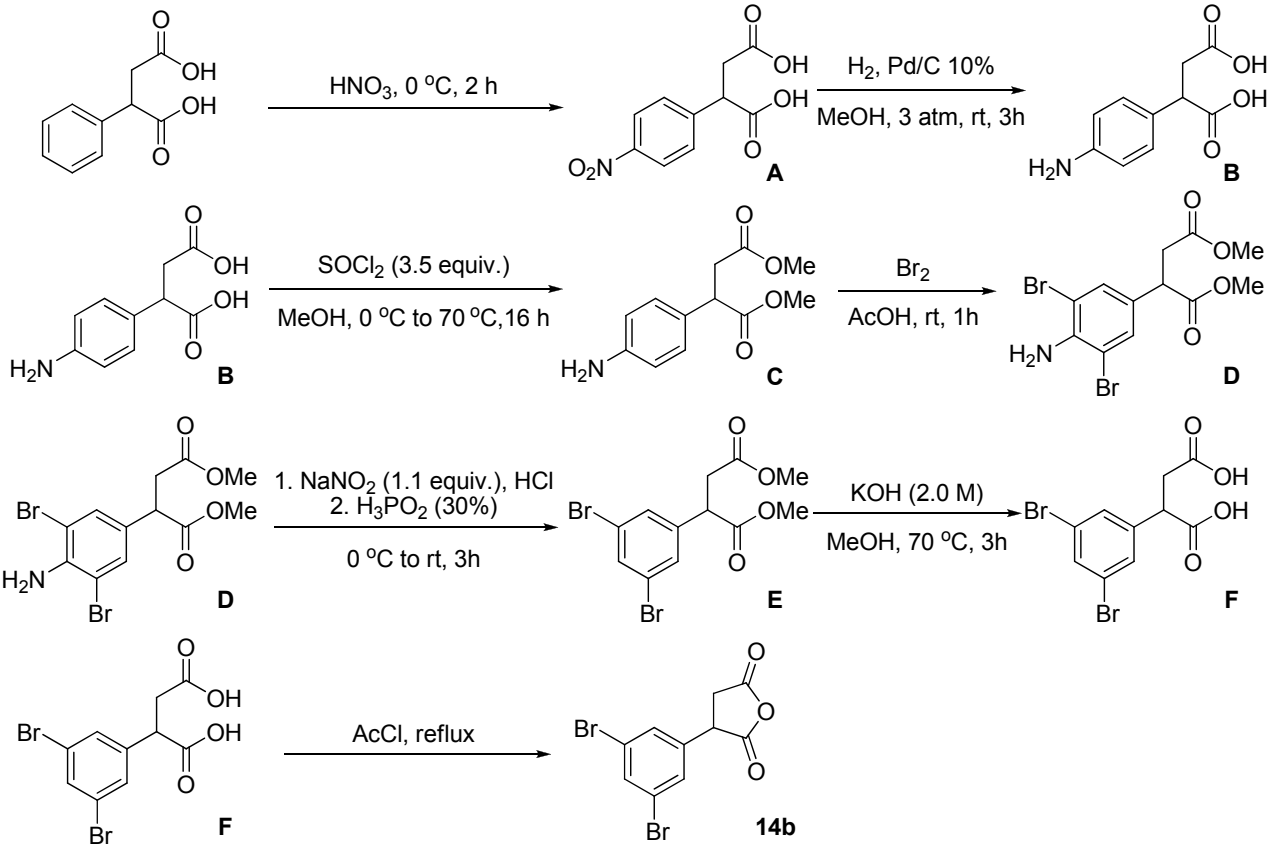
3-Phenyldihydrofuran-2,5-dione (Phenylsuccinic anhydride) (**14a**)



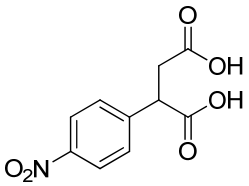
A 50 mL round-bottomed flask containinig a stirring bar was charged with phenylsuccinic acid (2.0 g, 10.30 mmol). Freshly distilled acetyl chloride (15.0 mL) was added, the flask was fitted with a condenser and the reaction mixture was heated at reflux temperature under an argon atmosphere for 16 h. The acetyl chloride was then removed *in vacuo* to obtain **14a** as a white solid (1.81 g, 100%).

M.p. 50-52 °C (lit.[1] m.p. 51-53 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.33 (m, 3H), 7.31-7.22 (m, 2H), 4.35 (dd, J = 6.5, 10.3, 1H), 3.47 (dd, J = 10.3, 19.1, 1H), 3.13 (dd, J = 6.5, 19.1, 1H).

3-(3,5-Dibromophenyl)dihydrofuran-2,5-dione (14b)



2-(4-Nitrophenyl)succinic acid (p-Nitrophenyl succinic acid) (**A**)

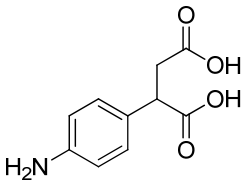


A three-neck oven-dried 100 mL round-bottomed flask fitted with a thermometer and containinig a stirring bar was charged with fuming HNO_3 (30.0 mL) and cooled to 0 °C. Phenylsuccinic acid (10.0 g, 51.5 mmol) was added portionwise while keeping the temperature below 20 °C. The solution was stirred at 0 °C for 2 h, then crushed ice (30.0 g) and H_2O (20.0 mL) were added to the reaction mixture. The white precipitate formed was filtered, washed with water, dried, and then recrystallised from water to obtain **A** as a white solid (7.2 g, 58%).

M.p. 233-235 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.6 (bs, 2H), 8.19 (d, J = 8.8, 2H), 7.60 (d, J = 8.8, 2H), 4.10 (dd, J = 5.5, 9.7, 1H), 3.00 (dd, J = 9.7, 17.0, 1H), 2.64 (dd, J = 5.5, 17.0, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.1, 172.4, 146.7, 146.4, 129.4, 123.7, 46.7, 36.9; IR (neat): 2862, 2576, 1703, 1596, 1520, 1435, 1347, 1255, 926, 732 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{10}H_8NO_6$ requires 238.0352, found 238.0353.

This journal is © The Royal Society of Chemistry 2012

2-(4-Aminophenyl)succinic acid (B)

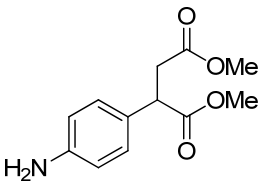


In a oven-dried 500 mL reaction vessel, **A** (4.50 g, 18.81 mmol) was dissolved in MeOH (25.0 mL). 10% Pd/C (2 mol%) was added, the flask was evacuated, placed under an atmosphere of hydrogen gas at a pressure of 3 atm and stirred for 3 h at room temperature. The flask was then evacuated and filled with an inert atmosphere. Water (30.0 mL) was added, the reaction mixture was heated under reflux for 10 minutes and then filtered hot through a pad of Celite and washed with hot water (5.0 mL). The filtrate was cooled to room temperature and the precipitate formed was collected by suction filtration and dried *in vacuo* to obtain **B** as a pale yellow solid (2.9 g, 74%). A second batch of product was obtained after removal of MeOH from the mother liquor under reduced pressure followed by extraction with EtOAc (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo* to afford a yellow solid (520 mg, 13%).

M.p. 202-204 °C; ^{1}H NMR (400 MHz, DMSO-d_6)*: δ = 6.91 (d, J = 8.3, 2H), 6.49 (d, J = 8.3, 2H), 3.66 (dd, J = 5.0, 10.5, 1H), 2.86 (dd, J = 10.5, 16.9, 1H), 2.42 (dd, J = 5.0, 16.9, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.8, 173.0, 147.8, 128.2, 125.5, 114.0, 46.0, 37.7; IR (neat): 3230, 2836, 2602, 1706, 1624, 1572, 1511, 1401, 1262, 1164, 632 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{10}H_{10}NO_4$ requires 208.0610, found 208.0612.

*The protic signals are not visible in DMSO-d_6.

Dimethyl 2-(4-aminophenyl)succinate (C)



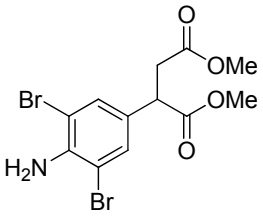
A oven-dried 100 mL round-bottomed flask containing a stirring bar was charged with **B** (2.60 g, 12.43 mmol) and anhydrous MeOH (20.0 mL) under an argon atmosphere. The reaction mixture was cooled to 0 °C then freshly distilled thionyl chloride (3.2 ml, 43.50 mmol) was added dropwise *via* syringe. The flask was fitted with a condenser and the reaction mixture was heated under reflux under an argon atmosphere for 16 h. The reaction was then cooled to room temperature and the excess thionyl chloride was quenched by addition of a saturated aqueous solution of $NaHCO_3$. MeOH was then removed *in vacuo*, and the mixture obtained was extracted with EtOAc (3 x 50

mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure to afford **C** as a peach colour solid (2.57 g, 87%).

M.p. 110-112 °C; ^{1}H NMR (400 MHz, DMSO-d_6) *: δ = 7.05 (d, J = 8.3, 2H), 6.62 (d, J = 8.3, 2H), 3.96 (dd J = 5.3, 10.2, 1H), 3.65 (s, 6H), 3.15 (dd J = 10.2, 17.0, 1H), 2.61 (dd J = 5.3, 17.0, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.0, 172.3, 146.0, 128.7, 127.5, 115.5, 52.4, 51.9, 46.3, 37.8; IR (neat): 3385, 3217, 2952, 1718, 1611, 1515, 1437, 1308, 1149, 1003, 730 cm^{-1}; HRMS (ESI): calcd. for [M-H] $C_{12}H_{14}NO_4$ requires 236.0923, found 236.0933.

*The protic signals are not visible in DMSO-d_6

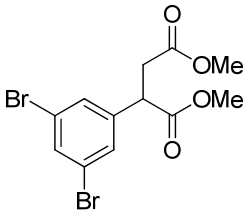
Dimethyl 2-(4-amino-3,5-dibromophenyl)succinate (D)



In a oven-dried 50 mL round-bottomed flask containing a stirring bar **C** (1.00 g, 4.21 mmol) was dissolved in AcOH (10.0 mL), then Br_2 (540 µL, 10.54 mmol) was added slowly at room temperature and the reaction mixture was stirred for 1 h. The excess Br_2 was then quenched by addition of a saturated aqueous solution of $Na_2S_2O_3$ and the resulting solution was adjusted to pH 8 by addition of a saturated aqueous solution of $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo* to obtain **D** as a yellow oil (1.61 g, 97%).

M.p. 274-276 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (s, 2H), 4.55 (bs, 2H), 3.90 (dd, J = 5.5, 9.8, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 3.12 (dd, J = 9.8, 17.1, 1H), 2.61 (dd, J = 5.5, 17.1, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 171.8, 141.7, 131.1, 128.8, 108.9, 52.7, 52.1, 45.6, 37.6; IR (neat): 3474, 3376, 2952, 1735, 1616, 1479, 1473, 1197, 1165, 735 cm^{-1}; HRMS (ESI): calcd. for [M+Na] $C_{12}H_{13}Br_2NO_4Na$ requires 415.9109, found 415.9126.

Dimethyl 2-(3,5-dibromophenyl)succinate (E)



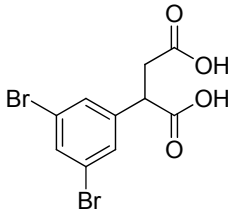
A three-neck oven-dried 100 mL round-bottomed flask fitted with a thermometer and containing a stirring bar was charged with **D** (1.50 g, 3.80 mmol) and concentrated HCl (15.0 mL) and it was

This journal is © The Royal Society of Chemistry 2012

cooled to 0 °C. A solution of $NaNO_2$ (288 mg, 4.28 mmol) in 10 mL of H_2O was added slowly to while keeping the temperature of the reaction mixture below 5 °C. The reaction was stirred at 0 °C for 20 minutes after which time it was added to a solution of H_3PO_2 (45.0 mL, 30% *m*/*v* in H_2O) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 2 h. Water (20 mL) was added and the reaction mixture was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo* to obtain a yellow oil which was purified by column chromatography (hexane:EtOAc 9:1 *v*/*v*) to afford **E** as a white solid (1.30 g, 90%).

M.p. 89-91 °C; TLC (hexanes:EtOAc, 8:2 *v*/*v*): R_f = 0.26; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59-7.56 (m, 1H), 7.38-7.34 (app. d, 2H), 4.01 (dd, *J* = 5.6, 9.7, 1H), 3.70 (s, 3H), 3.68 (s, 3H), 3.15 (dd, *J* = 9.7, 17.0, 1H) 2.64 (dd, *J* = 5.6, 17.0, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 171.5, 141.3, 133.6, 129.9, 123.4, 52.9, 52.2, 46.5, 37.3; IR (neat): 3070, 2953, 1725, 1584, 1556, 1435, 1338, 1170, 864, 740, 674 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{12}H_{11}O_4Br_2$ requires 376.9026, found 376.9024.

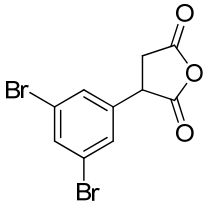
2-(3,5-Dibromophenyl)succinic acid (**F**)



In a 100 mL round-bottomed flask containing a stirring bar, **E** (1.15 g, 3.03 mmol) was dissolved in MeOH (15.0 mL). A 2.0 M aqueous solution of KOH (15.0 mL) was added and the reaction was heated under reflux for 3 h. The reaction mixture was cooled to room temperature, MeOH was removed under reduced pressure and the solution was adjusted to pH 2 by addition of a 2.0 M aqueous solution of HCl. The white precipitate formed was collected by suction filtration and dried *in vacuo* to yield **F** as a white solid (1.01 g, 95%).

M.p. 227-229 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.5 (bs, 2H), 7.76 (s, 1H), 7.54 (s, 2H), 3.94 (dd, *J* = 5.6, 9.6, 1H), 2.96 (dd, *J* = 9.6, 17.0, 1H), 2.63 (dd, *J* = 5.6, 17.0, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.2, 172.4, 143.3, 132.3, 130.1, 122.5, 46.1, 36.8; IR (neat): 2868, 2541, 1693, 1582, 1558, 1417, 1292, 1182, 945, 841, 746, 673 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{10}H_7Br_2O_4$ requires 348.8711, found 348.8720.

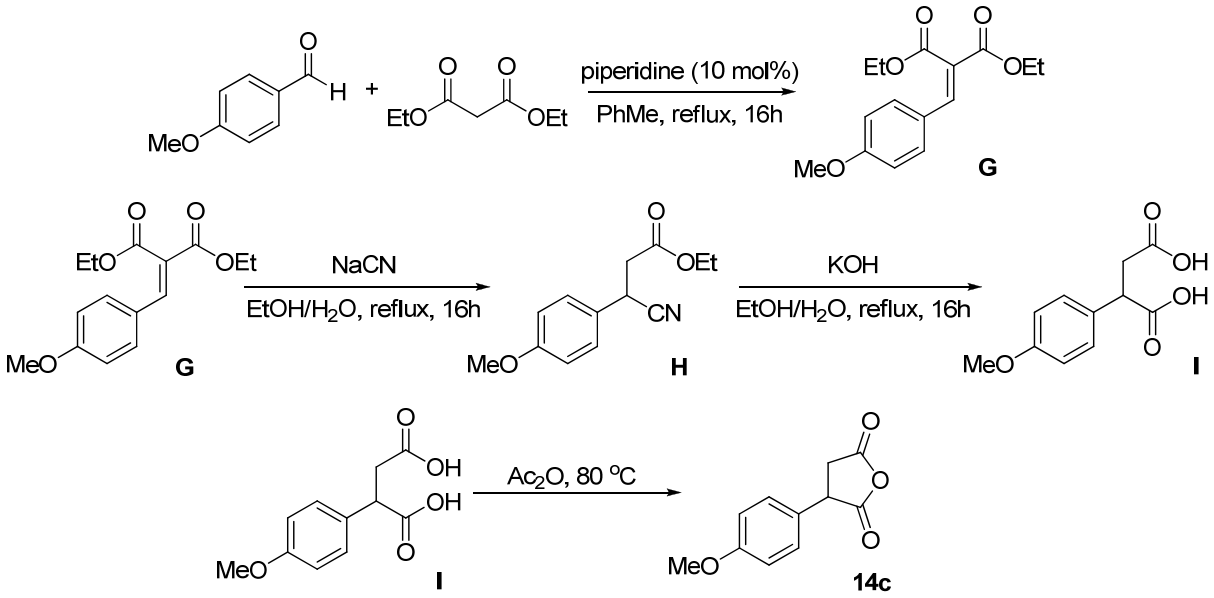
3-(3,5-Dibromophenyl)dihydrofuran-2,5-dione (3,5-Dibromophenyl succinic anhydride) (**14b**)



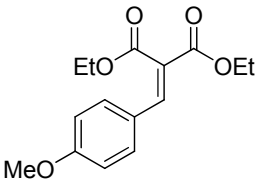
A 10 mL round-bottomed flask containing a stirring bar was charged with **F** (400 mg, 1.14 mmol). Freshly distilled acetyl chloride (4.0 mL) was added, the flask was fitted with a condenser and the reaction mixture was heated at reflux temperature under an argon atmosphere for 16 h. The acetyl chloride was then removed *in vacuo* to obtain **14b** as a white solid (379 mg, 100%).

M.p. 112-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (s, 1H), 7.38 (s, 2H), 4.31 (dd, J = 7.2, 10.3, 1H), 3.48 (dd, J = 10.3, 18.9, 1H), 3.11 (dd, J = 7.2, 18.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 168.4, 137.8, 134.7, 129.5, 124.1, 45.6, 36.2; IR (neat): 3072, 3004, 1846, 1778, 1557, 1429, 1220, 1044, 858, 813, 741, 679 cm^{-1}; HRMS (ESI): calcd. for [M-H] $C_{10}H_6Br_2O_3$ requires 330.8605, found 330.8614.

3-(4-Methoxyphenyl)dihydrofuran-2,5-dione (14c) (4-Methoxyphenyl succinic anhydride) (**14c**)



Diethyl 2-(4-methoxybenzylidene)malonate (G)

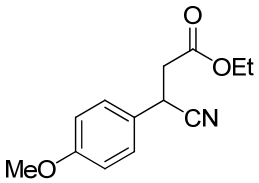


A three-neck oven-dried 100 mL round-bottomed flask containinig a stirring bar was fitted with a Dean-Stark apparatus and charged with diethyl malonate (9.50 mL, 62.6 mmol). Toluene (50.0 mL) followed by piperidine (620 µL, 6.26 mmol) and *p*-anisaldehyde (7.60 mL, 62.5 mmol) were added *via* syringe. The reaction was heated under reflux for 16 h with continuous removal of water. The reaction was then cooled to room temperature and toluene was removed *in vacuo*. The oily residue was taken up in EtOAc (50 mL) and then washed with an aqueous solution of HCl (2.0 N, 15 mL) and with a saturated aqueous solution of $NaHCO_3$ (20 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude oil was distilled by Kugelrohr to remove impurities and to leave **G** as a pale yellow oil (11.5 g, 66%).

Spectral data for this compound were consistent with those in the literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (s, 1H), 7.42 (d, J = 8.8, 2H), 6.89 (d, J = 8.8, 2H), 4.36 (q, J = 7.2, 2H), 4.35 (q, J = 7.1, 2H), 3.83 (s, 3H), 1.37-1.28 (m, 6H); HRMS (ESI): calcd. for [M+Na] $C_{15}H_{18}O_5Na$ requires 301.1052, found 301.1067.

Ethyl 3-cyano-3-(4-methoxyphenyl)propanoate (H)

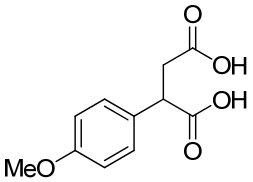


A 100 mL round-bottomed flask fitted with a condenser and containinig a stirring bar was charged with **G** (8.50 g, 30.5 mmol) and a mixture of EtOH (50.0 mL) and water (10.0 mL). NaCN (1.54 g, 30.6 mmol) was added portionwise to the solution and the reaction was heated under reflux for 16 h. The reaction mixture was then cooled to room temperature, filtered and EtOH was then removed *in vacuo*. The residue was partitioned between EtOAc (50 mL) and brine (20 mL) and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic extracts were then dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. A yellow oil was obtained which was purified by Kugelrohr distillation to obtain **H** as a pale yellow oil (4.26 g, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.7, 2H), 6.90 (d, J = 8.7, 2H), 4.24 (app. t, 1H), 4.17 (q, J = 7.1, 2H), 3.81 (s, 3H), 2.98 (dd, J = 8.1, 16.5, 1H), 2.80 (dd, J = 7.0, 16.5, 1H), 1.24 (t, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 159.8, 128.7, 126.5, 120.4, 114.7, 61.6, 55.5,

40.3, 32.6, 14.2; IR (neat): 2982, 2940, 2840, 2247, 1732, 1612, 1512, 1373, 1250, 1179, 1028, 832 cm^{-1}; HRMS (ESI): calcd. for [*M*+Na] $C_{13}H_{15}NO_3Na$ requires 256.0950, found 256.0949.

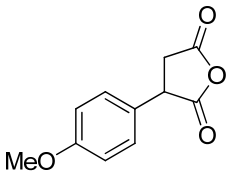
2-(4-Methoxyphenyl)succinic acid (I)



A 100 mL round-bottomed flask fitted with a condenser and containinig a stirring bar was charged with **H** (1.96 g, 8.40 mmol) and a mixture of EtOH (30.0 mL) and water (20.0 mL). KOH (2.12 g, 37.8 mmol) was added to the solution and the reaction was heated under reflux for 16 h. The reaction mixture was then cooled to room temperature and EtOH was removed *in vacuo*. The residue was acidified with conc. HCl and the precipitate formed was collected by suction filtration, washed with water (10.0 mL) and dried *in vacuo*. The crude solid was then recrystallised from H_2O/EtOH and dried to yield **I** as an off-white solid (1.72 g, 91%).

M.p. 199-202 °C (lit.[3] m.p. 197-199 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.30 (bs, 2H), 7.20 (d, *J* = 8.6, 2H), 6.88 (d, *J* = 8.6, 2H), 3.82 (dd, *J* = 5.1, 10.2, 1H), 3.72 (s, 3H), 2.93 (dd, *J* = 10.2, 16.9, 1H), 2.55-2.40 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.3, 172.8, 158.4, 130.6, 128.8, 114.0, 55.1, 46.0, 37.6; IR (neat): 2892, 2602, 1689, 1611, 1514, 1426, 1324, 1242, 1179, 1027, 917, 820 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{11}H_{11}O_5$ requires 223.0606, found 223.0606.

3-(4-Methoxyphenyl)dihydrofuran-2,5-dione (14c) (4-Methoxyphenyl succinic anhydride) (**14c**)

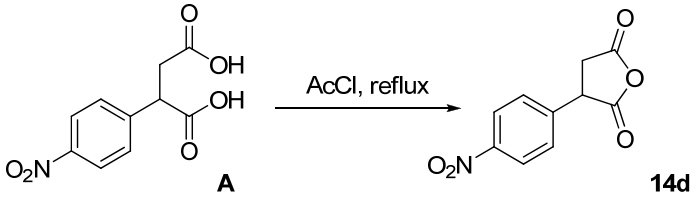


A 25 mL round-bottomed flask containinig a stirring bar was charged with **I** (600 mg, 2.68 mmol). Acetic anhydride (15.0 mL) was added, the flask was fitted with a condenser and the reaction mixture was heated at 80 ^{o}C under an argon atmosphere for 16 h. The acetic anhydride was then removed *in vacuo* to obtain a yellow oil. Et_2O (5 mL) was added and the mixture was stirred for 1 h at room temperature. The precipitate formed was collected by suction filtration, washed with Et_2O (2 x 2.0 mL) and dried *in vacuo* to afford **14c** as a white solid (320 mg, 58%).

M.p. 88-90 °C (lit.[4] m.p. 91-92 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.7, 2H), 6.93 (d, *J* = 8.7, 2H), 4.29 (dd, *J* = 6.6, 10.2, 1H), 3.81 (s, 3H), 3.44 (dd, *J* = 10.2, 18.9, 1H), 3.09 (dd, *J* =

6.6, 18.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 169.7, 159.9, 128.6, 126.6, 115.0, 55.5, 46.0, 36.9; IR (neat): 3062, 3019, 2972, 2891, 2843, 1854, 1763, 1619, 1518, 1228, 1026, 900, 843, 796 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{11}H_9O_4$ requires 205.0501, found 205.0500.

3-(4-Nitrophenyl)dihydrofuran-2,5-dione (p-Nitrophenyl succinic anhydride**) (14d)**

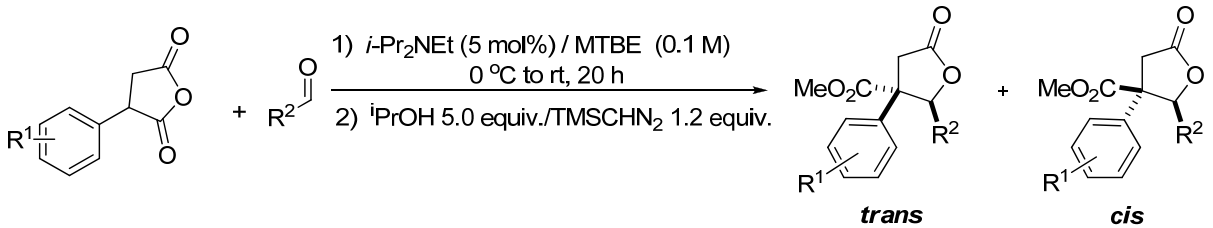


A 50 mL round-bottomed flask containinig a stirring bar was charged with **A** (2.0 g, 8.36 mmol). Freshly distilled acetyl chloride (15.0 mL) was added, the flask was fitted with a condenser and the reaction mixture was heated at reflux temperature under an argon atmosphere for 16 h. The acetyl chloride was then removed *in vacuo* to obtain a dark yellow oil that was purified by passing it through a plug of silica eluting with hexane:EtOAc 1:1 *v/v* to obtain **14d** as a thick yellow oil (1.31 g, 71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 8.8, 2H), 7.51 (d, *J* = 8.8, 2H), 4.51 (dd, *J* = 7.2, 10.4, 1H), 3.56 (dd, *J* = 10.4, 18.8, 1H), 3.18 (dd *J* = 7.2, 18.8, 1H); HRMS (ESI): calcd. for [*M*-H] $C_{10}H_6NO_5$ requires 220.0246, found 220.0243.

