Preparation of 2-diethoxyphosphoryl-4-alkenoates 8a-e. General Procedure.

A solution of ethyl diethoxyphosphoryl acetate (22.42g; 100 mmol) in THF (50 mL) was added dropwise to a stirred suspension of NaH (2.64 g; 110 mmol) in THF (200 mL) at 0°C. Stirring was continued for 0.5 h at the same temperature and then allyl bromide (105 mmol) in THF (100 mL) was added. The reaction mixture was left overnight at r.t. and cooled to 0°C before quenching with saturated ammonium chloride solution (150 mL). THF was evaporated under reduced pressure, water (100 mL) was added and the aqueous layer was extracted with Et_2O (2 x 100 mL). The combined organic extracts were dried and evaporated to give the crude product, which was purified by distillation.

Ethyl 2-diethoxyphosphoryl-4-pentenoate (8a); oil, 47 % yield, bp 108-114 °C/0.8 mbar; IR (film) *v* 1736 (C=O), 1640 (C=C), 1256 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, *J* = 7.00 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.34 (td, *J* = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 1.35 (td, *J* = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 2.50-2.82 (m, 2H, H_2C-3), 3.04 (ddd, *J* = 22.26, 11.00, 4.00 Hz, 1H, HC-2), 4.09-4.26 (m, 6H, $POCH_2$ and $COCH_2$), 5.02-5.17 (m, 2H, H_2C-5), 5.76 (ddt, *J* = 17.01, 10.26, 6.50 Hz, 1H, HC-4); ^{31}P NMR ($CDCl_3$) δ 22.78.

Ethyl 2-diethoxyphosphoryl-4-methyl-4-pentenoate (8b); oil, 64 % yield, bp 88-89 °C/0.013 mbar; IR (film) *v* 1736 (C=O), 1652 (C=C), 1260 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, *J* = 7.00 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.34 (t, *J* = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.35 (t, *J* = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.74 (s, 3H, CH_3C-4), 2.42-2.56 (m, 1H, HC-3), 2.72 (ddd, *J* = 15.26, 12.01, 6.75 Hz, 1H, HC-3), 3.19 (ddd, *J* = 22.76, 12.01, 3.25 Hz, 1H, HC-2), 4.14 (q, *J* = 7.00 Hz, 2H, $COCH_2$), 4.17 (quin, *J* = 7.00 Hz, 2H, $POCH_2$), 4.18 (quin, *J* = 7.00 Hz, 2H, $POCH_2$), 4.73 (s, 1H, HC-5), 4.78 (s, 1H, HC-5); ^{31}P NMR ($CDCl_3$) δ 23.29.

Ethyl (*E*) and (*Z*)-2-diethoxyphosphoryl-4-hexenoate (*E*-) and (*Z*)-(8c); mixture of isomers *(E)* / *(Z)* = 80/20, oil, 50 % yield, bp 96-99 °C/0.2 mbar; IR (film) *v* 1736 (C=O), 1260 (P=O) cm^{-1}; (*E*)-(**6c**); ^1H NMR[22] ($CDCl_3$) δ 1.24-1.40 (m, 9H, $CO_2CH_2\underline{CH_3}$ and $POCH_2\underline{CH_3}$), 1.60-1.75 (m, 3H, H_3C-6), 2.40-2.83 (m, 2H, H_2C-3), 2.97 (ddd, *J* = 22.01, 10.76, 4.00 Hz, HC-2), 4.08-4.26 (m, 6H, $POCH_2$ and $COCH_2$), 5.25-5.62 (m, 2H, HC-4 and HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 23.00. (*Z*)-(**6c**); ^1H NMR[22] ($CDCl_3$) δ 1.24-1.40 (m, 9H, $CO_2CH_2\underline{CH_3}$ and $POCH_2\underline{CH_3}$), 1.60-1.75 (m, 3H, H_3C-6), 2.40-2.83 (m, 2H, H_2C-3), 2.95 (dt, *J* = 22.51, 5.00 Hz, HC-2), 4.08-4.26 (m, 6H, $POCH_2$ and $COCH_2$), 5.25-5.62 (m, 2H, HC-4 and HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 23.00.

Ethyl (*E*) 2-diethoxyphosphoryl-4-octenoate) (*E*)-(8d); oil, 59 % yield, bp 96-98 °C/0.07 mbar; IR (film) *v* 1736 (C=O), 1256 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.50 Hz, 3H, H_3C-8), 1.27 (t, *J* = 7.25 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.33 (t, *J* = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.34 (td, *J* = 7.00, 0.25 Hz, 3H, $POCH_2\underline{CH_3}$), 1.25-1.42 (m, 2H, H_2C-7), 1.94 (q, *J* = 7.25 Hz, 2H, H_2C-6), 2.43-2.75 (m, 2H, H_2C-3), 2.98 (ddd, *J* = 21.76, 10.76, 4.00 Hz, 1H, HC-2), 4.09-4.25 (m, 6H, $POCH_2$ and $COCH_2$), 5.34 (dt, *J* = 15.26, 7.00 Hz, 1H, HC-4), 5.52 (dt, *J* = 15.26, 7.25 Hz, 1H, HC-5); ^{31}P NMR ($CDCl_3$) δ 23.00.

