Organic electrosynthesis using toluates as simple and versatile radical precursors.

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CONTENTS

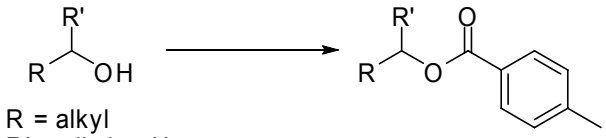
General Experimental Section.

- All experiments were performed in flame dried glass apparatus and under an argon atmosphere with magnetic stirring.
- All solvents and common reagents were purified by established procedures.
- Thin layer chromatography was performed on prepared thin layers precoated plates : Silicagel Merck 60 F_{254}. The visualization of spots on TLC plates was effected by exposure to UV or by using ethanolic phosphomolybdic acid solution. Column chromatography was performed over ROCC Silica gel 60 (40 – 63µ mesh) using relevant eluent.
- ^{1}H (300 MHz) and ^{13}C (75 MHz) spectra were recorded on Brucker AC-300 Avance II at ambient temperature in $CDCl_3$ (Aldrich). Chemical shifts are reported in ppm downfield to tetramethyl silane. Coupling constants are reported and expressed in Hz, splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), dt (double triplet), ddd (doublet of doublet of doublet), m (multiplet).
- NMR Fourier transform, integration and pick picking were done with Bruker TopSpin software or with MestRenova software.
- Infrared spectra were recorded on Shimadzu FTIR-8400S spectrometer and the absorption bands are reported in reciprocal centimeters (cm-1).
- The mass spectra were recorded on a Finigan TSQ 7000 or Varian Matt 44S.
- Cyclic voltammograms were recorded on a potentiostat PAR model 283 using PowerSuite software. DigitalSimulation were performed using DigiElch software.
- Electrolysis were carried out within a homemade H-type Cell consisting of two 100mL compartments separated by a sintered glass with a porosity of 40µm. Carbon graphite electrodes were purchased from Pierron, cut to the right dimension, and connected to a potentiostat PAR model 273A with standard copper wires.
- All reagents were purchased from Acros, Sigma-Aldrich, TCI or Strem and used directly as received without any further purification.
- Data for cyclohexanol, adamantane, fluorene, dibutylketone, 6-methylheptan-2-one and docosane were compared with authentic samples from Acros or TCI. 9-Methylfluorene[1], cholestane[2], cholestan-3-yl 4-methylbenzoate[3], cyclohexyl acetate[4], *t*-

[1] Cho, J.-Y., *Organometallics*, **2007**, *19*, 4816
[2] Park, H.S. ; *Org. Lett.* , **2005**, *7*, 787
[3] Leigh, W. J.; Frendo, D. T.; Klawunn, P. J., *Canadian Journal of Chemistry*, **1985**, *63*, 2131
[4] Nishikido, J., *Tetrahedron*, **2002**, *58*, 8345

butyl(cyclohexyl)dimethylsilane[5], 5-phenylpentan-2-one[6], dodecan-2-one[7], 6-phenylhexan-2-one[8], 1-methyl-2-phenylcyclopentanol[9] and 1-(pyrrolidin-1-yl)pentan-1-one[10], are known in the literature and their data were in good agreement with what has been previously reported.

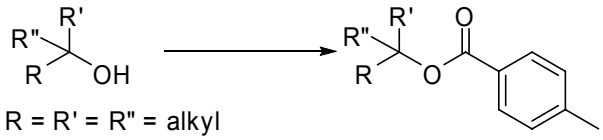
General procedure for preparing toluates from the corresponding primary or secondary alcohols.



R = alkyl
R' = alkyl or H

A solution of the alcohol (0,12M in dichloromethane) was cooled down to -78°C and TMEDA (0.6 equivalent) was added followed by the dropwise addition of toluolyl chloride (1,1 equivalent). The mixture was allowed to stand at -78°C for 30 minutes and the completion of the reaction was checked by TLC. Then, the mixture was quenched by addition of an aqueous saturated solution of NH_4Cl (same volume as dichloromethane). The resulting layers were separated and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel or by recrystallisation.

General procedure for preparing toluates from the corresponding tertiary alcohol.



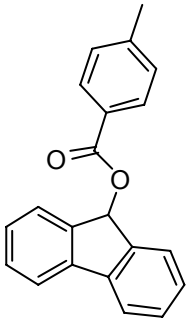
R = R' = R" = alkyl

A solution of the alcohol (1M in THF) was cooled down to 0°C and BuLi (1.6M in hexane, 1 equivalent) was added dropwise, followed, 15 minutes later, by the dropwise addition of toluolyl chloride (1,1 equivalent). The mixture was allowed to stand at 0°C for one hour and then at room temperature overnight. Afterwards, the mixture was quenched by the addition of an aqueous saturated solution of NH_4Cl (same volume as THF). The resulting mixture was extracted three times with dichloromethane. The combined organic layers were washed with

[5] Ito, H., *Org. Lett.*, **2005**, *7*, 1869
[6] Ochiai, M., *Org. Lett.,* **2004**, 9, 1505
[7] Mitsudo, K., *J. Am. Chem. Soc.*, **2007**, *8*, 2246
[8] Shukla, P., *J. Org. Chem.*, **2006**, *2*, 655
[9] Plate, A.F., *Zhurnal Obshchei Khimii*, **1960**, *30*, 1250
[10] Duffield, A.M., Djerassi, C., *J. Am. Chem. Soc.*, **1965**, *87*, 4554

water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel or by recrystallisation.

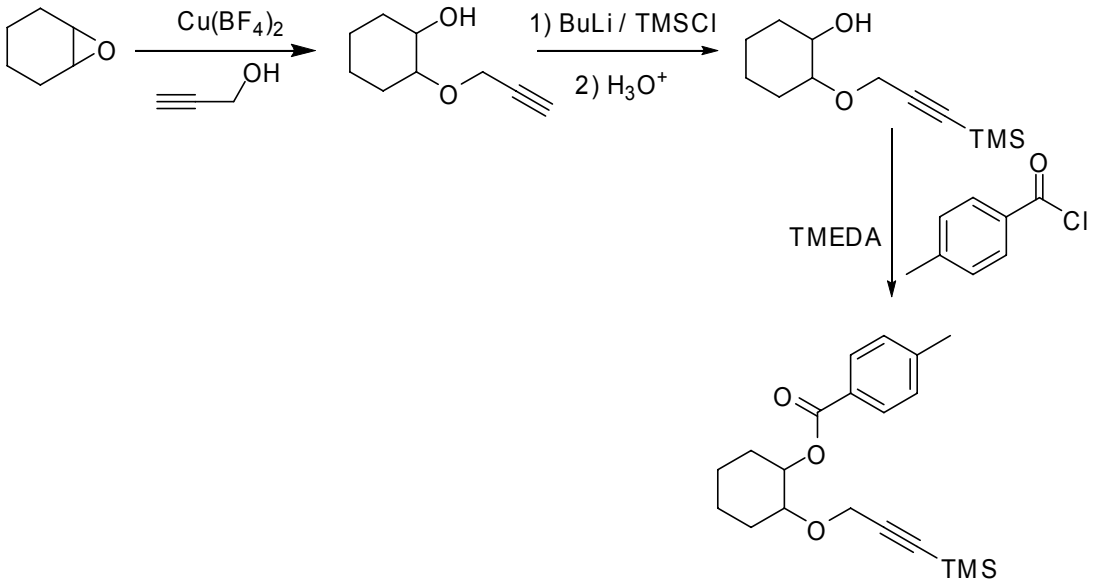
Data for 9*H*-fluoren-9-yl 4-methylbenzoate (7).