3.0 Synthesis of racemic γ-butyrolactones

General procedure for the preparation of racemic γ-butyrolactones *trans*-17a-d – *trans-26*



A oven-dried 10 mL reaction vessel containing a stirring bar under argon atmosphere was charged with the relevant anhydride (**14a-d**) (1.0 equiv.). Anhydrous MTBE (0.1 M) was added *via* syringe and the reaction mixture was then cooled to 0 °C. The relevant aldehyde (1.0 equiv.) was added to the reaction mixture followed by *N*,*N*-diisopropylethylamine (5 mol%) and the resulting mixture was allowed to warm to room temperature and stirred for 20 h. To the reaction mixture containing the corresponding carboxylic acids, anhydrous isopropyl alcohol (5.0 equiv.), followed by

trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 1.2 equiv.) were added *via* syringe at 0 ^{o}C and the reaction was allowed to stir for 1 h at room temperature. The solvent was then removed *in vacuo* and the crude mixture of diastereomeric esters was purified by flash chromatography to isolate the major diastereomer.

4.0 Catalyst evaluation at low temperature (general procedures)

Catalyst evaluation at low temperature (general procedure A) – Table 1 and Table 2

A oven-dried 10 mL reaction vessel containing a stirring bar under argon atmosphere was charged with the relevant anhydride (**14a-d**) (1.0 equiv.) Anhydrous MTBE (0.1 M) was added *via* syringe and the reaction mixture was then cooled to -15 °C. The relevant aldehyde (1.0 equiv.) was added to the reaction mixture followed by catalyst **10**[5], **15**[6] or **16**[7] (5 mol%) and the resulting mixture was stirred at -15 °C for the time indicated in Table 1. The yield and diastereomeric ratio of the products were monitored by ^{1}H-NMR spectroscopic analysis using either *p*-iodoanisole or styrene (0.5 equiv.) as an internal standard. The reaction was then diluted with EtOAc (15 mL) and extracted with an aqueous solution of $NaHCO_3$ (10% w/v, 3 x 15 mL). The combined aqueous extracts were acidified with HCl (2.0 N), a white precipitate formed and the mixture was then extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo* to yield the diastereomeric mixture of carboxylic acids. The acids were then dissolved in dry THF (0.1 M) and the solution was cooled to 0 ^{o}C, anhydrous isopropyl alcohol (5.0 equiv.), followed by trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 1.2 equiv.) were added *via* syringe at 0 ^{o}C and the reaction was allowed to stir for 1 h at room temperature. The solvent was then removed *in vacuo* and the crude mixture of diastereomeric esters was purified by flash chromatography to isolate the major diastereomer. The enantiomeric excess of the products was determined by CSP-HPLC using the conditions indicated for each case.

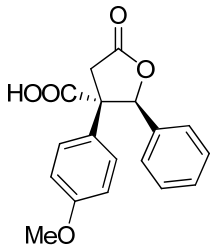
Catalyst evaluation at low temperature (general procedure B) – Table 2

A oven-dried 10 mL reaction vessel containing a stirring bar under argon atmosphere was charged with 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (1.0 equiv.) Anhydrous MTBE (0.1 M) was added *via* syringe and the reaction mixture was then cooled to -15 °C. The relevant aldehyde (1.0 equiv.) was added to the reaction mixture followed by catalyst **10**[6] (5 mol%) and the resulting

mixture was stirred at -15 °C for the time indicated in Table 2. The yield and diastereomeric ratio of the products were monitored by ^{1}H-NMR spectroscopic analysis using either *p*-iodoanisole or styrene (0.5 equiv.) as an internal standard. To the reaction mixture containing the corresponding carboxylic acids, anhydrous isopropyl alcohol (5.0 equiv.), followed by trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 1.2 equiv.) were added *via* syringe at 0 ^{o}C and the reaction was allowed to stir for 1 h at room temperature. The solvent was then removed *in vacuo* and the crude mixture of diastereomeric esters was purified by flash chromatography to isolate the major diastereomer. The enantiomeric excess of the products was determined by CSP-HPLC using the conditions indicated for each case.

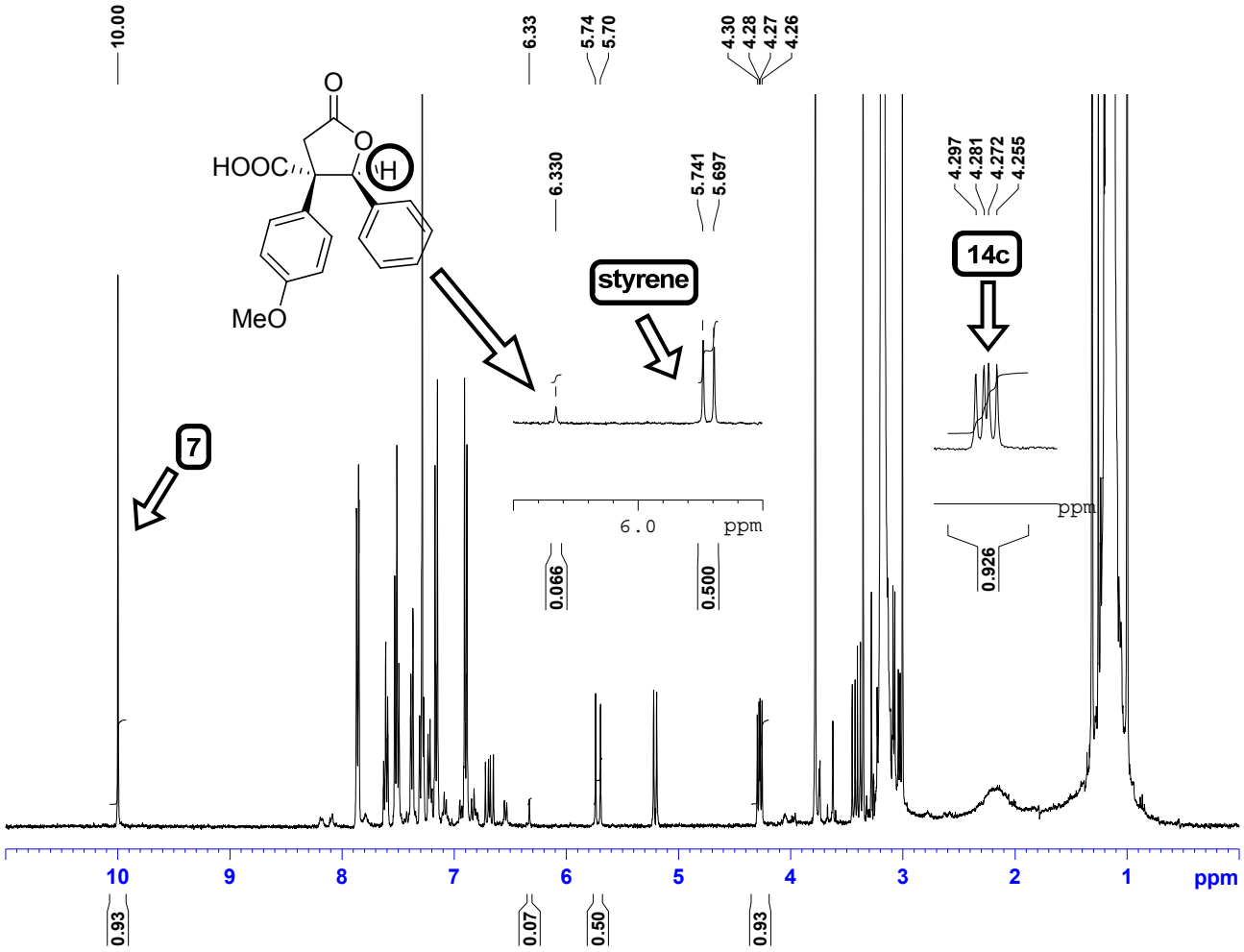
4.0.1 Reaction of anhydride 14c with benzaldehyde (7)

(2*S*,3*S*)-3-(4-Methoxyphenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylic acid (precursor of ***trans*-17c**, Table 1, entry 8)



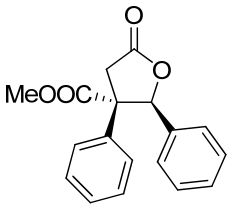
A oven-dried 10 mL reaction vessel containing a stirring bar under argon atmosphere was charged with 3-(4-methoxyphenyl)dihydrofuran-2,5-dione (**14c**) (50.7 mg, 0.246 mmol) Anhydrous MTBE (0.1 M, 2.4 mL) was added *via* syringe and the reaction mixture was then cooled to -15 °C. Freshly distilled benzaldehyde (**7**) (25.0 µL, 0.246 mmol) was added *via* syringe to the reaction mixture followed by catalyst **10**[6] (5 mol%, 8.7 mg) and the resulting mixture was stirred at -15 °C for 93 h. The yield of the products was monitored by ^{1}H-NMR spectroscopic analysis using styrene (0.5 equiv.) as an internal standard. The carboxylic acid precursor of ***trans*-17c** was formed in 7% yield after 93 h, (see ^{1}H-NMR spectrum that follows) while the yield of the precursor of ***cis*-17c** was not quantifiable by ^{1}H-NMR spectroscopic analysis.

Due to the low conversion of the reaction, esterification was not carried out and ***trans*-17c** was not isolated.



5.0 Characterisation data

(2*S*,3*S*)-Methyl 5-oxo-2,3-diphenyltetrahydrofuran-3-carboxylate (***trans*-17a**, Table 1, entry 2)



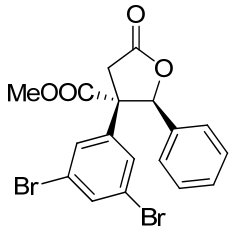
Prepared according to general procedure A using 3-phenyldihydrofuran-2,5-dione (**14a**) (43.3 mg, 0.492 mmol), anhydrous MTBE (0.1 M, 4.9 mL), freshly distilled benzaldehyde (50.0 µL, 0.492 mmol) and catalyst **10**[6] (5 mol%, 17.4 mg, 0.0246 mmol). The reaction was stirred for 24 h at room temperature to give a diastereomeric mixture of carboxylic acids in a 90:10 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-17a**) was isolated and purified by column

chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give a colourless thick oil (56.4 mg, 39%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 90/10, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 18.2 min. (minor enantiomer) and 31.0 min. (major enantiomer).

TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.35; $[\alpha]^{20}_D$ = -94.2° (*c* = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21-7.02 (m, 6H), 6.97 (d, *J* = 7.3, 2H), 6.81 (d, *J* = 7.3, 2H), 6.30 (s, 1H), 3.78 (s, 3H), 3.42 (d, *J* = 17.6, 1H); 3.33 (d, *J* = 17.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.1, 172.9, 134.9, 134.5, 128.5, 128.4, 128.1, 127.8, 127.0, 126.8, 85.6, 59.7, 53.3, 38.3; IR (neat): 3039, 2954, 1782, 1731, 1499, 1435, 1235, 1178, 1008, 898, 753, 695 cm^{-1}; HRMS (ESI): calcd. for [*M*+Na] $C_{18}H_{16}O_4Na$ requires 319.0946, found 319.0941.

(2*S*,3*S*)-Methyl 3-(3,5-dibromophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (*trans*-17b, Table 1, entry 7)

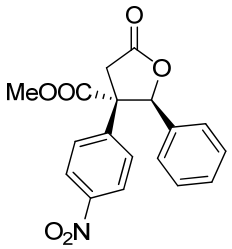


Prepared according to general procedure A using 3-(3,5-dibromophenyl)dihydrofuran-2,5-dione (**14b**) (77.4 mg, 0.232 mmol), anhydrous MTBE (0.1 M, 2.3 mL), freshly distilled benzaldehyde (23.6 µL, 0.232 mmol) and catalyst **10**[6] (5 mol%, 8.2 mg, 0.0116 mmol). The reaction was stirred for 97 h to give a diastereomeric mixture of carboxylic acids in a 94:6 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-17b**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 10% EtOAc in hexanes to give a white solid (68.5 mg, 65%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 0.6 mL min^{-1}, RT, UV detection at 254 nm, retention times: 23.9 min. (minor enantiomer) and 28.2 min. (major enantiomer).

M.p. 51-53 °C; TLC (hexanes:EtOAc, 9:1 *v/v*): R_f = 0.10; $[\alpha]^{20}_D$ = -78.0° (*c* = 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (s, 1H), 7.25-7.14 (m, 3H), 7.99 (d, *J* = 6.8, 2H), 6.89-6.78 (m, 2H), 6.27 (s, 1H), 3.81 (s, 3H), 3.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 171.8, 138.6, 133.9, 133.8, 129.1, 129.0, 128.2, 126.8, 122.3, 85.4, 59.4, 53.8, 37.7; IR (neat): 3074, 2954, 1785, 1732, 1584, 1556, 1434, 1411, 1238, 1174, 1012, 901, 855, 743, 698, 680 cm^{-1}.

(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate *trans*-17d, Table 2, entry 1)

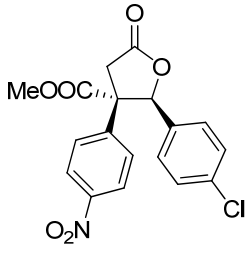


Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (55.1 mg, 0.249 mmol), anhydrous MTBE (0.1 M, 2.5 mL), freshly distilled benzaldehyde (25.3 µL, 0.249 mmol) and catalyst **10**[6] (5 mol%, 8.8 mg, 0.0125 mmol). The reaction was stirred for 99 h to give a diastereomeric mixture of carboxylic acids in a 97:3 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-17d**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give an off-white solid (78.2 mg, 92%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 80/20, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 36.2 min. (minor enantiomer) and 41.7 min. (major enantiomer).

M.p. 59-61 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.17; $[\alpha]^{20}_D$ = -94.0° (*c* = 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.8, 2H), 7.22-7.06 (m, 3H), 7.03-6.98 (m, 4H), 6.35 (s, 1H), 3.82 (s, 3H), 3.42 (app. s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 171.9, 147.4, 142.3, 133.8, 129.1, 128.3, 128.2, 126.7, 123.5, 85.3, 59.9, 53.8, 38.4; IR (neat): 3091, 2955, 2927, 1778, 1729, 1608, 1518, 1434, 1349, 1236, 1178, 1088, 999, 850, 731, 701 cm^{-1}.

(2*S*,3*S*)-Methyl 2-(4-chlorophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-18**, Table 2, entry 2)



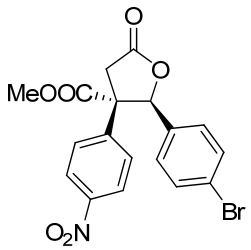
Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (59.6 mg, 0.269 mmol), anhydrous MTBE (0.1 M, 2.7 mL), recrystallised 4-chlorobenzaldehyde (37.8 mg, 0.269 mmol) and catalyst **10**[6] (5 mol%, 9.5 mg 0.0135 mmol). The reaction was stirred for 100 h to give a diastereomeric mixture of carboxylic acids in a 95:5 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-18**) was isolated and purified by column

chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give a white solid (93.8 mg, 93%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 76.3 min. (minor enantiomer) and 87.4 min. (major enantiomer).

M.p. 60-63 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.12; $[\alpha]^{20}_D$ = -59.0° (*c* = 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.8, 2H), 7.11 (d, *J* = 8.5, 2H), 7.03-6.92 (m, 4H), 6.28 (s, 1H), 3.82 (s, 3H), 3.41 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 171.7, 147.5, 142.0, 135.0, 132.2, 128.5, 128.2, 128.1, 123.7, 84.5, 59.6, 53.8, 38.7; IR (neat): 2956, 2934, 2855, 1790, 1734, 1568, 1522, 1349, 1243, 1176, 1091, 1010, 853, 737, 621 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{18}H_{13}NO_6Cl$ requires 374.0431, found 374.0418.

(2*S*,3*S*)-Methyl2-(4-bromophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-19**, Table 2, entry 3)



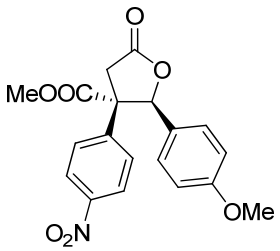
Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (312.3 mg, 1.41 mmol), anhydrous MTBE (0.1 M, 14.1 mL), recrystallised 4-bromobenzaldehyde (260.9 mg, 1.41 mmol) and catalyst **10**[6] (5 mol%, 49.8 mg, 0.0705 mmol). The reaction was stirred for 97 h to give a diastereomeric mixture of carboxylic acids in a 94:6 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-19**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give an off-white solid (547.4 mg, 92%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 86.5 min. (minor enantiomer) and 100.0 min. (major enantiomer).

M.p. 68-70 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.13; $[\alpha]^{20}_D$ = -49.0° (*c* = 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.6, 2H), 7.25 (d, *J* = 8.3, 2H), 6.98 (d, *J* = 8.6, 2H), 6.89 (d, *J* = 8.3, 2H), 6.26 (s, 1H), 3.81 (s, 3H), 3.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 171.7, 147.5, 142.0, 132.8, 131.5, 128.4, 128.1, 123.7, 123.2, 84.5, 59.6, 53.8, 38.7; IR (neat): 2955,

2928, 2853, 1787, 1734, 1603, 1520, 1490, 1348, 1251, 1173, 1006, 853, 823, 736, 710 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{18}H_{13}NO_6Br$ requires 417.9926, found 417.9916.

(2*S*,3*S*)-Methyl 2-(4-methoxyphenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-20**, Table 2, entry 4)

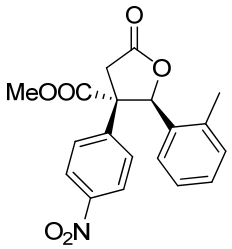


Prepared according to general procedure A using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (53.5 mg, 0.242 mmol), anhydrous MTBE (0.1 M, 2.4 mL), freshly distilled 4-methoxybenzaldehyde (29.4 µL, 0.242 mmol) and catalyst **10**[6] (5 mol%, 8.6 mg, 0.0121 mmol). The reaction was stirred for 164 h to give a diastereomeric mixture of carboxylic acids in a 92:8 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-20**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give a beige solid (64.1 mg, 71%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 85.0 min. (minor enantiomer) and 115.2 min. (major enantiomer).

M.p. 62-64 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.10; $[\alpha]^{20}_D$ = -47.0° (*c* = 0.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.7, 2H), 7.01 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 8.5, 2H), 6.64 (d, *J* = 8.5, 2H), 6.29 (s, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.41 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 171.9, 160.0, 147.4, 142.4, 128.3, 128.2, 125.6, 123.5, 113.6, 85.3, 59.8, 55.3, 53.7, 38.3; IR (neat): 2956, 2844, 1785, 1733, 1608, 1516, 1436, 1349, 1249, 1173, 1005, 854, 737, 702 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{19}H_{16}NO_7$ requires 370.0927, found 370.0910.

(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(o-tolyl)tetrahydrofuran-3-carboxylate (***trans*-21**, Table 2, entry 5)

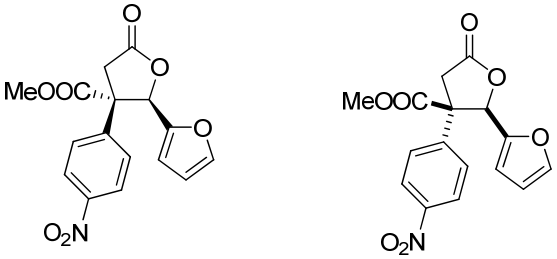


Prepared according to general procedure A using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (55.5 mg, 0.251 mmol), anhydrous MTBE (0.1 M, 2.5 mL), freshly distilled 2-methylbenzaldehyde (29.0 µL 0.251 mmol) and catalyst **10**[6] (5 mol%, 8.9 mg, 0.0126 mmol). The reaction was stirred for 161 h to give a diastereomeric mixture of carboxylic acids in a 95:5 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-21**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give an off-white solid (56.1 mg, 63%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 33.6 min. (minor enantiomer) and 44.7 min. (major enantiomer).

M.p. 61-64 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.18; $[\alpha]^{20}_D$ = -73.5° (*c* = 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.8, 2H), 7.12 (app. t, 1H), 7.07-6.91 (m, 4H), 6.74-6.63 (m, 2H), 3.87 (s, 3H), 3.55 (d, *J* = 17.6, 1H), 3.45 (d, *J* = 17.6, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 172.2, 147.4, 141.9, 136.4, 132.4, 131.1, 129.2, 128.7, 126.5, 126.1, 123.2, 82.8, 60.4, 54.1, 38.3, 19.7; IR (neat): 2957, 2929, 2857, 1772, 1737, 1597, 1522, 1349, 1239, 1177, 1000, 852, 731, 701 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{19}H_{16}NO_6$ requires 354.0978, found 354.0970.

Methyl 2-(furan-2-yl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-22**, ***cis*-22**, Table 2, entry 6)



Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (51.3 mg, 0.232 mmol), anhydrous MTBE (0.1 M, 2.3 mL), freshly distilled furan-2-

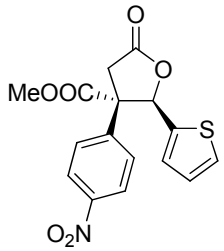
carboxaldehyde (19.2 µL, 0.232 mmol) and catalyst **10**[6] (5 mol%, 8.2 mg, 0.0116 mmol). The reaction was stirred for 98 h to give a diastereomeric mixture of carboxylic acids in a 99:1 (*trans*:*cis*) ratio. After esterification and purification by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes, ***trans*-22** and ***cis*-22** were obtained as a pale yellow solid (73.1 mg, 95%, combined yield for both diastereoisomers).

CSP-HPLC analysis. Chiralcel OD (4.6 mm x 25 cm), hexane/IPA: 75/25, 0.3 mL min^{-1}, RT, UV detection at 254 nm, retention times: ***trans*-22** 60.9 min. (minor enantiomer) and 64.2 min. (major enantiomer); ***cis*-22** 158.1 min. (both enantiomers).

M.p. 56-58 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.18; $[\alpha]^{20}_D$ = -135.5° (*c* = 0.20, $CHCl_3$)*; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.8, 2H), 7.34 (d, *J* = 8.8, 2H), 7.10 (app. s, 1H), 6.46-6.38 (m, 2H), 6.19-6.13 (m, 1H), 3.77 (s, 3H), 3.69 (d, *J* = 16.9, 1H), 3.60 (d, *J* = 16.9, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 173.0, 171.4, 147.61, 147.59, 144.0, 142.2, 128.2, 123.7, 112.9, 110.6, 78.9, 59.4, 54.3, 35.5; IR (neat): 3131, 3010, 2953, 2925, 1780, 1739, 1599, 1525, 1410, 1350, 1238, 1210, 1163, 978, 929, 877, 759, 736 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{16}H_{12}NO_7$ requires 330.0614, found 330.0600.

*** $[\alpha]^{20}_D$ referred to a mixture of *trans*-22:*cis*-22 – 99:1**

(2*R*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(thiophen-2-yl)tetrahydrofuran-3-carboxylate (***trans*-23**, Table 2, entry 7)



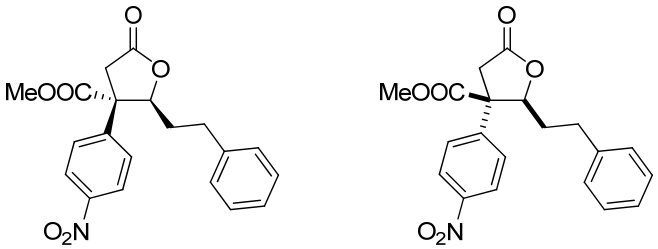
Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (50.0 mg, 0.226 mmol), anhydrous MTBE (0.1 M, 2.3 mL), freshly distilled 2-thiophenecarboxaldehyde (21.1 µL, 0.226 mmol) and catalyst **10**[6] (5 mol%, 8.0 mg, 0.0113 mmol). The reaction was stirred for 161 h to give a diastereomeric mixture of carboxylic acids in a 98:2 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-23**) was isolated and purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give a pale yellow solid (70.6 mg, 90%).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 50.0 min. (minor enantiomer) and 67.1 min. (major enantiomer).

M.p. 101-103 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.15; $[\alpha]^{20}_D$ = -112.0° (*c* = 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.8, 2H), 7.22 (d, *J* = 8.8, 2H), 7.13 (dd, *J* = 0.7, 5.0, 1H), 6.94 (d, *J* = 3.5, 1H), 6.82 (dd, *J* = 3.5, 5.0, 1H), 6.63 (s, 1H), 3.82 (s, 3H), 3.51 (d, *J* = 17.5, 1H), 3.45 (d, *J* = 17.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 171.5, 147.7, 142.2, 136.4, 128.3, 128.2, 127.2, 126.8, 123.7, 82.3, 59.9, 54.1, 36.7; IR (neat): 3115, 3086, 2956, 2931, 1789, 1731, 1603, 1519, 1437, 1349, 1244, 1160, 1009, 851, 704 cm^{-1}; HRMS (ESI): calcd. for [*M*-H] $C_{16}H_{12}NO_6S$ requires 346.0385, found 346.0388.

Methyl 3-(4-nitrophenyl)-5-oxo-2-phenethyltetrahydrofuran-3-carboxylate (***trans*-24**, ***cis*-24**

Table 2, entry 8)



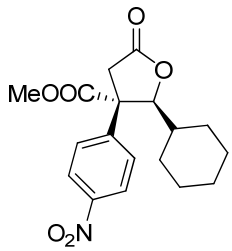
Prepared according to general procedure B using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (57.7 mg, 0.261 mmol), anhydrous MTBE (0.1 M, 2.6 mL), freshly distilled hydrocinnamaldehyde (34.4 µL 0.261 mmol) and catalyst **10**[6] (5 mol%, 9.3 mg, 0.0131 mmol). The reaction was stirred for 100 h to give a diastereomeric mixture of carboxylic acids in a 72:28 (*trans*:*cis*) ratio. After esterification and purification by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes, ***trans*-24** and ***cis*-24** were obtained as an off-white solid (94.5 mg, 98%, combined yield for both diastereoisomers).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: ***trans*-24** 41.9 min. (minor enantiomer) and 47.4 min. (major enantiomer); ***cis*-24** 91.4 min. (minor enantiomer) and 133.6 min. (major enantiomer).

M.p. 57-60 °C TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.19; ***trans*-24**: ^1H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 8.5, 2H), 7.50-6.95 (m, 7H), 5.14 (d, *J* = 10.9, 1H), 3.76 (s, 3H), 3.37 (d, *J* = 17.4, 1H), 3.14 (d, *J* = 17.4, 1H), 2.90-2.58 (m, 2H), 1.80-1.65 (m, 1H), 1.37-1.20 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 173.1, 171.7, 147.9, 142.8, 140.2, 128.7, 128.6, 128.2, 126.5, 124.3, 83.4, 58.2, 53.8, 37.6, 33.3, 32.2; ***cis*-24**: ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.4, 2H), 7.50-6.95 (m, 7H), 4.88 (d, *J* = 10.6, 1H), 3.75 (s, 3H), 3.52 (d, *J* = 17.1, 1H), 3.10-3.00 (m, 1H), 2.90-2.58 (m, 2H), 2.24-2.10 (m, 1H), 2.04-1.90 (m, 1H), ^{13}C NMR (151 MHz, $CDCl_3$): δ = 172.6, 170.9, 147.6, 145.8, 140.0, 129.0, 128.9, 127.4, 126.8, 124.3, 82.2, 58.0, 53.4, 40.5, 33.8, 32.3;

IR (neat): 2957, 2933, 2872, 1785, 1732, 1603, 1521, 1436, 1349, 1240, 1170, 1034, 952, 853, 751, 700; HRMS (ESI): calcd. for [*M*-H] $C_{20}H_{18}NO_6$ requires 368.1134, found 368.1136.