Ethyl (*E*) 2-diethoxyphosphoryl-5-phenyl-4-pentenoate (*E*)-(8e); oil, 53 % yield, bp 135-140 °C/0.13 mbar; IR (film) *v* 1732 (C=O), 1256 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, *J* = 7.25 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.35 (td, *J* = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 1.35 (td, *J* = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 2.67-2.96 (m, 2H, H_2C-3), 3.10 (ddd, *J* = 21.76, 10.51, 4.25 Hz, 1H, HC-2), 4.11-4.26 (m, 6H, $POCH_2$ and $COCH_2$), 6.13 (dt, *J* = 15.76, 7.00 Hz, 1H, HC-

4), 6.47 (dt, J = 15.76, 1.25 Hz, 1H, HC-5), 7.16-7.36 (m, 5H, Ph); ^{31}P NMR ($CDCl_3$) δ 22.68.

General Procedure for the Preparation of 2-Diethoxyphosphoryl-4-alkenoic acids (E)-4a-e. To a cold (0°C) solution of 2-diethoxyphosphoryl-4-alkenoate **8** (20 mmol) in EtOH (16 mL) a solution of KOH (1.68g; 30 mmol) in H_2O (2.2 mL) was added. The reaction mixture was left for 24 h at r.t. After this time EtOH was evaporated under reduced pressure and H_2O (10 mL) was added to the residue. The mixture was washed with Et_2O (3 x 15 mL), aqueous layer was acidified to pH ~1.5 with 10% aq. HCl and extracted with $CHCl_3$ (4 x 30 mL). The combined organic extracts were dried and evaporation gave crude product, which was used in the next step without further purification.

2-Diethoxyphosphoryl-4-pentenoic acid (4a); oil, 84 % yield; IR (film) ν 3000 (O-H), 1728 (C=O), 1640 (C=C), 1216 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (td, J = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 1.35 (td, J = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 2.45-2.80 (m, 2H, H_2C-3), 3.06 (ddd, J = 22.76, 10.76, 4.00 Hz, 1H, HC-2), 4.11-4.29 (m, 4H, $POCH_2$), 5.00-5.19 (m, 2H, H_2C-5), 5.79 (ddt, J = 17.01, 10.00, 6.75 Hz, 1H, HC-4), 9.25 (bs, 1H, O-H); ^{31}P NMR ($CDCl_3$) δ 23.73.

2-Diethoxyphosphoryl-4-methyl-4-pentenoic acid (4b); oil, 89 % yield; IR (film) ν 3050 (O-H), 1728 (C=O), 1652 (C=C), 1216 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.36 (t, J = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.74 (s, 3H, CH_3C-4), 2.38-2.52 (m, 1H, HC-3), 2.70 (ddd, J = 15.26, 11.50, 7.50 Hz, 1H, HC-3), 3.22 (ddd, J = 23.01, 11.50, 3.25 Hz, 1H, HC-2), 4.18 (quin, J = 7.00 Hz, 2H, $POCH_2$), 4.23 (quin, J = 7.00 Hz, 2H, $POCH_2$), 4.79 (s, 2H, H_2C-5), 8.09 (bs, 1H, O-H); ^{31}P NMR ($CDCl_3$) δ 24.10.

(*E*)- and (*Z*)-2-Diethoxyphosphoryl-4-hexsenoic acid (*E*)- and (*Z*)- (4c); mixture of isomers (*E*)/(*Z*) = 80/20, oil, 88 % yield; IR (film) ν 3050 (O-H), 1728 (C=O), 1216 (P=O) cm^{-1}; (*E*)-(**7c**); ^{1}H NMR[22] ($CDCl_3$) δ 1.30-1.40 (m, 6H, $POCH_2\underline{CH_3}$), 1.58-1.70 (m, 3H, H_3C-6), 2.38-2.82 (m, 2H, H_2C-3), 3.00 (ddd, J = 22.51, 10.76, 4.25 Hz, 1H, HC-2), 4.10-4.30 (m, 4H, $POCH_2$), 5.30-5.64 (m, 2H, HC-4 and HC-5), 8.51 (bs, 1H, O-H); ^{31}P NMR[22] ($CDCl_3$) δ 23.92. (*Z*)-(**7c**); ^{1}H NMR[22] ($CDCl_3$) δ 1.30-1.40 (m, 6H, $POCH_2\underline{CH_3}$), 1.58-1.70 (m, 3H, H_3C-6), 2.38-2.82 (m, 2H, H_2C-4), 2.98 (dt, J = 22.01, 6.00 Hz, 1H, HC-2), 4.10-4.30 (m, 4H, $POCH_2$), 5.30-5.64 (m, 2H, HC-4 and HC-4), 8.51 (bs, 1H, O-H); ^{31}P NMR[22] ($CDCl_3$) δ 23.92.