Yield : 78% - white solid

Purification : Recrystallization from ethanol **m.p.**= 186-189°C **IR** (neat) υ_{max}/cm^{-1} : 3066, 3043, 2920, 1708, 1612, 1450, 1325, 1261, 1176, 1101, 1091, 1020, 974, 945, 916, 838. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.43 (s, 3H) 7.09 (s, 1H) 7.26 (d, J=8.4 Hz, 2H) 7.34 (t, J=7.5 Hz, 2H) 7.46 (t, J=7.5, 2H) 7.68 (d, J=7.4 Hz, 2H) 7.74 (d, J=7.5 Hz, 2H) 8.03 (d, J=8.1 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): 21.6, 75.4, 120.0, 126.0, 127.2, 127.8, 129.1, 129.4, 129.9, 141.0, 142.2, 143.9, 167.3 **MSCI** *m/z* (%) 301.0 $[M+H]^+$ (32), 164.9 (100), 120.3 (3), 119.1 (50). **HRMS Calcd** for $[C_{12}H_{17}O]^+$: 117.12739 found : 117.12751 **Anal Calcd** for $C_{21}H_{16}O_2$ C, 83.98; H, 5.37 % Found : C, 83.64; H, 5.42 %.

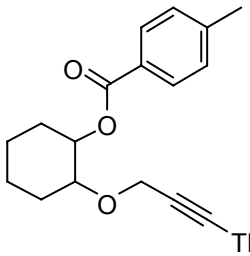
Preparation of 2-(3-(trimethylsilyl)prop-2-ynyloxy)cyclohexyl 4-methylbenzoate (8).



$CuBF_4.xH_2O$ (278mg, 1.17mmol, 0,01 equivalent) was suspended in 100ml of dichloromethane. The solution was cooled down to 0°C, and propargyl alcohol (27.7ml,

470mmol, 4 equivalent) was added, leading to an homogeneous greenish solution. Then, cyclohexane oxide (12ml, 117mmol, 1 equivalent) was added dropwise and the mixture was stirred at room temperature overnight. The crude mixture was washed three times with 40ml of water. The organic layer was dried over Na_2SO_4 and the solvent and excess propargyl alcohol were evaporated under reduced pressure. The resulting solution was distilled at 70°C, under vacuum (1mBar), affording 18.24 grams of a colourless oil which was directly engaged in the next step without any further purification. The crude, distilled, 2-(prop-2-ynyloxy)cyclohexanol (3.4g, 22.05mmol, 1 equivalent) was dissolved in 50ml of THF at -78°C. Then, BuLi (1.6M in hexane, 41.3ml, 66.1mmol, 3 equivalents) was added dropwise to the solution. After 20 minutes at -78°C, TMSCl was added (6.67ml, 77mmol, 3.5 equivalents) and the mixture was stirred at that temperature for one and a half hour. The dry ice/acetone bath was removed and was replaced by an ice bath. After stirring the reaction mixture at 0°C for 5 minutes, 20ml of an aqueous solution of 30% HCl was added. The cooling bath was removed and the solution was vigorously stirred during three hours at room temperature. The hydrolysis of the TMS ether was followed by TLC. The two layers were then separated and the aqueous layer was extracted with dichloromethane (3x20ml). The combined organic layers were washed with water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product (1.5g) was directly engaged in the esterification step using the standard protocol described for secondary alcohols. After purification by chromatography on silica gel using ether 1 to 10 / hexane 9 to 0 as eluent, 2.1g of a colourless oil, which solidified upon cooling were obtained. (42% over three steps).

Data for 2-(3-(trimethylsilyl)prop-2-ynyloxy)cyclohexyl 4-methylbenzoate (8).



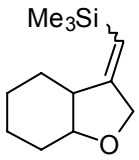
Yield : 42% over three steps - colourless oil.

Purification : Chromatography on silica gel : Eluent : Ether 1 to 10 / Hexane 9 to 0

IR (neat) υ_{max}/cm^{-1} 2927, 2858, 1716, 1612, 1454, 1321, 1269, 1176, 1108, 1089, 993, 840. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.17 (s, 9H) 1.35-1.46 (m, 4H) 1.73-1.76 (m, 2H) 2.11-2.13 (m, 2H) 2.41 (s, 3H) 3.67-3.69 (m, 1H) 4.33 (s, 2H) 4.96-5.03 (m, 1H) 7.23 (d, J=8.7 Hz, 2H) 7.96 (d, J=7.8 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$) : δ -0.2, 21.6, 23.11, 23.14, 29.7, 30.0, 57.9, 75.4, 78.0, 90.6, 102.3, 127.9, 128.9, 129.6, 130.8, 143.3, 165.8 **MSAPCI** *m/z* (%) 344.95 $[M+H]^+$ (5), 328.96 (13), 327.03 (5), 287.00 (32), 248.03 (6), 247.00 (100), 231.12 (22), 219.06 (95), 209.20 (23), 175.10 (6),

157.04 (7), 129.11 (17), 119.07 (37). **HRMS Calcd** for [$C_{20}H_{28}O_3Si+H^+$] : 345.1880 found : 345.1878

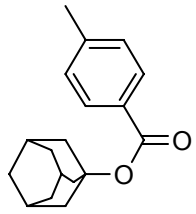
Data for ((hexahydrobenzofuran-3(2*H*)-ylidene)methyl)trimethylsilane (9).