(2*S*,3*S*)-Methyl 2-cyclohexyl-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-25**, Table 2, entry 9)

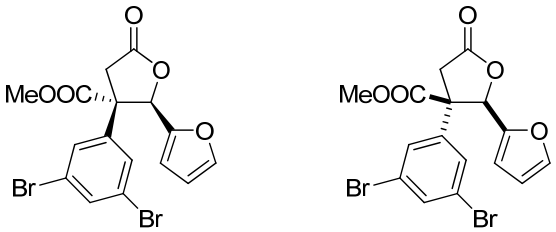


Prepared according to general procedure A using 3-(4-nitrophenyl)dihydrofuran-2,5-dione (**14d**) (47.4 mg, 0.214 mmol), anhydrous MTBE (0.1 M, 2.1 mL), freshly distilled cyclohexanecarboxaldehyde (25.9 μL, 0.214 mmol) and catalyst **10**[6] (20 mol%, 30.2 mg, 0.0428 mmol). The reaction was stirred for 98 h to give a diastereomeric mixture of carboxylic acids in a 88:12 (*trans*:*cis*) ratio. After esterification, the major diastereomer (***trans*-25**) was purified by column chromatography eluting in gradient from 100% hexanes to 20% EtOAc in hexanes to give an off-white solid (41.6 mg, 56%).

CSP-HPLC analysis. Chiralcel OD (4.6 mm x 25 cm), hexane/IPA: 90/10, 1.0 mL min^{-1}, RT, UV detection at 254 nm, retention times: 27.1 min. (minor enantiomer) and 29.6 min. (major enantiomer).

M.p. 49-51 °C TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.19; $[\alpha]^{20}_D$ = -100.7° (*c* = 0.15, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.8, 2H), 7.46 (d, *J* = 8.8, 2H), 5.20 (d, *J* = 3.4, 1H), 3.75 (s, 3H), 3.37 (d, *J* = 17.4, 1H), 3.19 (d, *J* = 17.4, 1H), 1.79-0.70 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 172.3, 147.7, 142.8, 128.5, 124.0, 88.2, 58.3, 54.0, 39.2, 37.8, 30.2, 26.3, 26.0, 25.6, 25.5; IR (neat): 2929, 2855, 1779, 1734, 1602, 1521, 1449, 1348, 1245, 1172, 988, 853, 704 cm^{-1}.

Methyl 3-(3,5-dibromophenyl)-2-(furan-2-yl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-26, *cis*-26**, Scheme3).



Prepared according to general procedure A using 3-(3,5-dibromophenyl)dihydrofuran-2,5-dione (**14b**) (75.7 mg, 0.227 mmol), anhydrous MTBE (0.1 M, 2.3 mL), freshly distilled furan-2-carboxaldehyde (18.8 μL, 0.227 mmol) and catalyst **10**[6] (5 mol%, 8.1 mg, 0.0114 mmol). The reaction was stirred for 97 h to give a diastereomeric mixture of carboxylic acids in a 98:2 (*trans*:*cis*) ratio. After esterification and purification by column chromatography eluting in gradient from 100% hexanes to 10% EtOAc in hexanes, ***trans*-26** and ***cis*-26** were obtained as a white solid (81.5 mg, 81%, combined yield for both diastereoisomers).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 0.6 mL min^{-1}, RT, UV detection at 254 nm, retention times: ***trans*-26** 29.0 min. (minor enantiomer) and 32.2 min. (major enantiomer); ***cis*-26** 48.4 min. (both enantiomers).

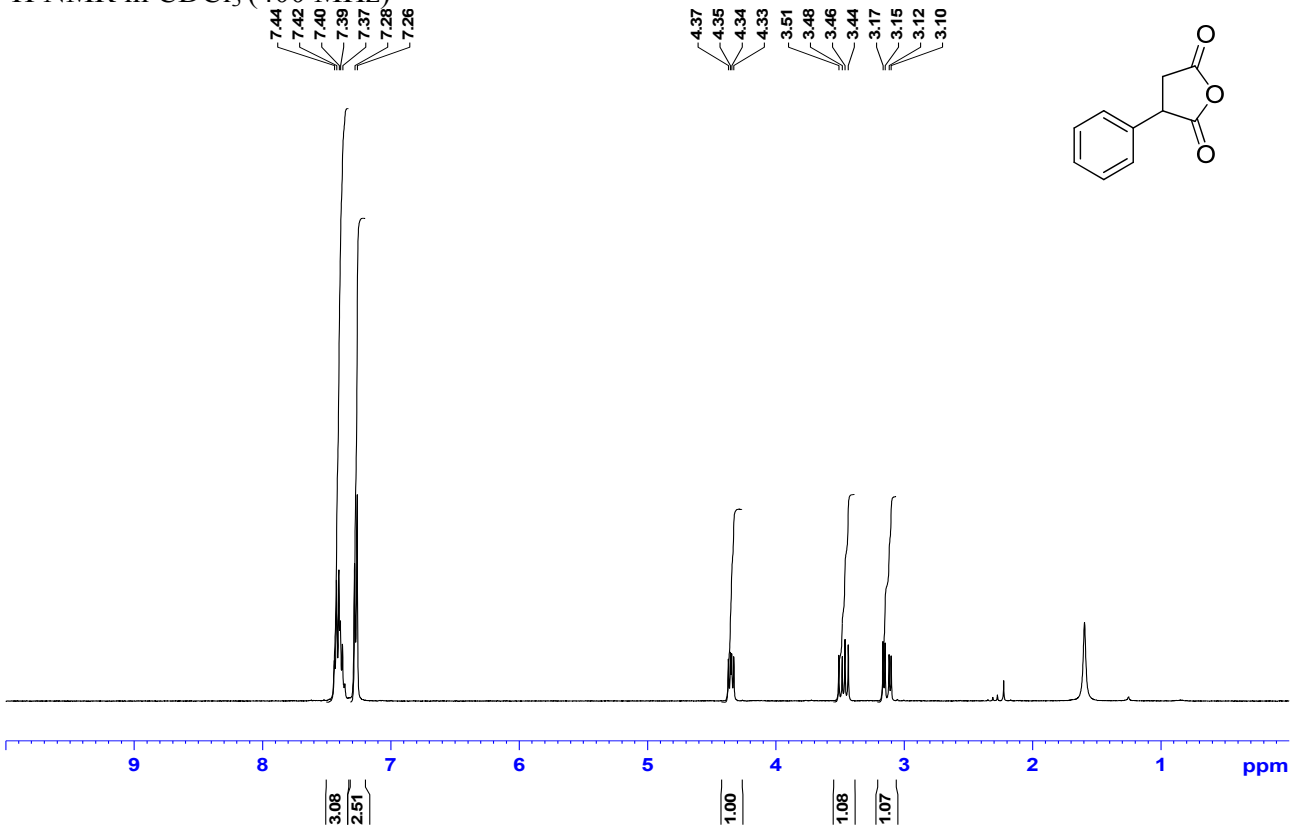
M.p. 96-98 °C; TLC (hexanes:EtOAc, 8:2 *v/v*): R_f = 0.14; $[\alpha]^{20}_D$ = -102.0° (*c* = 0.20, $CHCl_3$)*; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 (s, 1H), 7.22 (s, 2H), 7.18 (app. s, 1H), 6.42 (d, *J* = 3.2, 1H), 6.35 (s, 1H), 6.23-6.18 (m, 1H), 3.79 (s, 3H), 3.58 (d, *J* = 16.9, 1H), 3.50 (d, *J* = 16.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 171.5, 147.5, 144.0, 138.9, 134.1, 129.0, 123.0, 112.9, 110.6, 78.9, 58.8, 54.4, 35.3; IR (neat): 2955, 2922, 2853, 1789, 1731, 1584, 1555, 1434, 1412, 1248, 1154, 1044, 1013, 988, 923, 743, 681 cm^{-1}.

*** $[\alpha]^{20}_D$ referred to a mixture of *trans*-26:*cis*-26 – 98:2**

6.0 NMR spectra

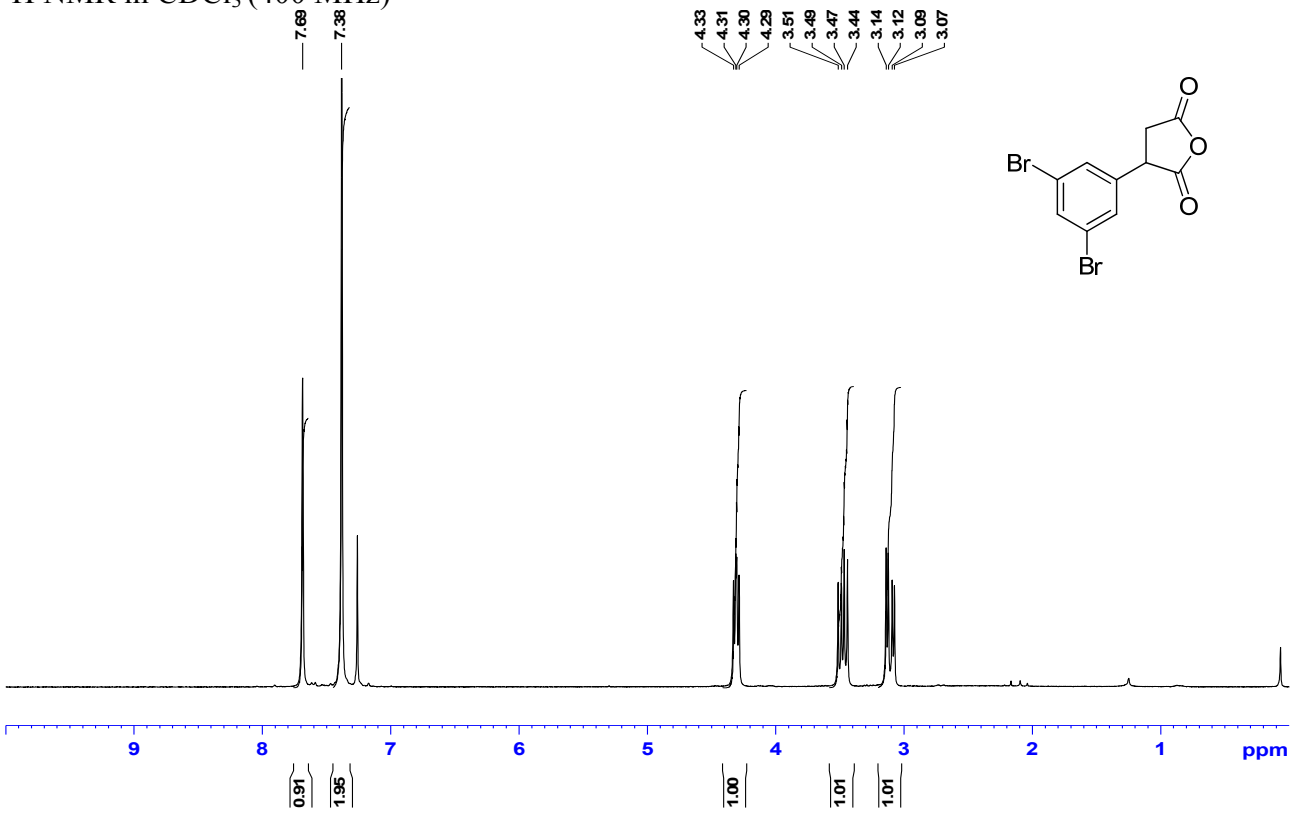
3-Phenyldihydrofuran-2,5-dione (Phenylsuccinic anhydride) (**14a**).

^{1}H NMR in $CDCl_3$ (400 MHz)



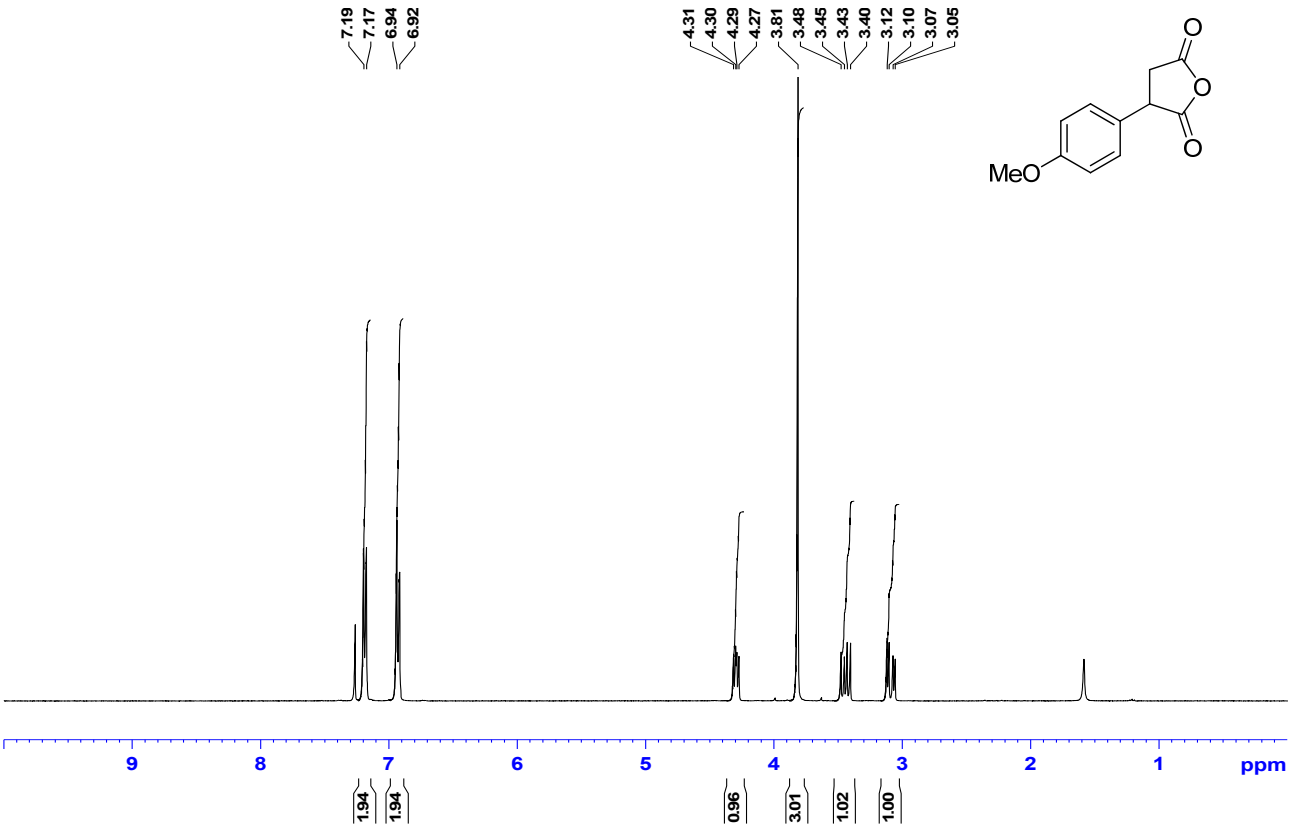
3-(3,5-Dibromophenyl)dihydrofuran-2,5-dione (3,5-Dibromophenyl succinic anhydride) (**14b**)

^{1}H NMR in $CDCl_3$ (400 MHz)



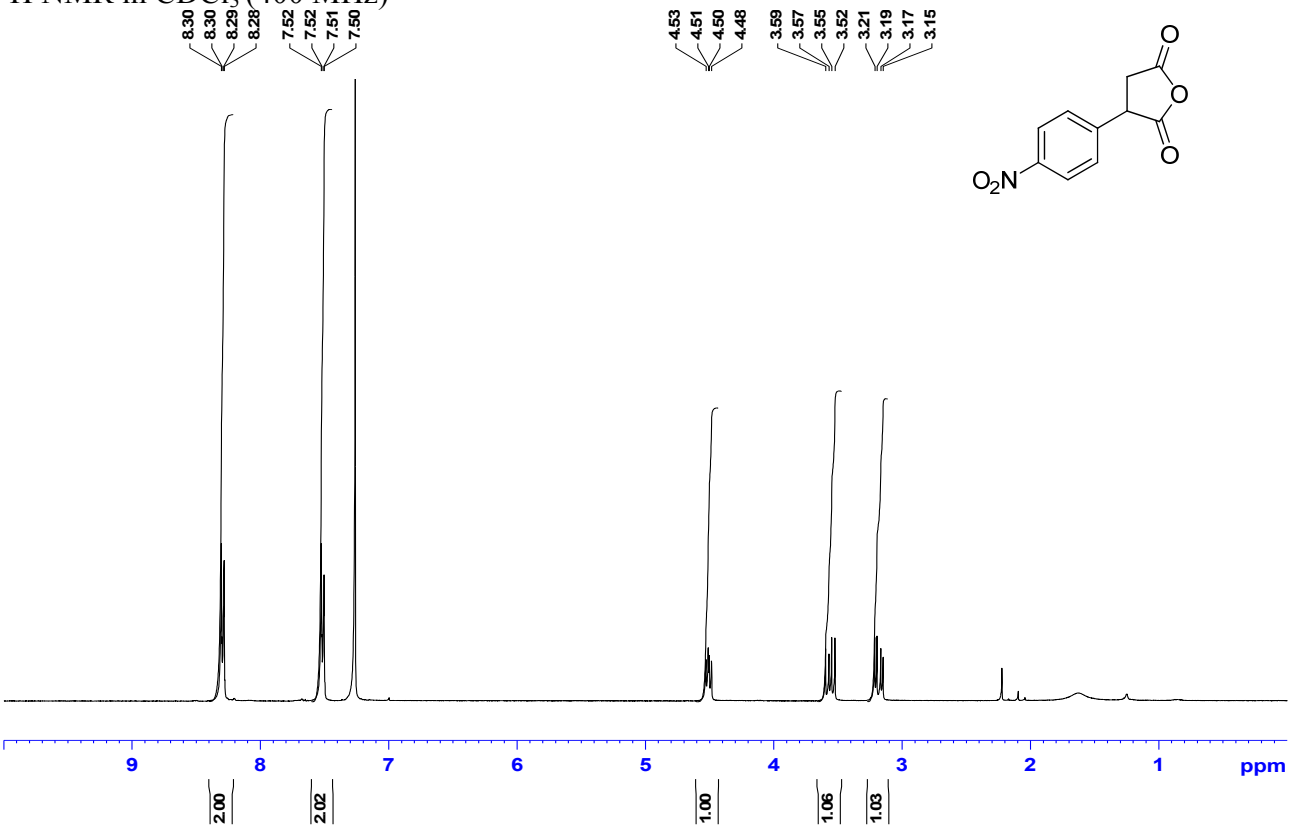
3-(4-Methoxyphenyl)dihydrofuran-2,5-dione (14c) (4-Methoxyphenyl succinic anhydride) (**14c**)

^{1}H NMR in $CDCl_3$ (400 MHz)



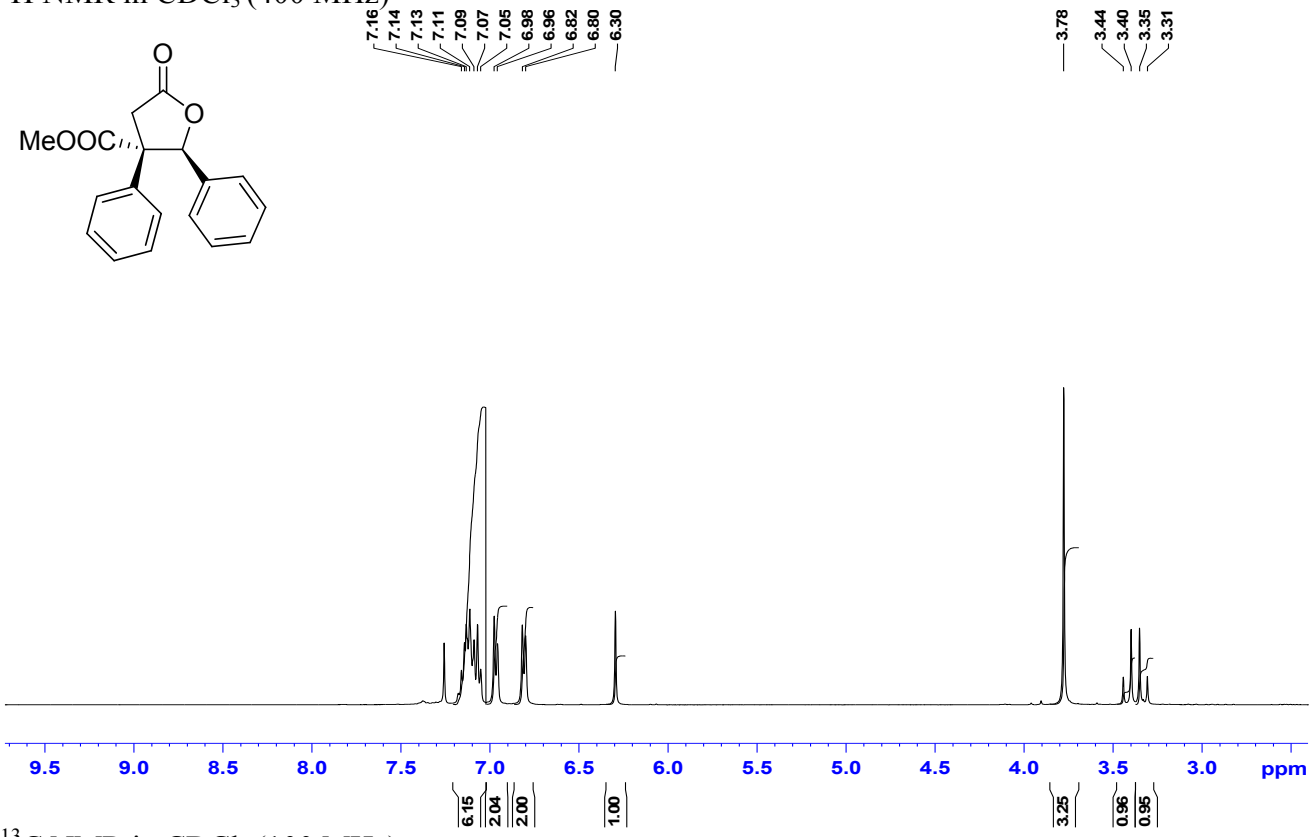
3-(4-Nitrophenyl)dihydrofuran-2,5-dione (p-Nitrophenyl succinic anhydride) **(14d)**

^{1}H NMR in $CDCl_3$ (400 MHz)

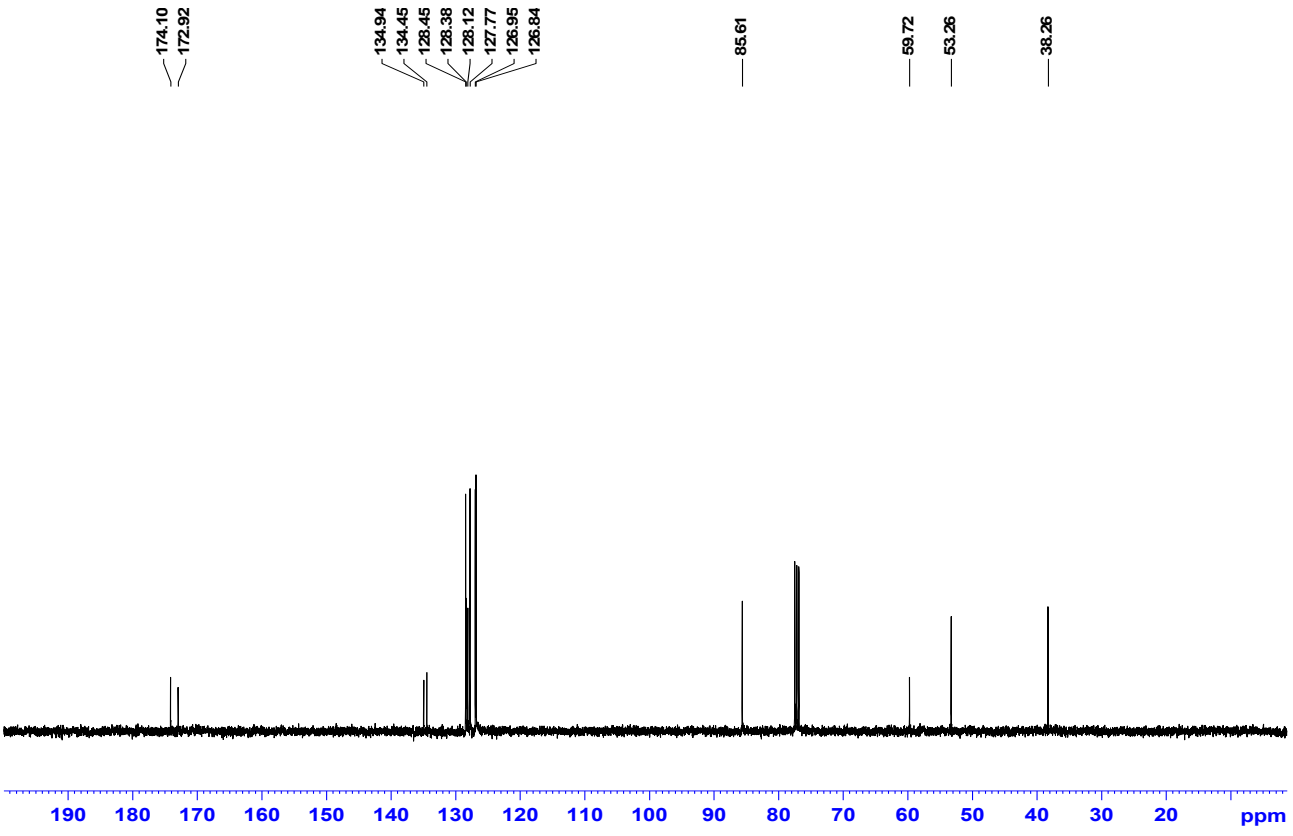


(2*S*,3*S*)-Methyl 5-oxo-2,3-diphenyltetrahydrofuran-3-carboxylate (***trans*-17a**, Table 1, entry 2).

