Microwave-assisted ester formation using *O*–alkylisoureas: a convenient method for the synthesis of esters with inversion of configuration

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Supporting Information

1. General procedures: reaction solvents were used as follows: THF was distilled from Na/benzophenone, Toluene was distilled from Na. Chromatography refers to column chromatography and was performed on 230-400 mesh silica gel. Reactions were monitored by TLC (Merck) with detection by UV illumination or through alkaline $KMnO_4$ oxidation. Melting points are reported uncorrected. ^{1}H and ^{13}C-NMR spectra were recorded on a 250 and 300 MHz NMR, using $CDCl_3$ referenced to residual solvent peaks; chemical shifts are

quoted in ppm and *J* values given in Hz. IR spectra were recorded with a FT-IR spectrometer. Abbreviations used for reporting data are s = strong, m = medium, w = weak, br = broad. HPLC/ELSD analyses were obtained using eluent A: water + 0.1% formic acid, eluent B: methanol + 0.1% formic acid. Gradient: 95 % to 5 % A over 10 min). Eluents used were analytical grade. Reagents were purchased from commercial sources and used without further purification. *N*-cyclohexyl-*N*'-methylpolystyrenecarbodiimide was purchased from Polymer Laboratories. HRMS analyses were performed by the Mass Spectrometry Service of the University of Southampton and the University of Edinburgh. The temperature measurement in the microwave oven was achieved using an external IR temperature sensor.

2. Characterisation for compounds in Table 1

-Methyl 3-phenylpropanoate (7a): spectral data (IR, NMR) were identical to those previously reported.[1]

-(*E*)-Methyl cinnamate (8a): spectral data (IR, NMR) were identical to those previously reported .[2]

-Methyl 2-hydroxy-2-phenylacetate (9a): spectral data (IR, NMR) were identical to those previously reported.[3]

-Methyl 2-hydroxy-3-methylbenzoate (10a): spectral data (IR, NMR) were identical to those previously reported.[4]

-Methyl 4-phenoxybenzoate (11a): spectral data (IR, NMR) were identical to those previously reported.[5]

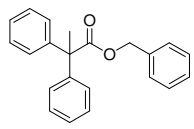
-Methyl 2,2-diphenylpropanoate (12a): spectral data (IR, NMR) were identical to those previously reported.[6]

-Benzyl 3-phenylpropanoate (7b): spectral data (IR, NMR) were identical to those previously reported.[7]

-(*E*)-benzyl cinnamate (8b): spectral data (IR, NMR) were identical to those previously reported.[1]

-Benzyl 2-hydroxy-2-phenylacetate (9b): spectral data (IR, NMR) were identical to those previously reported.[3]

-Benzyl 2-hydroxy-3-methylbenzoate (10b): spectral data (IR, NMR) were identical to those previously reported.[8]



-Benzyl 2,2-diphenylpropanoate (12b): 80%. Rf: 0.70 (Eluant: hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3032 (w); 1730 (s); 1495 (m); 1213 (s); 737 (m); 697 (m). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.56-7.42 (m, 15H); 5.44 (s, 2H); 2.22 (s, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_c: 174.8; 144.4; 135.9; 128.4; 128.2; 128.1; 128.1; 127.9; 126.9; 66.9; 56.7; 27.1. LRMS [FAB(+)] *m/z* (%): 317 (7); 239 (16); 181 (82); 91 (100); 77 (33). HRMS [FAB(+)] *m/z*: calcd. for $C_{22}H_{21}O_2$ $[M+H]^+$ 317.1536, found 317.1542. Purity (ELSD): ≥98%.

-Benzyl 2-phenylacetate (13b): spectral data (IR, NMR) were identical to those previously reported.[9]

-Benzyl adamantate (14b): spectral data (IR, NMR) were identical to those previously reported.[10]

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-Allyl 3-phenylpropanoate (7c): spectral data (IR, NMR) were identical to those previously reported.[11]

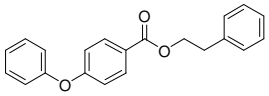
-(*E*)-Allyl cinnamate (8c): spectral data (IR, NMR) were identical to those previously reported.[12]

(E)-*tert*-Butyl cinnamate (8d): spectral data (IR, NMR) were identical to those previously reported. [13]

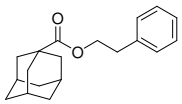
- *tert*-Butyl 2-hydroxy-3-methylbenzoate (10d): spectral data (IR, NMR) were identical to those previously reported.[8]

3. Synthesis of (L,L)-Cbz-Gly-Phe-Val-OMe[14] 16: a microwave vial was charged with Cbz-Gly-Phe-Val-OH **15** (0.256 mmol) and CH_3CN (2 mL), and *O*-methylisourea **1a** (0.300 mmol) was added. The vial was capped and the mixture heated at 80 °C for 20 min and at 100 °C for 20 min using a focused microwave oven. The 1,3-diisopropylurea was filtered off, the solvent evaporated and the residue purified by chromatography (Yield 75%). Spectral data (IR, NMR) were identical to those previously reported. ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H : 7.23-7.10 (11 H, m, Ar-H, NH), 6.85 (1H, br, NH), 5.77 (1H, br, NH), 5.11 (2H, s, Ph-CH_2-O), 4.84 (1H, m, CH^*_{Phe}), 4.44 (1H, dd, *J* = 8.0, 5.1 Hz, CH^*_{Val}), 3.87 (2H, m, NH-CH_2), 3.67 (3H, s, OCH_3), 3.03 (2H, d, *J* = 4.0 Hz, $CHCH_2Ph$), 2.07 (1H, m, $CH(CH_3)_2$), 0.85 (3 H, d, *J* = 6.5 Hz, CH_3), 0.81 (3H, d, *J* = 6.5 Hz, CH_3). LRMS [ES+] *m/z* (%): 470 $[M+H]^+$ (100). HPLC (Method A): t_R = 10.30 min.

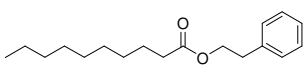
4. Characterisation for compounds in Table 2



Phenethyl-4-phenoxybenzoate (11f): 84%. Rf: 0.55 (hexane/ethyl acetate; 8/2). IR (neat): ν_{max}/(cm^{-1}) 3062 (br); 1720 (s); 1268 (s); 1176 (m); 1007 (s); 752 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 8.21 (d, *J* = 9.0 Hz, 2H); 7.65-7.18 (m, 12H); 4.74 (t, *J* = 7.0 Hz, 2H); 3.29 (t, *J* = 7.0 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 166.1; 161.9; 155.7; 138.1; 131.8; 130.1; 129.1; 128.6; 126.7; 124.7; 124.6; 120.2; 117.4; 65.5; 35.4. [FAB(+)] *m/z* (%): 319 (41); 197 (82); 105 (100); 91 (32); 77 (64); 43 (14). Purity (ELSD): ≥98%.



Phenethyl adamantate (14f): 70%. Rf: 0.50 (hexane/ethyl acetate; 98/2). IR (neat): ν_{max}/(cm^{-1}) 3027 (w); 2851 (s); 1725 (s); 1497 (m); 1233 (s); 741 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.45-7.33 (m, 5H); 4.38 (t, *J* = 7.0 Hz, 2H); 3.07 (t, *J* = 7.0 Hz, 2H). 2.11-1.82 (m, 15H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 177.8; 138.2; 129.1; 128.5; 126.6; 64.7; 40.8; 38.9; 36.6; 35.3; 28.1. LRMS [FAB(+)] *m/z* (%): 285 (16); 135 (81); 105 (100); 91 (55); 77 (52); 43 (13). HRMS [FAB(+)] *m/z*: calcd. for $C_{19}H_{25}O_2$ $[M+H]^+$ 285.1849, found 285.1851. Purity (ELSD): ≥98%.



Phenethyl decanoate (17f): 70%. Rf: 0.50 (hexane/ethyl acetate; 98/2). IR (neat): ν_{max}/(cm^{-1}) 3028 (w); 2925 (s); 2855 (s); 1737 (s); 699 (m). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.47-7.34 (m, 5H); 4.40 (t, *J* = 7.0 Hz, 2H); 3.08 (t, *J* = 7.0 Hz, 2H); 2.43 (t, *J* = 7.0 Hz,

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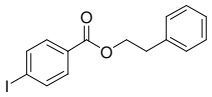
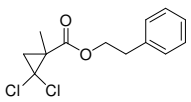
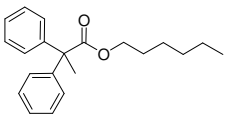
2H); 1.77-1.71 (m, 2H); 1.41 (m, 12H); 1.04 (t, *J* =7.0 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_c: 173.1; 137.4; 128.3; 127.9; 126.0; 64.1; 34.6; 33.8; 31.4; 28.9; 28.8; 28.6; 24.4; 22.2; 13.6. [FAB(+)] *m/z* (%): 277 (14); 105 (100); 91 (41); 77 (28); 43 (81); 27 (64). [FAB(+)] *m/z* : calcd. for $C_{18}H_{29}O_2$ $[M+H]^+$ 277.2162, found 277.2168.). HRMS [FAB(+)] m/z: calcd. for $C_{21}H_{18}O_3$ $[M]^{+\bullet}$ 318.1256, found 318.1250. Purity (ELSD)**:** ≥98%.



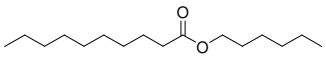
Phenethyl-4-iodobenzoate (18f): 87%. Rf: 0.70 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3053 (br); 1719 (s); 1587 (s); 1266 (s); 1117 (s); 739 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.69-7.57 (m, 4H); 7.24-7.11 (m, 5H); 4.40 (t, *J* = 7.0 Hz, 2H); 2.95 (t, *J* = 7.0 Hz, 2H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 166.1; 137.8; 131.1; 129.8; 129.0; 128.7; 126.8; 100.8; 65.8; 35.3. LRMS [FAB(+)] *m/z* (%): 353 (46); 305 (12); 231 (56); 127 (57); 105 (100); 91 (74); 77 (43); 73 (62); 45 (77); 29 (35). HRMS [FAB(+)] *m/z*: calcd. for $C_{15}H_{14}IO_2$ $[M+H]^+$ 353.0033, found 353.0031. Purity (ELSD): ≥98%.