(*E*)-2-Diethoxyphosphoryl-4-octenoic acid (*E*)-(4d); oil, 84 % yield; IR (film) ν 3000 (O-H), 1728 (C=O), 1216 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 7.25 Hz, 3H, H_3C-8), 1.33 (t, J = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.34 (t, J = 7.25 Hz, 3H, $POCH_2\underline{CH_3}$), 1.25-1.42 (m, 2H, H_2C-7), 1.94 (q, J = 7.00 Hz, 2H, H_2C-6), 2.40-2.74 (m, 2H, H_2C-3), 3.00 (ddd, J = 22.26, 10.76, 4.00 Hz, 1H, HC-2), 4.17 (dq, J = 8.00, 7.00 Hz, 2H, $POCH_2$), 4.22 (quin, J = 7.25 Hz, 2H, $POCH_2$), 5.37 (dt, J = 15.26, 6.50 Hz, 1H, HC-4), 5.54 (dt, J = 15.26, 7.00 Hz, 1H, HC-5), 8.34 (bs, 1H, O-H); ^{31}P NMR ($CDCl_3$) δ 23.89.

(*E*)-2-Diethoxyphosphoryl-5-phenyl-4-pentenoic acid (*E*)-(4e); oil, 96 % yield; IR (film) ν 3000 (O-H), 1728 (C=C), 1216 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 1.33 (t, J = 7.00 Hz, 3H, $POCH_2\underline{CH_3}$), 2.62-2.95 (m, 2H, H_2C-3), 3.13 (ddd, J = 22.51, 10.50, 4.25 Hz, 1H, HC-2), 4.17 (quin, 2H, J = 7.00 Hz, 2H, $POCH_2$), 4.23 (quin,

2H, J = 7.00 Hz, 2H, $POCH_2$), 6.15 (dt, J = 15.76, 7.00 Hz, 1H, HC-4), 6.48 (d, J = 15.76 Hz, 1H, HC-5), 7.15-7.35 (m, 5H, Ph), 9.30 (bs, 1H, O-H); ^{31}P NMR ($CDCl_3$) δ 23.72.

General Procedure for the Preparation of Diethyl (5*R,1'*R**)-5-(1'-hydroxyalkyl)-2-oxotetrahydrofuran-3-ylphosphonates (5*R**,1'*R**)-6a-e.** To a stirred mixture of 4-alkenoic acid **4** (5.0 mmol), N-methylmorpholine N-oxide (0.743g; 5.5 mmol) water (2 mL) and acetone (2.5 mL), 0.02 M solution of OsO_4 in *t*-BuOH (1.4 mL) was added at r.t. The reaction mixture was stirred for 24h and sodium metabisulphite (0.114g; 0.6 mmol) was added. After 0.5 h the precipitate was filtered off, the filtrate was acidified to pH ~2 with 1N H_2SO_4, and finally acetone and water were evaporated in vacuum. The residue was extracted with $CHCl_3$ (4 x 20 mL), the chloroform layer was dried over $MgSO_4$ and evaporated to give crude (5*R**, 1'*R**)-**6**, which were purified by column chromatography (silica gel, EtOAc : MeOH = 95 : 5 as eluent).

Diethyl 5-(hydroxymethyl)-2-oxotetrahydrofuran-3-ylphosphonate (6a); mixture of diastereoisomers in a 70/30 ratio, oil, 73 % yield; R_f = 0.21 (AcOEt : MeOH = 95 : 5); IR (film) ν 3400 (O-H), 1772 (C=O), 1248 (P=O) cm^{-1}; major diastereoisomer (70%) ^{1}H NMR[22] ($CDCl_3$) δ 1.36 (t, J = 7.00 Hz, 6H, $POCH_2\underline{CH_3}$), 2.05 (bs, 1H, O-H), 2.34-2.70 (m, 2H, H_2C-4), 3.24 (ddd, J = 23.51, 10.26, 5.75 Hz, 1H, HC-3), 3.64 (dd, J = 12.51, 3.75 Hz, 1H, HC-1'), 3.95 (dd, J = 12.51, 2.75 Hz, 1H, HC-1'), 4.10-4.40 (m, 4H, $POCH_2$), 4.76 (tdd, J = 7.25, 3.75, 2.75 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.59; minor diastereoisomer (30%) ^{1}H NMR[22] ($CDCl_3$) δ 1.37 (t, J = 7.00 Hz, 6H, $POCH_2\underline{CH_3}$), 2.05 (bs, 1H, O-H), 2.34-2.70 (m, 2H, H_2C-4), 3.21 (dt, J = 24.51, 10.25 Hz, 1H, HC-3), 3.75 (dd, J = 12.51, 5.00 Hz, 1H, HC-1'), 3.91 (dd, J = 12.51, 3.25 Hz, 1H, HC-1'), 4.10-4.40 (m, 4H, $POCH_2$), 4.63 (tdd, J = 7.75, 5.00, 3.25 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.59.

