A new photocleavable linker in solid phase chemistry for ether cleavage

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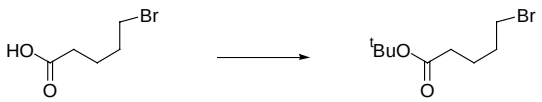
Supporting Information: Full experimental procedures for the synthesis of **9**. General procedures for the attachment of alcohols to resin bound ethers **1** and general procedures for the photolytic cleavage of the ethers **1a-c**.

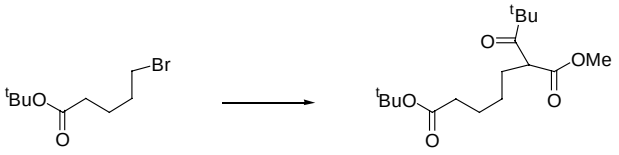
General Methods: All quoted temperatures are uncorrected. Materials and reagents were of the highest grade available commercially and used without further purification. Commercial resin (TentaGel S NH_2) was purchased from Rapp Polymere, Tübingen, Germany. The polystyrene resin (200 μm beads, 1% DVB) was obtained from Novartis AG. THF was distilled from potassium/benzophenone before use. The level of attachment of the resin was estimated by Fmoc-cleavage/UV-detection, picrate monitoring or combustion analysis of bromine. All NMR spectra were recorded on Varian instruments 300 MHz or 400 MHz or on a Bruker instrument 500 MHz. ^{1}H and ^{13}C NMR data were measured in the indicated solvent with tetramethylsilane as internal standard. The gel phase data was obtained by NMR-measurement of the resin, swollen in $CDCl_3$. Fast atom bombardment (FAB) mass spectra were obtained with *m*-nitrobenzyl alcohol as matrix. Elementary analyses were performed by Mikroanalytisches Labor, University of Basel, or Mikroanalytisches Labor Novartis AG Basel. Analytical HPLC (reverse phase) was performed on Hewlett Packard 1050 series or Waters Alliance 2690 using a column from Merck Lichrospher 100, RP 18 (5μm), 250 mm x 4 mm, flow: 1ml/min. Gradients used for elution were as follows: 0-20 min, 40–100% B in A with A = water and B = acetonitrile. Gas chromatography was performed on Carlo Erba Instruments GC 6000 Vega Series 2, using a column from Machery Nagel Optima δ3, 25 m x 0.20 mm. The temperature program was as follow: 60°C (5min), 10°C/min, 300°C (10 min). Photolyses were performed on Oriel 68810 with Osram 500W mercury arc high-pressure lamp in combination with a cut-off filter or on Rayonet RPR-100 with up to 16 x 21W lamps of a spectral energy distribution from 370-250 nm with the maximum at 300 nm. The solvents for photolysis were deoxygenated before use by bubbling argon through it for 15 minutes.



3 **3a**

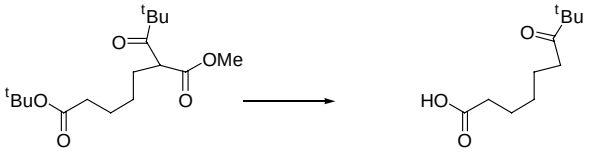
5-Bromovaleric acid-*tert.*-butylester (3a). 5-Bromovaleric acid **(3)** (7.05 g, 37.8 mmol) was stirred with isobutylene (35.0 ml, 375 mmol, 10 eq) in presence of conc. sulfuric acid (520 μl, 9.42 mmol, 0.25 eq) in a pressure apparatus for 5 h at room temperature. The reaction mixture was diluted with sat. $NaHCO_3$ (100 ml) and extracted with ether (3 x 100 ml). The organic