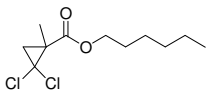
Phenethyl-2,2-dichloro-1-methylcyclopropanecarboxylate (19f): 87%. Rf: 0.50 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3055 (br); 2982 (br); 1733 (s); 1455 (m); 1266 (s); 741 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.56-7.46 (m, 5H); 4.63 (t, *J* = 7.0 Hz, 2H); 3.24 (t, *J* = 7.0 Hz, 2H); 2.50 (d, *J* = 7.5 Hz, 1H); 1.79 (s, 3H); 1.64 (d, *J* = 7.5 Hz, 1H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 169.2; 137.6; 129.0; 128.6; 126.8; 66.4; 62.7; 35.5; 35.1; 30.9; 18.3. LRMS [FAB(+)] *m/z* (%): 151 (61); 105 (100); 91 (76); 77 (63). HRMS [FAB(+)] *m/z*: calcd. for $C_{13}H_{15}Cl_2O_2$ $[M+H]^+$ 273.0444, found 273.0443. Purity (ELSD): ≥98%.



Hexyl-2,2-diphenylpropanoate (12g): 90%. Rf: 0.65 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3058 (br); 2359 (s); 1725 (s); 1494 (m); 1265 (s); 739 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.60-7.48 (m, 10H); 4.41 (t, *J* = 7.0 Hz, 2H); 2.20 (s, 3H); 1.86-1.81 (m, 2H); 1.53-1.47 (m, 6H); 1.12 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 175.2; 144.7; 128.2; 128.1; 126.8; 65.4; 56.7; 31.4; 28.5; 27.2; 25.6; 22.6; 14.1. LRMS [FAB(+)] *m/z* (%): 311 (37); 91 (24); 77 (28); 55 (25); 43 (100). HRMS [FAB(+)] *m/z*: calcd. for $C_{21}H_{27}O_2$ $[M+H]^+$ 311.2006, found 311.2012. Purity (ELSD): ≥98%.

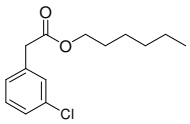


Hexyl decanoate (17g): 74%. Rf: 0.70 (hexane/ethyl acetate; 98/2). IR (neat): ν_{max}/(cm^{-1}) 3054 (w); 2957 (br); 1731 (s); 1466 (m); 1265 (s); 740 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 4.03 (t, *J* = 6.6 Hz, 2H); 2.26 (t, *J* = 7.6 Hz, 2H); 1.61-1.53 (m, 4H); 1.27-1.23 (m, 18H); 0.86-0.82 (m, 6H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 174.0; 64.4; 34.5; 32.0; 31.6; 29.5; 29.4; 29.4; 29.3; 28.7; 25.7; 25.1; 22.8; 22.7; 14.2; 14.1. LRMS [FAB(+)] *m/z* (%): 257 (37); 173 (42); 155 (27); 127 (15); 83 (35); 69 (40); 57 (66); 43 (100); 29 (73). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{16}H_{33}O_2$ $[M+H]^+$ 257.2475, found 257.2481. Purity (ELSD): ≥98%.

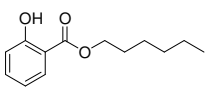


Hexyl-2,2-dichloro-1-methylcyclopropanecarboxylate (19g): 72%. Rf: 0.70 (hexane/ethyl acetate; 98/2). IR (neat): ν_{max}/(cm^{-1}) 3054 (br); 2959 (br); 1730 (s); 1265 (s); 1175 (m); 739 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 4.14 (t, *J* = 6.6 Hz, 2H); 2.24 (d,

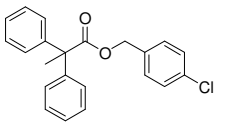
J = 7.4 Hz, 1H); 1.67-1.59 (m, 2H); 1.56 (m, 3H); 1.38 (d, *J* = 7.5 Hz, 1H); 1.36-1.24 (m, 6H); 0.87 (t, *J* = 6.5, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 169.3; 66.2; 62.8; 35.6; 31.5; 30.9; 28.6; 25.6; 22.6; 18.4; 14.1. LRMS [FAB(+)] *m/z* (%): 253 (6); 217 (52); 91 (67); 45 (100); 29 (63). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{11}H_{19}Cl_2O_2$ $[M+H]^+$ 253.0757, found 253.0765. Purity (ELSD): ≥98%.



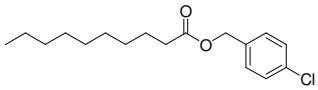
Hexyl-2-(3-chlorophenyl)acetate (20g): 87%. Rf: 0.56 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3053 (br); 2960 (br); 1731 (s); 1422 (s); 1265 (s); 895 (s); 740 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.29-7.15 (m, 4H); 4.12 (t, *J* = 6.5 Hz, 2H); 3.58 (s, 2H); 1.61-1.58 (m, 2H); 1.33-1.27 (m, 6H); 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 171.1; 136.1; 134.4; 129.8; 129.5; 127.6; 127.4; 65.3; 41.1; 31.5; 28.6; 25.6; 22.6; 14.1. LRMS [FAB(+)] *m/z* (%): 255 (37); 125 (72); 91 (20); 43 (100); 27 (60). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{14}H_{20}ClO_2$ $[M+H]^+$ 255.1146, found 255.1147. Purity (ELSD): ≥98%.



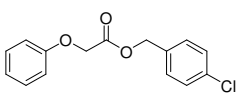
Hexyl-2-hydroxybenzoate (21g): 82%. Rf: 0.75 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3183 (br); 2958 (s); 2932 (s); 2858 (s); 1675 (s); 1614 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 10.88 (s, 1H); 7.84 (dd, *J* = 7.9, 1.7 Hz, 1H); 7.43 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 1H); 6.97 (dd, *J* = 8.5, 1.0 Hz, 1H); 6.86 (ddd, *J* = 8.1, 7.6, 1.2 Hz, 1H); 4.33 (t, *J* = 6.6 Hz, 2H); 1.82-1.71 (m, 2H); 1.49-1.28 (m, 6H); 0.91 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 170.2; 161.7; 135.5; 129.9; 119.0; 117.6; 112.7; 65.5; 31.5; 28.6; 25.7; 22.6; 14.0. LRMS [FAB(+)] *m/z* (%): 223 (51); 121 (100); 43 (86); 29 (53). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{13}H_{19}O_3$ $[M+H]^+$ 223.1329, found 223.1334. Purity (ELSD): ≥98%.



4-Chlorobenzyl-2,2-diphenylpropanoate (12h): 80%. Rf: 0.50 (hexane/ethyl acetate; 9/1). IR (neat): δ_{max}/(cm^{-1}) 3087 (br); 1729 (s); 1493 (s); 1445 (s); 1212 (s); 1076 (s); 699 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.60-7.36 (m, 14H); 5.42 (s, 2H); 2.02 (s, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 174.8; 144.2; 134.4; 134.0; 129.3; 128.7; 128.2; 127.0; 66.1; 56.7; 27.2. LRMS [FAB(+)] *m/z* (%): 351 (5); 181 (96); 125 (100); 91 (39); 77 (40). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{22}H_{20}ClO_2$ $[M+H]^+$ 351.1146, found 351.1152. Purity (ELSD): ≥98%.

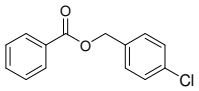


4-Chlorobenzyl decanoate (17h): 80%. Rf: 0.70 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3053 (br); 2928 (br); 2856 (br); 1733 (s); 1265 (s); 1094 (m); 744 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.53-7.44 (m, 4H); 5.25 (s, 2H); 2.53 (t, *J* = 7.3 Hz, 2H); 1.83-1.79 (m, 2H); 1.44-1.09 (m, 12H); 1.06 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 173.7; 134.8; 134.2; 129.7; 128.8; 65.3; 34.4; 32.0; 29.5; 29.4 (2C); 29.2; 25.0; 22.8; 14.2. LRMS [FAB(+)] *m/z* (%): 296 (18); 155 (75); 91 (58); 77 (39); 55 (100). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{17}H_{25}ClO_2$ $[M]^{+\cdot}$ 296.1543, found 296.1542. Purity (ELSD): ≥98%.

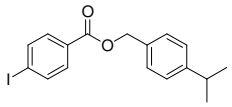


4-Chlorobenzyl-2-phenoxyacetate (22h): 87%. Rf: 0.35 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 3054 (br); 2986 (br); 1760 (s); 1265 (s); 1089 (s); 743 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.47-7.36 (m, 6H); 7.15-7.00 (m, 3H); 5.32 (s, 2H); 4.79 (s, 2H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 168.9; 157.8; 135.2; 129.6; 128.7; 128.6; 128.5; 121.8; 114.7; 67.0; 65.4. LRMS [FAB(+)]

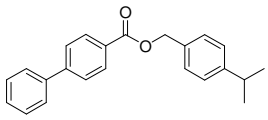
m/z (%): 276 (22); 125 (100); 91 (96); 77 (50). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{15}H_{13}ClO_3$ $[M]^{+\cdot}$ 276.0553, found 276.0553. Purity (ELSD): ≥98%.



4-Chlorobenzyl benzoate (23h): 90%. Rf: 0.57 (Eluant: hexane/ethyl acetate; 9/1). IR (neat): $\nu_{max}/(cm^{-1})$ 3062 (br); 2957 (br); 1720 (s); 1493 (s); 1270 (s); 738 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 8.11-8.07 (m, 2H); 7.60-7.33 (m, 7H); 5.33 (s, 2H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 166.2; 134.6; 134.1; 133.1; 130.0; 129.7; 129.6; 128.8; 128.4; 65.8. LRMS [FAB(+)] *m/z* (%): 246 (28); 125 (94); 105 (100); 77 (85); 51 (60). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{14}H_{12}ClO_2$ $[M+H]^+$ 247.0520, found 247.0526. Purity (ELSD): ≥98%.