Diethyl 5-(hydroxymethyl)-5-methyl-2-oxotetrahydrofuran-3-ylphosphonate (6b); mixture of diastereoisomers in a 70/30 ratio, oil, 74 % yield; R_f = 0.38 (AcOEt : MeOH = 95 : 5);IR (film) ν 3384 (O-H), 1772 (C=O), 1244 (P=O) cm^{-1}; major diastereoisomer (70%) ^{1}H NMR[22] ($CDCl_3$) δ 1.36 (t, J = 7.00 Hz, 6H, $POCH_2\underline{CH_3}$), 1.43 (s, 3H, CH_3C-5), 2.28 (ddd, J = 21.26, 13.26, 9.50 Hz, 1H, HC-4), 2.68 (ddd, J = 13.26, 10.76, 8.75 Hz, 1H, HC-4), 2.80 (bs, 1H, O-H), 3.50 (ddd, J = 23.76, 10.76, 9.50 Hz, 1H, HC-3), 3.51 (d, J = 12.01 Hz, 1H, HC-1'), 3.72 (d, J = 12.01 Hz, 1H, HC-1'), 4.12-4.35 (m, 4H, $POCH_2$); ^{31}P NMR[22] ($CDCl_3$) δ 21.91; minor diastereoisomer (30%) ^{1}H NMR[22] ($CDCl_3$) δ 1.36 (td, J = 7.00, 0.50 Hz, 6H, $POCH_2\underline{CH_3}$), 1.39 (s, 3H, CH_3C-5), 2.19 (ddd, J = 13.50, 10.76, 9.25 Hz, 1H, HC-4), 2.71 (ddd, J = 20.51, 13.50, 9.25 Hz, 1H, HC-4), 2.80 (bs, 1H, O-H), 3.33 (ddd, J = 24.76, 10.76, 9.25 Hz, 1H, HC-3), 3.59 (d, J = 12.26 Hz, 1H, HC-1'), 3.73 (d, J = 12.26 Hz, 1H, HC-1'), 4.12-4.35 (m, 4H, $POCH_2$); ^{31}P NMR[22] ($CDCl_3$) δ 22.04.

Diethyl (5*R,1'*R**)-5-(1'-hydroxyethyl)-2-oxotetrahydrofuran-3-ylphosphonate (5*R**,1'*R**)-(6c)**; mixture of four diastereoisomers in 45/25/20/10 ratio, oil, 82 % yield; R_f = 0.20 (AcOEt : MeOH = 95 : 5); IR (film) ν 3376 (O-H), 1776 (C=O), 1248 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15-1.30 (m, 3H, CH_3-C-1'), 1.32-1.42 (m, 6H, $POCH_2\underline{CH_3}$), 2.28-2.80 (m, 3H, H_2C-4 and O-H), 3.10-3.30 (m, 1H, HC-3), 3.74-4.57 (m, 6H, $POCH_2$, HC-5 and HC-1'); ^{31}P NMR ($CDCl_3$) δ 21.54 (45%), 21.43 (25%), 21.75 (20%), 21.67 (10%).

Diethyl (5*R,1'*R**)-5-(1'-hydroxybutyl)-2-oxotetrahydrofuran-3-ylphonate (5*R**,1'*R**)-(6d)**; mixture of diastereoisomers in 65/35 ratio, oil, 81 % yield; R_f = 0.36 (AcOEt : MeOH = 95 : 5); IR (film) ν 3376 (O-H), 1772 (C=O), 1244 (P=O) cm^{-1}; major

diastereoisomer (65%); ^{1}H NMR[22] ($CDCl_3$) δ 0.95 (t, J = 7.00 Hz, 3H, H_3C-4'), 1.36 (t, J = 7.25 Hz, 6H, $POCH_2\underline{CH_3}$), 1.32-1.63 (m, 4H, H_2C-2' and H_2C-3'), 2.31 (bs, 1H, O-H), 2.35-2.70 (m, 2H, H_2C-4), 3.23 (ddd, J = 23.50, 10.30, 5.00 Hz, 1H, HC-3), 3.58 (dt, J = 8.00, 4.00 Hz, 1H, HC-1'), 4.15-4.35 (m, 4H, $POCH_2$), 4.57 (td, J = 7.00, 4.00 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.50; minor diastereoisomer (35%) ^{1}H NMR[22] ($CDCl_3$) δ 0.95 (t, J = 7.00 Hz, 3H, H_3C-4'), 1.37 (t, J = 7.25 Hz, 6H, $POCH_2\underline{CH_3}$), 1.32-1.63 (m, 4H, H_2C-2' and H_2C-3'), 2.31 (bs, 1H, O-H), 2.35-2.70 (m, 2H, H_2C-4), 3.20 (dt, J = 24.60, 10.24 Hz, 1H, HC-3), 3.66 (q, J = 5.00 Hz, 1H, HC-1'), 4.15-4.35 (m, 4H, $POCH_2$), 4.39 (ddd, J = 9.00, 8.00, 5.00 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.27.