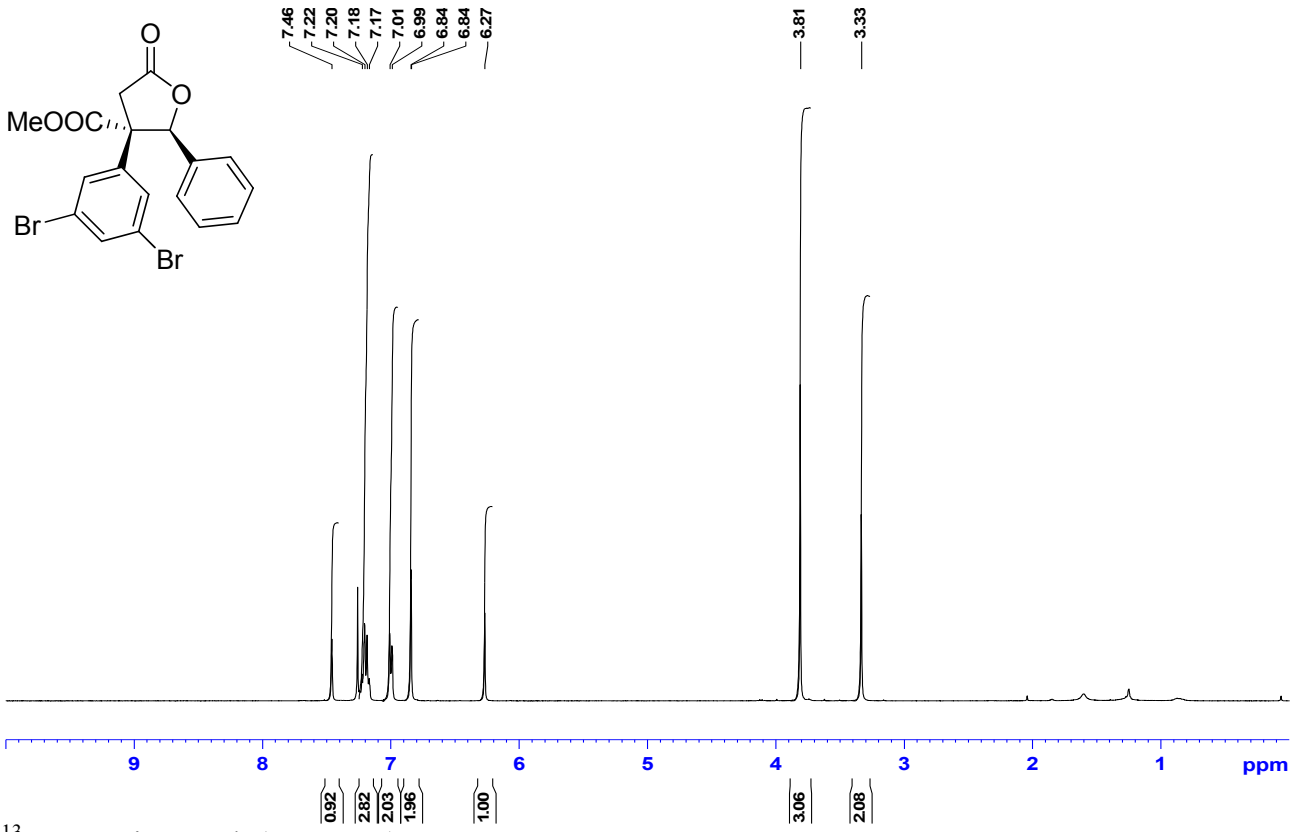
^{1}H NMR in $CDCl_3$ (400 MHz)



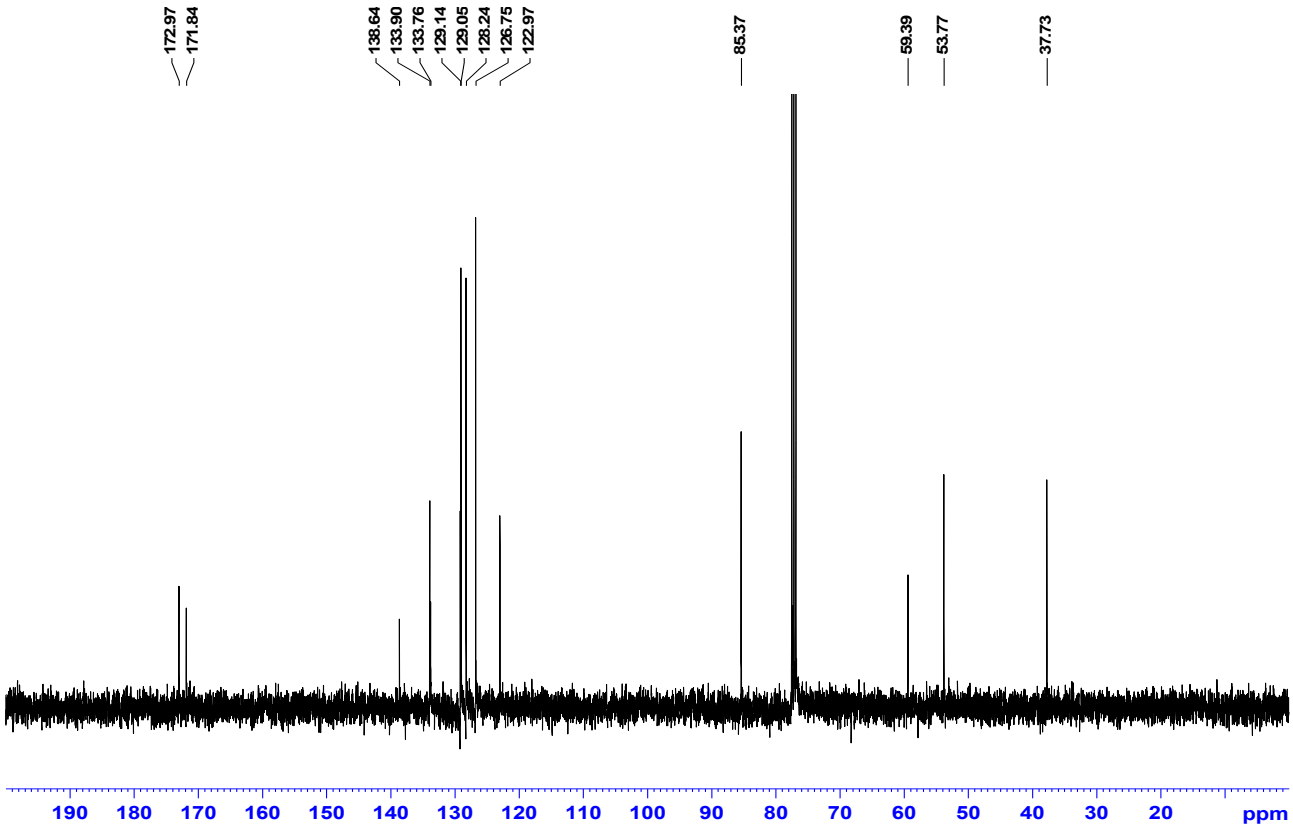
^{13}C NMR in $CDCl_3$ (100 MHz)



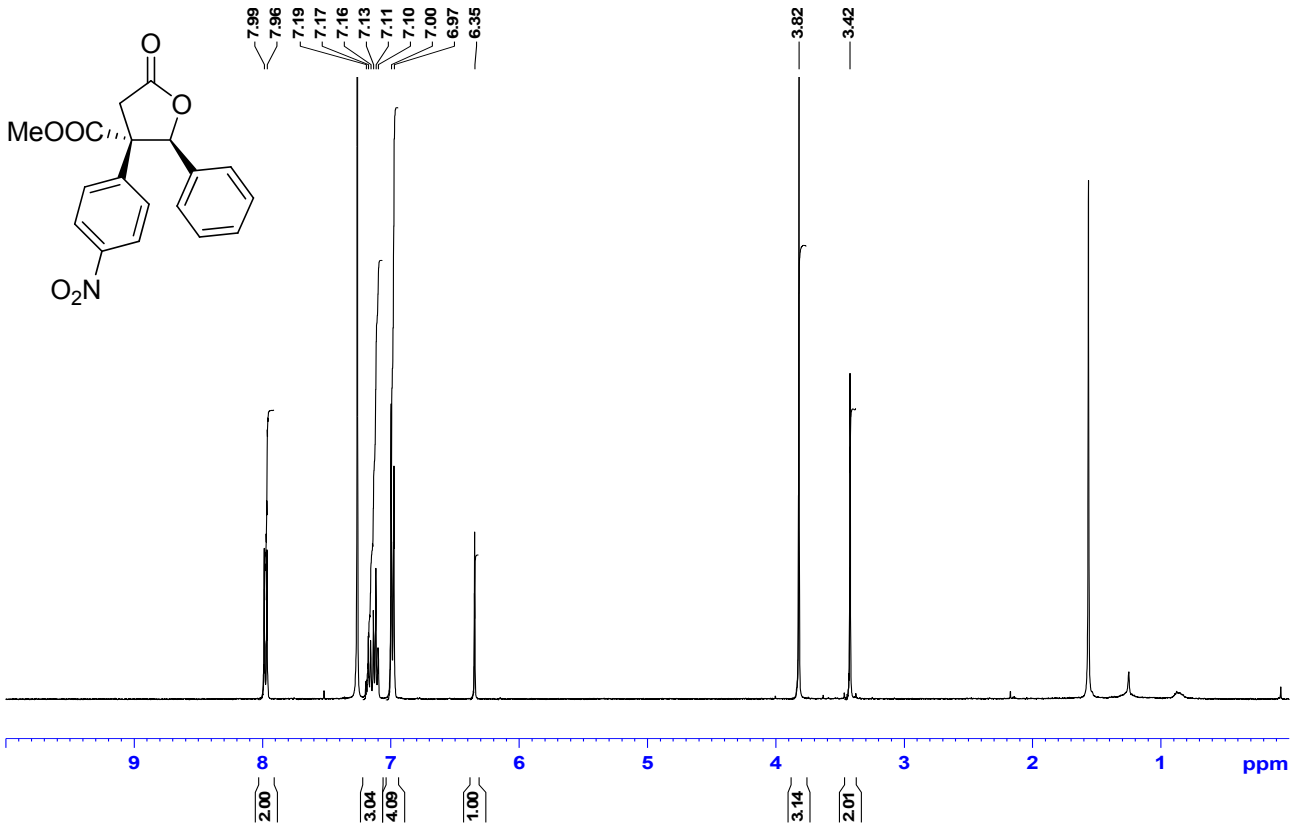
(2*S*,3*S*)-Methyl 3-(3,5-dibromophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (*trans*-17b, Table 1, entry 7). ^{1}H NMR in $CDCl_3$ (400 MHz)



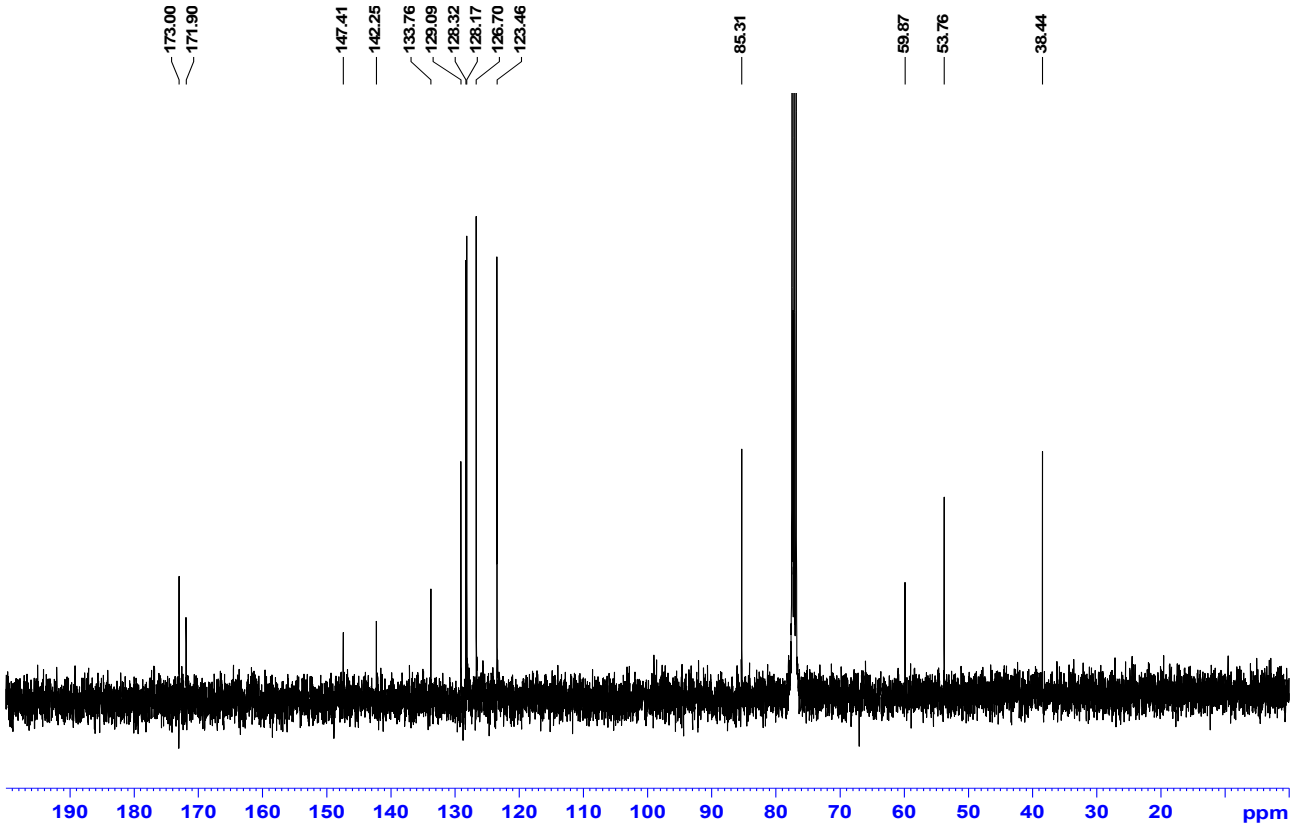
^{13}C NMR in $CDCl_3$ (100 MHz)



(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate *trans*-17d, Table 2, entry 1). ^{1}H NMR in $CDCl_3$ (400 MHz)

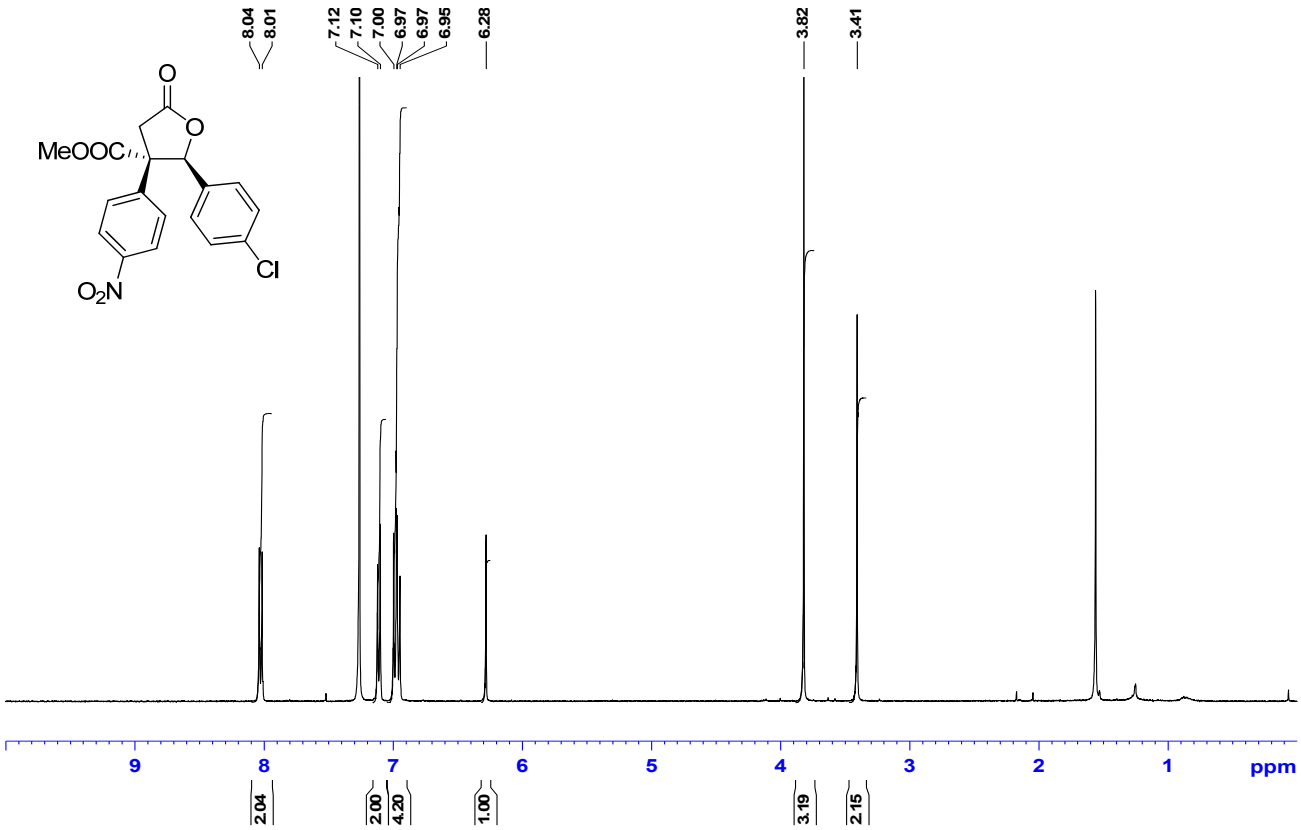


^{13}C NMR in $CDCl_3$ (100 MHz)

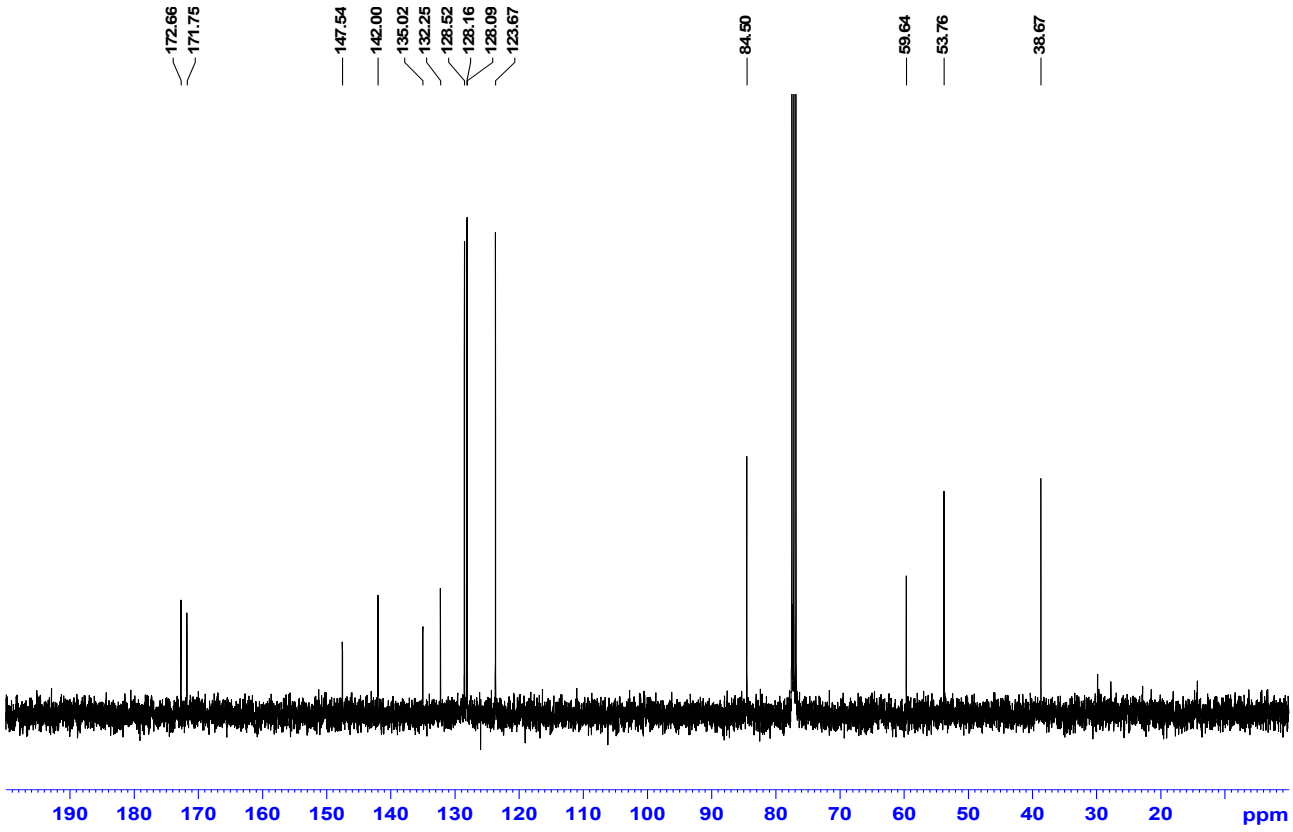


(2*S*,3*S*)-Methyl 2-(4-chlorophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate

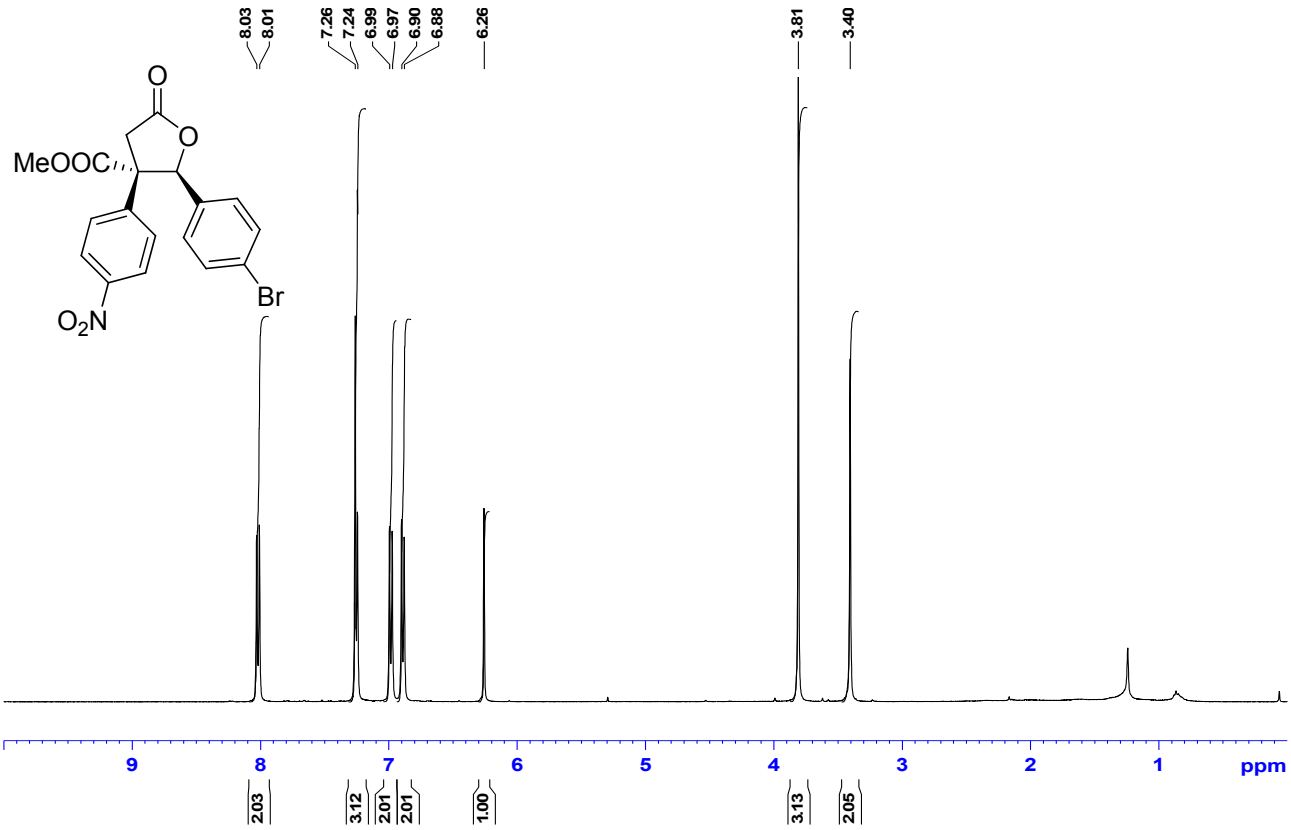
(***trans*-18**, Table 2, entry 2) ^{1}H NMR in $CDCl_3$ (400 MHz)



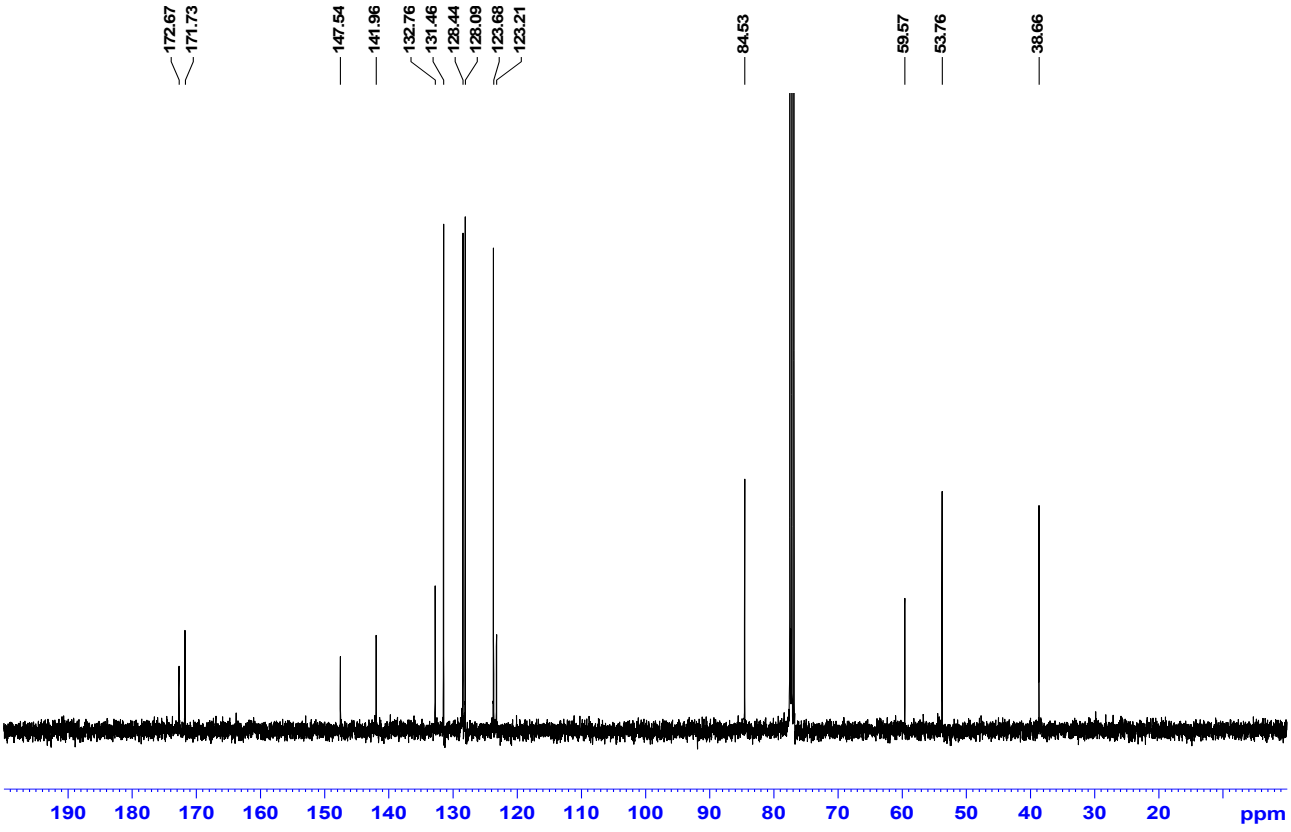
^{13}C NMR in $CDCl_3$ (100 MHz)