4-Isopropylbenzyl-4-iodobenzoate (18i): 83%. Rf: 0.62 (hexane/ethyl acetate; 9/1). IR (neat): $\nu_{max}/(cm^{-1})$ 3053 (br); 1720 (s); 1586 (s); 1113 (s); 739 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.73-7.65 (m, 4H); 7.34-7.18 (m, 4H); 5.28 (s, 2H); 2.86 (m, 1H); 1.20 (d, J = 7.0 Hz, 6H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 165.7; 149.0; 137.6; 133.1; 131.0; 129.6; 128.4; 126.6; 100.8; 66.8; 33.8; 23.9. LRMS [FAB(+)] *m/z* (%): 380 (11); 105 (40); 91 (51); 77 (31). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{17}H_{17}IO_2$ $[M]^{+\cdot}$ 380.0273, found 380.0275. Purity (ELSD): ≥98%.



4-Isopropylbenzyl-4-phenylbenzoate (24i): 82%. Rf: 0.56 (hexane/ethyl acetate; 9/1). IR (neat): $\nu_{max}/(cm^{-1})$ 3054 (br); 2986 (br); 1721 (s); 1525 (s); 1348 (s); 1265 (s); 740 (s). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 8.47 (d, J = 9.0 Hz, 2H); 7.93-7.56 (m, 11H); 5.68 (s, 2H); 3.23 (m, 1H); 1.58 (d, J = 7.0 Hz, 6H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 166.2; 149.0; 145.5; 139.8; 133.5; 130.2; 128.9; 128.9; 128.4; 128.1; 127.2; 126.9; 126.6; 66.6; 33.8; 23.9. LRMS [FAB(+)] *m/z* (%): 331 (5); 307 (79); 154 (100); 91 (62); 77 (80). HRMS [FAB(+)] *m/z* (%): calcd. for $C_{23}H_{23}O_2$ $[M+H]^+$ 331.1693, found 331.1698. Purity (ELSD): ≥98%

5. *O*-alkylisoureas *rac- and* (*S*)-1j, (*R*)-1k

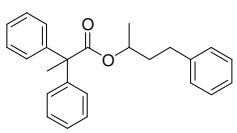
-4-Phenylbutan-2-ylisourea (*rac*-1j): 80%. Spectral data (IR, NMR) were identical to those previously reported.[15]

-Octan-2-ylisourea (*rac*-1k): 80%. Spectral data (IR, NMR) were identical to those previously reported.[16]

-(*S*)-(+)-4-phenylbutan-2-ylisourea (52) ((*S*)-1j): 83%. The compound was synthesized using general method described on page S11. Spectral data (IR, NMR) were identical to those previously reported.[15]

-(*R*)-(-)-octan-2-ylisourea (51) ((*R*)-1k): 83%. The compound was synthesized using general method described on page S11. Spectral data (IR, NMR) were identical to those previously reported.[16]

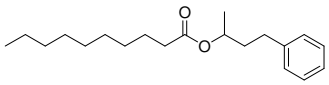
6. Characterisation for racemic esters in Table 3



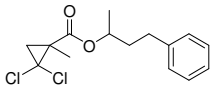
4-Phenylbutan-2-yl 2,2-diphenylpropanoate (*rac*-12j): 96%. Rf: 0.62 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^1) 2976 (w); 1720 (s); 1445 (m); 1375 (m); 1216 (s);

[15] Li, Z.; Crosignani, S.; Linclau, B. *Tetrahedron Lett.* **2003**, *44*, 8143–8147.
[16] Collingwood, S. P.; Davies, A. P.; Golding, B. T. *Tetrahedron Lett.* **1987**, *28*, 4445–4448.

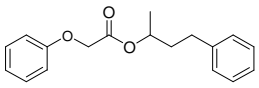
695 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.43-7.09 (m, 15H); 5.09 (m, 1H); 2.54-2.40 (m, 2H), 2.05 (s, 3H); 1.97-1.79 (m, 2H); 1.34 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 174.6; 144.8; 144.6; 141.7; 128.5; 128.4, (2C); 128.2, (2C); 128.1; 126.9, (2C); 126.0; 71.6; 56.8; 37.8; 31.6; 27.3; 19.8. LRMS [FAB(+)] *m/z* (%): 359 (41); 227 (64); 181 (87); 91 (100); 77 (61); 43 (30). HRMS [FAB(+)] *m/z* calcd. for $C_{25}H_{27}O_2$ $[M+H]^+$ 359.2006, found 359.2012. Purity (ELSD): ≥98%.



4-Phenylbutan-2-yl decanoate (*rac*-17j): 48%. Rf: 0.45 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2923 (w); 1731 (s); 1495 (m); 1173 (m); 746 (m); 698 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.23-7.07 (m, 5H), 4.87 (m, 1H); 2.66-2.46 (m, 2H); 2.20 (t, *J* = 7.3 Hz, 2H); 1.94-1.64 (m, 2H); 1.57-1.52 (m, 2H); 1.21-1.15 (m, 15H); 0.82-0.77 (t, *J* = 6.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 173.6; 141.7; 128.5; 128.4; 126.0; 70.3; 37.8; 34.8; 32.0; 31.9; 29.6; 29.4; 29.4; 29.3; 25.2; 22.8; 20.2; 14.2. LRMS [FAB(+)] *m/z* (%): 305 (29); 133 (69); 91 (87); 77 (49); 43 (100). HRMS [FAB(+)] *m/z* calcd. for $C_{20}H_{33}O_2$ $[M+H]^+$ 305.2475, found 305.2481. Purity (ELSD): ≥98%.

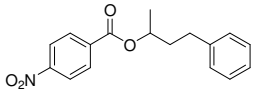


4-Phenylbutan-2-yl-2,2-dichloro-1-methylcyclopropanecarboxylate (*rac*-19j) (mixture of two diastereomers): 70%. Rf: 0.37 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max}/(cm^{-1}) 2977 (w); 1729 (s); 1454 (s); 1278 (s); 1175 (s); 744 (s); 697(s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.27-7.06 (m, 5H), 4.91 (m, 1H); 2.60-2.55 (m, 2H); 2.17 (dd, *J* = 7.4, 3.5 Hz, 1H); 1.89-1.74 (m, 2H); 1.49 (d, *J* = 4.8 Hz, 3H); 1.3 (dd, *J* = 7.5, 2.2 Hz, 2H); 1.2 (dd, *J* = 6.3, 3.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 168.8; 168.7; 141.5; 141.4; 128.6; 128.42; 128.37; 126.1; 126.0; 72.63; 72.55; 62.8; 62.7; 37.6; 37.5; 35.7; 35.6; 31.9; 31.8; 30.8; 30.7; 20.1; 19.9; 18.5; 18.4. LRMS [FAB(+)] *m/z* (%): 301 (29); 215 (27); 133 (63); 91 (88); 29 (100). HRMS [FAB(+)] *m/z* calcd. for $C_{15}H_{19}Cl_2O_2$ $[M+H]^+$ 301.0757 found 301.0762. Purity (ELSD)**:** ≥98%.



4-Phenylbutan-2-yl-2-phenoxyacetate (*rac*-22j): 90%. Rf: 0.35 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2932 (w); 1754 (s); 1728 (s); 1599 (s); 1085 (m); 750 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.46-7-03 (m, 10H); 5.20 (m, 1H); 4.71 (s, 2H), 2.79-2.66 (m, 2H); 2.16-1.90 (m, 2H); 1.41 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 168.8; 158.0; 141.4; 129.7; 128.5; 128.4; 126.1; 121.8; 114.7; 72.0; 65.5; 37.5; 31.8; 20.1. LRMS [FAB(+)] *m/z* (%): 285 (25); 133 (75); 91 (100); 77 (80); 43 (63). HRMS [FAB(+)] *m/z* calcd. for $C_{18}H_{20}O_3$ $[M]^{+\cdot}$ 284.1412, found 284.1412. Purity (ELSD): ≥98%.

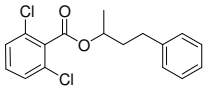
4-phenylbutan-2-yl benzoate (*rac*-23j): 90%. Spectral data (IR, NMR) were identical to those previously reported.[17]



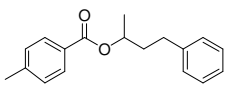
4-Phenylbutan-2-yl 4-nitrobenzoate (*rac*-25j): 95%. Rf: 0.35 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2977 (w); 1717 (s); 1524 (s); 1217 (s); 1117 (m); 717 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 8.15 (d, *J* = 8.9 Hz, 2H); 8.04 (d, *J* = 8.9 Hz, 2H); 7.19-7.03 (m, 5H), 5.12 (m, 1H); 2.63 (t, *J* = 8.0 Hz, 2H); 2.10-1.80 (m, 2H); 1.31 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 164.2; 150.4; 141.2; 136.1; 130.6; 128.5; 128.3; 126.1; 123.5; 72.6; 37.4; 31.9; 20.0. LRMS [FAB(+)]

[17] Werner, T.; Barrett, A. G. M. *J. Org. Chem.* **2006**, *71*, 4302–4304.

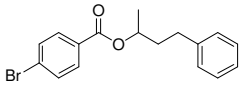
m/z (%): 300 (10); 150 (79); 91 (100); 77 (16); 43 (96). HRMS [FAB(+)] *m/z* calcd. for $C_{17}H_{18}NO_4$ $[M+H]^+$ 300.1230, found 300.1236. Purity (ELSD): ≥98%.



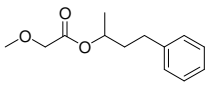
4-Phenylbutan-2-yl 2,6-dichlorobenzoate (*rac*-26j): 96%. Rf: 0.50 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2978 (w); 1733 (s); 1563 (m); 1432 (s); 1274 (s); 1149 (s); 1015 (s); 779 (m). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.25-7.07 (m, 8H); 5.21 (m, 1H); 2.83-2.56 (m, 2H), 2.06-1.75 (m, 2H); 1.33 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 164.5; 141.6; 134.1; 131.8; 130.8; 128.6; 128.5; 128.0; 126.1; 73.3; 37.8; 31.8; 20.0. LRMS [FAB(+)] *m/z* (%): 323 (14); 173 (24); 133 (62); 91 (100); 77 (48); 43 (45). HRMS [FAB(+)] *m/z* calcd. for $C_{17}H_{17}Cl_2O_2$ $[M+H]^+$ 323.0600, found 323.0606. Purity (ELSD): ≥98%.