Diethyl (5*R,1'*R**)-5-(hydroxy-phenyl-methyl)-2-oxotetrahydrofuran-3-ylphosphonate (5*R**,1'*R**)-(6e)**; mixture of diastereoisomers in 65/35 ratio, white solid, 85 % yield; R_f = 0.38 (AcOEt : MeOH = 95 : 5); IR (CCl_4) ν 3368 (O-H), 1756 (C=O), 1232 (P=O) cm^{-1}; major diastereoisomer (65%) ^{1}H NMR[22] ($CDCl_3$) δ 1.32 (t, J = 7.25 Hz, 6H, $POCH_2\underline{CH_3}$), 2.38-2.47 (m, 2H, H_2C-4), 2.96-3.23 (m, 2H, HC-3 and O-H), 4.07-4.33 (m, 4H, $POCH_2$), 4.70 (d, J = 5.50 Hz, 1H, HC-1'), 4.80 (td, J = 7.25, 5.50 Hz, 1H, HC-5), 7.29-7.45 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 21.19; minor diastereoisomer (35%) ^{1}H NMR[22] ($CDCl_3$) δ 1.35 (t, J = 7.25 Hz, 6H, $POCH_2\underline{CH_3}$), 2.38-2.47 (m, 2H, H_2C-4), 2.96-3.23 (m, 1H, HC-3 and O-H), 4.07-4.33 (m, 4H, $POCH_2$), 4.60 (q, J = 7.50 Hz, 1H, HC-5), 4.78 (d, J = 7.50 Hz, 1H, HC-1'), 7.29-7.45 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 21.17.

General Procedure for the Preparation of Ethyl (4*R,5*R**)-4,5-epoxy-2-diethoxyphosphoryl alkanoate (4*R**,5*R**)-9c-e.** To a stirred solution of 4-alkenoate **8** (7.0 mmol) in CH_2Cl_2 (15 mL) a solution of m-chloroperbenzoic acid (70%)(1.9 g; 7.7 mmol) in CH_2Cl_2 (25 mL) was added at r.t. The reaction mixture was stirred at this temperature for 24 h (**9c,d**) or 48 h (**9e**) and 10% aqueous Na_2CO_3 solution was added until the iodine test for the presence of peracid was negative. The organic layer was separated, washed with 5% Na_2CO_3 (10 mL), H_2O (10 mL), and brine (10 mL) dried and evaporated to give crude product which was purified by column chromatography (silica gel, $CHCl_3$: acetone = 9 : 1 as eluent).

Ethyl 4,5-epoxy-2-diethoxyphosphorylhexanoate (9c); mixture of diastereoisomers, oil, 82 % yield; R_f = 0.33 ($CHCl_3$: acetone = 8 : 1); IR (film) ν 1736 (C=O), 1252 (P=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25-1.39 (m, 6H, $CO_2CH_2\underline{CH_3}$ and $POCH_2\underline{CH_3}$), 1.80-2.42 (m, 2H, H_2C-3), 22.64-3.25 (m, 3H, HC-2, HC-4 and HC-5), 4.08-4.32 (m, 6H, $POCH_2$ and $COCH_2$); ^{31}P NMR ($CDCl_3$) δ 22.50, 22.60.

Ethyl (4*R,5*R**)-4,5-epoxy-2-diethoxyphosphoryloctanoate (4*R**,5*R**)-(9d)**; mixture of diastereoisomers in 60/40 ratio, oil, 91 % yield; R_f = 0.37 ($CHCl_3$: acetone = 8 : 1); IR (film) ν 1756 (C=O), 1260 (P=O) cm^{-1}; major diastereoisomer (60%) ^{1}H NMR[22] ($CDCl_3$) δ 0.94 (t, J = 7.25 Hz, 3H, H_3C-8), 1.25-1.60 (m, 13H, $CO_2CH_2\underline{CH_3}$, $POCH_2\underline{CH_3}$, H_2C-6 and H_2C-7), 1.93 (dddd, J = 13.20, 9.76, 6.25, 3.25 Hz, 1H, HC-3), 2.32 (dddd, J = 13.20, 12.01, 7.00, 4.75 Hz, 1H, HC-3), 2.66-2.98 (m, 2H, HC-4 and HC-5), 3.13 (ddd, J = 23.51, 12.01, 3.25 Hz, 1H, HC-2), 4.08-4.32 (m, 6H, $POCH_2$ and $COCH_2$); ^{31}P NMR[22] ($CDCl_3$) δ 22.39; minor diastereoisomer (40%) ^{1}H NMR[22] ($CDCl_3$) δ 0.98 (t, J = 7.00 Hz, 3H, H_3C-8), 1.25-1.60 (m, 13H, $CO_2CH_2\underline{CH_3}$, $POCH_2\underline{CH_3}$, H_2C-6 and H_2C-7), 2.00-2.23 (m, 2H, H_2C-3), 2.66-2.98 (m, 2H, HC-4 and HC-5), 3.07 (ddd, J = 23.01, 5.50, 3.50 Hz, 1H, HC-2), 4.08-4.32 (m, 6H, $POCH_2$ and $COCH_2$); ^{31}P NMR[22] ($CDCl_3$) δ 22.46.