layers were dried ($MgSO_4$) and concentrated in vacuo to yield 5-Bromovaleric acid-*tert.*-butylester **(3a)** (8.81 g, 37.1 mmol, 98%) as a clear oil: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.41 (t, 2H, J = 6.5 Hz), 2.25 (t, 2H, J = 7.2 Hz), 1.92-1.85 (m, 2H), 1.78-1.71 (m, 2H), 1.45 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.4, 80.2, 34.4, 33.0, 31.9, 28.0, 23.5; IR (film) 2977, 2933, 1729, 1457, 1392, 1367, 1256, 1218, 1156, 848 cm^{-1}; MS (EI) m/z 223, 221, 183, 181, 165, 163, 137, 135, 101, 57, 41; Anal. Calcd for $C_9H_{17}BrO_2$: (237.14) C 45.58, H 7.23, O 13.49; Found: C 45.60, H 7.24, O 13.59.



3a **4**

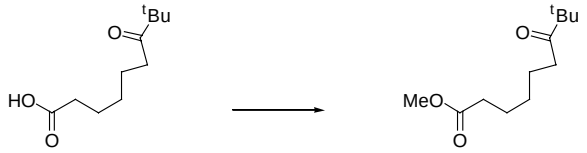
2-*tert.*-Butylcarbonylpimelic acid-1-methyl-7-*tert.*-butyldiester (4). To a cooled (-10°C) suspension of sodium hydride (3.00 g, 76.8 mmol, 3.0 eq) in DMF (200 ml) was added methyl-4,4-dimethyl-3-oxo-pentanoate (12.3 g, 76.8 mmol, 3.0 eq) and allowed to warm to room temperature. After stirring for 30 min at room temperature, the solution was cooled to 0°C and a solution of 5-Bromovaleric acid-*tert.*-butylester **(3a)** (6.07 g, 25.6 mmol) in DMF (20 ml) was added. The resulting solution was allowed to warm to room temperature and stirred for 65 h. The colorless solution was diluted with water (200ml) and extracted with ether (3 x 300 ml). The organic layers were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography on silica gel (pentane/ether 20:1, 5:1) yielded diester **4** (6.31 g, 20.1 mmol, 78%) as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.89 (t, 1H, J = 7.1 Hz), 3.68 (s, 3H), 2.20 (t, 2H, J = 7.4 Hz), 1.91-1.80 (m, 1H), 1.79-1.72 (m, 1H), 1.59 (qu, 2H, J = 7.2 Hz), 1.44 (s, 9H), 1.34-1.22 (m, 2H), 1.16 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 209.6, 172.8, 169.9, 80.0, 52.2, 52.2, 45.3, 35.1, 29.6, 28.0, 27.2, 26.1, 24.8; IR (film) 2973, 2870, 1731, 1709, 1479, 1458, 1435, 1392, 1367, 1255, 1224, 1157, 1097, 1052 cm^{-1}; MS (EI) m/z 258, 241, 227, 209, 201, 183, 174, 156, 128, 123, 101, 85, 69, 57, 41; Anal. Calcd for $C_{17}H_{30}O_5$: (314.42) C 64.94, H 9.62, O 25.44; Found: C 65.10, H 9.65, O 25.53.



4 **4a**

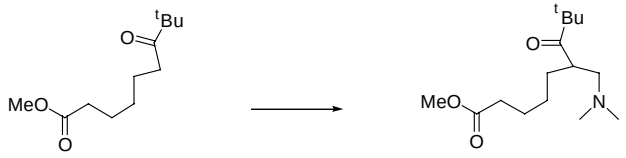
8,8-Dimethyl-7-oxo-pelargonic acid (4a). To a solution of 2-*tert.*-butylcarbonylpimelic acid-1-methyl-7-*tert.*-butyldiester **(4)** (4.30 g, 13.7 mmol) in methanol/water 3:1 (60 ml) was added powdered potassium hydroxide (1.53 g, 27.4 mmol, 2.0 eq). After refluxing the reaction mixture for 6 h, the solution was acidified with 1 M hydrochloric acid (20 ml) concentrated on vacuo to 20 ml and extracted with ether (3 x 50 ml). The organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield 8,8-Dimethyl-7-oxo-pelargonic acid **(4a)** (2.70 g, 13.5 mmol, 99%) which crystallizes out of hexane: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.49 (t, 2H, J = 7.2 Hz), 2.36 (t, 2H, J = 7.4 Hz), 1.70-1.60 (m, 2H), 1.62-1.53 (m, 2H), 1.38-1.30 (m, 2H), 1.13 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 216.0, 179.5, 44.1, 36.1, 33.8, 28.6, 26.3, 24.5, 23.4; IR (KBr) 3300-2500, 2968, 2938, 2870, 1715, 1698, 1478, 1429, 1413,