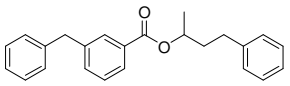
4-Phenylbutan-2-yl 4-methylbenzoate (*rac*-27j): 80%. Rf: 0.37 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2933 (w); 1704 (s); 1276 (s); 1110 (m); 904 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.84 (d, *J* = 7.9 Hz, 2H); 7.21-7.08 (m, 7H), 5.08 (m, 1H); 2.73-2.54 (m, 2H); 2.32 (s, 3H); 2.04-1.77 (m, 2H); 1.28 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 166.3; 143.5; 141.7; 129.7; 129.1; 128.5; 128.4; 128.1; 126.0; 71.0; 37.9; 32.0; 21.7; 20.3. LRMS [FAB(+)] *m/z* (%): 269 (55); 133 (69); 91 (97); 77 (66); 43 (100). HRMS [FAB(+)] *m/z* calcd. for $C_{18}H_{21}O_2$ $[M+H]^+$ 269.1536, found 269.1542. Purity (ELSD): ≥98%.



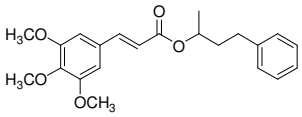
4-Phenylbutan-2-yl-4-bromobenzoate (*rac*-28j): 87%. Rf: 0.37 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2976 (w); 1713 (s); 1589 (m); 1356 (s); 1115 (s); 735 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.78 (d, *J* = 8.5 Hz, 2H); 7.47 (d, *J* = 8.5 Hz, 2H); 7.21-7.07 (m, 5H), 5.08 (m, 1H); 2.72-2.53 (m, 2H); 2.11-1.77 (m, 2H); 1.29 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 165.5; 141.5; 131.7; 131.2; 129.7; 128.6; 128.4; 128.0; 126.1; 71.7; 37.7; 31.9; 20.2. LRMS [FAB(+)] *m/z* (%): 333 (8); 183 (69); 133 (69); 91 (100); 77 (62); 43 (76). HRMS [FAB(+)] *m/z* calcd. for $C_{17}H_{18}BrO_2$ $[M+H]^+$ 333.0485, found 333.0490. Purity (ELSD): ≥98%.



4-Phenylbutan-2-yl-2-methoxyacetate (*rac*-29j): 82%. Rf: 0.48 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2931 (w); 1747 (s); 1191 (s); 1124 (s); 947 (w); 698 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.21-7.05 (m, 5H), 5.00 (m, 1H); 3.88 (s, 2H); 3.35 (s, 3H); 2.65-2.49 (m, 2H); 2.03-1.66 (m, 2H); 1.20 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 169.9; 141.3; 128.4; 128.3; 126.0; 71.2; 69.9; 59.3; 37.4; 31.8; 20.0. LRMS [FAB(+)] *m/z* (%): 445 (23); 133 (62); 91 (80); 45 (100). HRMS [FAB(+)] *m/z* calcd. for $C_{13}H_{19}O_3$ $[M+H]^+$ 223.1329, found 223.1334. Purity (ELSD): ≥98%.



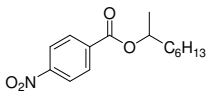
4-Phenylbutan-2-yl-3-benzylbenzoate (*rac*-30j): 85%. Rf: 0.60 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2974 (w); 1711 (s); 1251 (s); 1125 (s); 1071 (s); 737 (s); 695 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.76 (d, *J* = 7.7 Hz, 1H); 7.35-7.02 (m, 13H); 5.02 (m, 1H); 4.31 (s, 2H); 2.60-2.43 (m, 2H); 1.94-1.66 (m, 2H); 1.16 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 167.4; 141.9; 141.6; 141.1; 131.9; 131.7; 131.0; 130.5; 129.0; 128.5; 128.43; 128.41; 126.4; 126.0; 71.2; 39.6; 37.8; 32.0; 20.1. LRMS [FAB(+)] *m/z* (%): 345(5); 91 (100); 77 (46); 39 (62). HRMS [FAB(+)] *m/z* calcd. for $C_{24}H_{25}O_2$ $[M+H]^+$ 345.1849, found 345.1855. Purity (ELSD): ≥98%.



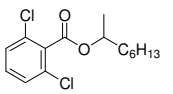
(*E*)-4-Phenylbutan-2-yl 3-(3,4,5-trimethoxyphenyl)acrylate (*rac*-31j): 47%. Rf: 0.60 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2937 (w); 1704 (m); 1582 (m); 1273 (s); 1126 (s); 1005 (w). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.51 (d, *J* = 15.9 Hz, 1H); 7.24-7.10 (m, 5H); 6.70 (s, 2H), 6.27 (d, *J* = 15.9 Hz, 1H); 5.01 (m, 1H); 3.82 (s, 9H); 2.73-2.53 (m, 2H); 2.03-1.74 (m, 2H); 1.26 (d; *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 166.7; 153.6; 144.6; 141.7; 140.0; 130.1; 128.6; 128.5; 126.0; 118.0; 105.3; 70.8; 61.1; 56.3; 37.9; 32.0; 20.3. LRMS [FAB(+)] *m/z* (%): 371 (48); 221 (63); 91 (84); 77 (60); 43 (89). HRMS [FAB(+)] *m/z* calcd. for $C_{22}H_{26}O_5$ $[M]^{+\cdot}$ 370.1780, found 370.1780. Purity (ELSD): ≥98%.

-Octan-2-yl decanoate (*rac*-17k): 60%. Spectral data (IR, NMR) were identical to those previously reported.[18]

-Octan-2-yl benzoate (*rac*-23k): 80%. Spectral data (IR, NMR) were identical to those previously reported.[19]

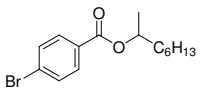


Octan-2-yl-4-nitrobenzoate (*rac*-25k): 95%. Rf: 0.53 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2929 (w); 1719 (s); 1526 (s); 1272 (s); 1167 (s); 718 (m). ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 8.29-8.17 (m, 4H); 5.17 (m, 1H); 1.80-1.55 (m, 2H), 1.36-1.26 (m, 11H); 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (62 MHz, $CDCl_3$) δ_C: 164.4; 150.5; 136.4; 130.7; 123.6; 73.2; 36.0; 31.8; 29.2; 25.5; 22.7; 20.1; 14.1. HRMS [FAB(+)] *m/z* calcd. for $C_{15}H_{22}NO_4$ $[M+H]^+$ 280.1543, found: 280.1542. Purity (ELSD): ≥98%.

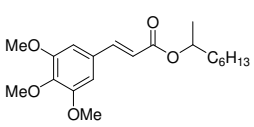


Octan-2-yl-2,6-dichlorobenzoate (*rac*-26k): 90%. Rf: 0.53 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2928 (w); 1732 (s); 1431 (s); 1271 (s); 727 (m). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.54-7.14 (m, 3H); 5.16 (m, 1H); 1.71-1.50 (m, 2H); 1.31-1.20 (m, 11H); 0.80 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 164.5; 134.3; 131.8; 130.7; 128.0; 127.9; 73.9; 35.9; 31.9; 29.1; 25.4; 22.7; 20.0; 14.2. LRMS [FAB(+)] *m/z* (%): 303 (19); 173 (62); 91 (24); 77 (32); 43 (97). HRMS [FAB(+)] *m/z* calcd. for $C_{15}H_{21}Cl_2O_2$ $[M+H]^+$ 303.0913, found 323.0919. Purity (ELSD): ≥98%.

-Octan-2-yl-4-methylbenzoate (*rac*-27k): 78%. Spectral data (IR, NMR) were identical to those previously reported.[18]



Octan-2-yl-4-bromobenzoate (*rac*-28k): 72%. Rf: 0.40 (hexane/ethyl acetate; 95/5). IR (neat): ν_{max} / (cm^{-1}) 2928 (w); 1714 (s); 1268 (s); 1101 (s); 1011 (s); 755 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.89 (d, *J* = 8.7 Hz, 2H); 7.55 (d, J = 8.7 Hz, 2H); 5.13 (m, 1H); 1.76-1.52 (m, 2H); 1.33-1.27 (m, 11H); 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 165.6; 131.7; 131.2; 129.9; 127.9; 72.3; 36.1; 31.8; 29.2; 25.5; 22.7; 20.1; 14.2. LRMS [FAB(+)] *m/z* (%): 313 (20); 183 (46); 91 (15); 77 (32); 43 (100). Purity (ELSD): ≥98%.



(*E*)-octan-2-yl 3-(3,4,5-trimethoxyphenyl)acrylate (*rac*-31k): 74%. Rf: 0.31 (hexane/ethyl acetate; 8/2). IR (neat): ν_{max} / (cm^{-1}) 2929 (w); 1703 (s); 1635 (s); 1272 (s); 1123 (s); 826 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.60 (d, *J* = 15.8 Hz, 2H); 6.74

[18] Barrett, A. G. M.; Braddock, D. C.; James, R. A.; Koike, N.; Procopiou, P. A. *J. Org. Chem.* **1998**, *63*, 6273–6280.
[19] Moore, J. D.; Byrne, R. J.; Vedantham, P.; Flynn, D. L.; Hanson, P. R. *Org. Lett.* **2003**, *5*, 4241–4244.

(s, 2Hok); 6.33 (d, *J* = 15.8 Hz, 1Hok; 5.03 (m, 1H); 3.88 (s, 6H); 3.87 (s, 3H); 1.68-1.47 (m, 2H); 1.32-1.27 (m, 11H); 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 166.7; 153.5; 144.4; 140.1; 130.2; 118.2; 105.3; 71.3; 61.1; 56.2; 36.2; 31.9; 29.3; 25.5; 22.7; 20.2; 14.2. LRMS [FAB(+)] *m/z* (%): 351 (39); 221 (50); 91 (35); 77 (33); 43 (87); 29 (100). HRMS [FAB(+)] *m/z* calcd. for $C_{20}H_{30}O_5$ $[M]^{+\cdot}$ 350.2093, found 350.2093. Purity (ELSD): ≥98%.