Yield : 58% - colourless liquid

Purification : Chromatography on silica gel : Eluent : Ether 0.25 / Pentane 10 **IR** (neat) υ_{max}/cm^{-1} : 2929, 2852, 1637, 1448, 1247, 1051, 1029, 910, 877, 837. **^{1}H NMR mixture of 2 isomers (2:1)** (300 MHz, $CDCl_3$): δ 0.07(major) and 0.10(minor) (s, 9H) 1.20-1.61 (m, 8H) 2.45 (m, 1H) 3.89-3.96(m and q J=4.6 Hz, 1H) 4.28(major) and 4.16(minor) (ddd and dd, J=14.0 Hz, 3.4Hz, 0.9 Hz and 13.9 Hz, 2.0Hz, 1H) 4.42-4.52 (m, 1H) 5.19(minor) and 5.36(major) (dd and dd, J=2.0 Hz, 1.1 Hz and 2.5 Hz, 2.2 Hz, 1H) **^{13}C NMR mixture of 2 isomers (2:1)** (75 MHz, $CDCl_3$): δ -0.59(major) -0.1(minor) 20.1(minor) 21.4(major) 23.0(major) 24.5(minor) 27.1(major) 27.6(major) 27.7(minor) 27.9(minor) 43.0(minor) 46.1(major) 69.3(major) 72.4(minor) 77.1(major) 78.0(minor) 116.0(minor) 116.1(major) 161.2(major) 162.5(minor) **MSESI** *m/z* (%) 211.13 [M^++H] (15), 194.82 (5), 194.07 (10), 180.98 (10), 180.05 (4), 168.96 (10), 142.79 (10), 129.65 (10), 127.72 (2), 120.94 (36), 105.93 (100), 100.14 (4), 94.08 (7), 93.00 (16), 87.86 (10), 73.09 (4). **HRMS Calcd** for [$C_{12}H_{22}OSi+H^+$] : 211.1513 found : 211.1511

Data for 1-adamantyl-4-methylbenzoate (12).

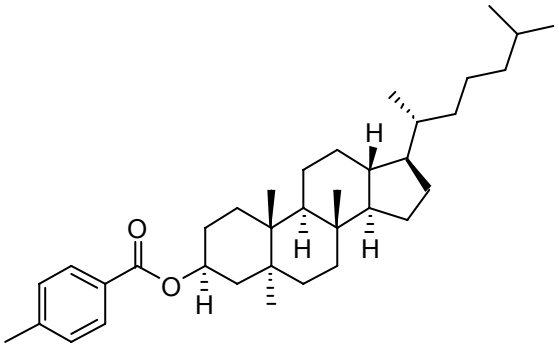


Yield : 76% - white powder

Purification : Chromatography on silica gel : Eluent : Ether 0,5 / Hexane 9,5 or recrystallisation from a mixture of ethanol/water.

m.p.= 66-69°C. **IR** (neat) υ_{max}/cm^{-1} 2910, 2852, 1708, 1612, 1456, 1311, 1272, 1176, 1105, 1053, 1020, 968, 854, 840. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 1.68-1.77 (br, 4H) 2.23 (br, 2H) 2.27 (d, J=2,4 Hz, 4H), 2.40 (s, 3H), 7.21 (d, J=8.1 Hz, 2H), 7.90 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 21.5, 30.8, 36.2, 41.4, 80.6, 128.8, 129.4, 142.8, 165.5 **MSAPCI** *m/z* (%) 270.9 (1) $[M+H]^+$, 256.2 (1), 135.1 (100), 134 (1). **Anal Calcd** for $C_{18}H_{22}O_2$ C, 79.96; H, 8.20 % Found : C, 79.81; H, 8.19 %.

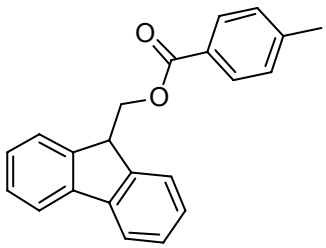
Data for cholestan-3-yl 4-methylbenzoate (14).



Yield : 82% - white powder

Purification : Chromatography on silica gel : Eluent : Ether 0.5 / Hexane 9.5 **m.p.**= 158-160°C **IR** (neat) υ_{max}/cm^{-1} 2933, 2866, 2852, 1714, 1612, 1465, 1363, 1274, 1176, 1108, 1020, 841 **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.67 (s, 3H) 0.86-2.00 (m, 33H) 2.17 (s, 12H) 2.41 (s, 3H) 4.93 (tt, J=11.5, 4.9 Hz, 1H) 7.23 (d, J=8.0, 2H) 7.93 (d, J=8.2, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 12.1, 12.3, 18.7, 21.2, 21.6, 22.5, 22.8, 23.8, 24.2, 27.6, 28.0, 28.2, 28.6, 32.0, 34.1, 35.5, 35.8, 36.2, 36.8, 39.5, 40.0, 42.6, 44.7, 54.2, 56.3, 56.4, 74.1, 125.3, 128.2, 128.3, 128.9, 129.0, 129.5, 143.2, 166.2 **MSAPCI** *m/z* (%) 507.23 (10) $[M+H]^+$, 505.23 (57), 488.23 (21), 487.19 (55), 469.08 (7), 459.18 (5 413.41 (6), 370.12 (30), 369.14 (100) 301.13 (5), 287.08 (5), 257.07 (5), 254.94 (10), 237.06 (7), 225.10 (7), 199.04 (8), 172.88 (3), 161.02 (4).

Data for (9*H*-fluoren-9-yl)methyl 4-methylbenzoate (16).



Yield : 91% - white powder

Purification : Chromatography on silica gel : Eluent : Ether 0,2 / Hexane 9,8 or recrystallisation from a mixture of ethanol/water.

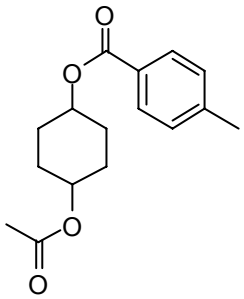
m.p.= 118-201°C. **IR** (neat) υ_{max}/cm^{-1} : 3064, 1715, 1610, 1448, 1269, 1176, 1105, 1020, 841. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.46 (s, 3H) 4.41 (t, J=7,3, 1H) 4.63 (d, J=7.3, 2H) 7.30-7.37 (m, 4H) 7.44 (t, J=7.4, 2H) 7.69 (d, J=7,4, 2H) 7.83 (d, J=7.5, 2H) 8.05 (d, J=8,1, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 21.7, 46.9, 66.8, 120.0, 125.1, 127.1, 127.3, 127.7, 129.2, 129.64, 141.3, 143.8, 143.9, 166.5 **MSAPCI** *m/z* (%) 315.43 (10) $[M+H]^+$, 251.12 (20), 233.07 (100), 229.37 (20), 171.07 (30). **Anal Calcd** for $C_{22}H_{18}O_2$ C, 84.05; H, 5.77 % Found : C, 83.69; H, 5.50 %.

Preparation of 4-acetoxycyclohexyl 4-methylbenzoate (18).