1368, 1345, 1302, 1264, 1240, 1200, 1100, 1059, 982, 936, 728 cm^{-1}; MS (EI) m/z 200 (M^+), 183, 143, 125, 115, 97, 85, 69, 57, 41; mp 49-51°C; Anal. Calcd for $C_{11}H_{20}O_3$: (200.28) C 65.97, H 10.07, O 23.97; Found: C 65.92, H 9.93, O 24.04.



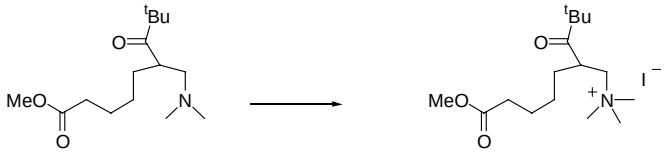
4a **5**

8,8-Dimethyl-7-oxo-pelargonic acid methylester (5). To a solution of 8,8-Dimethyl-7-oxo-pelargonic acid **(4a)** (2.79 g, 13.9 mmol) in methanol (40 ml) were added 2 spatula tips *p*-toluenesulfonic acid. After stirring this solution under argon for 6 h at room temperature the solvent was removed on vacuo, diluted with water (50 ml) and extracted with ether (3 x 50 ml). The organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield 8,8-Dimethyl-7-oxo-pelargonic acid methylester **(5)** (2.92 g, 13.6 mmol, 98%) as a pale yellow oil without further purification: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.67 (s, 3H), 2.48 (t, 2H, J = 7.2 Hz), 2.31 (t, 2H, J = 7.4 Hz), 1.67-1.59 (m, 2H), 1.62-1.52 (m, 2H), 1.36-1.25 (m, 2H), 1.13 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 215.7, 174.1, 51.4, 44.0, 36.1, 33.8, 28.7, 26.3, 24.7, 23.4; IR (film) 2953, 2868, 1740, 1705, 1478, 1463, 1437, 1366, 1256, 1199, 1172, 1099, 1060, 991 cm^{-1}; MS (EI) m/z 214 (M^+), 183, 157, 139, 125, 111, 97, 87, 69, 57, 41; Anal. Calcd for $C_{12}H_{22}O_3$: (214.31) C 67.25, H 10.35, O 22.40; Found: C 67.03, H 10.42, O 22.40.