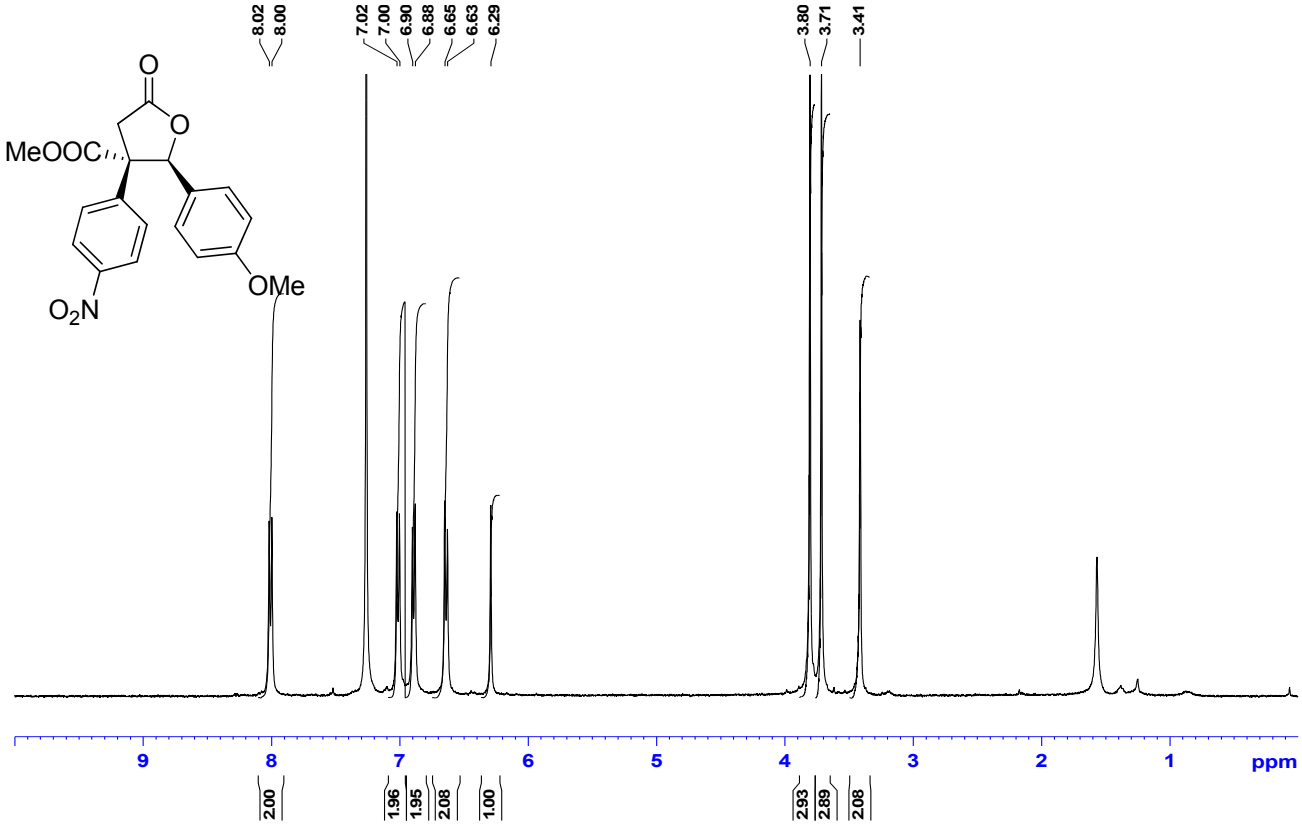
(2*S*,3*S*)-Methyl2-(4-bromophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-19**, Table 2, entry 3). ^{1}H NMR in $CDCl_3$ (400 MHz)



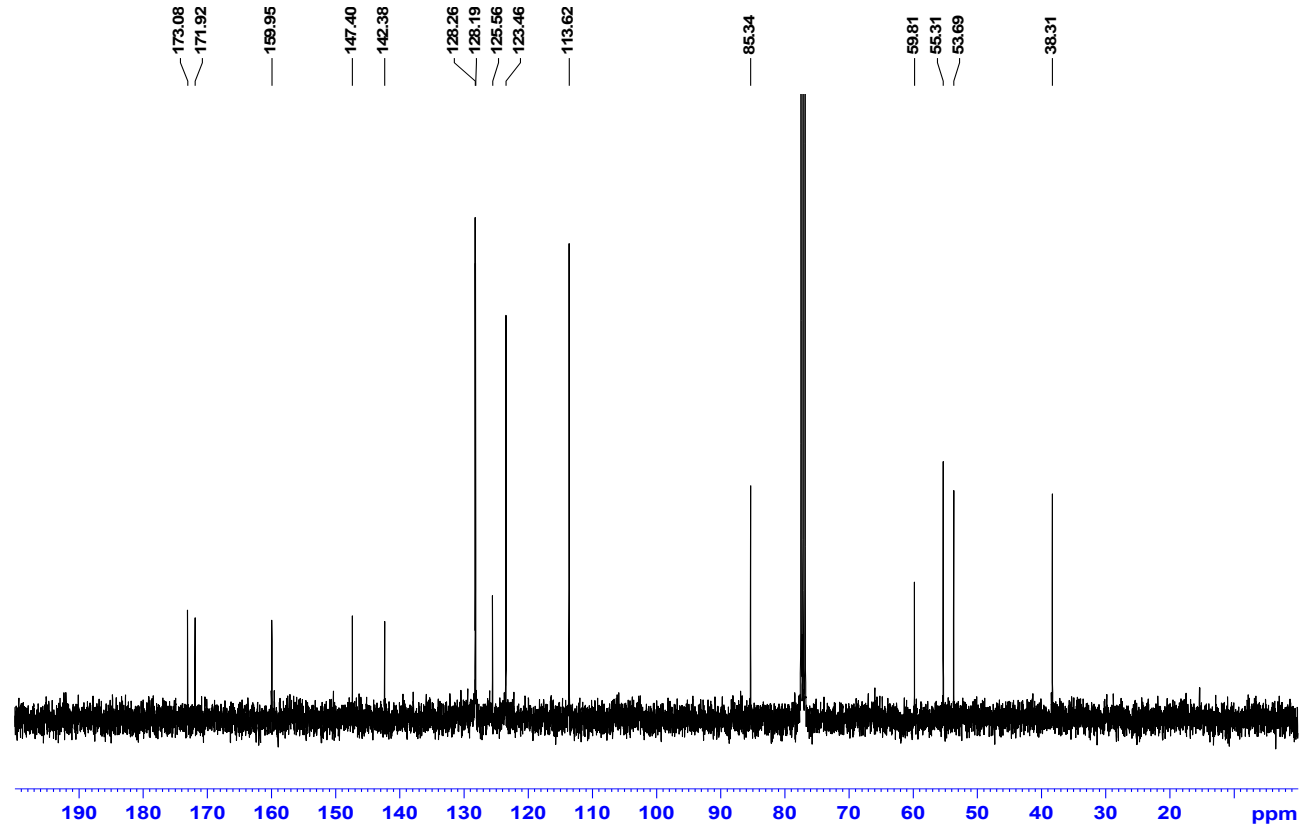
^{13}C NMR in $CDCl_3$ (100 MHz)



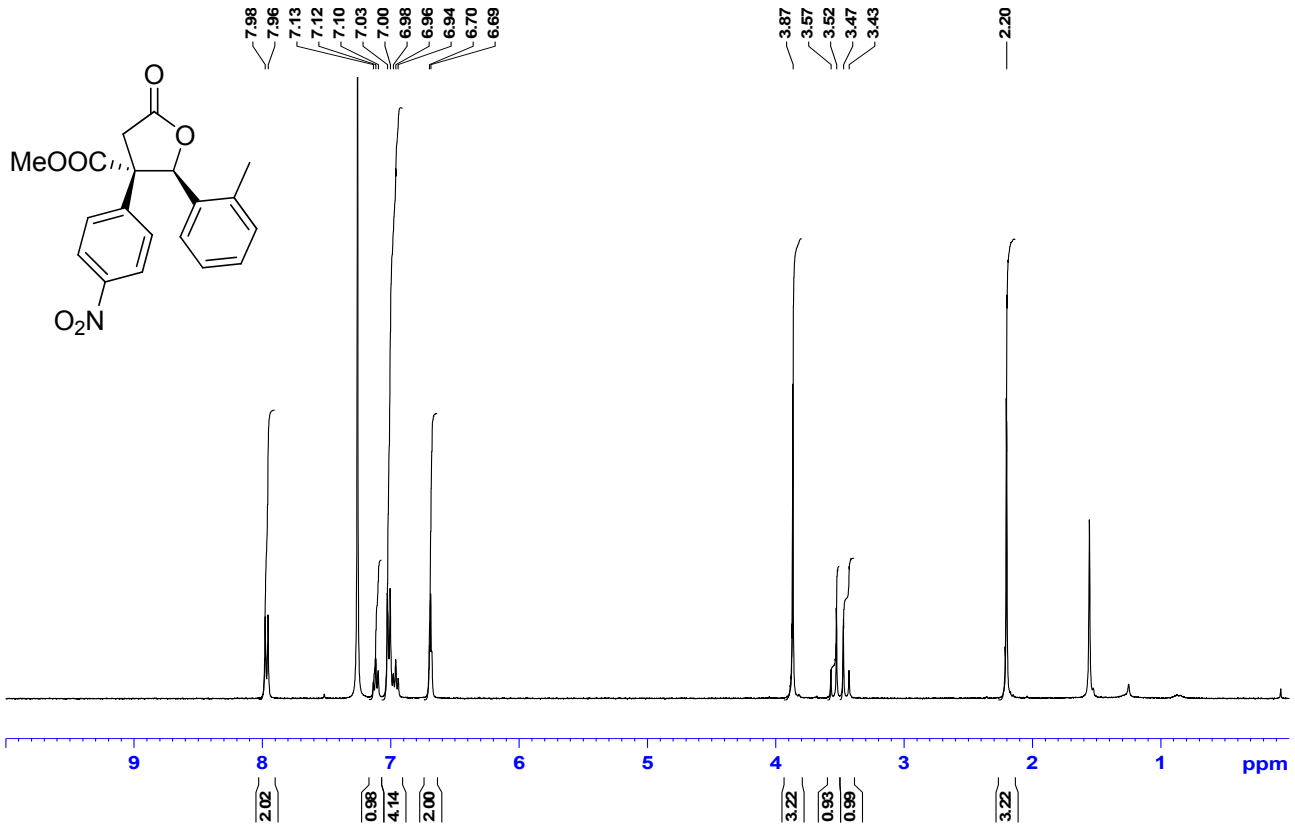
(2*S*,3*S*)-Methyl 2-(4-methoxyphenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-20**, Table 2, entry 4). ^{1}H NMR in $CDCl_3$ (400 MHz)



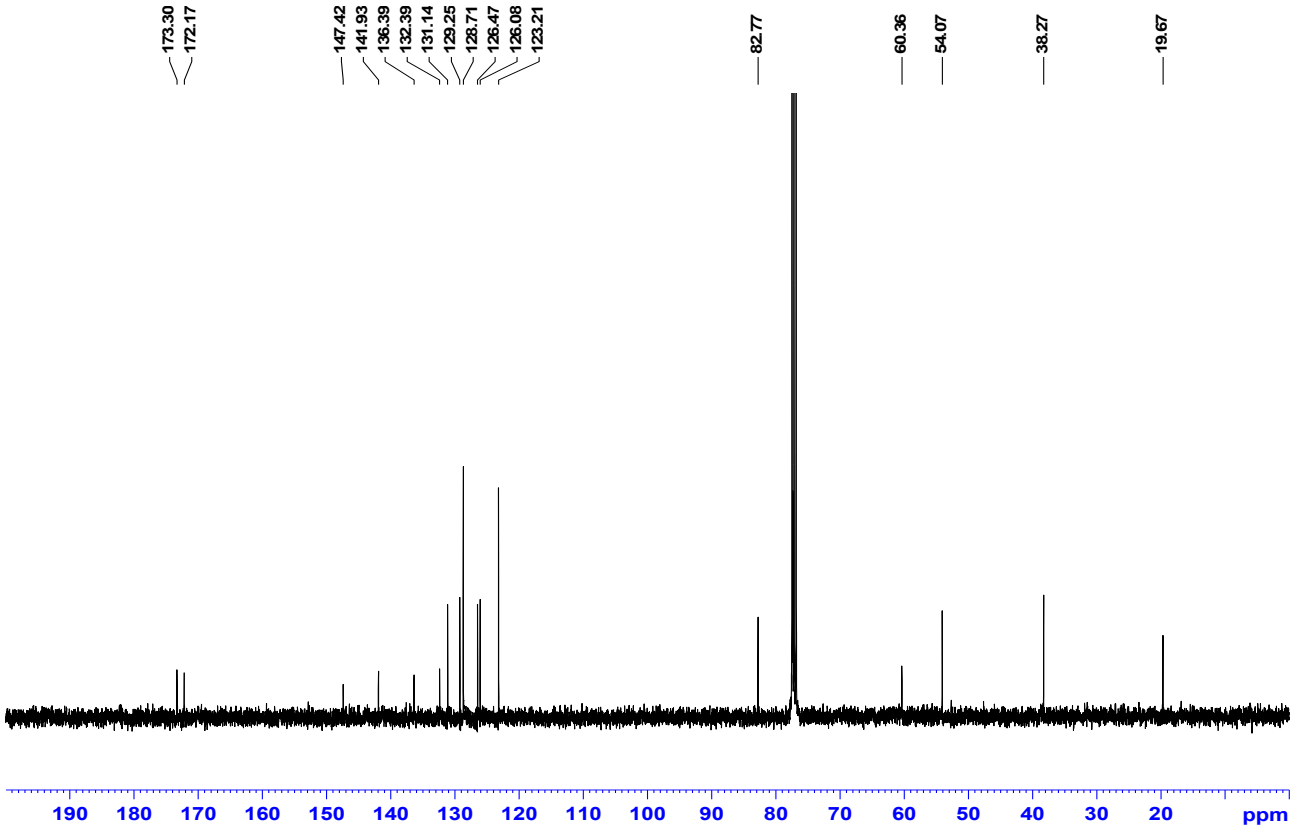
^{13}C NMR in $CDCl_3$ (100 MHz)



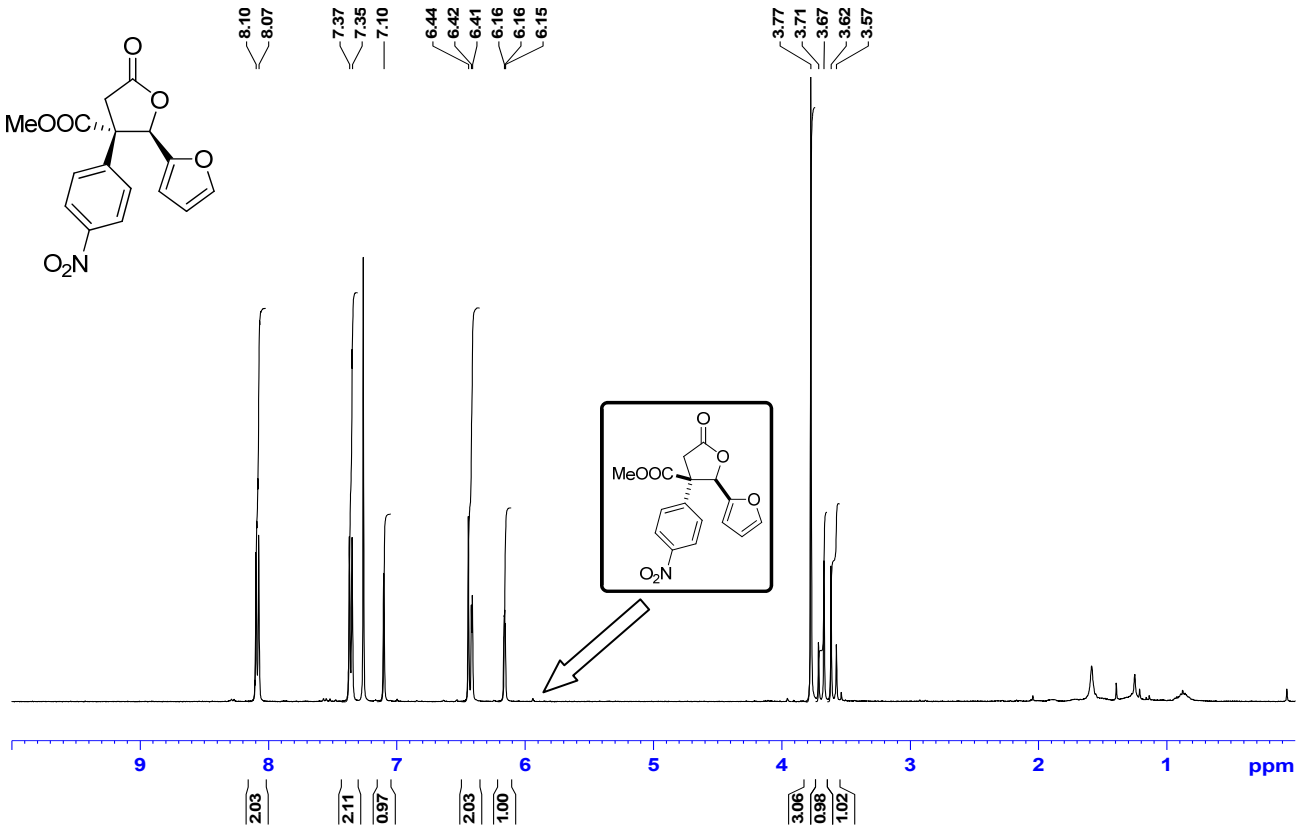
(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(o-tolyl)tetrahydrofuran-3-carboxylate (***trans*-21**, Table 2, entry 5). ^{1}H NMR in $CDCl_3$ (400 MHz)



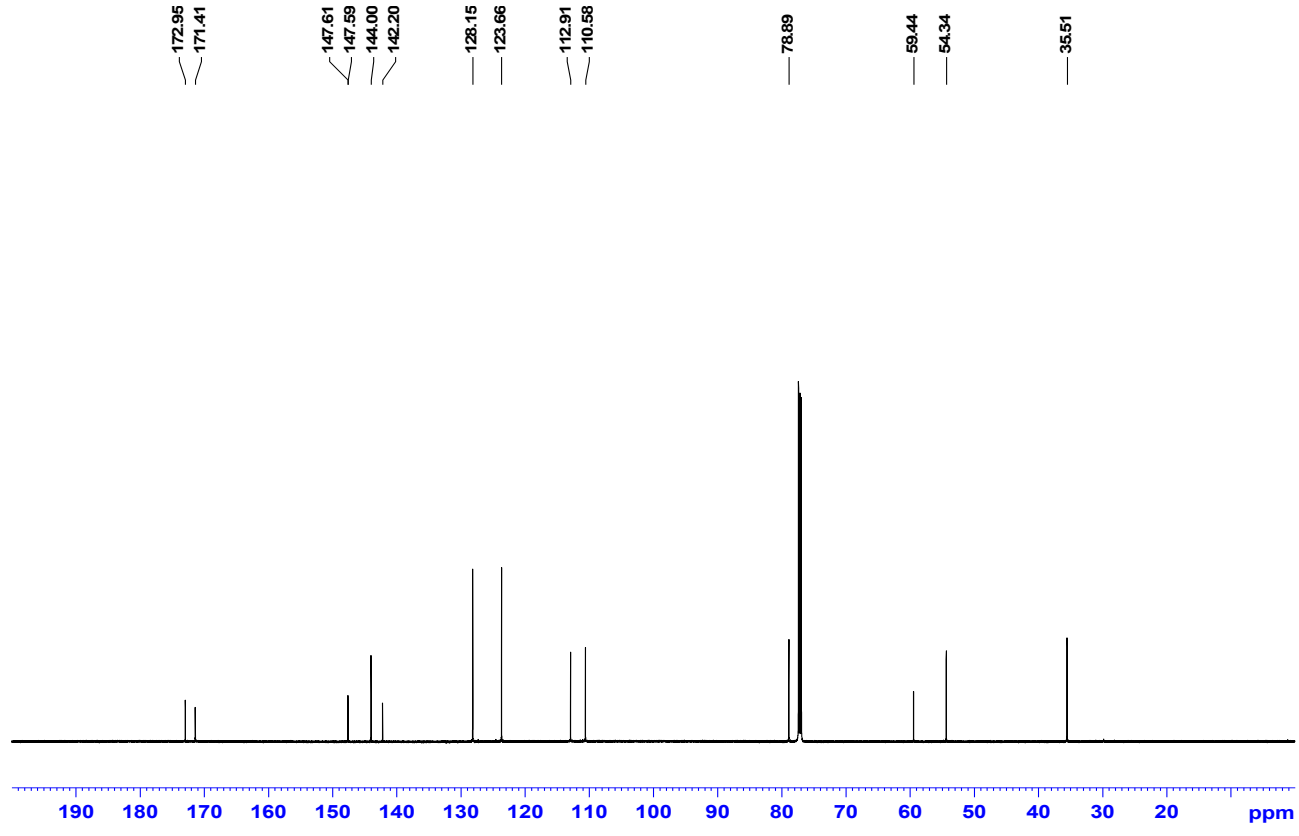
^{13}C NMR in $CDCl_3$ (100 MHz)



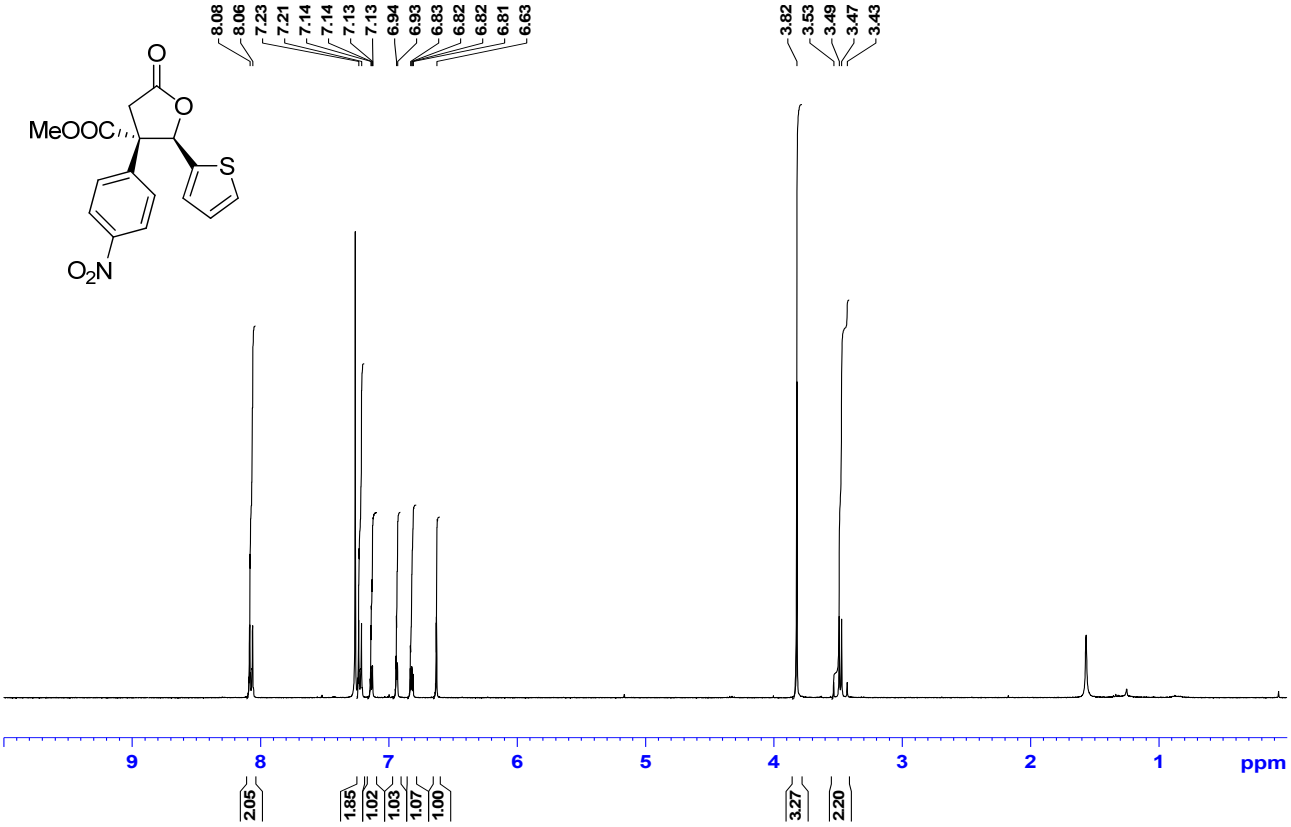
Methyl 2-(furan-2-yl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-22**, ***cis*-22**, Table 2, entry 6). ^{1}H NMR in $CDCl_3$ (400 MHz)