4-hydroxycyclohexyl 4-methylbenzoate (905mg, 3.86mmol, 1 equivalent) was dissolved in a mixture of 100ml of dichloromethane and 10ml of pyridine which was cooled to 0°C. Then, DMAP (23mg, 0,19mmol, 0.05 equivalent) was added to the mixture followed by the dropwise addition of acetic anhydride (1,8ml, 19.31mmol, 5 equivalents). The mixture was stirred at room temperature overnight and then quenched with 40ml of a saturated aqueous solution of $NaHCO_3$. The two layers were separated and the aqueous layer was extracted with

dichloromethane (3x40ml). The combined organic layers were washed with water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel using ether 0.5 / hexane 9.5 as eluent, yielding 865mg of a colourless oil which solidified into a white solid upon cooling (81%).

Data for 4-acetoxycyclohexyl 4-methylbenzoate (18).



Yield : 81% - colourless oil.

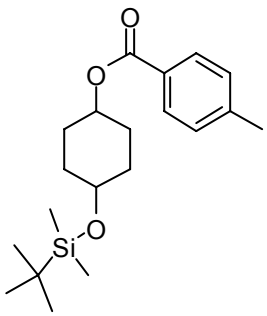
Purification : Chromatography on silica gel : Eluent : Ether 0.5 / Hexane 9.5.

IR (neat) υ_{max}/cm^{-1} 2921, 2850, 1731, 1712, 1612, 1361, 1272, 1242, 1211, 1176, 1108, 1043, 1018, 910. **^{1}H NMR mixture of 2 dia (1:1)** (300 MHz, $CDCl_3$): δ 1.57-2.00 (m, 8H) 2.05 and 2.07 (s, 3H) 2.39 and 2.40 (s, 3H) 4.86-4.88 (m, 1H) 5.00-5.11 (m, 1H) 7.20 and 7.21 (d, J=8.4 Hz, 2H) 7.9 ((two overlaped d), J=8.4Hz, 2H) **^{13}C NMR mixture of 2 dia (1:1)** (75 MHz, $CDCl_3$) : δ 21.2, 21.3, 21.5, 27.2, 27.5, 27.8, 69.9, 70.3, 70.8, 71.0, 127.7, 127.8, 128.9, 129.4, 143.4, 165.8, 165.9, 170.4, 170.5 **MSCI/CH$_4$** *m/z* (%) 277.2 $[M+H]^+$ (1), 216.9 (2), 141.0 (90), 136.9 (45), 119.1 (1), 81 (100), 79.8 (1), 60.6 (1). **Anal Calcd** for $C_{16}H_{20}O_4$ C, 69.54; H, 7.30 % Found : C, 69.67; H, 7.38 %.

Preparation of 4-(*tert*-butyldimethylsilyloxy)cyclohexyl 4-methylbenzoate (20).

4-hydroxycyclohexyl 4-methylbenzoate (980mg, 4.19mmol, 1 equivalent) was dissolved in 42 ml of dichloromethane which was cooled to 0°C. Then, imidazole (0.427mg, 6.28mmol, 1.5 equivalents) was added to the mixture followed by the dropwise addition of TBDMSCl (694mg, 4.60mmol, 1,1 equivalents) diluted in 10ml of dichloromethane. The mixture was allowed to warm up to room temperature. After stirring overnight, it was quenched with 20ml of a saturated aqueous solution of $NaHCO_3$. The two layers were separated and the aqueous layer was extracted with dichloromethane (3x40ml). The combined organic layers were washed with water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel using ether 1 / hexane 1000 as eluent, yielding 914mg of a colourless oil (63%).

Data for 4-(*tert*-butyldimethylsilyloxy)cyclohexyl 4-methylbenzoate (20).



Yield : 63% - colourless oil.

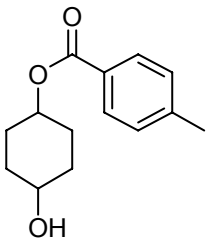
Purification : Chromatography on silica gel : Eluent : Ether 1 / Hexane 1000.

IR (neat) υ_{max}/cm^{-1} 2948, 2856, 1712, 1612, 1461, 1274, 1257, 1176, 1095, 1018, 910, 889. **^{1}H NMR mixture of 2 dia (1:1)** (300 MHz, $CDCl_3$): δ 0.07 and 0.08 (s, 6H) 0.91 and 0.93 (s, 9H) 1.54-1.96 (m, 8H) 2.41 (s, 3H) 3.76-3.82 (m, 1H) 5.0-5.05 (m, 1H) 7.24 (br d, J=7.5 Hz, 2H) 7.9 and 8.0 (d, J=8.4 Hz, 2H) **^{13}C NMR mixture of 2 dia(1:1)** (75 MHz, $CDCl_3$) : δ -4.8, 18.12, 18.17, 21.6, 25.82, 25.85, 27.3, 27.9, 31.4, 31.8, 65.8, 67.9, 68.9, 71.0, 71.8, 128.1, 128.9, 129.5, 129.6, 143.3, 166.1. **MSAPCI** *m/z* (%) 349.06 $[M+H]^+$ (1), 250.95 (7), 231.05 (2), 216.82 (5), 212.82 (100), 212.00 (2), 184.97 (2), 164.68 (6), 146.88 (22), 136.97 (9), 132.82 (34), 118.93 (1). **Anal Calcd** for $C_{20}H_{32}O_3Si$ C, 68.92; H, 9.25 % Found : C, 68.77; H, 9.31 %.

Preparation of 4-hydroxycyclohexyl 4-methylbenzoate (22).

1,4-cyclohexanediol (5g, 42.2mmol, 1,02 equivalents) was dissolved in a mixture of 16ml of chloroform and 12ml of pyridine at 0°C. Toluolyl chloride (5.58ml, 41.4mmol, 1 equivalent), dissolved in 13ml of chloroform was added dropwise. Afterwards, the mixture was stirred during 5 hours at 0°C and then quenched with 20ml of a saturated aqueous solution of NH_4Cl. The two layers were separated and the aqueous layer was extracted with dichloromethane (3x20ml). The combined organic layers were washed with water, dried over a mixture of Na_2SO_4 and K_2CO_3 and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel using ether 1 / hexane 1 as eluent and yielding 6.46g of a colourless oil (67%).

Data for 4-hydroxycyclohexyl 4-methylbenzoate (22).



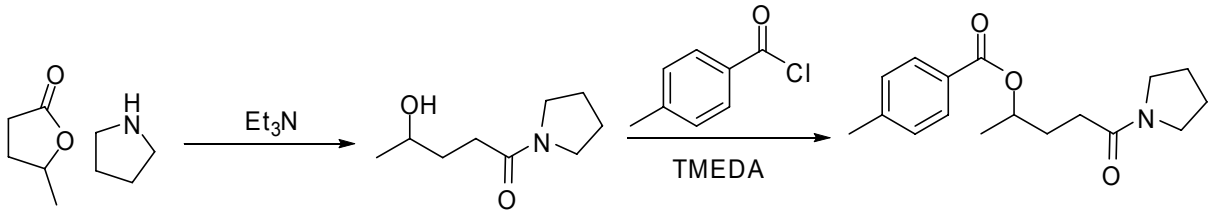
Yield : 67% - colourless oil

Purification : Chromatography on silica gel : Eluent : Ether 1 / Hexane 1.