-Octan-2-yl 4-methoxybenzoate (*rac*-32k): 74%. Spectral data (IR, NMR) were identical to those previously reported.[18]

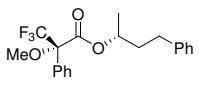
7. Characterisation of enantiopure esters in Table 4

-(*R*)-(4-Phenylbut-2-yl)-2-phenoxyacetate ((*R*)-22j): 90%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-22j)**. Prepared using racemic 4-phenyl-2-butanol. The enantiomeric excess was determined by chiral HPLC (Method C). Retention time: 6.54 min, *ee* ≥99.9%.

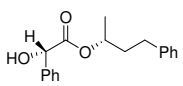
-(*R*)-(4-Phenylbut-2-yl)-4-nitrobenzoate ((*R*)-25j): 95%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-25j)**. Prepared using racemic 4-phenyl-2-butanol. The enantiomeric excess was determined by chiral HPLC (Method C). Retention time: 10.40 min, *ee* ≥99.9%.

-(*R*)-(4-phenylbut-2-yl)-2,6-dichlorobenzoate ((*R*)-26j): 95%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-26j)**. Prepared using racemic 4-phenyl-2-butanol. The enantiomeric excess was determined by chiral HPLC (Method C). Retention time: 7.39 min, *ee* ≥99.9%.

-(*R*)-(4-phenylbut-2-yl)-4-bromobenzoate ((*R*)-28j): 87%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-28j)** prepared using racemic 4-phenyl-2-butanol.



(2*S*,2'*R*)-(4-phenylbut-2'-yl)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ((*R*)-33j): 78%. Rf: 0.36 (hexane/ethyl acetate; 95/5). IR (neat): ν_{max} / (cm^{-1}) 2947 (w); 1738 (s); 1504 (m); 1271 (s); 1162 (s); 987 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.85-7.81 (m, 2H); 7.68-7.62 (m, 3H); 7.54-7.33 (m, 3H); 7.33-7.29 (m, 2H); 5.39 (m, 1H); 3.83 (q, *J* = 1.3 Hz, 3H); 2.87-2.70 (m, 2H); 2.31-2.00 (m, 2H); 1.62 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 166.2; 141.2; 132.7; 129.7; 128.6; 128.5; 128.4; 127.4; 126.1; 125.9; 84.7 (q, J_{CF} = 28.0 Hz); 73.5; 55.5; 37.5; 31.4; 19.9. The CF_3 quartet was not observed. LRMS [FAB(+)] m/z (%): 367 (63); 105 (100); 91 (100); 77 (97); 43 (24); 29 (19). HRMS [FAB(+)] m/z: calcd for $C_{20}H_{22}F_3O_3$ $[M+H]^+$ 367.1516, found 367.1521. Purity (ELSD): ≥98%.



(2*S*,2'*R*)-(4-Phenylbut-2'-yl)-2-hydroxy-2-phenylacetate ((*R*)-9j): 60% Mp: 34-36 °C. Rf: 0.30 (hexane/ethyl acetate; 8/2). IR (neat): ν_{max} / (cm^{-1}) 3500 (s); 2929 (s); 1729 (s); 1184 (m); 1066 (s); 698 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.23-7.06 (m, 10H); 5.01 (s, 1H); 4.91 (m, 1H); 3.38 (m, 1H); 2.60-2.53 (m, 2H); 1.97-1.59 (m, 2H); 1.02 (d, *J* = 6.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 173.4; 141.3; 138.6; 128.62; 128.60; 128.44; 128.42; 126.6; 126.2; 73.1; 73.0; 37.3; 31.8; 19.7. LRMS [FAB(+)] *m/z* (%): 285 (81); 239 (81); 91 (100); 77 (96); 43 (52); 29 (32). HRMS [FAB(+)] *m/z*: calcd for $C_{18}H_{21}O_3$ $[M+H]^+$ 285.1485, found 285.1491. Purity (ELSD): ≥98%.

-(*S*)-(Oct-2-yl) benzoate ((*S*)-23k): 80%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-23k)** prepared using racemic 2-octanol. The enantiomeric excess was determined by chiral HPLC (Method C). Retention time: 8.64 min, *ee* ≥99.9.

-(*S*)-(Oct-2-yl)-4-methylbenzoate ((*S*)-27k): 77%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-27k)** prepared using racemic 2-octanol. The enantiomeric excess was determined by chiral HPLC (Method D). Retention time: 14.58 min, *ee* ≥99.9.

-**(*S*)-(Oct-2-yl)-4-bromobenzoate ((*S*)-28k)**: 70%. Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-28k)** prepared using racemic 2-octanol. The enantiomeric excess was determined by chiral HPLC (Method E). Retention time: 16.94 min, *ee* ≥99.9.

-(2*S*,2'*S*)-(Oct-2'-yl)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ((*S*)-33k): 80%. Spectral data (IR, NMR) were identical to those previously reported.[20]

-(2*S*,2'*S*)-Oct-2'-yl)-2-hydroxy-2-phenylacetate ((*S*)-9k): 90%. Spectral data (IR, NMR) were identical to those previously reported.[21]

8. Synthesis of (*R*)-(4-phenylbut-2-yl)-2-phenoxyacetate ((*R*)-22j) using Mitsunobu conditions under microwave irradiations (Scheme 4).[22]

A microwave vial was charged with a stir bar, alcohol **5j** (0.195 g, 1.30 mmol) was added followed by PPh_3 (0.760 g, 2.88 mmol), 2-phenoxyacetic acid (0.438 g, 2.88mmol) and DIAD (0.257 g, 1.27 mmol) in 4 mL of anhydrous THF. The vial was capped and the mixture heated at 180 °C using a focused microwave ovenfor 7 min. The residue was purified by chromatography (0.31 g, 83% yield colourless oil). Spectral data (IR, NMR) obtained were in agreement with that obtained for **(*rac*-22j)** prepared using racemic 4-phenyl-2-butanol. The enantiomeric excess was determined by chiral HPLC (Method C). Retention time: 6.45 min, *ee* ≥99.9%.

9. 1,3-Diisopropyl-2-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)isourea (1l): 82%. Spectral data (IR, NMR) were identical to those previously reported.[23]

10. Characterisation of the neomentyl esters (Table 6).

-(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl benzoate (23l): 68% Spectral data (IR, NMR) were identical to those previously reported.[24]

-(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-nitrobenzoate (25l): 90% Spectral data (IR, NMR) were identical to those previously reported.[24]

-**(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-methoxybenzoate (32l)**: 66% Spectral data (IR, NMR) were identical to those previously reported.[24]

-**(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl ethanethioate (36l)**: 31% Spectral data (IR, NMR) were identical to those previously reported.[25]

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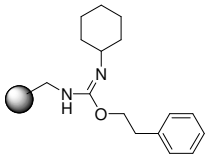
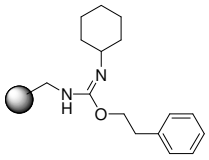
[20] Omata, K.; Fujiwara, T.; Kabuto, K. *Tetrahedron: Asymmetry* **2002**, *13*, 1655–1662.
[21] Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548–3551.
[22] Steinreiber, A.; Stadler, A.; Mayer, S. F.; Faber, K.; Kappe, O. C. *Tetrahedron Lett.* **2001**, *42*, 6283–6286.
[23] Poelert, M. A.; Hulshof, L. A.; Kellogg, R. M. *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 365–368.
[24] Dodge, J. A.; Trujillo, J. I.; Presnell, M. *J. Org. Chem.* **1994**, *59*, 234–236.
[25] Strijtveen, B.; Kellogg, R. M. *J. Org. Chem.* **1986**, *51*, 3664–3671.

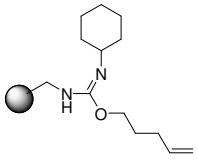
11. Characterisation of PS-*O*-alkylisoureas (38e,f,m)



PS-*O*-(3-phenyl-1-propyl)isourea (38e): IR (neat): ν_{max} / (cm^{-1}) 2926 (s); 1657 (s); 1450 (m); 1240 (m); 1029 (s).



PS-*O*-phenethylisourea (38f): IR (neat): ν_{max} / (cm^{-1}) 2923 (s); 1653 (s); 1448 (m); 1239 (m); 1029 (m).



PS-*O*-pentenylisourea (38m): IR (neat): ν_{max} / (cm^{-1}) 2924 (s); 1652 (s); 1238 (s); 1029 (s); 890 (m).

12. Characterisation of the product esters in table 7.

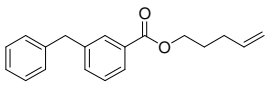
-3-Phenylpropyl acetate (35e): 90% Spectral data (NMR) were identical to those previously reported.[26]

-Phenethyl-4-phenoxybenzoate (11f): 53% Spectral data (IR, NMR) were identical to those reported above.

-Phenethyl adamantate (14f): 56% Spectral data (IR, NMR) were identical to those reported above.

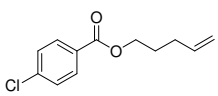
-Phenethyl decanoate (17f): 90% Spectral data (IR, NMR) were identical to those reported above.

-Phenethyl-2,2-dichloro-1-methylcyclopropanecarboxylate (19f): 68% Spectral data (IR, NMR) were identical to those reported above.