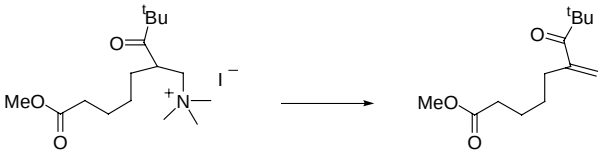
5 **6**

8,8-Dimethyl-6-*N*,*N*-dimethylaminomethyl-7-oxo-pelargonic acid methylester (6). To a solution of 8,8-Dimethyl-7-oxo-pelargonic acid methylester **(5)** (2.58 g, 12.0 mmol) in acetonitrile (100 ml) was added *N*,*N*-Dimethylmethyleniminiumchloride (Eschenmoser salt) (5.81 g, 60.2 mmol, 5.0 eq) and *p*-toluenesulfonic acid (2.29 g, 12.0 mmol, 1.0 eq). After refluxing the solution under argon for 16 h at 80°C the colorless mixture was cooled to room temperature, treated with 2 N sodium hydroxide solution (15 ml), diluted with water (50 ml) and extracted with ether (3 x 50 ml). The organic layers were washed with water (150 ml) dried ($MgSO_4$) and concentrated in vacuo to yield 8,8-Dimethyl-6-*N*,*N*-dimethyl-aminomethyl-7-oxo-pelargonic acid methylester **(6)** (2.94 g, 10.8 mmol, 90%) without further purification as a yellow oil, which crystallizes at 4°C: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.66 (s, 3H), 3.11 (qu, 1H, J = 6.6 Hz), 2.38 (dd, 1H, J = 12.3; 6.5 Hz), 2.29 (t, 2H, J = 7.5 Hz), 2.19 (dd, 1H, J = 12.2; 6.6 Hz), 2.18 (s, 6H), 1.65-1.55 (m, 2H), 1.55-1.44 (m, 2H), 1.31-1.17 (m, 2H), 1.15 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 218.3, 174.0, 62.5, 51.4, 46.0, 44.5, 44.1, 33.8, 30.8, 27.3, 26.3, 25.1; IR (film) 2951, 2862, 2818, 2767, 1739, 1702,1462, 1366, 1264, 1196, 1174, 1045, 982 cm^{-1}; MS (EI) m/z 271 (M^+), 256, 240, 214, 186, 156, 141, 125, 98, 84, 69, 58, 41; Anal. Calcd for $C_{15}H_{29}NO_3$: (271.40) C 66.38, H 10.77, N 5.16, O 17.69; Found: C 66.32, H 10.76, N 5.32, O 17.89.



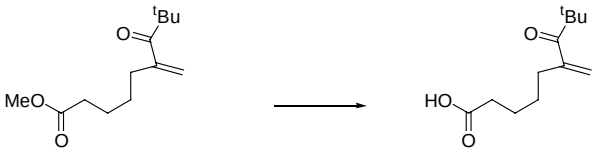
6 **6a**

8,8-Dimethyl-7-oxo-6-(methyl-*N*,*N*,*N*-trimethylammoniumiodide)-pelargonic acid methylester (6a). To 8,8-Dimethyl-6-*N*,*N*-dimethylaminomethyl-7-oxo-pelargonic acid methyl ester **(6)** (2.78 g, 10.2 mmol) was added methyl iodide (20 ml, 321 mmol, 31.0 eq). After stirring this solution under argon for 48 h at room temperature it was concentrated on vacuo to yield 8,8-Dimethyl-7-oxo-6-(methyl-*N*,*N*,*N*-trimethyl-ammoniumiodid)-pelargonic acid methylester **(6a)** (4.15 g, 10.0 mmol, 98%) as a pale yellow solid without further purification: ^{1}H-NMR (400 MHz, CD_3OD) δ 3.76 (dd, 1H, J = 13.5, 8.2 Hz), 3.34 (s, 3H), 3.01 (d, 1H, J = 13.4 Hz), 2.98 (d, 1H, J = 8.4 Hz), 2.82 (s, 9H), 2.06 (t, 2H, J = 7.3 Hz), 1.45-1.27 (m, 4H), 1.16-1.08 (m, 2H), 0.97 (s, 9H); ^{13}C-NMR (101 MHz, CD_3OD) δ 216.6, 176.4, 68.1, 55.4, 52.9, 46.5, 43.3, 35.1, 33.1, 28.9, 27.7, 26.5; IR (KBr) 3000, 2952, 2940, 2865, 1734, 1699, 1479, 1459, 1438, 1403, 1368, 1302, 1288, 1198, 1180, 1157, 1134, 971, 957 cm^{-1}; MS (FAB) m/z 286 $(M\text{-}I)^+$, 200, 69, 57, 43, 41; mp 159-161°C; Anal. Calcd for $C_{16}H_{32}INO_3$: (413.34) C 46.49, H 7.80, N 3.39, O 11.61; Found: C 46.21, H 7.78, N 3.45, O 11.72.