IR (neat) υ_{max}/cm^{-1} 3404, 2941, 2250, 1697, 1612, 1272, 1178, 1107, 1064, 1018, 906, 840. **^{1}H NMR mixture of 2 dia (1:1)** (300 MHz, $CDCl_3$): δ 1.73-1.81 (m, 5H) 1.99-2.13 (m, 3H) 2.41 (s, 3H) 3.79-3.83 (m, 1H) 5.00-5.12 and 5.13-5.15 (m, 1H) 7.22 (d, J=8.2 Hz, 2H) 7.92 ((two overlapped d), J=8.5 Hz, 2H) **^{13}C NMR mixture of 2 dia (1:1)** (75 MHz, $CDCl_3$) : δ 21.5,27.6, 28.4, 30.5, 31.9, 68.1, 68.7, 69.8, 71.9, 127.8, 127.9, 128.90, 128.93, 129.44, 129.46, 143.40, 143.41, 165.9, 166.0

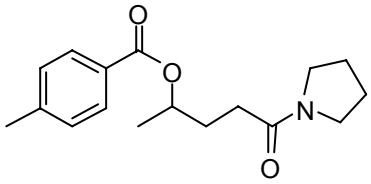
MSAPCI *m/z* (%) 235.05 $[M+H]^+$ (40), 216.24 (15), 168.80 (7), 137.07 (100), 98.94 (7), 80.99 (14). **Anal Calcd** for $C_{14}H_{18}O_3$ C, 71.77; H, 7.74 % Found : C, 71.71; H, 7.75 %.

Preparation of 5-oxo-5-(pyrrolidin-1-yl)pentan-2-yl 4-methylbenzoate (24).



Pyrrolidine (5.5ml, 65.8mmol, 2 equivalents) was mixed with gamma-valerolactone (3.33ml, 34.3mmol, 1 equivalent) and with triethylamine (23.8ml, 171mmol, 5 equivalents). The mixture was refluxed during 3 days and the excess of triethylamine and pyrrolidine was removed under vacuum. The crude oil was directly used in the esterification step. The crude product was then purified by chromatography on silica gel, using ether as eluant, yielding 8.13g of a white powder (82% over two steps).

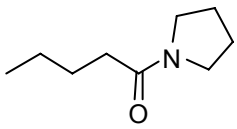
Data for 5-oxo-5-(pyrrolidin-1-yl)pentan-2-yl 4-methylbenzoate (24).



Yield : 82% over two steps - white powder

Purification : Chromatography on silica gel : Eluent : Ether **m.p.**= 61-63°C. **IR** (neat) υ_{max}/cm^{-1} 2976, 2237, 1704, 1670, 1444, 1274, 1178, 1076, 906. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 1.36 (d, J=6.2 Hz, 3H) 1.73-1.78 (m, 2H) 1.80-1.86 (m, 2H) 1.99-2.08 (m, 2H) 2.31-2.39 (m, 2H) 2.40 (s, 3H) 3.33 (t, J=6.8 Hz, 2H) 3.38-3.42 (m, 2H) 5.13-5.28 (m, 1H) 7.23 (d, J=8.2 Hz, 2H) 7.92 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 20.3, 21.6, 24.3, 26.0, 30.8, 31.2, 45.6, 46.5, 71.1, 127.8, 128.9, 129.5, 144.4, 166.2, 170.7 **MSAPCI** *m/z* (%) 291.02 $[M+H]^+$ (1), 270.84 (1), 154.09 (1), 154.03 (100), 153.31 (1), 97.91 (2) **HRMS Calcd** for $[C_{17}H_{23}NO_3+H^+]$: 290.1751 found : 290.1750

Data for 1-(pyrrolidin-1-yl)pentan-1-one (25).

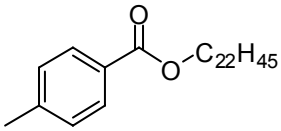


Yield : 69% - colourless liquid

Purification : Chromatography on silica gel : Eluent : dichloromethane **IR** (neat) υ_{max}/cm^{-1} 3053, 2983, 2927, 2883, 2850, 1456, 1421, 1296, 1265, 1147, 985, 908 **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.85 (t, J=7.3 Hz, 3H) 1.29 (tq, J=7.5 Hz, 2H) 1.54 (quint, J=7.5 Hz, 2H) 1.77 (quint, J=7.6 Hz, 2H) 1.87 (quint, J=6.4 Hz, 2H) 2.18 (t, J=7.9 Hz, 2H) 3.36 (dt, J=10.6 Hz, 6.8 Hz, 4H) **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 13.6, 22.3,

24.1, 25.8, 26.7, 34.2, 45.2, 46.3, 171.4 **MSEI** *m/z* (%) 155.1 [M] (20), 140 (6), 127 (5), 126 (17), 114 (10), 113.0 (100), 111.9 (10), 97.9 (17), 85.0 (24), 71.0 (16), 70.0 (33), 57.0 (12), 55.0 (19)

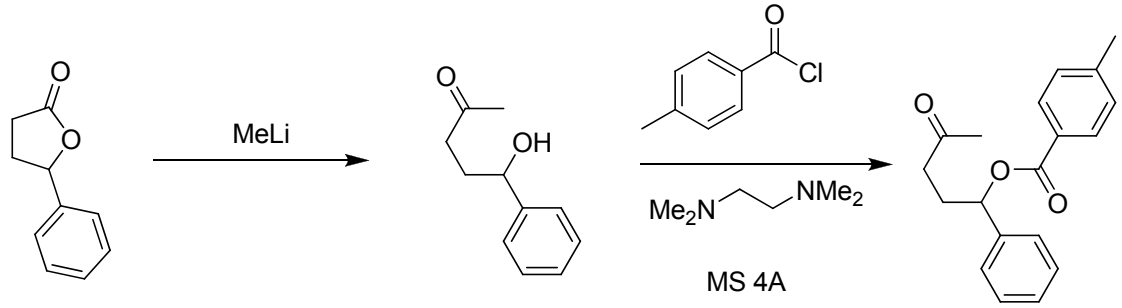
Data for docosyl 4-methylbenzoate (28).