Pent-4-enyl-2-benzylbenzoate (30m): 85%. Rf: 0.63 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2927 (w); 2359 (w); 1718 (s), 1494 (w). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.81 (d, J = 9.4 Hz, 1H); 7.33 (td, J = 7.5, 1.5 Hz, 1H); 7.26-7.04 (m, 7H); 5.71 (m, 1H); 4.97 (dd, J_{trans} = 17.7, 1.9 Hz, 1H); 4.92 (dd, J_{cis} = 9.5, 1.4 Hz, 1H); 4.39 (s, 2H): 4.24 (t, J = 6.4 Hz, 2H); 2.17-2.10 (m, 2H); 1.80-1.73 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 167.7; 142.0; 140.9; 137.5; 131.9; 131.6; 130.6; 130.4; 128.9; 128.3; 126.3; 125.9; 115.3; 64.3; 39.5; 30.1; 27.8. LRMS [EI] *m/z* (%): 211 (12); 194 (100); 165 (49); 133 (4). HRMS [EI] *m/z* calcd. for $C_{19}H_{20}O_2$ $[M]^{+\cdot}$ 280.1463, found 280.1462.

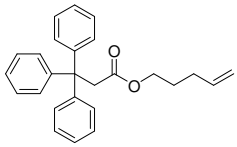
-Pent-4-enyl-4-methoxybenzoate (32m): 80%. Spectral data (IR, NMR) were identical to those previously reported.[27]



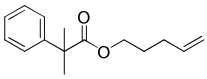
Pent-4-enyl-4-chlorobenzoate (39m): 90%. Rf: 0.60 (hexane/ethyl acetate; 8/2). IR (neat): ν_{max} / (cm^{-1}) 2931 (br); 1720 (s), 1595 (w); 1488 (w); 1401 (w), 849 (w). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.96 (d, J = 9.2 Hz, 2H); 7.40 (d, J = 8.8 Hz, 2H); 5.83 (m, 1H); 5.05 (dd, J_{trans} = 17.3, 1.9 Hz, 1H); 5.03 (dd, J_{cis} = 10.9, 1.2 Hz, 1H); 4.33 (t, J = 6.6 Hz, 2H); 2.25-2.17 (m, 2H); 1.91-1.78 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 163.9; 137.4; 135.5; 129.1; 126.8; 126.4; 113.6; 62.7; 28.2; 25.9.

[26] Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4560–4567.
[27] Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 10805–10816.

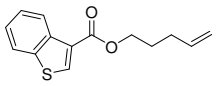
LRMS [EI] m/z (%): 139 (74); 111 (48); 77 (4); 68 (100); 51 (6). HRMS [EI] *m/z* calcd. for $C_{12}H_{13}ClO_2$ $[M]^{+\cdot}$ 224.0604, found 224.0601.



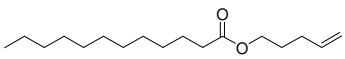
Pent-4-enyl-3,3,3-triphenylpropanoate (40m): 90%. Rf: 0.60 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} /(cm^{-1}) 2935 (br); 1732 (m); 1445 (m); 750 (m); 698 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.24-7.09 (m, 15H); 5.60 (m, 1H); 4.87 (dd, J_{trans} = 17.0, 1.8 Hz, 1H); 4.84 (dd, J_{cis} = 10.7, 1.1 Hz, 1H); 3.72 (t, J = 6.4 Hz, 2H); 3.65 (s, 2H); 1.95-1.77 (m, 2H); 1.40-1.31 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 169.2; 144.8; 135.7; 127.4; 126.0; 124.4; 113.3; 62.0; 54.0; 44.7; 28.1; 25.7. LRMS [EI] *m/z* (%): 243 (100); 165 (56); 77 (4); 51 (2). HRMS [EI] *m/z* calcd. for $C_{26}H_{26}O_2$ $[M]^{+\cdot}$ 370.1933, found 370.1936.



Pent-4-enyl-2-methyl-2-phenylpropanoate (41m): 90%. Rf: 0.50 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2931 (br); 1726 (s); 1253 (s); 1144 (s); 1100 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 7.29-7.13 (m, 5H); 5.72 (m, 1H); 4.89 (dd, J_{trans} = 17.6, 1.8 Hz, 1H); 4.84 (dd, J_{cis} = 9.8, 1.4 Hz, 1H); 4.07 (t, J = 6.8 Hz, 2H); 2.02-1.95 (m, 2H); 1.72-1.60 (m, 2H); 1.58 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 174.9; 142.8; 135.6; 126.5; 124.8; 123.8; 113.4; 62.3; 44.7; 28.0; 25.8; 24.6. LRMS [EI] *m/z* (%): 119 (100); 91 (35); 77 (6); 68 (10); 51 (4). HRMS [EI] *m/z* calcd. for $C_{15}H_{20}O_2$ $[M]^{+\cdot}$ 232.1463, found 232.1464.



Pent-4-enyl benzo[b]thiophene-3-carboxylate (42m): 90%. Rf: 0.70 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2928 (br); 1718 (s); 1494 (w); 1450 (w); 1256 (s); 741 (s). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 8.59 (d, J = 8.0 Hz, 1H); 8.38 (s, 1H); 7.86 (d, J = 8.0 Hz, 1H); 7.51-7.38 (m, 2H); 5.86 (m, 1H); 5.01 (dd, J_{trans} = 17.3, 1.7 Hz, 1H); 4.95 (dd, J_{cis} = 10.2, 1.5 Hz, 1H); 4.39 (t, J = 6.4 Hz, 2H); 2.29-2.02 (m, 2H); 1.97-1.87 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 161.0; 138.2; 135.6; 134.9; 134.7; 125.5; 123.6; 123.2; 122.9; 120.7; 113.6; 62.3; 28.4; 26.2. LRMS [EI] *m/z* (%): 246 (6); 178 (100); 161 (60); 133 (14); 89 (34); 68 (4). HRMS [EI] *m/z* calcd. for $C_{14}H_{14}O_2S$ $[M]^{+\cdot}$ 246.0715, found 246.0716.



Pent-4-enyl dodecanoate (43m): 66%. Rf: 0.63 (hexane/ethyl acetate; 9/1). IR (neat): ν_{max} / (cm^{-1}) 2923 (s); 1737 (s); 1465 (br); 1170 (br); 912 (m). ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H: 5.78 (m, 1H); 4.97 (dd, J_{trans} = 16.8, 1.8 Hz, 1H); 4.91 (dd, J_{cis} = 10.0, 1.5 Hz, 1H); 4.06 (t, J = 6.6 Hz, 2H); 2.28 (t, J = 7.7 Hz, 2H); 2.15-2.07 (m, 2H); 1.76-1.66 (m, 2H); 1.65-1.58 (m, 2H); 1.24 (br, 16H); 0.86 (t, J = 6.6 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C: 173.9; 137.5; 115.2; 63.6; 34.4; 31.9; 29.6; 29.5 (3C); 29.3 (2C); 29.3; 27.8; 25.0; 22.7; 14.1. LRMS [EI] *m/z* (%): 183 (10); 113 (5); 100 (28); 68 (100); 55 (24). HRMS [EI] *m/z* calcd. for $C_{17}H_{32}O_2$ $[M]^{+\cdot}$ 268.2402, found: 268.2405.

13. Characterisation of esters in Table 8.

-Pent-4-enyl-4-chlorobenzoate (39m): 40%. Spectral data (IR, NMR) were identical to those reported above.

-Pent-4-enyl dodecanoate (43m): 70%. Spectral data (IR, NMR) were identical to those reported above.

-3-Phenylpropyl decanoate (17e): 40%. Spectral data (IR, NMR) were identical to those previously reported.[28]

-3-Phenylpropyl acetate (35e): 90% Spectral data (NMR) were identical to those previously reported.[26]

-Phenethyl-4-phenoxybenzoate (11f): 23%. Spectral data (IR, NMR) were identical to those reported above.

-Phenethyl adamantate (14f): 40%. Spectral data (IR, NMR) were identical to those reported above.

-Phenethyl decanoate (17f): 30%. Spectral data (IR, NMR) were identical to those reported above.

-Phenethyl-2,2-dichloro-1-methylcyclopropanecarboxylate (19f): 30%. Spectral data (IR, NMR) were identical to those reported above.

-Hexyl-2-(3-chlorophenyl)acetate (20g): 80%. Spectral data (IR, NMR) were identical to those reported above.

-Hexyl-2-hydroxybenzoate (21g): 72%. Spectral data (IR, NMR) were identical to those reported above.

14. Determination of the enantiomeric purities by chiral HPLC

Optical purity of the chiral esters was established by chiral HPLC analysis using a Chiralpak® AD-RH (150×4.6 mm), λ = 220 nm, λ = 254 nm. The following methods were used:

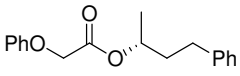
Method C: gradient from 40% water / 60% acetonitrile to 20% water / 80% acetonitrile over 16 min. Flow = 1.00 mL/min.

Method D: gradient from 30% water / 70% acetonitrile to 14% water / 76% acetonitrile /10% water + 0.1% formic acid over 15 min. Flow = 0.40 mL/min.

Method E: gradient from 30% water / 70% acetonitrile to 27% water / 73% acetonitrile over 15 min. Flow = 0.40 mL/min.

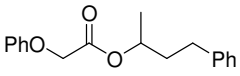
[28] Manabe, K.; Iimura, S.; Sun, X-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2002**, *124*, 11971–11978.