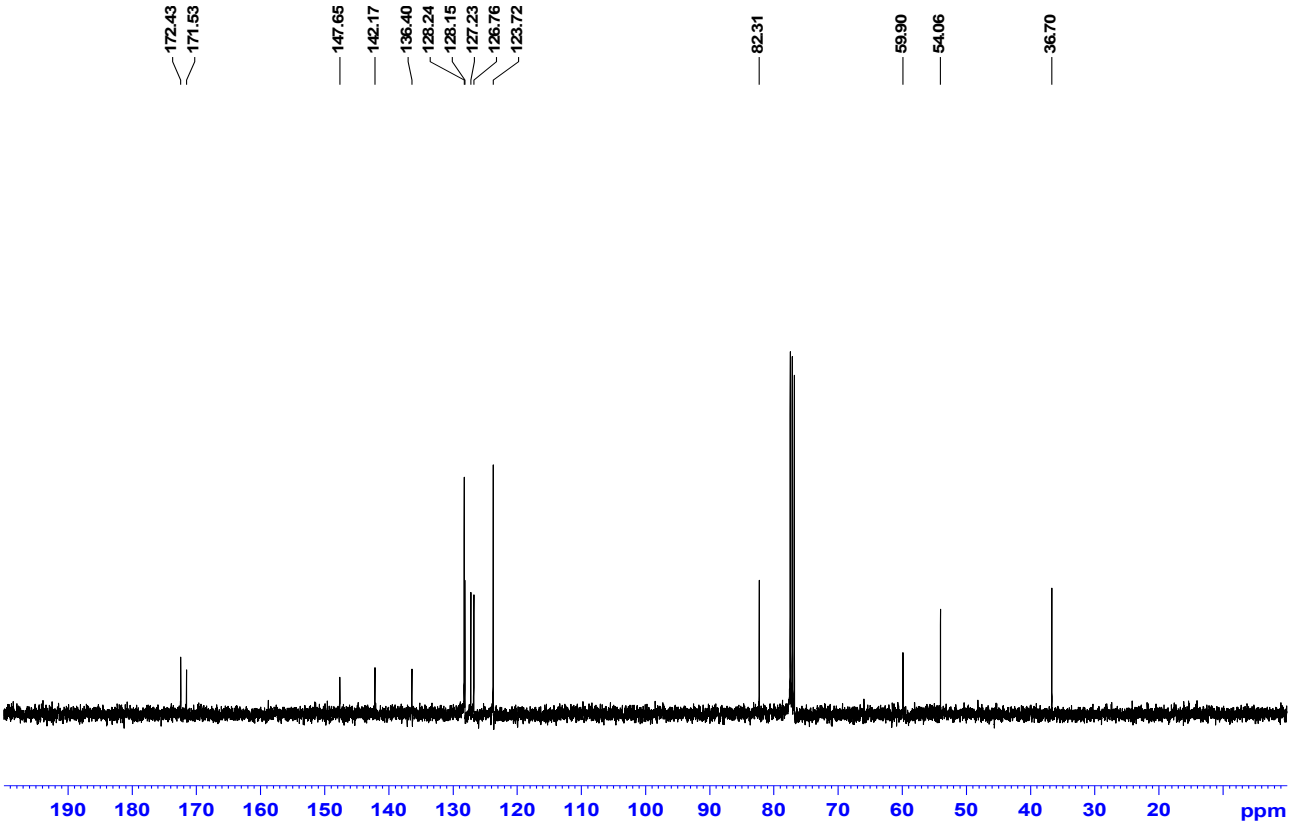
^{13}C NMR in $CDCl_3$ (151 MHz)



(2*R*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(thiophen-2-yl)tetrahydrofuran-3-carboxylate (***trans*-23**, Table 2, entry 7). ^{1}H NMR in $CDCl_3$ (400 MHz)

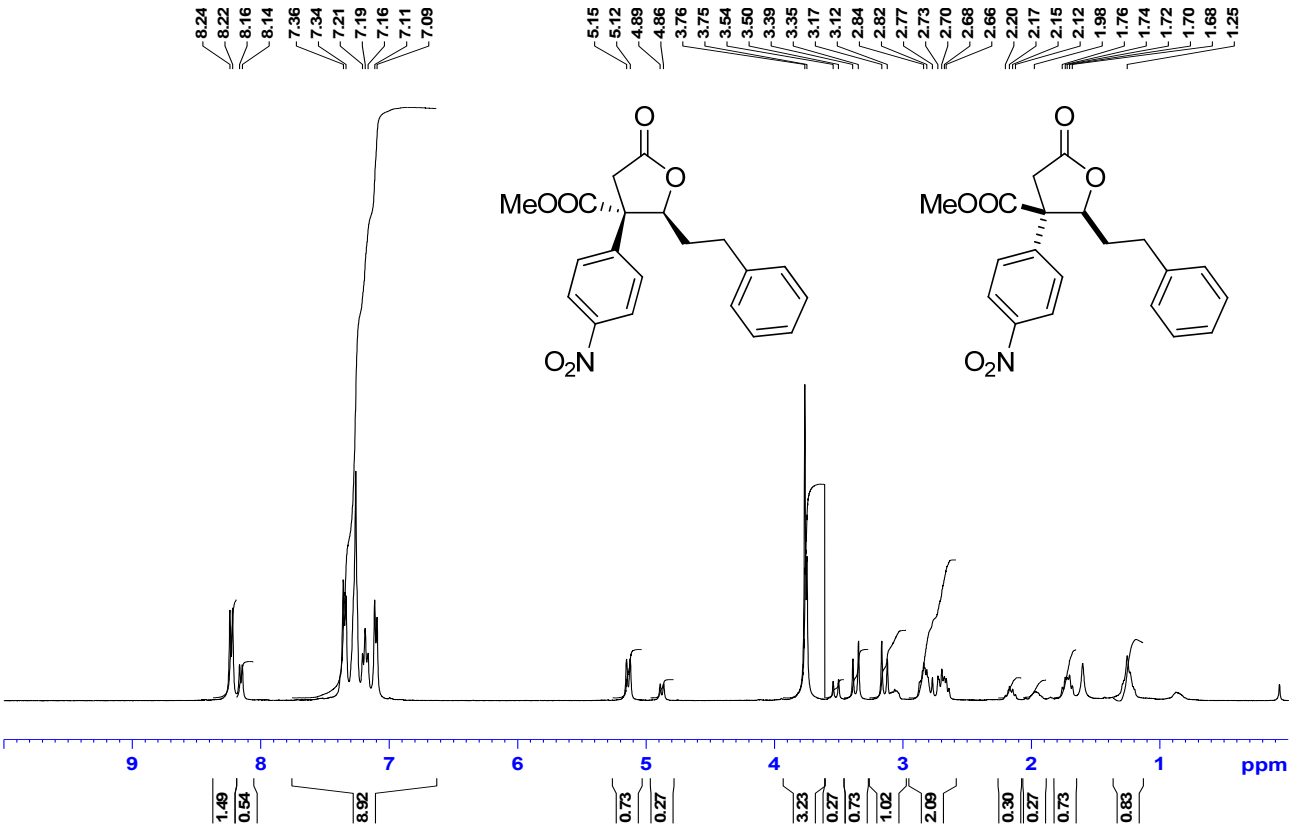


^{13}C NMR in $CDCl_3$ (100 MHz)

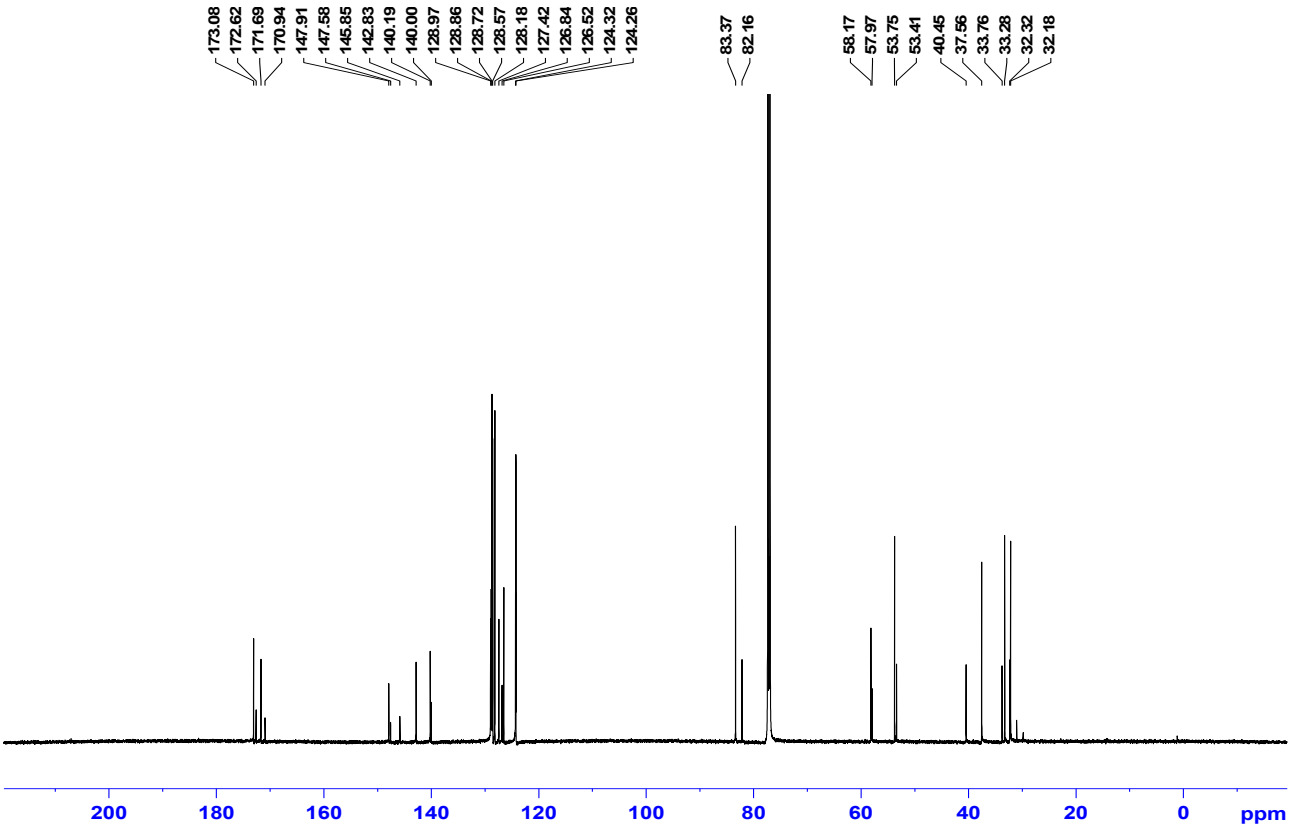


Methyl 3-(4-nitrophenyl)-5-oxo-2-phenethyltetrahydrofuran-3-carboxylate (*trans*-24, *cis*-24

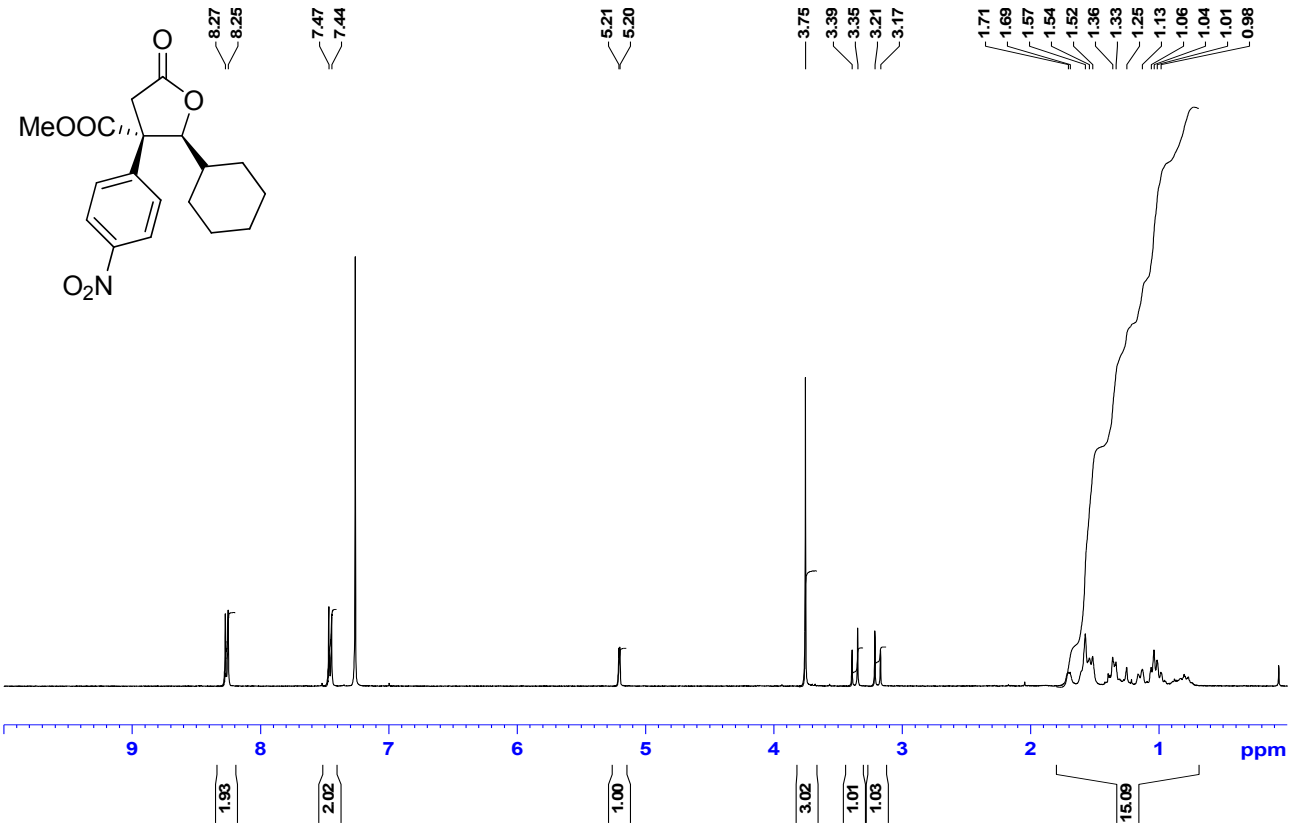
Table 2, entry 8). ^{1}H NMR in $CDCl_3$ (400 MHz)



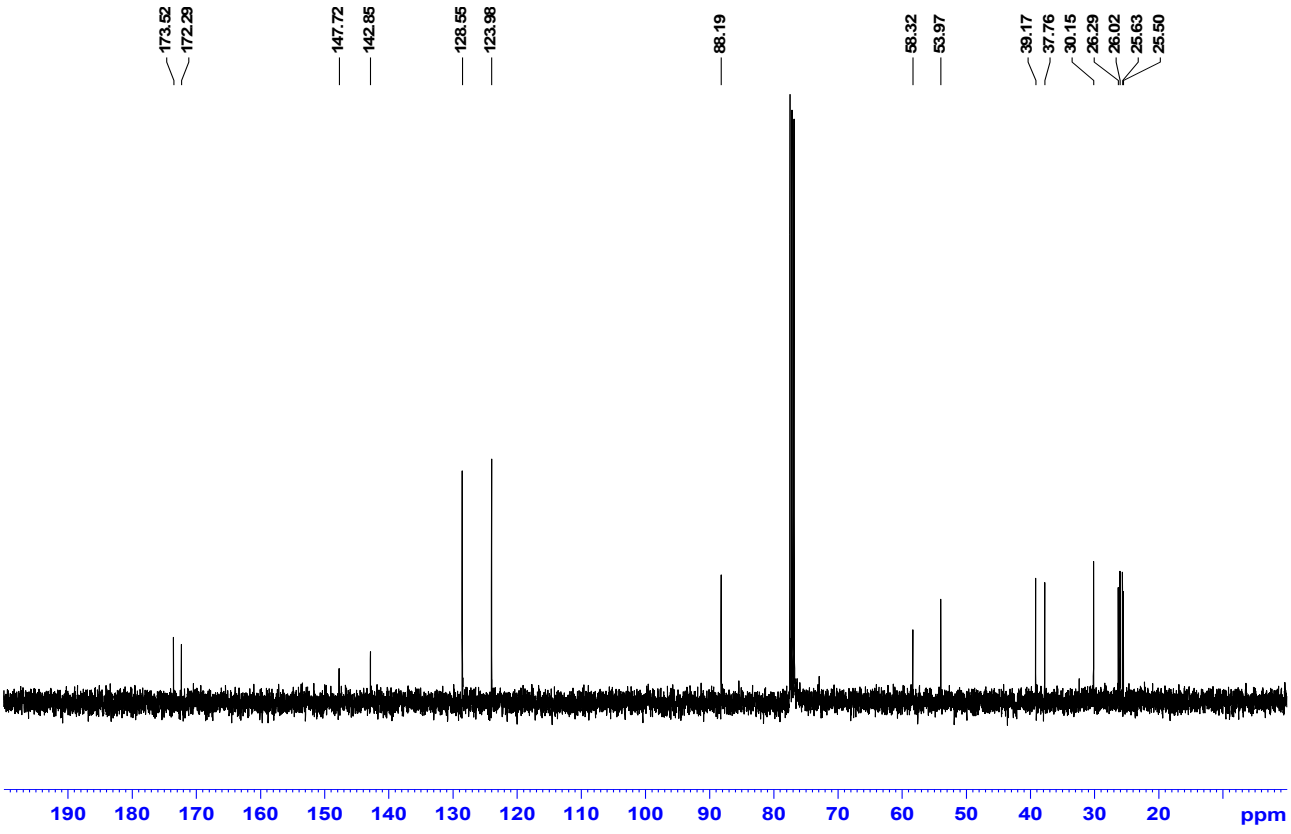
^{13}C NMR in $CDCl_3$ (151 MHz)



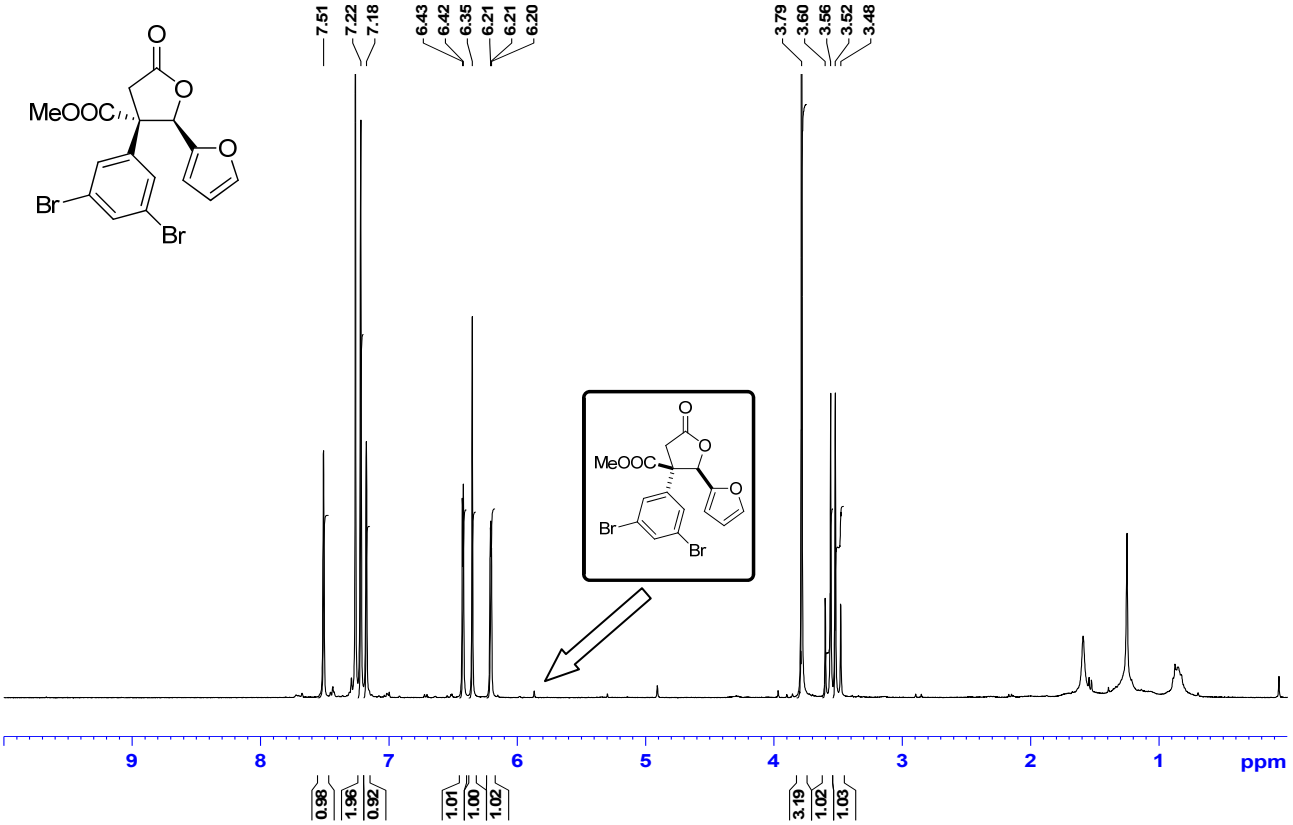
(2*S*,3*S*)-Methyl 2-cyclohexyl-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-25**, Table 2, entry 9)**.** ^{1}H NMR in $CDCl_3$ (400 MHz)



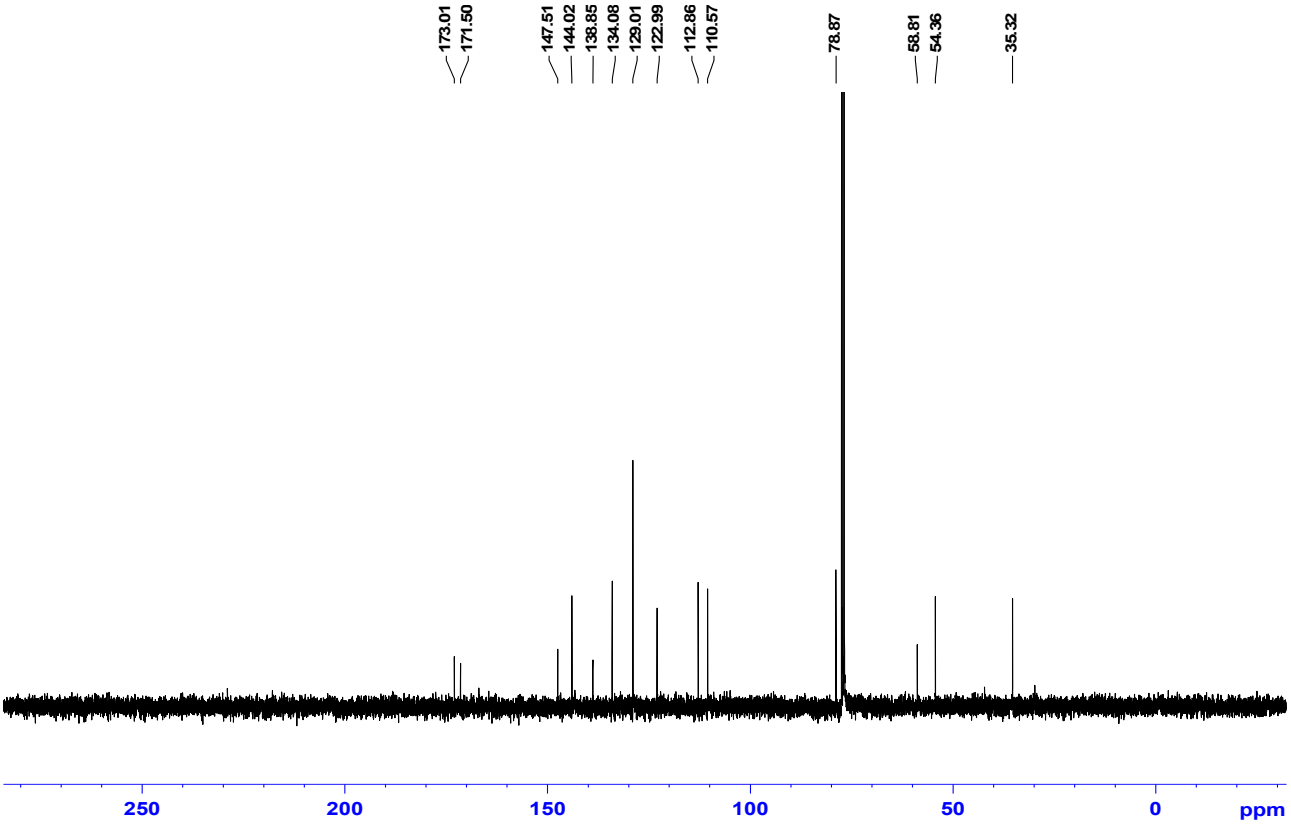
^{13}C NMR in $CDCl_3$ (100 MHz)



Methyl 3-(3,5-dibromophenyl)-2-(furan-2-yl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-26**, ***cis*-26**, Scheme 3). ^{1}H NMR in $CDCl_3$ (400 MHz)



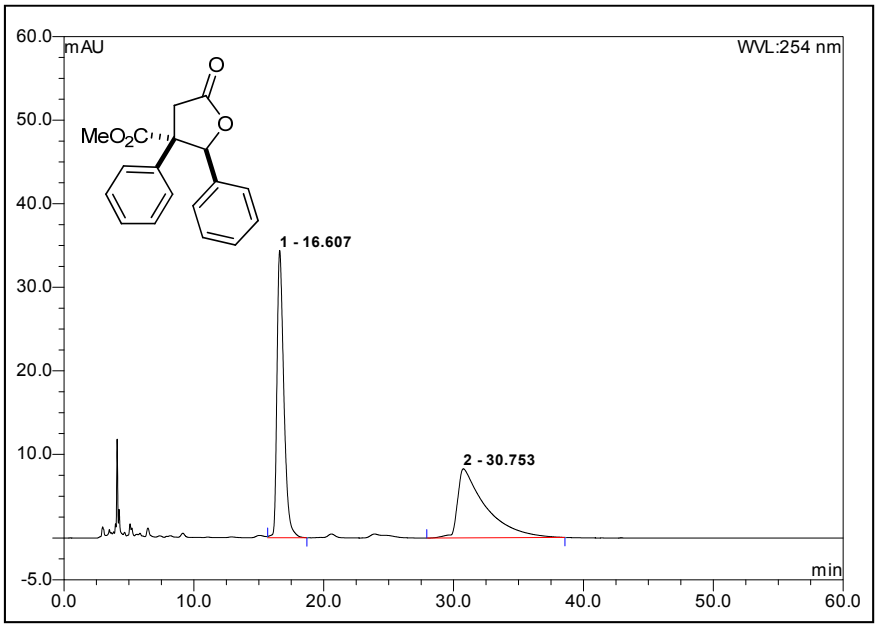
^{13}C NMR in $CDCl_3$ (100 MHz)



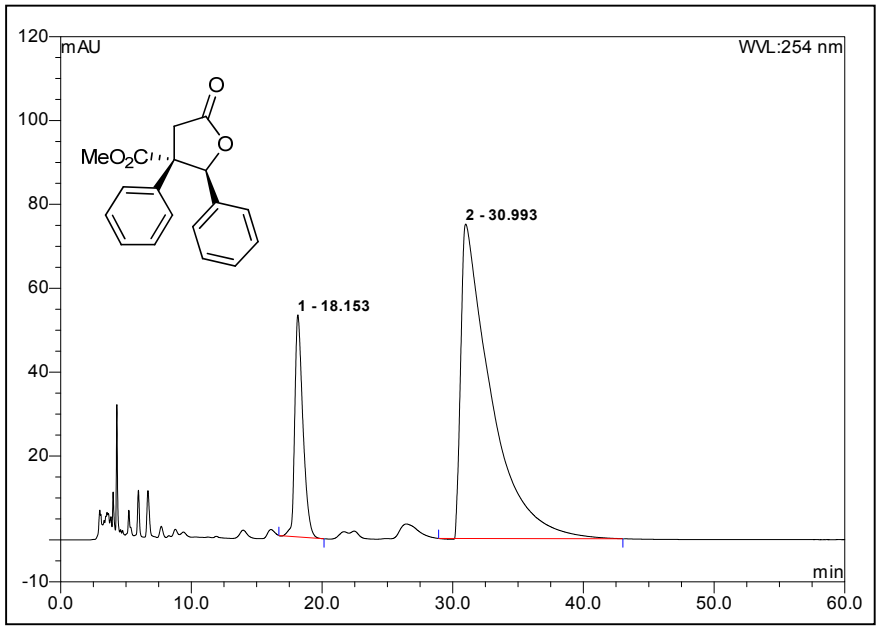
7.0 HPLC chromatograms

(2*S*,3*S*)-Methyl 5-oxo-2,3-diphenyltetrahydrofuran-3-carboxylate (***trans*-17a**, Table 1, entry 2). Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 90/10, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	16.61	50.58
2	30.75	49.42
Total:		100.00