Yield : 94% - White powder

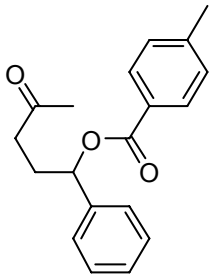
Purification : Recrystallization from ethanol **m.p.**= 52-54°C **IR** (neat) υ_{max}/cm^{-1} : 2952, 2914, 2848, 1716, 1612, 1467, 1275, 1176, 1109, 1020, 841. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.89 (t, 3H, J=6.9 Hz) 1.26 (br s, 38H) 1.76 (quint, J=5.2 Hz) 2.41 (s, 3H) 4.30 (t, 2H, J=6.7 Hz) 7.24 (d, 2H, J= 8.0 Hz) 7.94 (d, 2H, J=8.2 Hz) **^{13}C NMR** (75 MHz, $CDCl_3$): δ 14.1, 21.6, 22.7, 26.0, 28.7, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9, 64.9, 127.8, 129.0, 129.5, 143.3, 166.7 **MSAPCI** *m/z* (%) 445.12 $[M+H]^+$ (1), 137.89 (8),136.91 (100) **Anal Calcd** for $C_{30}H_{52}O_2$ C, 80.48; H, 11.71 % Found : C, 80.82; H, 11.74 %.

Preparation of 4-oxo-1-phenylpentyl 4-methylbenzoate (30).



Phenylgamma butyrolactone (3.45g, 3ml, 20.63mmol, 1 equivalent) was dissolved in 42ml of dry diethylether. The solution was cooled down to -30°C, and methyllithium (1.6 M in diethylether, 12.9ml, 20.63mmol, 1 equivalent) was added dropwise. After two hours, the solution was allowed to come back to room temperature and stirred for 30 more minutes. Then the reaction was quenched by slow addition of 50ml of saturated aqueous solution of ammonium chloride. The two layers were separated and the aqueous layer was extracted three times with 10ml of diethylether. Finally all organic layers were combined, dried over Na_2SO_4 and the solvent and was evaporated under reduced pressure. The resulting oil was directly engaged in the esterification step using the standard protocol described for secondary alcohols. After purification by chromatography on silica gel using ether 1 to 3 / hexane 9 to 7 as eluent, 2.6g of a colourless oil were obtained. (56% over two steps).

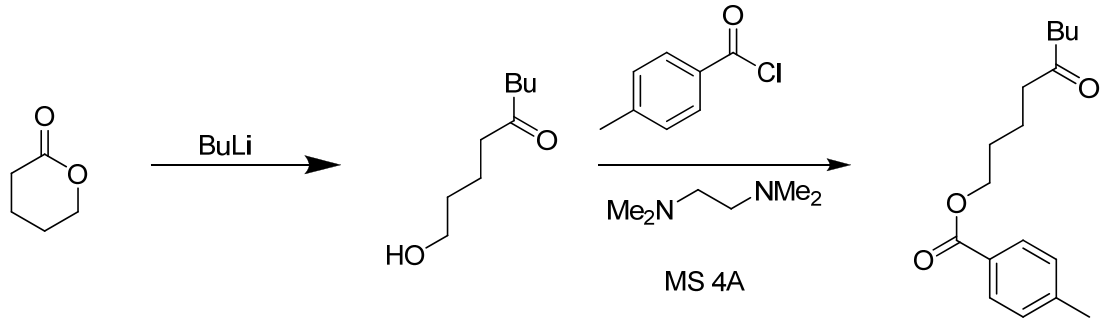
Data for 4-oxo-1-phenylpentyl 4-methylbenzoate (30).



Yield : 56% over two steps - colourless liquid

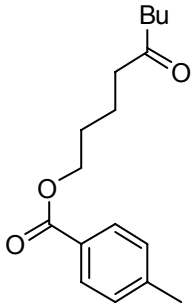
Purification : Chromatography on silica gel : Eluent : Ether 1 to 3 / Hexane 9 to 7 **IR** (neat) υ_{max}/cm^{-1} : 3062, 3033, 2956, 2923, 2852, 1708, 1610, 1494, 1454, 1309, 1267, 1176, 1105, 1064, 1020, 958, 840. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.12 (s, 3H) 2.28-2.35 (m, 2H) 2.42 (s, 3H) 2.55 (t, J=7.0 Hz, 2H) 6.0-6.05 (m, 1H) 7.25-7.46 (m, 7H) 8.00 (d, J=8.1 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): δ 21.5, 29.9, 30.3, 39.3, 75.3, 126.2, 127.3, 127.9, 128.4, 129.0, 129.6, 140.1, 143.7, 165.7, 207.4 **MSESI** *m/z* (%) 319.05 $[M+Na]^+$ (100), 314.10 (5), 242.49 (20), 161.11 (7). **HRMS Calcd** for $[C_{19}H_{20}O_3Na]$: 319.1310 found : 319.1332

Preparation of 5-oxononyl 4-methylbenzoate (32a).



Delta-valerolactone (3.30g, 3ml, 32.6mmol, 1 equivalent) was dissolved in 36ml of dry diethylether. The solution was cooled down to -30°C, and buthyllithium (1.6 M in hexane, 20.4ml, 32.6mmol, 1 equivalent) was added dropwise. After two hours, the solution was allowed to come back to room temperature and stirred for 30 more minutes. Then the reaction was quenched by slow addition of 50ml of saturated aqueous solution of ammonium chloride. The two layers were separated and the aqueous layer was extracted three times with 10ml of diethylether. Finally all organic layers were combined, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The resulting oil was directly engaged in the esterification step using the standard protocol described for secondary alcohols. After purification by chromatography on silica gel using ether 1 / hexane 9 as eluent, 7.5g of a colourless oil were obtained. (61 % over two steps).

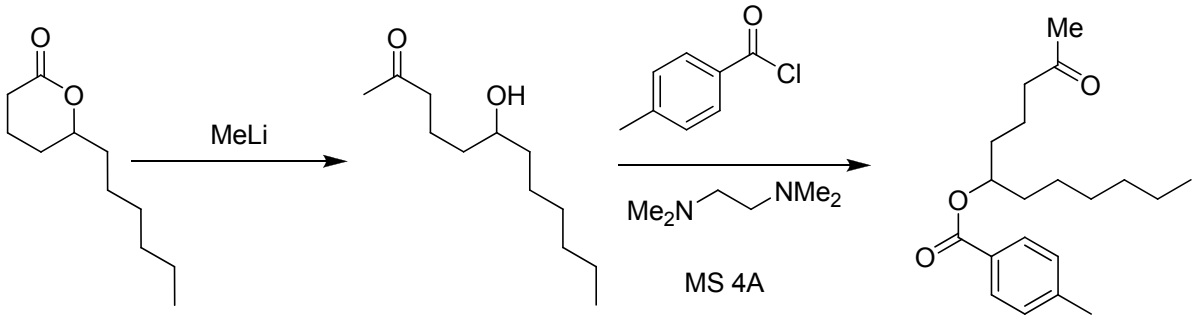
Data for 5-oxononyl 4-methylbenzoate (32a).