Ethyl (4*R,5*R**)-4,5-epoxy-2-diethoxyphosphoryl-5-phenylpentanoate (4*R**,5*R**)-(9e)**; mixture of diastereoisomers in 65/35 ratio, oil, 88 % yield; R_f = 0.35 ($CHCl_3$: acetone = 8 : 1); IR (film) ν 1732 (C=O), 1260 (P=O) cm^{-1}; major diastereoisomer (65%) ^1H NMR[22] ($CDCl_3$) δ 1.27 (t, *J* = 7.25 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.33 (td, *J* = 7.25, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 1.34 (td, *J* = 7.00, 0.50 Hz, 3H, $POCH_2\underline{CH_3}$), 2.08-2.52 (m, 2H, H_2C-3), 3.01 (td, *J* = 5.50, 2.00 Hz, 1H, HC-4), 3.20 (ddd, *J* = 23.51, 11.51, 3.25 Hz, 1H, HC-2), 3.69 (d, *J* = 2.00 Hz, 1H, HC-5), 4.10-4.30 (m, 6H, $POCH_2$ and $COCH_2$), 7.19-7.37 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 22.25; minor diastereoisomer (35%) ^1H NMR[22] ($CDCl_3$) δ 1.29 (t, *J* = 7.25 Hz, 3H, $CO_2CH_2\underline{CH_3}$), 1.31 (td, *J* = 7.25, 0.25 Hz, 3H, $POCH_2\underline{CH_3}$), 1.33 (td, *J* = 7.25, 0.25 Hz, 3H, $POCH_2\underline{CH_3}$), 2.08-2.52 (m, 2H, H_2C-3), 3.12 (td, *J* = 5.50, 1.75 Hz, 1H, HC-4), 3.15 (ddd, *J* = 20.76, 8.50, 5.50 Hz, 1H, HC-2), 3.65 (d, *J* = 1.75 Hz, 1H, HC-5), 4.10-4.30 (m, 6H, $POCH_2$ and $COCH_2$), 7.19-7.37 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 22.36.

General Procedure for the Preparation of Diethyl (5*R,1'*S**)-5-(1'-hydroxyalkyl)-2-oxotetrahydrofuran-3-ylphosphonate** (5*R**,1'*S**)**-6c-e.** To the epoxide **9** (5.0 mmol) 30% $HClO_4$ (5mL) was added and the mixture was left overnight at r.t. The reaction mixture was extracted with $CHCl_3$ (4 x 15 mL), combined organic layers were dried and evaporated to give crude product, which was purified by column chromatography (silica gel, EtOAc : MeOH = 95 : 5 as eluent).

Diethyl 5-(1'-hydroxyethyl)-2-oxotetrahydrofuran-3-ylphosphonate (6c); Mixture of four diastereoisomers in 45/25/20/10 ratio, oil, 82 % yield; R_f = 0.20 (AcOEt : MeOH = 95 : 5); IR (film) ν 3376 (O-H), 1776 (C=O), 1248 (P=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15-1.30 (m, 3H, CH_3-C-1'), 1.32-1.42 (m, 6H, $POCH_2\underline{CH_3}$), 2.28-2.80 (m, 3H, H_2C-4 and O-H), 3.10-3.30 (m, 1H, HC-3), 3.74-4.57 (m, 6H, $POCH_2$, HC-5 and HC-1'); ^{31}P NMR ($CDCl_3$) δ 21.75 (45%), 21.67 (25%), 21.54 (20%), 21.43 (10%).

Diethyl (5*R,1'*S**)-5-(1'-hydroxybutyl)-2-oxotetrahydrofuran-3-ylphosphonate (5*R**,1'*S**)-(6d)**; mixture of diastereoisomers in 60/40 ratio, oil, 72 % yield; R_f = 0.36 (AcOEt : MeOH = 95 : 5); IR (film) ν 3384 (O-H), 1772 (C=O), 1236 (P=O) cm^{-1}; major diastereoisomer (60%) ^1H NMR[22] ($CDCl_3$) δ 0.95 (t, *J* = 7.00 Hz, 3H, H_3C-4'), 1.36 (td, *J* = 7.25, 0.50 Hz, 6H, $POCH_2\underline{CH_3}$), 1.25-1.65 (m, 4H, H_2C-2' and H_2C-3'), 2.36-2.88 (m, 3H, H_2C-4 and O-H), 3.31 (dt, *J* = 23.76, 10.25 Hz, 1H, HC-3), 3.88-4.00 (m, 1H, HC-1'), 4.13-4.30 (m, 4H, $POCH_2$), 4.57 (td, *J* = 7.25, 2.75 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.63; minor diastereoisomer (40%) ^1H NMR[22] ($CDCl_3$) δ 0.95 (t, *J* = 7.00 Hz, 3H, H_3C-4'), 1.39 (t, *J* = 7.25 Hz, 6H, $POCH_2\underline{CH_3}$), 1.25-1.65 (m, 4H, H_2C-2' and H_2C-3'), 2.36-2.88 (m, 3H, H_2C-4 and O-H), 3.33 (dt, *J* = 23.76, 10.25 Hz, 1H, HC-3), 3.88-4.00 (m, 1H, HC-1'), 4.13-4.30 (m, 4H, $POCH_2$), 4.44 (ddd, *J* = 9.00, 7.00, 4.00 Hz, 1H, HC-5); ^{31}P NMR[22] ($CDCl_3$) δ 21.37.