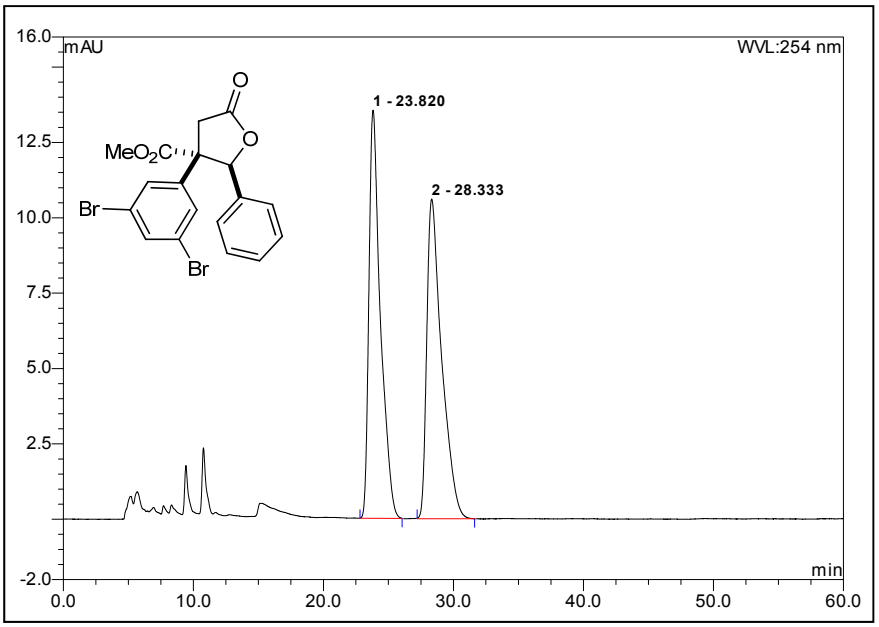
No.	Ret.Time min	Rel.Area %
1	18.15	16.14
2	30.99	83.86
Total:		100.00



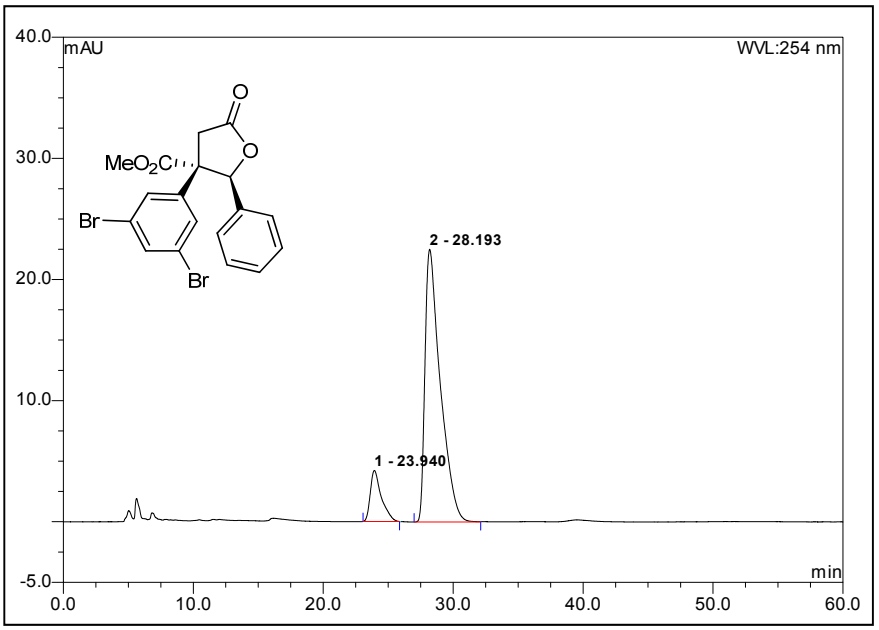
(2*S*,3*S*)-Methyl 3-(3,5-dibromophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (*trans*-17b, Table 1, entry 7).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 0.6 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	23.82	49.63
2	28.33	50.37
Total:		100.00



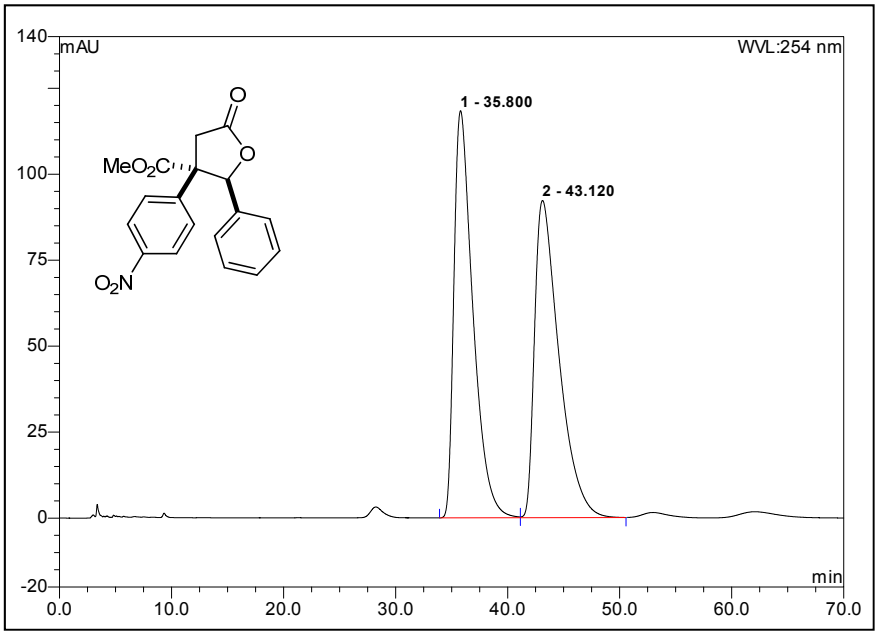
No.	Ret.Time min	Rel.Area %
1	23.94	11.86
2	28.19	88.14
Total:		100.00



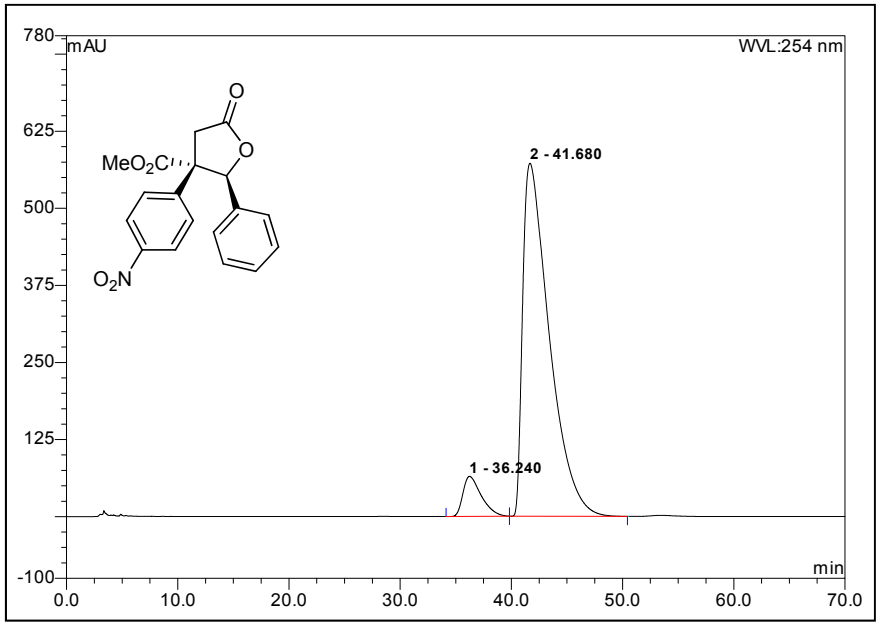
(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate *trans*-17d, Table 2, entry 1).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 80/20, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	35.80	49.99
2	43.12	50.01
Total:		100.00



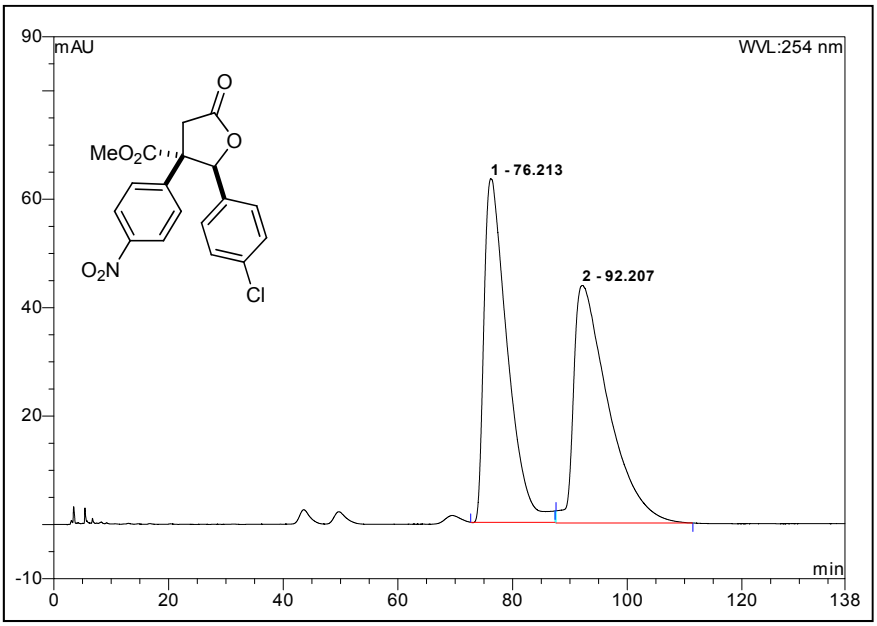
No.	Ret.Time min	Rel.Area %
1	36.24	7.24
2	41.68	92.76
Total:		100.00



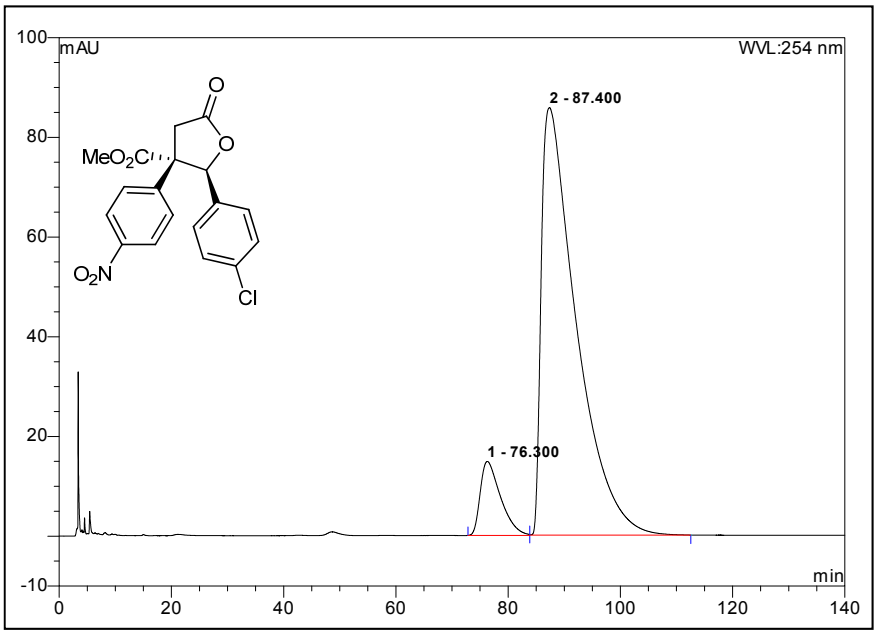
(2*S*,3*S*)-Methyl 2-(4-chlorophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-18**, Table 2, entry 2).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	76.21	49.38
2	92.21	50.62
Total:		100.00



No.	Ret.Time min	Rel.Area %
1	76.30	9.16
2	87.40	90.84
Total:		100.00

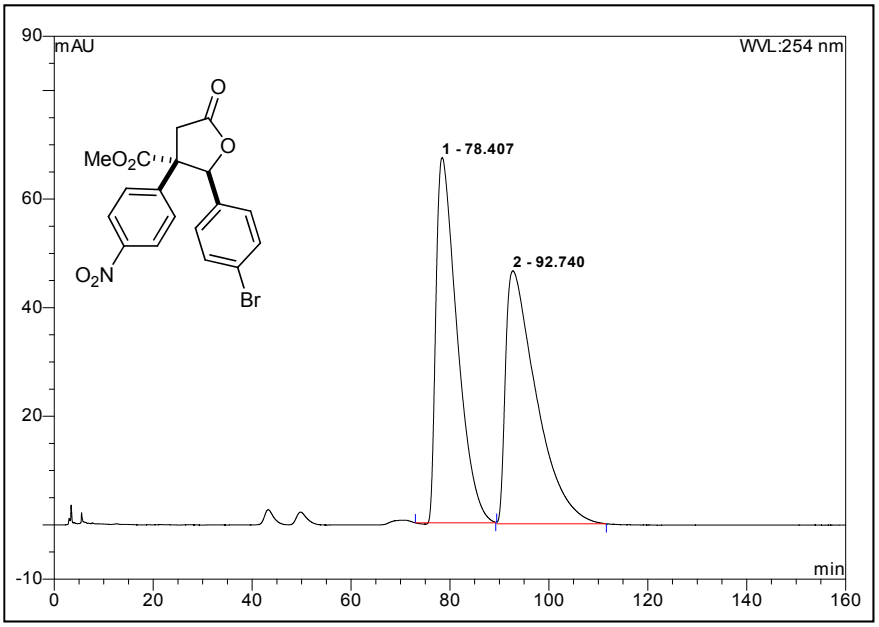


(2*S*,3*S*)-Methyl2-(4-bromophenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate

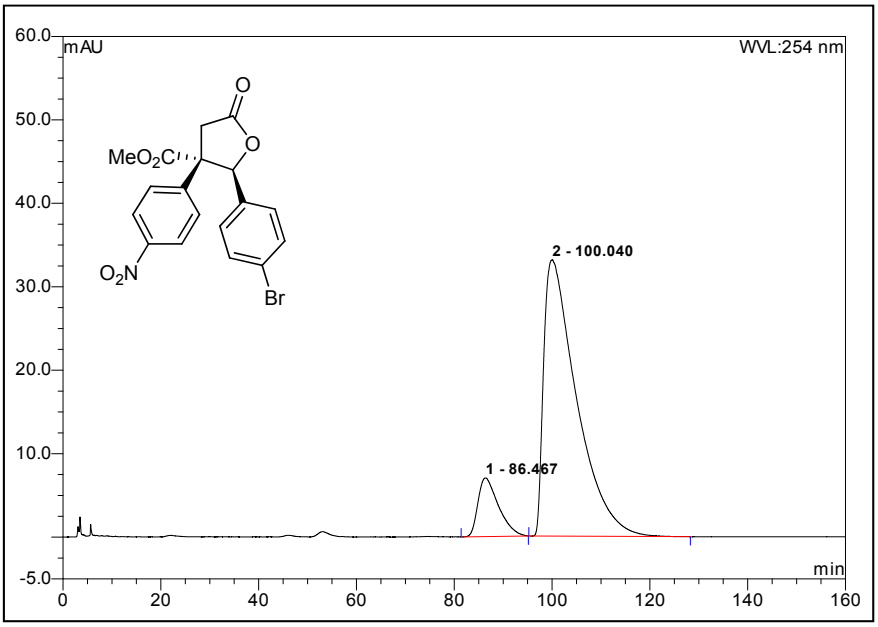
(***trans*-19**, Table 2, entry 3).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	78.41	49.76
2	92.74	50.24
Total:		100.00



No.	Ret.Time min	Rel.Area %
1	86.47	11.69
2	100.04	88.31
Total:		100.00

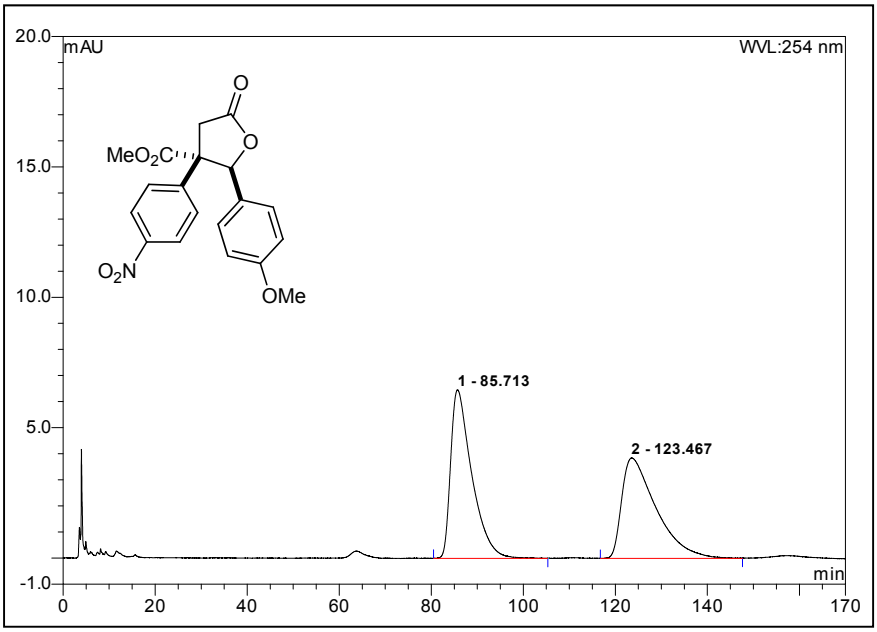


(2*S*,3*S*)-Methyl 2-(4-methoxyphenyl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate

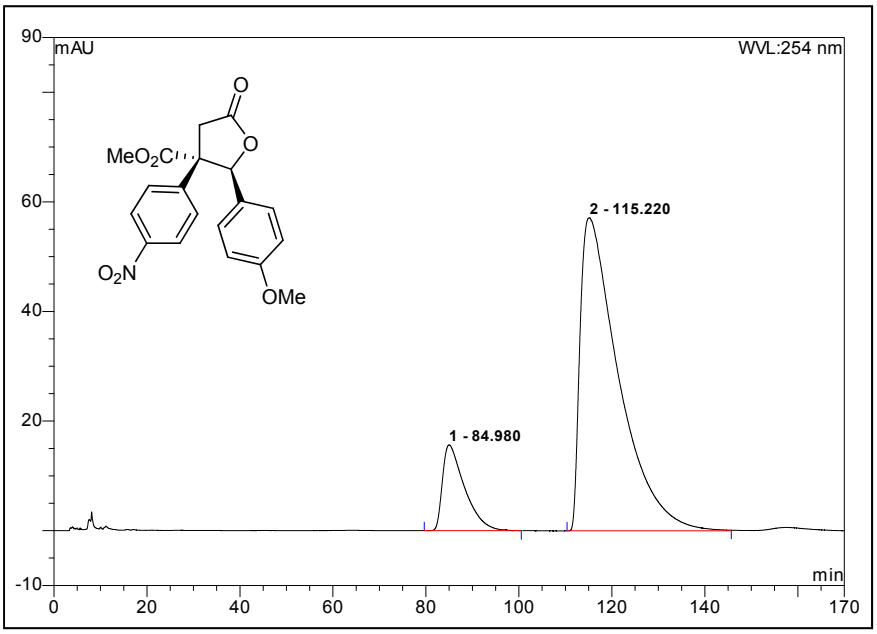
(***trans*-20**, Table 2, entry 4)

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	85.71	50.76
2	123.47	49.24
Total:		100.00



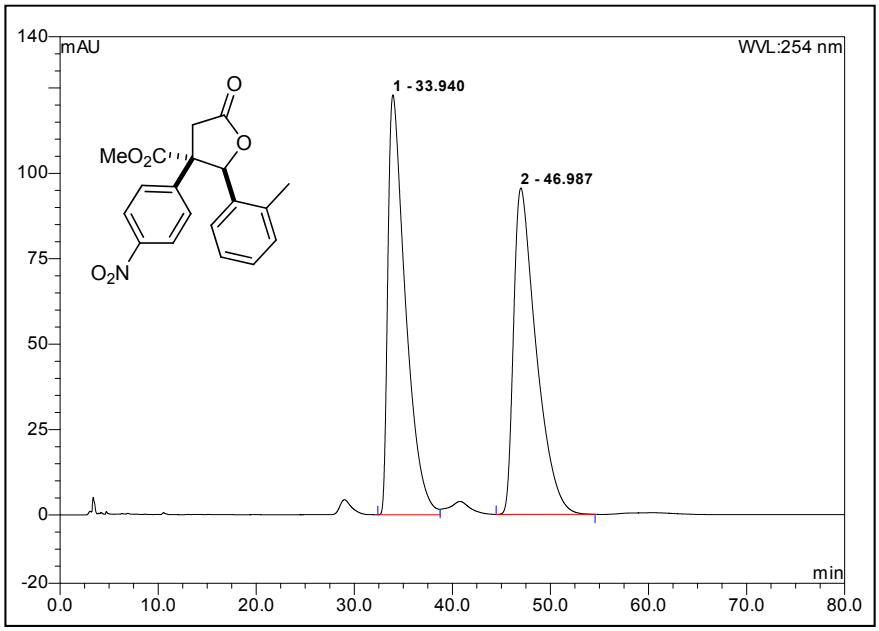
No.	Ret.Time min	Rel.Area %
1	84.98	13.55
2	115.22	86.45
Total:		100.00



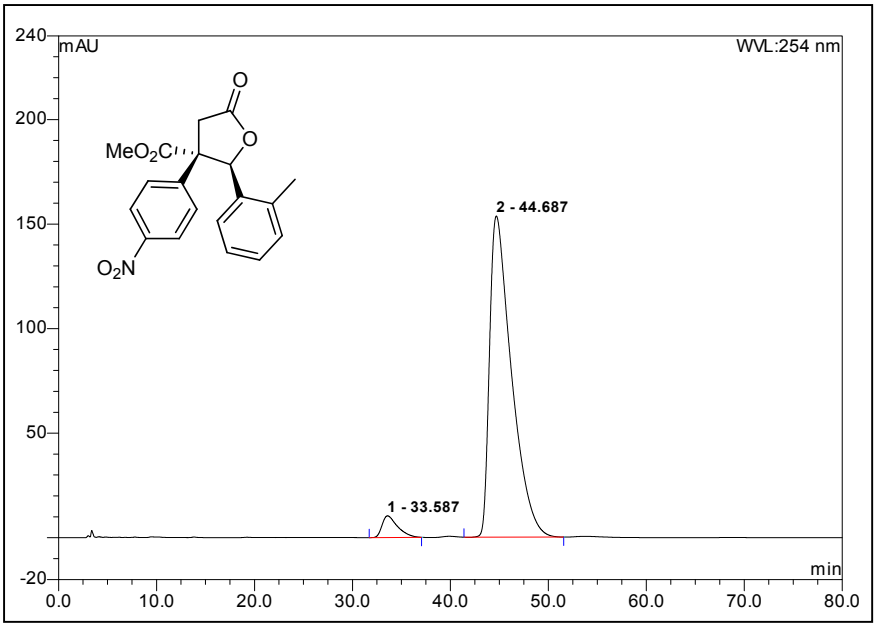
(2*S*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(o-tolyl)tetrahydrofuran-3-carboxylate (***trans*-21**, Table 2, entry 5).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	33.94	50.12
2	46.99	49.88
Total:		100.00

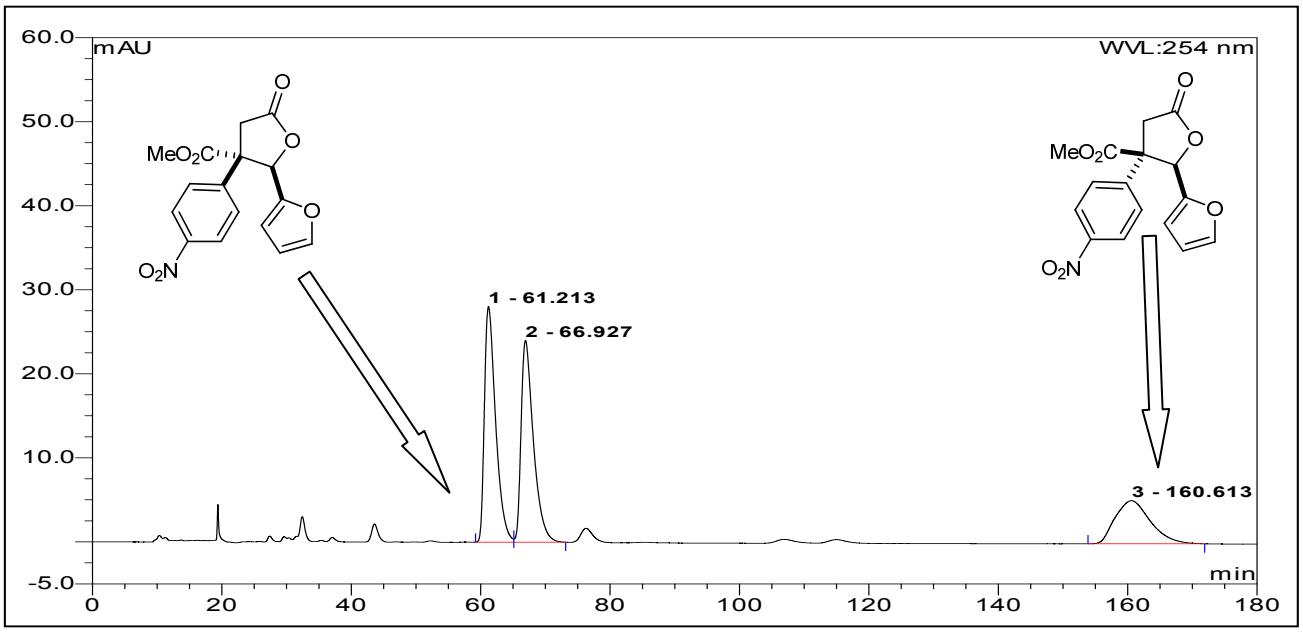


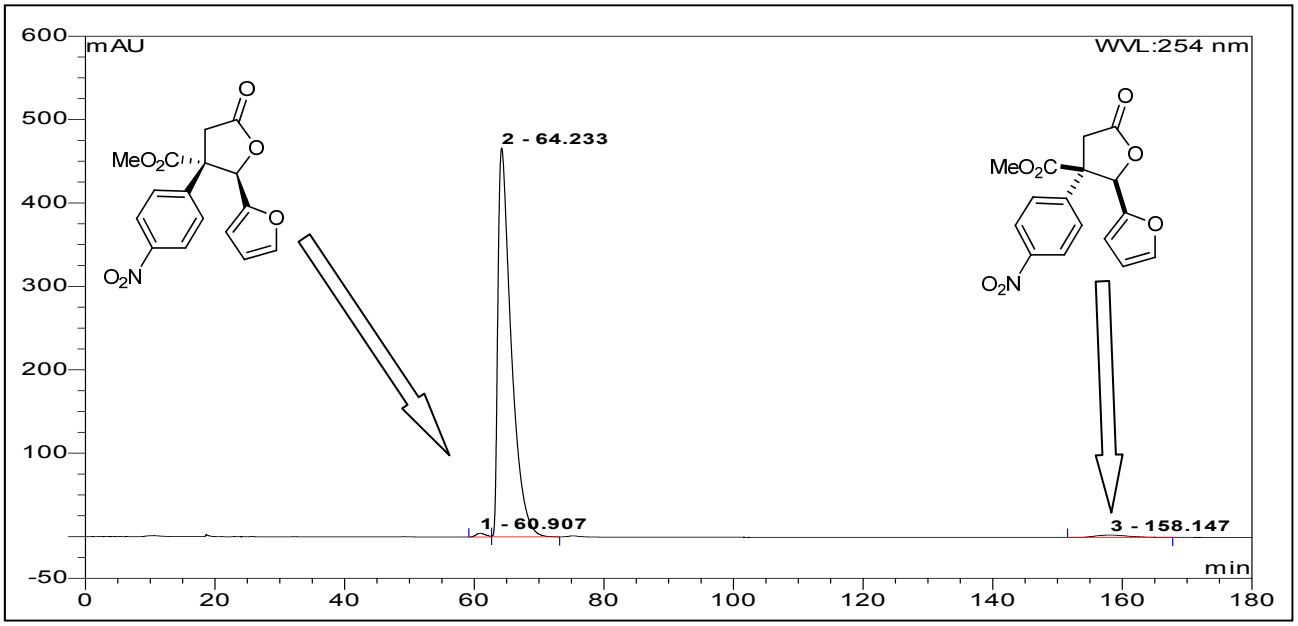
No.	Ret.Time min	Rel.Area %
1	33.59	4.54
2	44.69	95.46
Total:		100.00



Methyl 2-(furan-2-yl)-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (*trans*-22, *cis*-22, Table 2, entry 6)

Chiralcel OD (4.6 mm x 25 cm), hexane/IPA: 75/25, 0.3 mL min^{-1}, RT, UV detection at 254 nm.