Yield : 61% over two steps - colourless oil

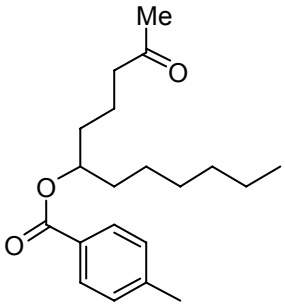
Purification : Chromatography on silica gel : Eluent : Ether 1 / Hexane 9 **IR** (neat) υ_{max}/cm^{-1} : 3004, 2854, 1735, 1716, 1612, 1448, 1365, 1272, 1217, 1178, 1107, 1020. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.90 (t, J=7.3 Hz, 3H) 1.30 (td, J=7.6 Hz 2H) 1.53 (tt, J= 7.3Hz, 2H) 1.73-1.75 (m, 4H) 2.40 (s + overlapped t, 5H) 2.48 (t, J= 6.8 Hz, 2H) 4.39 (t, J=6.0 Hz, 2H) 7.23 (d, J=8.1 Hz, 2H) 7.92 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): δ 13.8, 20.2, 21.6, 22.3, 25.9, 28.2, 42.0, 42.5, 64.3, 127.5, 129.0, 129.5, 143.5, 166.6, 210.8 **MSCI** *m/z* (%) 277.2 $[M+H]^+$ (7), 234.2 (4), 157.1 (5), 142.5 (8), 141.2 (100), 137.1 (15), 119.1 (20), 98 (13). **HRMS Calcd** for $[C_{17}H_{25}O_3]^+$: 277.18037 found : 277.18149

Preparation of 1-(4-oxopentyl)heptyl 4-methylbenzoate (32b).



6-hexyltetrahydro-2*H*-pyran-2-one (2.91g, 3ml, 15.46mmol, 1 equivalent) was dissolved in 30ml of dry diethylether. The solution was cooled down to -30°C, and buthyllithium (1.6 M in hexane, 9.66ml, 15.46mmol, 1 equivalent) was added dropwise. After two hours, the solution was allowed to come back to room temperature and stirred for 30 more minutes. Then the reaction was quenched by slow addition of 50ml of saturated aqueous solution of ammonium chloride. The two layers were separated and the aqueous layer was extracted three times with 10ml of diethylether. Finally all organic layers were combined, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The resulting oil was directly engaged in the esterification step using the standard protocol described for secondary alcohols. After purification by chromatography on silica gel using ether 0 to 2 / hexane 10 to 8 as eluent, 4.75g of a colourless oil were obtained. (59 % over two steps).

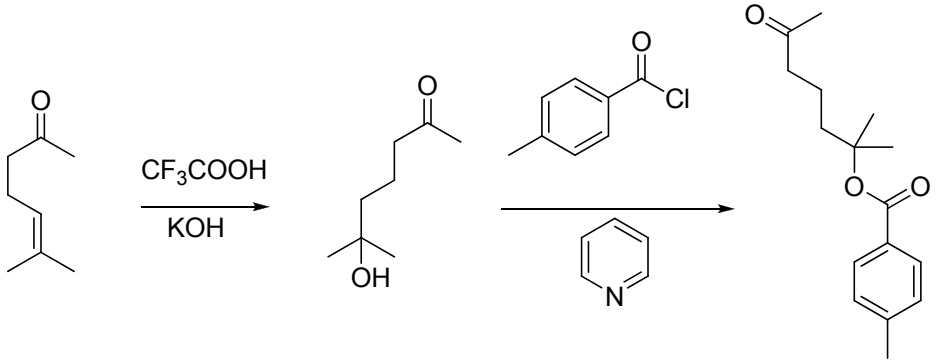
Data for 1-(4-oxopentyl)heptyl 4-methylbenzoate (32b).



Yield : 59% over two steps - colourless oil

Purification : Chromatography on silica gel : Eluent : Ether 0 to 2 / Hexane 10 to 8 **IR** (neat) υ_{max}/cm^{-1} : 3002, 2952, 2856, 1735, 1716, 1612, 1436, 1365, 1272, 1226, 1217, 1207, 1176, 1108. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.84-0.90 (m, 5H) 1.26-1.31 (m, 7H) 1.64-1.68 (m, 5H) 2.12 (s, 3H) 2.41 (s, 3H) 2.45-2.49 (m, 2H) 5.10-5.13 (m, 1H) 7.24 (d, J=8.2 Hz, 2H) 7.93 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): 14.0, 19.4, 21.6, 22.5, 25.2, 29.2, 29.8, 31.6, 33.44, 34.1, 43.2, 74.1, 127.8, 129.0, 129.5, 143.4, 166.4, 208.6 **MSAPCI** *m/z* (%) 319.00 $[M+H]^+$ (1), 318.88 (3), 182.75 (100), 164.73 (33), 136.62 (10), 122.68 (13), 108.65 (55), 94.67 (80), 82.67 (47), 80.67 (33), 68.69 (20), 66.69 (10), 42.74 (25). **HRMS Calcd** for $[C_{20}H_{31}O_3]^+$: 319.22732 found : 319.22814

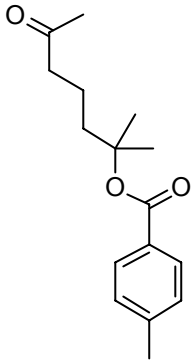
Preparation of 1,1-dimethyl-5-oxohexyl 4-methylbenzoate (32c).



6-methylhept-5-en-2-one (8.50g, 10ml, 65.7mmol, 1 equivalent) was added dropwise, at 0°C, to 82ml of trifluoroacetic acid. The red solution was stirred at room temperature during two hours before the addition of 600ml of a cold aqueous solution of KOH (5M, 45 equivalents). Then the aqueous solution was extracted three times with 100ml of dichloromethane. Finally all organic phases were combined, dried over Na_2SO_4 and the solvent and was evaporated under reduced pressure. 2g (13.87 mmol, 1 equivalent) of the resulting oil was directly dissolved in 14ml of pyridine and toluoyl chloride (21.88g, 18.71ml, 139mmol, 10 equivalents) was added dropwise, afterward the solution was stirred overnight at room temperature. After what, the reaction was cooled down to 0°C and aqueous 1M KOH solution was added until the pH reached 8. The solution was extracted 3 times with 20ml of diethylether and all organic phases were collected, dried over sodium sulphate and finally the solvent was removed under reduced pressure. After purification by chromatography on silica

gel using ether 0 to 2 / hexane 10 to 8 as eluent, 2.00g of a colourless oil was obtained. (47 % over two steps).