Diethyl (5*R,1'*S**)-5-(1'-hydroxyphenylmethyl)-2-oxotetrahydrofuran-3-ylphosphonate (5*R**,1'*S**)-(6e)**; mixture of diastereoisomers in 65/35 ratio, oil, 90 % yield; R_f = 0.36 (AcOEt : MeOH = 95 : 5); IR (film) ν 3344 (O-H), 1772 (C=O), 1252 (P=O) cm^{-1}; major diastereoisomer (65%) ^1H NMR[22] ($CDCl_3$) δ 1.27-1.40 (m, 6H, $POCH_2\underline{CH_3}$), 2.15-2.75 (m, 2H, H_2C-4), 3.20 (ddd, *J* = 23.26, 10.76, 5.75 Hz, 1H, HC-4), 4.08-4.37 (m, 4H, $POCH_2$), 4.81 (ddd, *J* = 7.75, 6.25, 3.00 Hz, 1H, HC-5), 5.15 (d, *J* = 3.00 Hz, 1H, HC-5), 7.30-7.41 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 21.52; minor diastereoisomer (35%) ^1H NMR[22] ($CDCl_3$) δ 1.27-1.40 (m, 6H, $POCH_2\underline{CH_3}$), 2.15-2.75 (m, 2H, H_2C-4), 3.13 (dt, *J* = 24.01, 10.26 Hz, 1H,

HC-4), 4.08-4.37 (m, 4H, $POCH_2$), 4.65 (td, J = 6.75, 3.75 Hz, 1H, HC-5), 5.14 (d, J = 3.75 Hz, 1H, HC-5), 7.30-7.41 (m, 5H, Ph); ^{31}P NMR[22] ($CDCl_3$) δ 21.63.

Preparation of (5*R*,1'*R*)-5-(Hydroxy-phenyl-methyl)-3-methylidenetetrahydro-2-furanone (5*R*,1'*R*)-(**7e**). A mixture of AD-mix-β (2.80 g) and potassium osmate dihydrate (6.0 mg, 0.8 mol%) in 50% aqueous *tert*-BuOH (20 mL) was stirred at r.t. until two clear phases were formed. Then $CH_3SO_2NH_2$ (0.19 g, 2.0 mmol) was added. The resultant mixture was cooled to 0°C and a solution of alkenoic acid **4e** (0.625g; 2 mmol) in 50% aqueous *tert*-BuOH (4 mL) was added in one portion. After stirring for 2 h the mixture was allowed to warm to r.t. and was stirred for additional 48 h. The reaction was quenched with Na_2SO_3 (6.0 g), stirred for 1 h and acidified to pH ~2 with 3N HCl. Then solvents were evaporated under reduced pressure and the residue was extracted with $CHCl_3$ (5 x 20 mL). Combined chloroform extracts were dried over $MgSO_4$ and evaporated. Crude product was purified by column chromatography (silica gel, AcOEt/MeOH, 95/5, as eluent) to give 0.29g (71 %) of (5*R*,1'*R*)-(**7e**); $[\alpha]_D^{20}$ = -42.7° (c 1.038, $CHCl_3$). Spectral data identical with the data of (5*R**,1'*R**)-(**7e**). Anal ($C_{12}H_{12}O_3$) C, H.

Preparation of Mosher's ester of (5*R*,1'*R*)-7e.

To a solution of 2-furanone (5*R*,1'*R*)-**7e** (16 mg; 0.08 mmol) in CH_2Cl_2 (2 mL) and pyridine (0.5 mL), (R)-(-)- α-methoxy-α-(trifluoromethyl)phenylacetic acid chloride (40 mg; 0.16 mmol) was added and the reaction mixture was stirred at r.t. for 14 h. Solvents were evaporated under reduced pressure and the residue was extracted with Et_2O (4 x 5 mL). Combined ether layers were washed with 0.1N HCl (5 mL) and H_2O (5mL), dried and evaporated. Yield 32 mg (95%); mixture of diastereoisomers in 95/5 ratio.

(2*S*, 1'*R*, 2''*R*)-(4''-methylidene-5''-oxo-tetrahydrofuran-2''-yl)-(phenyl)-methyl 3,3,3-trifluoro-2-methoxy-2-phenyl-propionate; oil; major diastereoisomer (95%); ^{1}H NMR[22] ($CDCl_3$) δ 2.58 (ddt, J = 17.76, 5.75, 2.50 Hz, 1H, HC-4), 2.81 (ddt, J = 17.76, 8.25, 2.50 Hz, 1H, HC-4), 3.47 (q, J = 1.25 Hz, 3H, OCH_3), 4.82 (td, J = 8.25, 5.75 Hz, 1H, HC-5), 5.46 (t, J = 2.50 Hz, 1H, =CH), 6.01 (d, J = 5.75 Hz, 1H, HC-1'), 6.13 (t, J = 2.50 Hz, 1H, =CH), 7.22-7.50 (m, 10H, Ph).