Racemic

No.	Ret.Time min	Rel.Area %	
1	61.21	39.76	*cis*-22
2	66.93	37.38	*cis*-22
3	160.61	22.86	*trans*-22
Total:		100.00	

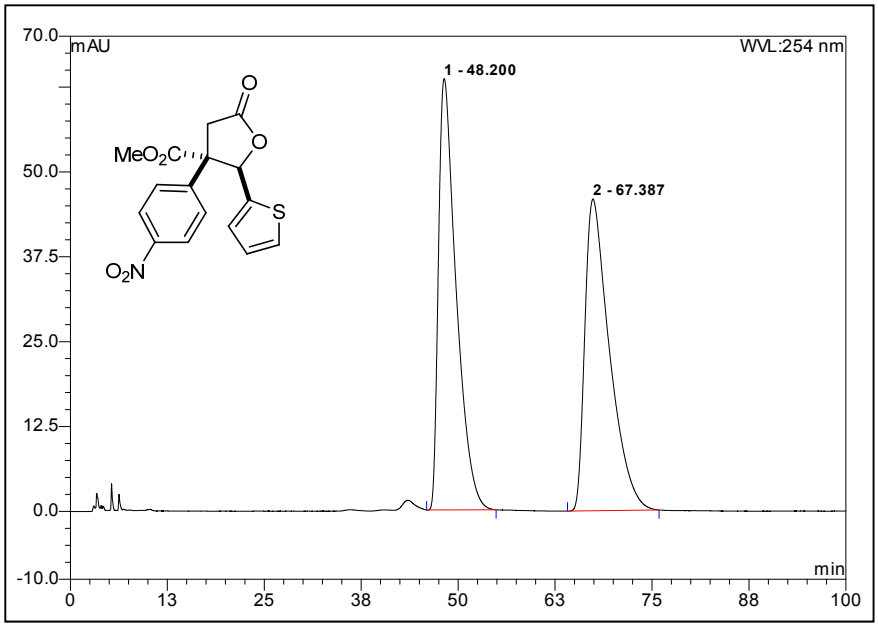
Enantioselective

No.	Ret.Time min	Rel.Area %	
1	60.91	0.67	*cis*-22
2	64.23	97.92	*cis*-22
3	158.15	1.41	*trans*-22
Total:		100.00	

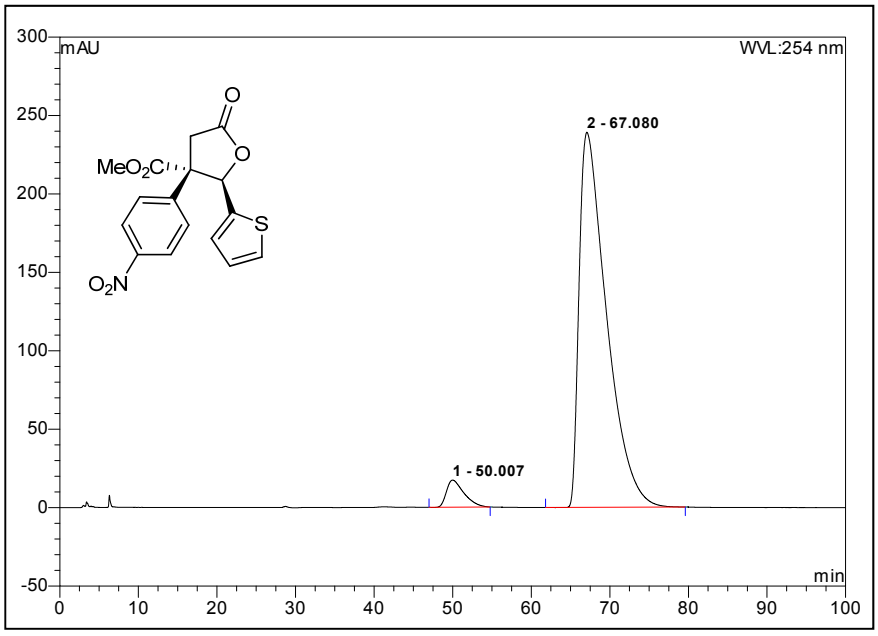
(2*R*,3*S*)-Methyl 3-(4-nitrophenyl)-5-oxo-2-(thiophen-2-yl)tetrahydrofuran-3-carboxylate (***trans*-23**, Table 2, entry 7).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	48.20	49.91
2	67.39	50.09
Total:		100.00



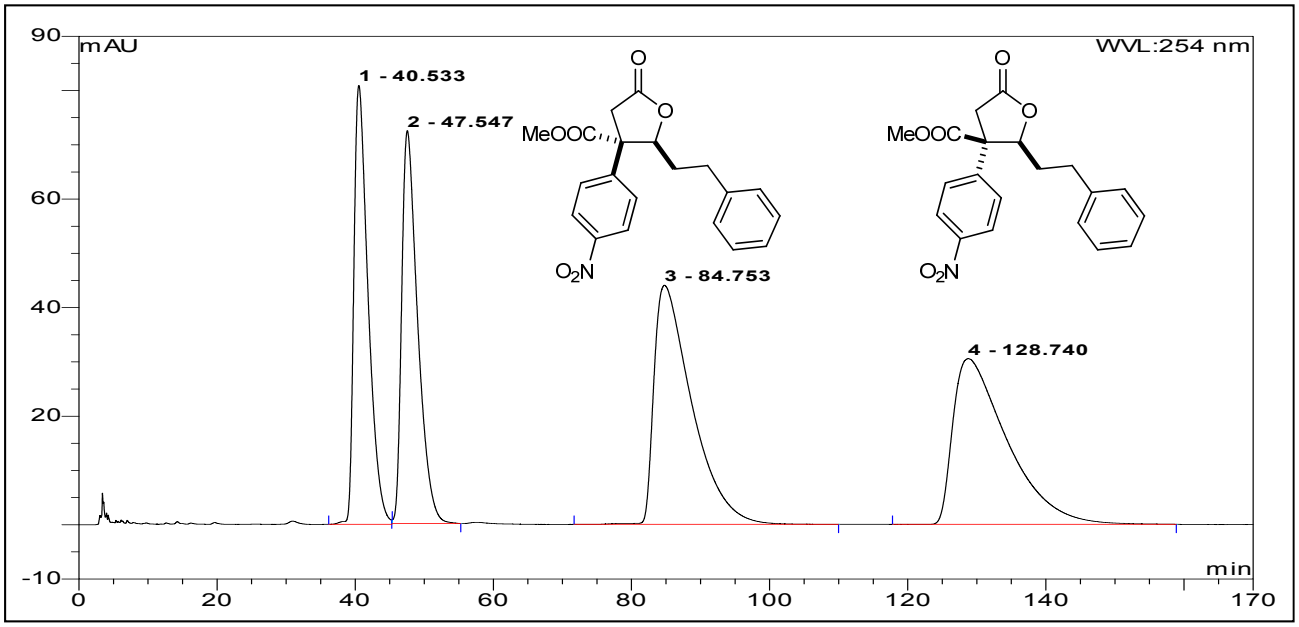
No.	Ret.Time min	Rel.Area %
1	50.01	4.42
2	67.08	95.58
Total:		100.00

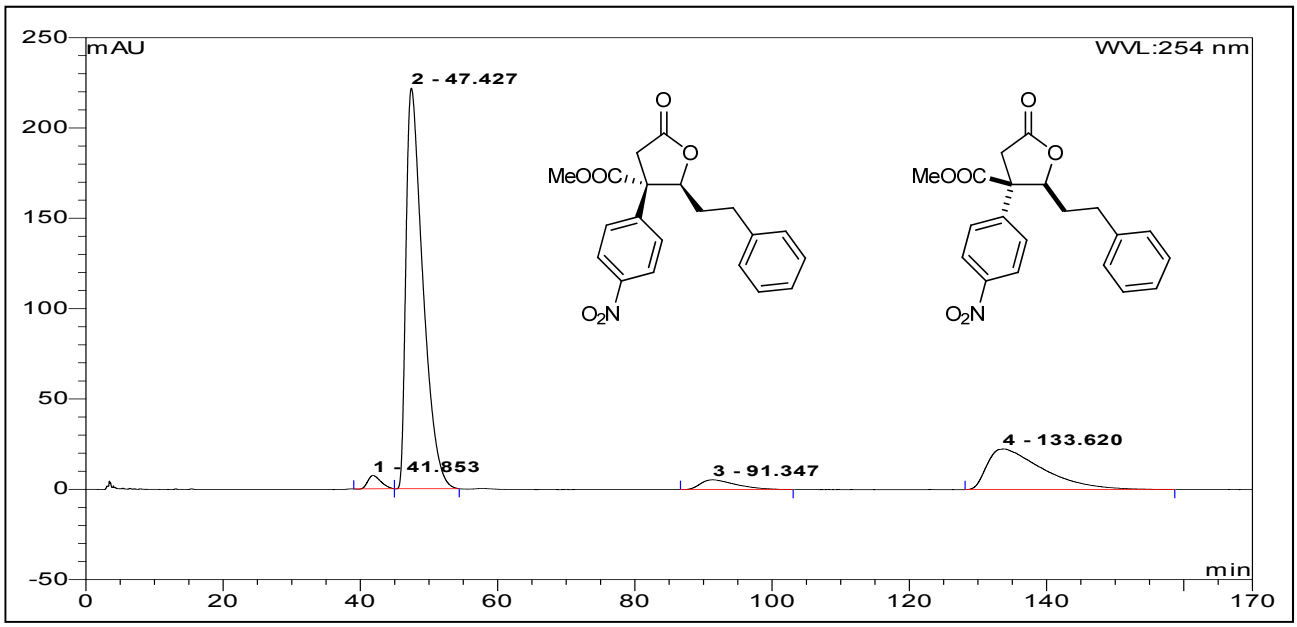


Methyl 3-(4-nitrophenyl)-5-oxo-2-phenethyltetrahydrofuran-3-carboxylate (*trans*-24, *cis*-24

Table 2, entry 8).

Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 1.0 mL min^{-1}, RT, UV detection at 254 nm.





Racemic

No.	Ret.Time min	Rel.Area %	
1	40.53	20.52	***cis*-24**
2	47.55	20.55	***cis*-24**
3	84.75	29.52	***trans*-24**
4	128.74	29.40	***trans*-24**
Total:		100.00	

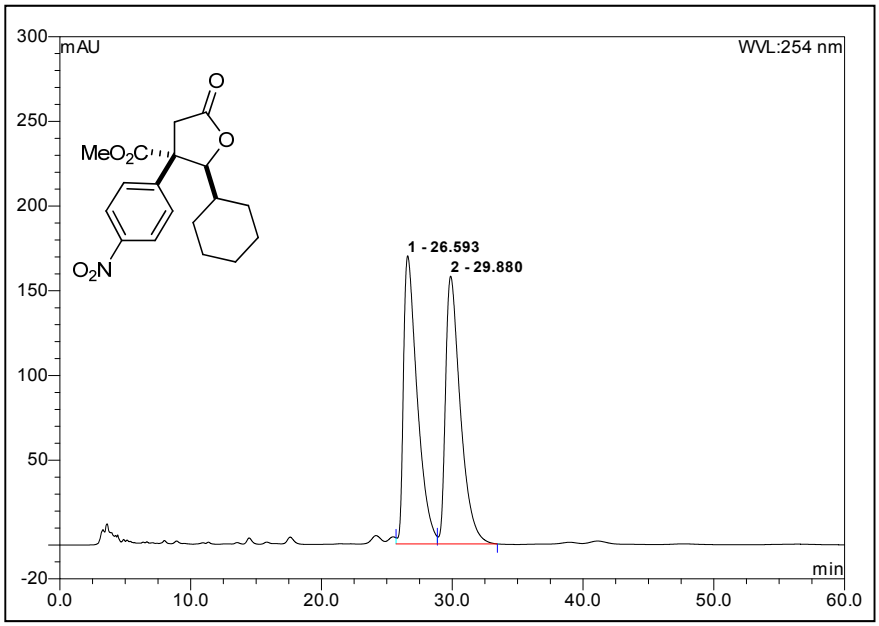
Enantioselective

No.	Ret.Time min	Rel.Area %	
1	41.85	1.80	***cis*-24**
2	47.43	70.94	***cis*-24**
3	91.35	3.60	***trans*-24**
4	133.62	23.66	***trans*-24**
Total:		100.00	

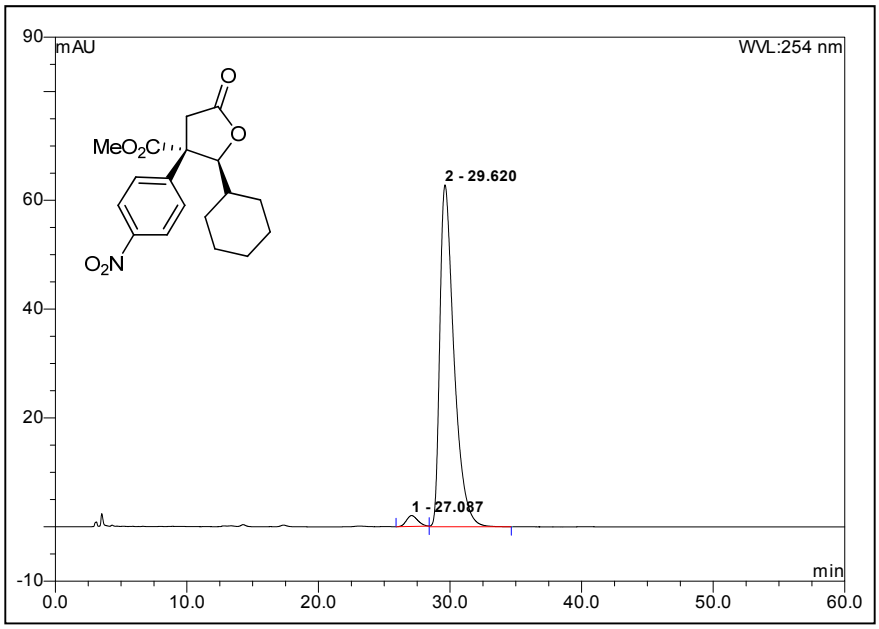
(2*S*,3*S*)-Methyl 2-cyclohexyl-3-(4-nitrophenyl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-25**, Table 2, entry 9)**.**

Chiralcel OD (4.6 mm x 25 cm), hexane/IPA: 90/10, 1.0 mL min^{-1}, RT, UV detection at 254 nm.

No.	Ret.Time min	Rel.Area %
1	26.59	49.89
2	29.88	50.11
Total:		100.00

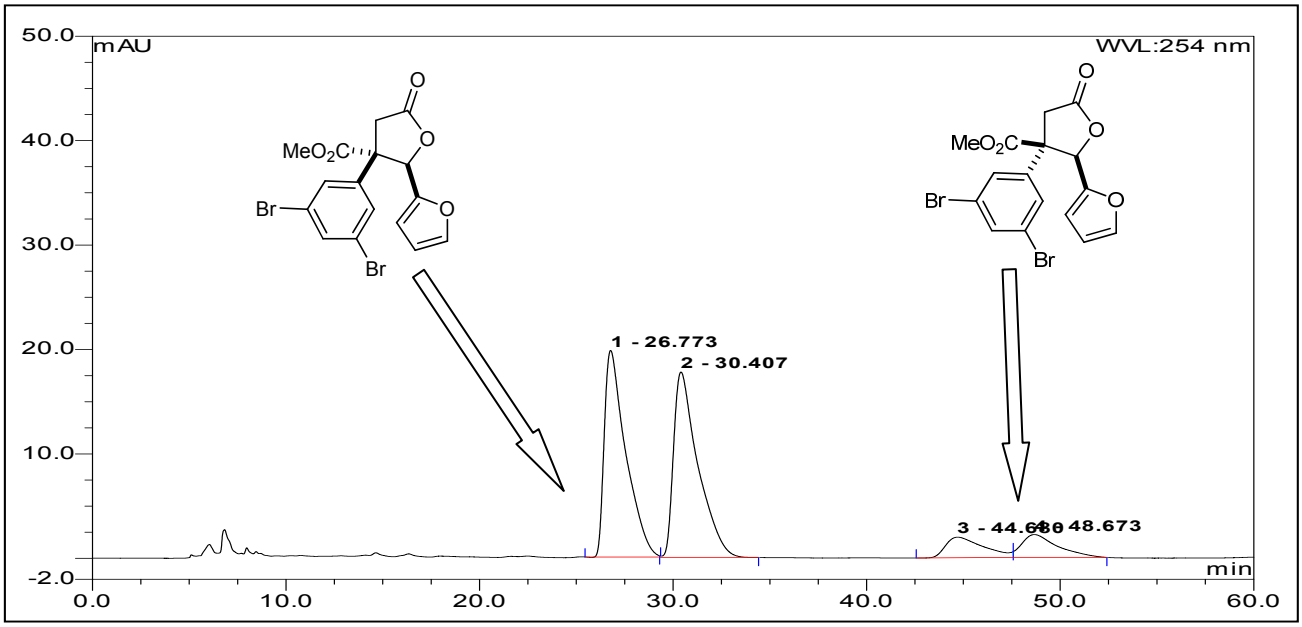


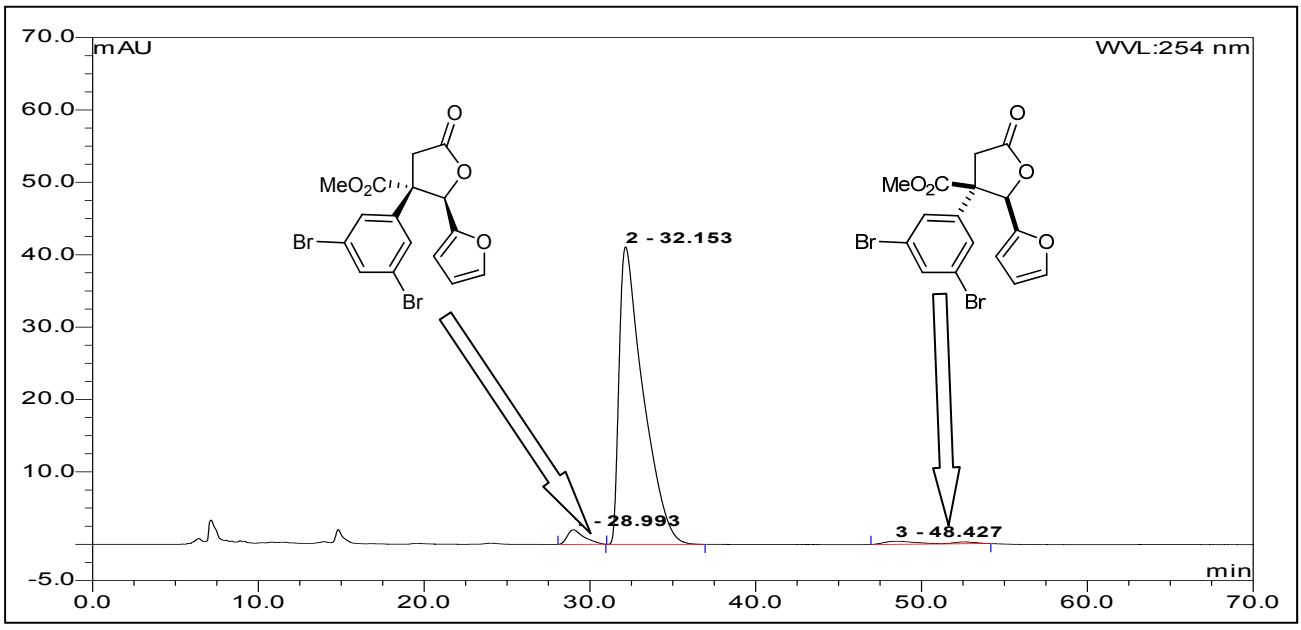
No.	Ret.Time min	Rel.Area %
1	27.09	2.45
2	29.62	97.55
Total:		100.00



Methyl 3-(3,5-dibromophenyl)-2-(furan-2-yl)-5-oxotetrahydrofuran-3-carboxylate (***trans*-26**, ***cis*-26**, Scheme 3).

CSP-HPLC analysis. Chiralcel OD-H (4.6 mm x 25 cm), hexane/IPA: 85/15, 0.6 mL min^{-1}, RT, UV detection at 254 nm.





Racemic

No.	Ret.Time min	Rel.Area %	
1	26.77	42.01	***trans*-26**
2	30.41	42.87	***trans*-26**
3	44.68	7.42	***cis*-26**
4	48.67	7.70	***cis*-26**
Total:		100.00	

Enantioselective

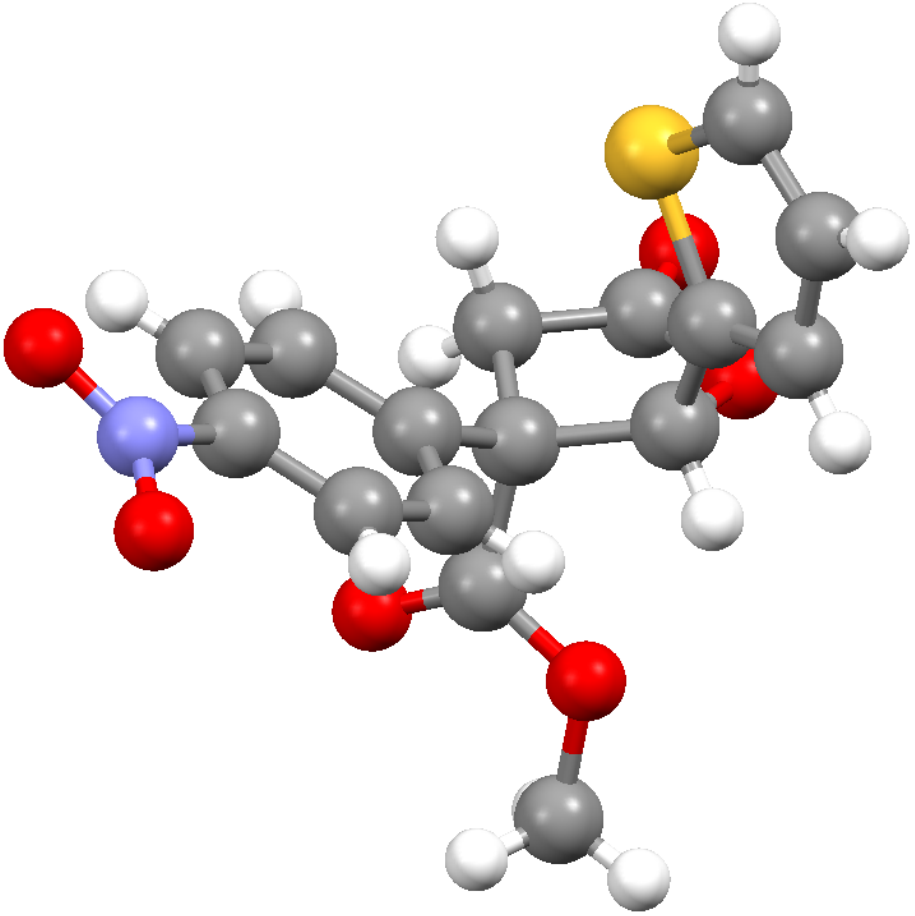
No.	Ret.Time min	Rel.Area %	
1	28.99	3.25	***trans*-26**
2	32.15	94.95	***trans*-26**
3	48.43	1.80	***cis*-26**
Total:		100.00	

8.0 Crystal structures of *trans*-23

Note – the structure has been deposited in the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 872935

Unit cell parameters: a 12.4236(4) b 8.6723(3) c 15.4909(4) beta 111.6880(10)

space group P21



9.0 References

1 H. E. Zimmerman, H. G. Durr, R. S. Givens and R. G. Lewis, *J. Am. Chem. Soc.*, 1967, **89**, 1863.

2 O. Kaumanns, R. Lucius, Roland and H. Mayr, *Chem. Eur. J.*, 2008 , **14**, 9675.

3 A.W. Murray and R.W. Bradshaw, *Tetrahedron*, 1967, **23**, 2333.

4 B. B. Corson and R. W. Stoughton, *J. Am. Chem. Soc.*, 1928 , **50**, 2836.

5 Synthesised according to the procedure described by C. Cornaggia, F. Manoni, E. Torrente, S. Tallon and S. J. Connon, *Org. Lett*., 2012, **14**, 1850.

6 Synthesised according to the procedure described by W. Yang and D. -M. Du, *Org. Lett*., 2010, **12**, 5450.

7 Synthesised according to the procedure described by B. Vakulya, S. Varga, A. Csámpai and T. Soós, *Org. Lett.*, 2005, **7**, 1967.