1) **22j**

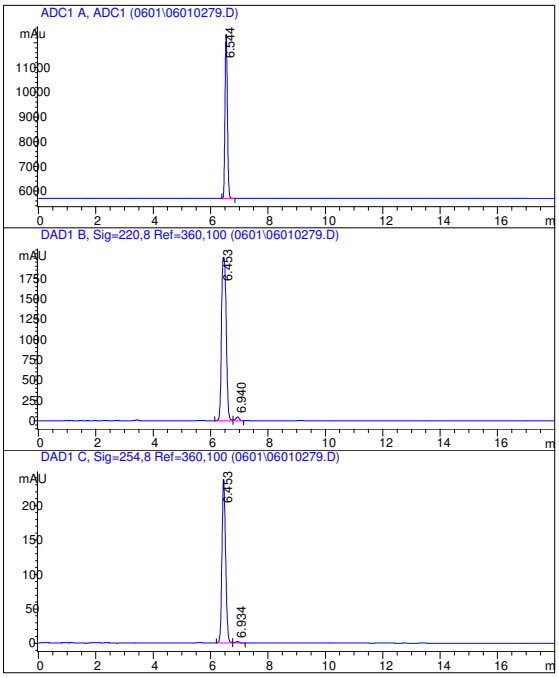


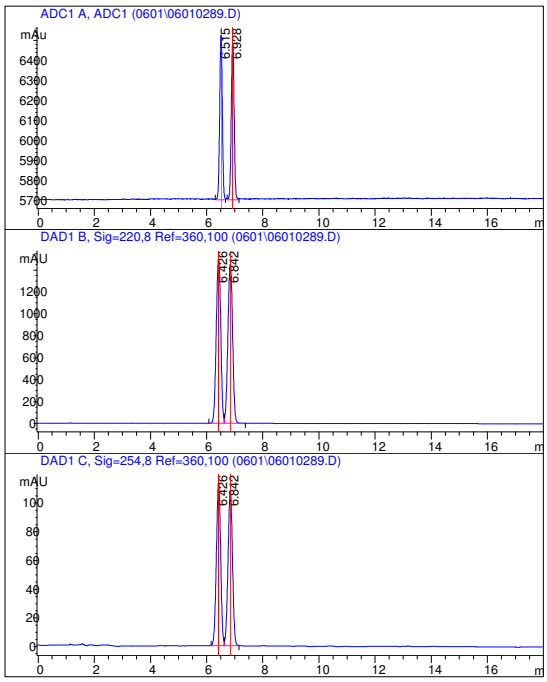
(*R*)-22j

(Method C)

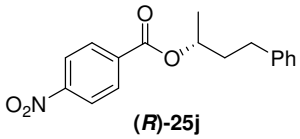


***rac*-22j**



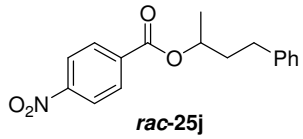


2) **25j**

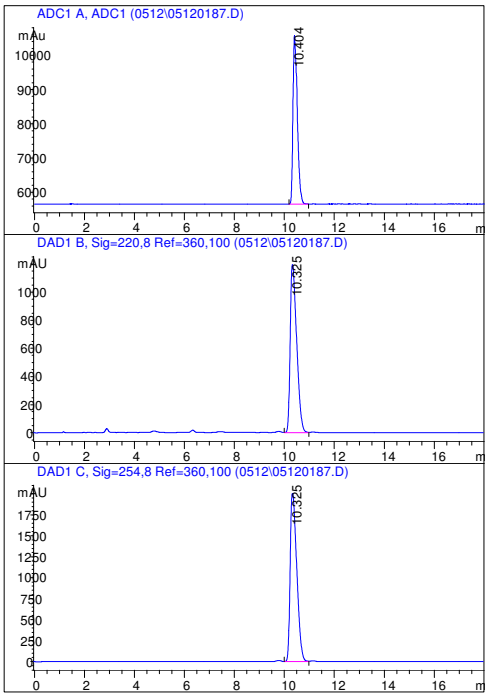


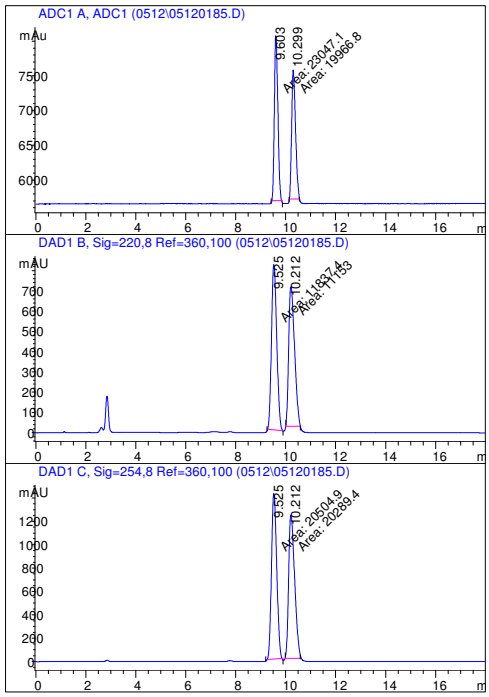
(***R***)-25j

(Method C)

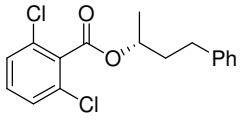


***rac*-25j**



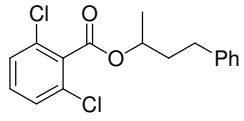


3) **26j**

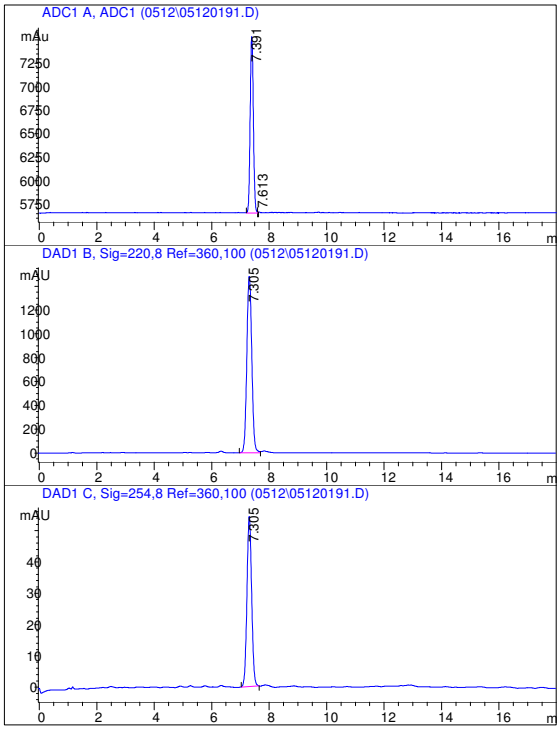


(***R***)-**26j**

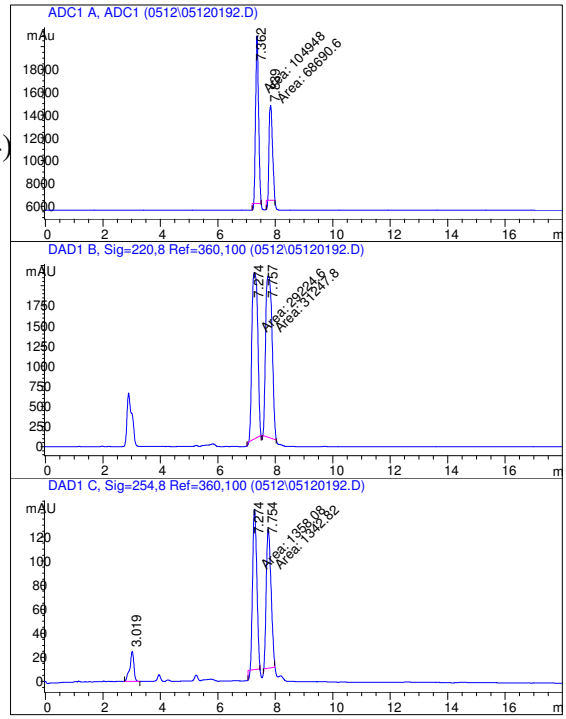
(Method C)



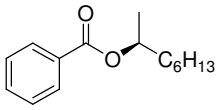
***rac*-26j**



4)

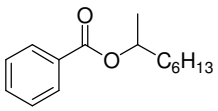


4) **23k**

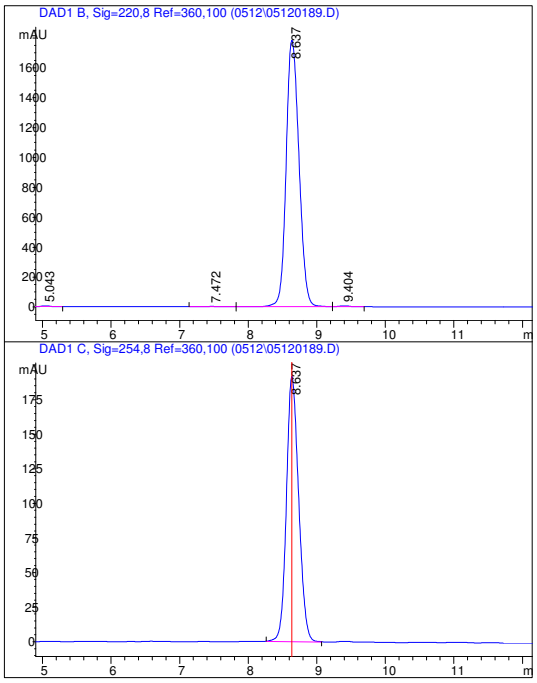


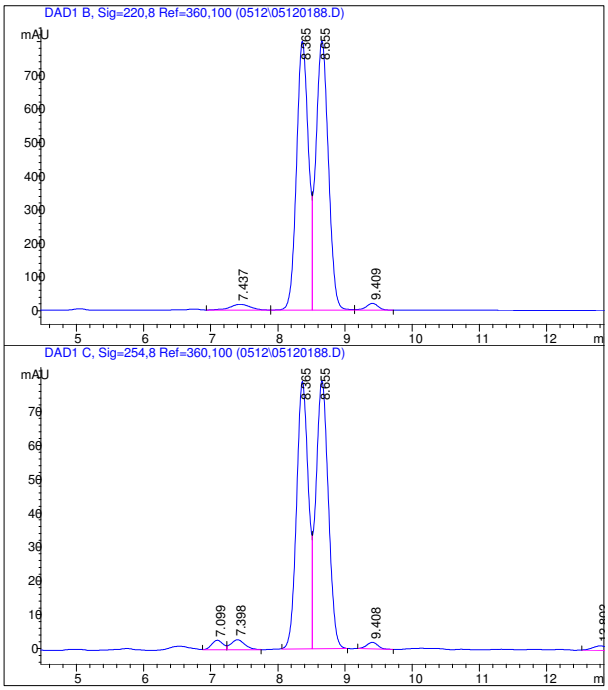
(*S*)-23k

(Method C)