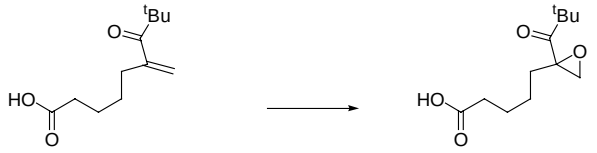
6a **7**

8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid methylester (7). To a solution of 8,8-Dimethyl-7-oxo-6-(methyl-*N*,*N*,*N*-trimethylammoniumiodide)-pelargonic acid methylester **(6a)** (3.18 g, 7.69 mmol) in acetonitrile (50 ml) was added potassium-*tert.*-butoxide (890 mg, 7.93 mmol, 1.1 eq.). After stirring this suspension at room temperature for 2.5 h, 1 N hydrochloric acid (10 ml) was added. The aqueous layer was separated and extracted with ether (2 x 10 ml). Combined organic layers were washed with 10 % sodiumthiosulfate solution (20 ml) dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography on silica gel (pentane/ether 20:1, 0:1) yielded 8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid methylester **(7)** (1.39 g, 6.15 mmol, 80%) as a pale yellow oil: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.39 (d, 2H, J = 11.5 Hz), 3.67 (s, 3H), 2.32 (t, 2H, J = 7.4 Hz), 2.25 (t, 2H, J = 7.6 Hz), 1.70-1.60 (m, 2H), 1.49-1.40 (m, 2H), 1.23 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 211.6, 174.0, 148.1, 117.0, 51.4, 44.0, 33.9, 33.7, 27.7, 27.5, 24.4; IR (film) 2953, 2870, 1740, 1685, 1670, 1478, 1462, 1436, 1366, 1206, 1174, 1079, 995, 921 cm^{-1}; MS (EI) m/z 226 (M^+), 195, 169, 137, 109, 95, 81, 67, 57, 41; Anal. Calcd for $C_{13}H_{22}O_3$: (226.32) C 68.99, H 9.80, O 21.21; Found: C 68.89, H 9.72, O 21.01.



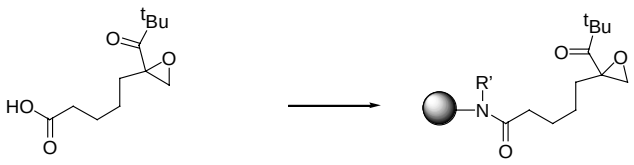
7 **7a**

8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid (7a). To a solution of 8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid methylester **(7)** (300 mg, 1.33 mmol) in methanol/water 3:1 (10 ml) was added lithiumhydroxide monohydrate (168 mg, 3.98 mmol, 3.0 eq). After strirring at room temperature for 3 h the solution was concentrated on vacuo to 3 ml, acidified with sat. NH_4Cl (15 ml) and extracted with ether (3 x 25 ml). The organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield 8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid **(7a)** (266 mg, 1.25 mmol, 95%) without further purification as a yellow oil: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 11.14 (s, br, 1H), 5.40 (d, 2H, J = 12.1 Hz), 2.37 (t, 2H, J = 7.4 Hz), 2.26 (t, 2H, J = 7.6 Hz), 1.71-1.61 (m, 2H), 1.51-1.40 (m, 2H), 1.24 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 211.7, 179.9, 148.0, 117.2, 44.0, 33.9, 33.8, 27.7, 27.4, 24.1; IR (film) 3500-2500, 2955, 2871, 1710, 1685, 1670, 1483, 1479, 1414, 1395, 1366, 1288, 1221, 1062, 995, 932 cm^{-1}; MS (EI) m/z 212 (M^+), 194, 155, 137, 127, 109, 95, 85, 81, 69, 57, 41; Anal. Calcd for $C_{12}H_{20}O_3$: (212.29) C 67.89, H 9.50, O 22.61; Found: C 67.67, H 9.66, O 22.76.