(2*S*, 1'*S*, 2''*S*)-(4''-methylidene-5''-oxo-tetrahydrofuran-2''-yl)-(phenyl)-methyl 3,3,3-trifluoro-2-methoxy-2-phenyl-propionate; oil; minor diastereoisomer (5%); ^{1}H NMR[22] ($CDCl_3$) δ 2.60 (ddt, J = 17.76, 6.50, 2.50 Hz, 1H, HC-4), 2.77 (ddt, J = 17.76, 8.25, 2.50 Hz, 1H, HC-4), 3.61 (q, J = 1.25 Hz, 3H, OCH_3), 4.84 (td, J = 8.25, 6.50 Hz, 1H, HC-5), 5.58 (t, J = 2.50 Hz, 1H, =CH), 5.88 (d, J = 6.50 Hz, 1H, HC-1'), 6.23 (t, J = 2.50 Hz, 1H, =CH), 7.22-7.50 (m, 10H, Ph).

Lipophilicity calculations. Logarithms of the n-octanol/water partition coefficients (*logP*) of the new furanones were calculated by means of software package Pallas (CompuDrug Chemistry, Hungary). In these calculations $logP_{CDR}$, $logP_{ATOMIC}$ and $logP_{ATOMICA}$ were obtained using three different sets of additive and constitutive atomic constants reflecting furanones structures. Additionally, the values of $logP_{combined}$ were predicted according to the formula derived as the weighed average of lipophilicity obtained in three individual procedures:

$$logP_{combined} = 0.313\ logP_{CDR} + 0.208\ logP_{ATOMIC} + 0.479\ logP_{ATOMICA}$$

where $logP_{CDR}$ means that calculated *log*P values have taken into account the lipophilic fragmental constants and their correction terms derived from an extended set of about 1000 experimental n-octanol/water partition coefficients, by using the constrained least-squares technique as proposed by Rekker and De Kort[24] and further modified by producer of Pallas software; $logP_{ATOMIC}$ means that calculated *log*P values have taken into account the additive and constitutive predefined lipophilicity of 222 atomic contributions calculated by applying the Monte Carlo optimization and linear regression analysis to the matrix of experimental values of the n-octanol/water partition coefficients determined for 1868 compounds as reported by Broto et al.[25]; $logP_{ATOMICA}$ means that calculated *log*P value have taken into account the predefined lipophilicity values of 120 atomic state subtypes (which included their oxidation and hybridized state and the influence of immediately bonded atoms) estimated by using the simple least-squares fitting method to the set of experimental values of the n-octanol/water partition coefficients collected for 893 compounds as described by Viswanadhan et al.[26]

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26. Viswanadhan V.N.; Ghose A.K.; Revankar, G.N., Robins R.K. Hydrophobicity and residue-residue constants in globular proteins. *J. Chem. Inf. Comput. Chem.* **1987**, *29*, 163-171.

Experimental determination of logP for 7a. The partition coefficient P was determined as described[4,27] using a Pharmacia LKB Ultraspec III spectrophotometer. Three experiments were made in which furanone **7a** (1 mg) was partitioned between 100 mL of water and 1-octanol in different volume ratios (water/1-octanol: 25/75, 50/50 and 75/25) and absorbance for the water layer was measured (A = 0.585, 0.620 and 0.656 respectively, λ_{max} = 215 nm). Concentration in the water layer was then determined and concentration in the octanol layer was obtained by difference. From these concentrations partition coefficients P were calculated (P = 1.244, 1.228 and 1.219 respectively). The average value for P was then calculated $P_{average}$ = 1.230 and logP = 0.09 ± 1.

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Log*P* prediction for 7e

Database: a:7e.cdb

$\log P_{CDR} = 1.79$
$\log P_{ATOMIC} = 1.32$
$\log P_{ATOMICA} = 2.01$
$\log P_{combined} = 0.313 \log P_{CDR} + 0.208 \log P_{ATOMIC} + 0.479 \log P_{ATOMICA} = 1.80$

PREDICTION DETAILS
Fragment database CDR

Occ.	Name of contributor	Value
1	CONJUGATION II.	0.29
1	PROXIMITY: 2C SEPARATION	0.58
7	-CH-	0.34
2	-CH2-	0.52
1	AL-COO-AL	-1.29
1	AL-OH	-1.49
2	C-ATOM	0.16

$\log P_{CDR} = 1.79$

Fragment database ATOMIC

Occ.	Name of contributor	Value
1	CONJUGATION 1	0.54
1	C11	0.46
2	C111	0.03
2	C112	-0.55
1	C144	0.09
1	C2	0.74
5	C44	0.31
12	H	0.00
1	O11C11C12	0.59
1	O1C11	-0.94
1	O2C11	-0.68

$\log P_{ATOMIC} = 1.32$

Fragment database ATOMICA

Occ.	Name of contributor	Value
1	002_C:CH2R2	-0.20
2	008_C: =CHR2X	-0.41
1	015_C: =CH2	0.14
1	017_C: =CR2	0.02
5	024_C: R[CH]R	0.14
1	025_C: R[CR]R	0.18
1	040_C: R-C(=X)-X,R-C#X, X=C=X	-1.07
9	047_H: C1(SP3), C0(SP2)	0.21
1	050_H: H-HETEROATOM	-0.15
2	052_H: H-C0(SP3)[1X ON THE NEXT C]	0.28
1	056_O: IN ALCOHOL	-0.37
1	058_O: =O	0.74
1	060_O: AL-O-AR,AR20, R%O%R, R-O-C=X	0.38

$\log P_{ATOMICA} = 2.01$