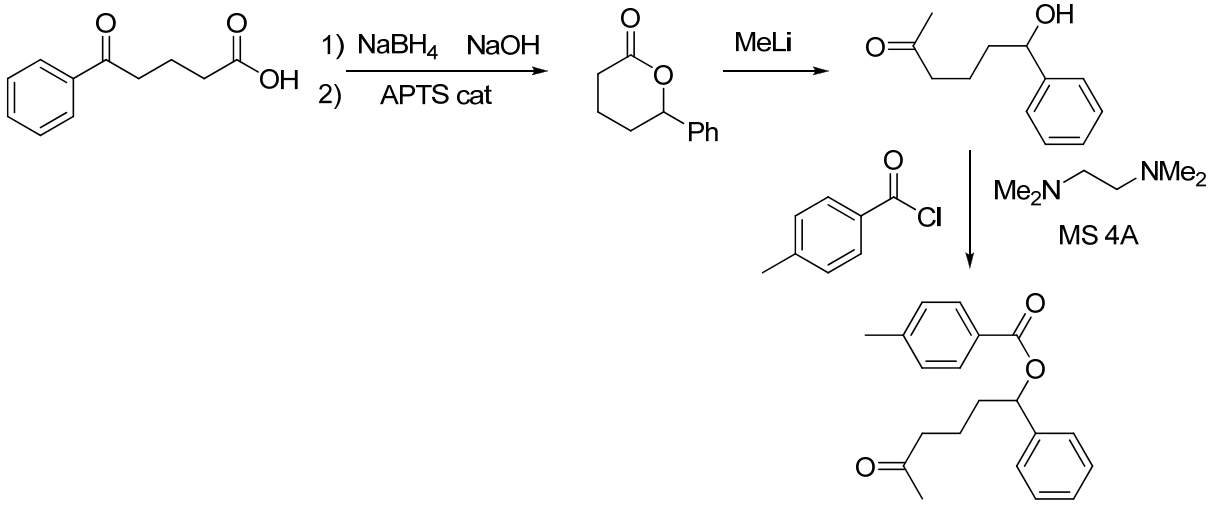
Data for 1,1-dimethyl-5-oxohexyl 4-methylbenzoate (32c).



Yield : 47% over two steps - colourless oil

Purification : Chromatography on silica gel : Eluent : Ether 0 to 2 / Hexane 10 to 8 **IR** (neat) υ_{max}/cm^{-1} : 2970, 2920, 1708, 1674, 1610, 1577, 1448, 1367, 1282, 1261, 1207, 1174, 1107, 1020, 960, 840. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 1.55 (s, 6H) 1.60-1.69 (m, 2H) 1.83-1.84 (m, 2H) 2.11 (s, 3H) 2.37 (s, 3H) 2.44 (t, J=7.2 Hz, 2H) 7.19 (d, J=8.1 Hz, 2H) 7.85 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): 18.1, 21.5, 26.0, 29.8, 40.1, 43.5, 82.4, 128.8, 128.9, 129.3, 142.9, 165.7, 208.5 **MSCI** *m/z* (%) 263.1 $[M+H]^+$ (1), 248.5 (1), 154.5 (1), 136.8 (3), 126.9 (100), 109.0 (40).. **HRMS Calcd** for $[C_{16}H_{23}O_3]^+$: 263.16472 found : 263.16568

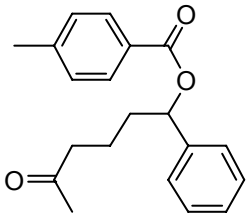
Preparation of 5-oxo-1-phenylhexyl 4-methylbenzoate (32d).



Benzoyl butyric acid (5g, 26mmol, 1 equivalent) and sodium hydroxide (2,1g, 2 equivalents) were dissolved in 100ml of water. The solution was cooled down to 0°C, and sodium borohydride (3,94g, 104mmol, 4 equivalents) was added by portion. After two hours, concentred hydrochloric acid was carefully added until the solution reached pH 2. Then the solution was extracted three times with 50ml of ether. All organic layers were combined, dried over Na_2SO_4 and the solvent and were evaporated under reduced pressure. The resulting oil was directly dissolved in 100ml of benzene with few APTS crystals and the water was azeotropicaly removed by using a Dean-Starck apparatus. When no more water evolved from the reaction, the solution was cooled down and washed with 30ml of a saturated solution of

sodium hydrogenocarbonate. The benzene layer was dried over sodium sulphate and evaporated under reduced pressure. The crude product was pure enough to be directly engaged in the next step. The lactone was opened by methyllithium to afford the corresponding methylketone by using the same procedure as described for the phenylgamma butyrolactone. Finally, the resulting oil was directly engaged in the esterification step using the standard protocol described for secondary alcohols. After purification by chromatography on silica gel using ether 2.5 / hexane 7.5 as eluent, 2.9g of a colourless oil were obtained. (36% over three steps).

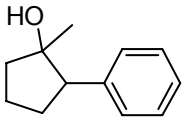
Data for 5-oxo-1-phenylhexyl 4-methylbenzoate (32d).



Yield : 36% over three steps - colourless oil

Purification : Chromatography on silica gel : Eluent : Ether 2.5 / Hexane 7.5 **IR** (neat) υ_{max}/cm^{-1} : 2952, 1708, 1612, 1454, 1407, 1309, 1269, 1176, 1107, 1020, 840. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 1.64-1.97 (m, 4H) 2.12 (s, 3H) 2.42 (s, 3H) 2.49 (t, J=7.3 Hz, 2H) 5.98-6.03 (m, 1H) 7.24-7.45 (m, 7H) 8.00 (d, J=8.2 Hz, 2H) **^{13}C NMR** (75 MHz, $CDCl_3$): δ 19.6, 21.5, 29.8, 35.7, 42.9, 75.8, 126.2, 127.5, 127.8, 128.4, 129.0, 129.6, 140.4, 143.6, 165.7, 208.2 **MSAPCI** *m/z* (%) 311.04 $[M+H]^+$ (13), 309.97 (17), 291.03 (5), 263.01 (12), 218.02 (7), 217.02 (40), 175.12 (16), 174.12 (100), 146.11 (6), 119.02 (6). **HRMS Calcd** for $[C_{20}H_{22}O_3H]^+$: 311.16417 found : 311.16400

Data for 1-methyl-2-phenylcyclopentanol (34d).



Yield : 62% - colourless oil

Purification : Chromatography on silica gel : Eluent : Ethyl acetate 3 / Hexane 7 **IR** (neat) υ_{max}/cm^{-1} : 3406, 2958, 2925, 2873, 1602, 1494, 1452, 1406, 1272, 1178, 1109, 1020, 943. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 0.96 (s, 3H) 1.60 (s, 1H) 1.86-2.16 (m, 6H) 3.10 (t, J=9 Hz, 1H) 7.14-7.42 (m, 5H) **^{13}C NMR** (75 MHz, $CDCl_3$): 20.7, 24.4, 29.0, 40.3, 56.4, 81.3, 126.3, 128.0, 128.2, 141.3 **MSCI** *m/z* (%) 177.0 $[M+H]^+$ (65), 158.9 (66), 129.8 (25), 117.0 (100).