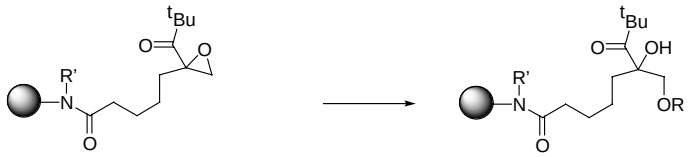
7a **8**

8,8-Dimethyl-6-methylenoxide-7-oxo-pelargonic acid (8). To a solution of 8,8-Dimethyl-6-methylen-7-oxo-pelargonic acid **(7a)** (616 mg, 2.90 mmol) in acetone (10 ml) was added dimethyldioxirane solution (180 ml, ~0.05 M in acetone). After stirring at room temperature for 12h, the solution was concentrated in vacuo to 10 ml. Another addition of dimethyldioxirane solution (250 ml, ~0.05 M in acetone) with stirring for 12 h followed. The reaction mixture was concentrated in vacuo to 10 ml, diluted with ether (150 ml) and washed with sat. NH_4Cl (2 x 100 ml). The organic layer was separated, dried ($MgSO_4$) and the solvent was removed in vacuo. Flash chromatography on silica gel (pentane/*tert*.butyl-methylether 3:1) yielded 8,8-Dimethyl-6-methylenoxide-7-oxo-pelargonic acid **(8)** (622 mg, 2.73 mmol, 94%) as colorless crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 11.20 (s, br, 1H), 2.77 (s, 2H), 2.35 (t, 2H, J = 7.5 Hz), 2.27 - 2.17 (m, 1H), 1.64 (quint, 2H, J = 7.5), 1.53 - 1.41 (m, 2H), 1.39 – 1.28 (m, 1H), 1.18 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 213.1, 178.9, 64.1, 51.1, 44.4, 33.5, 33.6, 25.7, 24.6, 24.3; IR (film) 3500-2600, 2957, 2872, 1709, 1701, 1480, 1462, 1414, 1393, 1366, 1285, 1241, 1108, 1065, 978, 915, 734 cm^{-1}; MS (FAB) m/z 229 (MH^+), 211, 127, 85, 69, 57, 41; mp 57-60°C; Anal. Calcd for $C_{12}H_{20}O_4$: (228.29) C 63.13, H 8.83, O 28.03; Found: C 63.19, H 8.70, O 27.95.



8 **9**

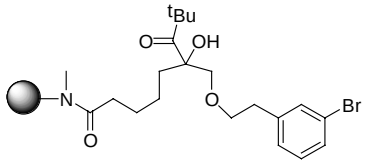
Photolinker-solid support (9). TentaGel S NH_2 (1.00g , 0.28 mmol/g loading) or polystyrene NHMe (1% DVB) (215 mg, 1.3 mmol/g loading) was suspended in dry CH_2Cl_2 (5 ml) and photolinker **8** (96.0 mg, 420 mmol, 1.5 eq), DMAP (9 mg, 0.07 mmol, 0.25 eq) and diisopropylcarbodiimid (DIC, 110 µl, 0.7 mmol, 2.5 eq) were added. The resin was shaken for 18 h at room temperature and washed with CH_2Cl_2, DMD, CH_2Cl_2 and dried to yield the photolabile support **1**. Kaiser test revealed complete reaction. TentaGel: Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 213.0, 172.7, 64.1, 51.1, 44.4, 36.2, 36.1, 25.8, 25.6, 24.6; IR (KBr) 1734 (CO), 1695 (CO) cm^{-1}; Anal. Found: C 65.60, H 8.46, N 0.42, O 24.18. Polystyrene: Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 213.1, 162.5, 64.1, 51.1, 44.4, 33.7, 33.6, 25.8, 24.8, 24.6; IR (KBr) 1735 (CO), 1697 (CO) cm^{-1}; Anal. Found: C 80.24, H 8.24, N 2.11, O 8.14.