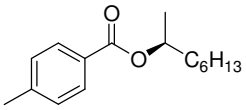


***rac*-23k**



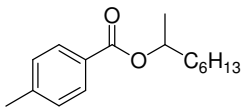


5) **27k**

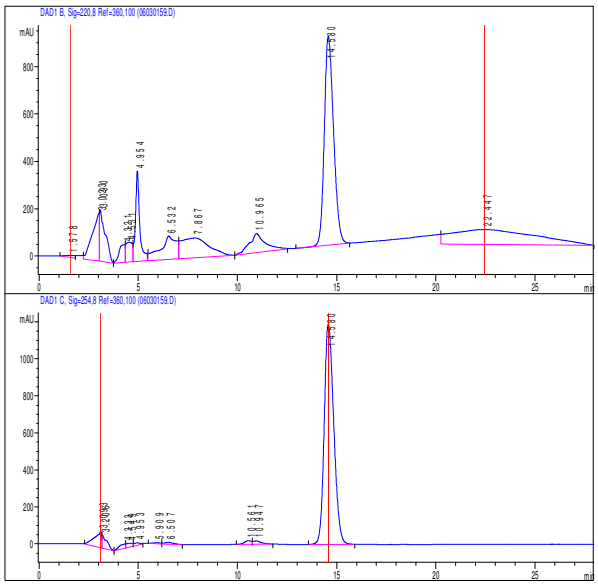


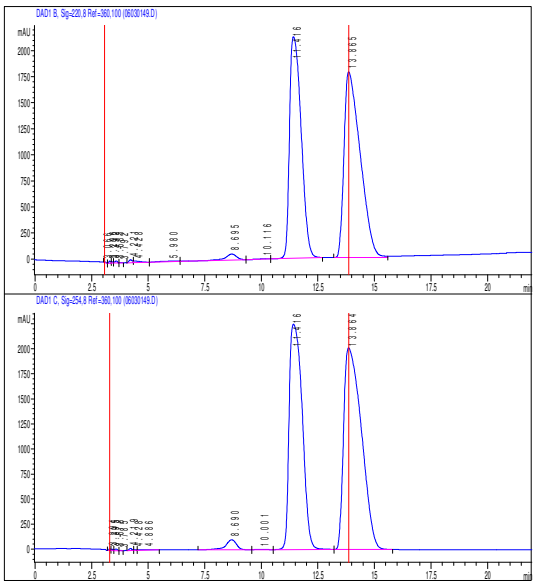
(*S*)-27k

(Method D)

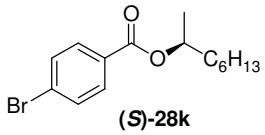


***rac*-27k**



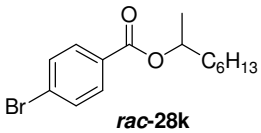


6) **28k**

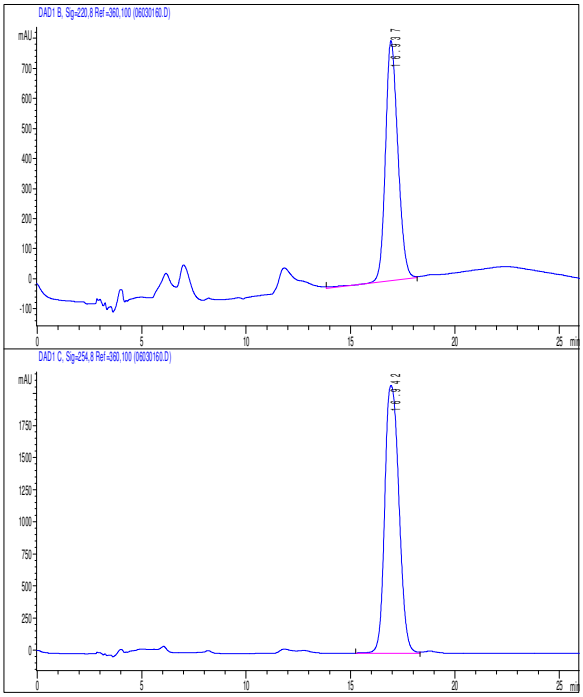


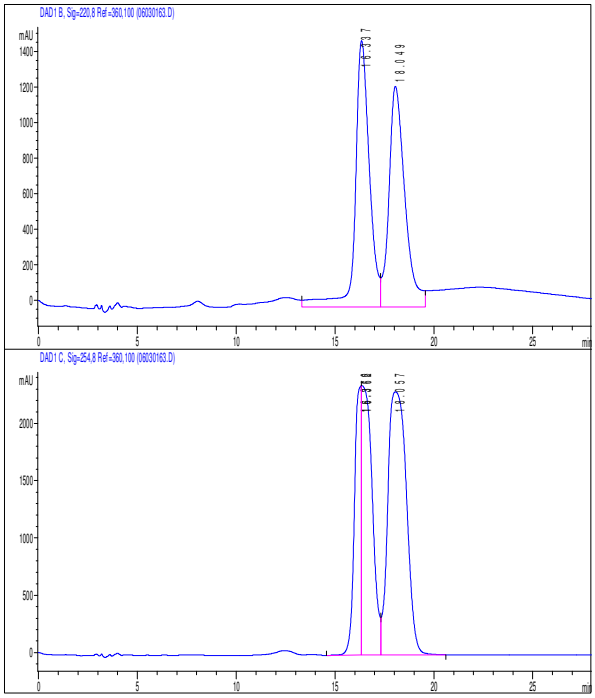
(***S***)-28k

(Method E)

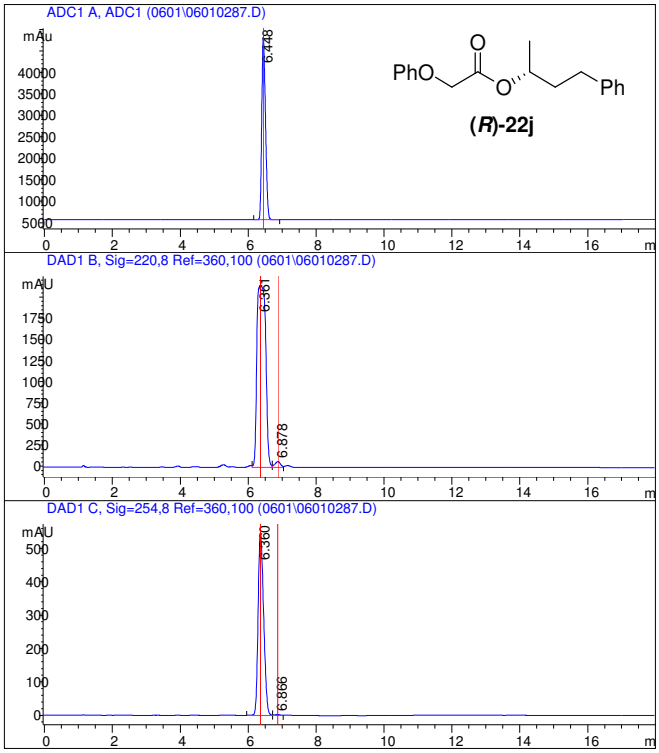


***rac*-28k**

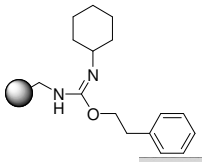




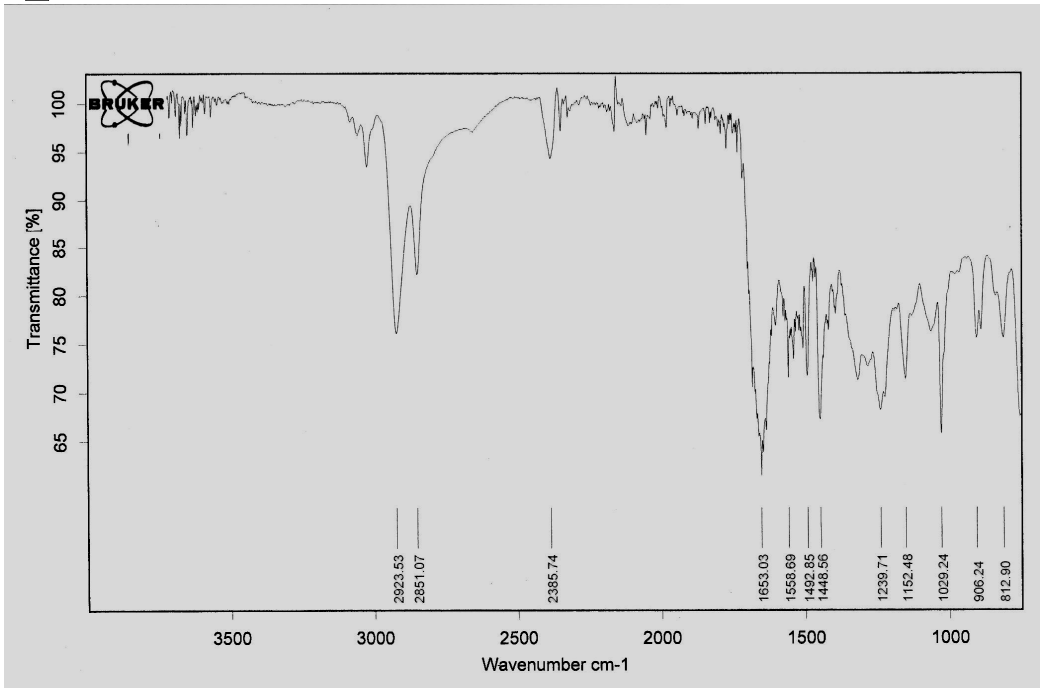
Control Experiments: Mitsunobu inversion under microwave conditions:

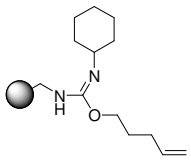


15. IR spectra of resins 38f,m



PS-*O*-phenethylisourea (38f): IR (neat): ν_{max} / (cm^{-1}) 2923 (s); 1653 (s); 1448 (m); 1239 (m); 1029 (m).





PS-*O*-pentenylisourea (39m): IR (neat): ν_{max} / (cm^{-1}) 2924 (s); 1652 (s); 1238 (s); 1029 (s); 890 (m).