9 **1**

General Procedure for Base Induced Epoxide Opening. To a suspension of photolinker resin **9** (~100 mg, PS or TentaGel) in THF (5 ml) were added the alcohol (20 eq) and potassium-*tert.*-butoxide (10 eq) and the mixture was shaken for 15 h at 60°C. Washing (THF, 5% HOAc in MeOH, DMF, CH_2Cl_2, THF) after cooling to room temperature and drying afforded the ether-photolinker resin **1**.

General Procedure for Lewis Acid Induced Epoxide Opening. To a suspension of photolinker resin **9** (~100 mg, PS or TentaGel) in toluene (3 ml) were added the alcohol (6 eq) and $BF_3{\cdot}Et_2O$ (100 µl) and the mixture was shaken for 2.5 days at 100°C. Washing (toluene, DMF, THF, CH_2Cl_2) after cooling to room temperature and drying afforded the ether-photolinker **1**.

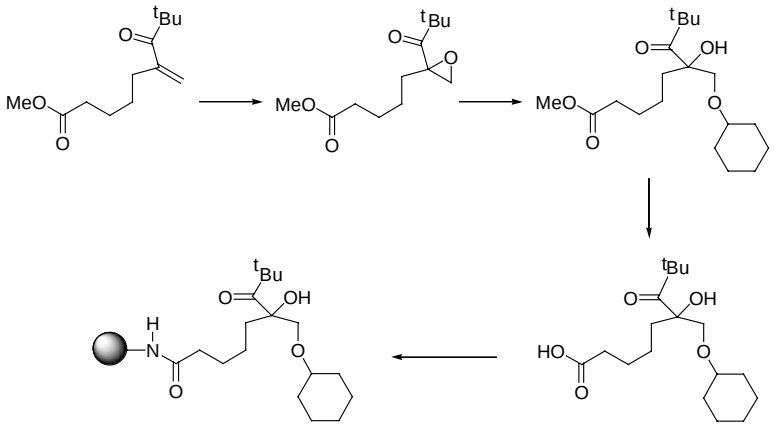


1a

Ether-Photolinker 1a. Ether-Photolinker **1a** was prepared following the general procedure for base induced epoxide opening with polystyrene photolinker resin **9** (149 mg, ~0.19 mmol), *o*-Bromophenyl-ethanol (532 µl, 3.87 mmol, 20 eq), potassium-*tert.*-butoxide (223 mg, 1.93 mmol, 10 eq) and THF (7 ml). Loading: 0.22 mmol/g; Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 213.0, 162.5, 138.9, 134.8, 132.0, 129.3, 127.6, 122.4, 84.2, 72.0, 70.5, 44.6,

40.4, 36.5, 35.7, 31.4, 27.2, 26.5, 25.9; IR (KBr) 3432 (OH), 1729 (CO), 1701 (CO) cm^{-1}; Anal. Found: C 79.79, H 7.82, N 1.73, O 6.25, Br 1.9.

Ether-Photolinker 1b. As there was no possibility of determining the loading with photolinker **1b** after the epoxide opening on solid phase, the alcohol was preloaded onto the linkage unit in solution. The ether bound photolinker was then attached in a last step onto the solid support:



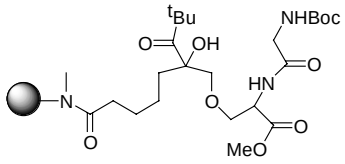
1b

The epoxidation of the olefin was conducted in analogy to the epoxidation described above (**7a→8**) in 91% yield: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.77 (s, 2H), 2.30 (t, 2H, J = 7.5 Hz), 2.25 - 2.20 (m, 1H), 1.63 (quint, 2H, J = 7.5 Hz), 1.52 - 1.38 (m, 2H), 1.37 – 1.22 (m, 1H), 1.18 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 213.1, 173.8, 64.1, 51.5, 51.0, 44.4, 33.8, 33.6, 25.7, 24.8, 24.4; IR (film) 2954, 2871, 1739, 1697, 1481, 1461, 1437, 1392, 1365, 1241, 1198, 1174, 1066, 978, 919 cm^{-1}; MS (EI) m/z 227, 185, 169, 157, 141, 127, 111, 97, 83, 57, 41; Anal. Calcd for $C_{13}H_{22}O_4$: (242.32) C 64.44, H 9.15, O 26.41; Found: C 64.25, H 9.16, O 26.45.

The epoxide opening was performed acid catalyzed by stirring the epoxide (150 mg, 619 µmol) in cyclohexanol (+1% H_2SO_4) (2 ml) at room temperature for 6 h. The reaction mixture was diluted with ether (20 ml) and washed with sat. $NaHCO_3$ (2 x 20 ml) and water (20 ml). The organic layer was separated, dried ($MgSO_4$) and the solvent was removed in vacuo. Flash chromatography on silica gel (pentane/ether 10:1) yielded the cyclohexylether (134 mg, 391 µmol, 63%) as colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.75 (d, 1H, J = 8.7 Hz), 3.66 (s, 3H), 3.46 (s br, 1H), 3.33 (d, 1H, J = 8.7 Hz), 3.25 (td, 1H, J = 8.5 Hz; 3.7 Hz), 2.29 (t, 2H, J = 7.5 Hz), 1.82 – 1.77 (m, 2H), 1.76 – 1.70 (m, 1H), 1.69 - 1.63 (m, 2H), 1.61 – 1.54 (m, 1H), 1.59 (t, 2H, J = 7.6 Hz), 1.49 – 1.46 (m, 1H), 1.43 – 1.37 (m, 1H), 1.30 – 1.22 (m, 6H), 1.25 (s, 9H); ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 218.3, 174.0, 84.1, 77.9, 73.2, 51.5, 44.6, 36.8, 33.9, 31.8, 27.0, 25.7, 25.2, 23.6, 23.2; IR (film) 3520, 2935, 2863, 1740, 1696, 1461, 1433, 1367, 1239, 1172, 1100 cm^{-1}; MS (EI) m/z 293, 257, 230, 199, 175, 143, 117, 99, 83, 55, 41; Anal. Calcd for $C_{19}H_{34}O_5$: (342.48) C 66.63, H 10.01, O 23.36; Found: C 66.77, H 10.24, O 23.22.

Deprotection of the methylester to the free acid was performed in analogy to the reaction described above (**7→7a**) in 82% yield: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 10.05 (s br, 1H), 3.76 (d, 1H, J = 8.8 Hz), 3.34 (d, 1H, J = 8.8 Hz), 3.28 – 3.24 (m, 1H), 2.33 (t, 2H, J = 7.4 Hz), 1.83 – 1.74 (m, 2H), 1.71 – 1.52 (m, 6H), 1.50 – 1.30 (m, 2H), 1.28 – 1.21 (m, 6H), 1.25 (s, 9H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 218.3, 179.5, 84.1, 78.0, 73.3, 44.6, 36.8, 33.9, 31.8, 27.0, 25.7, 25.0, 23.6, 23.0; IR (film) 3600-2850, 2933, 2859, 1709, 1694, 1482, 1462, 1391,

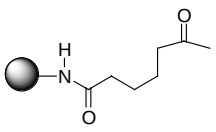
1366, 1244, 1098 cm^{-1}; MS (ESI) m/z 693 ($2M^-$+K), 677 ($2M^-$+Na), 327 (M^-); Anal. Calcd for $C_{18}H_{32}O_5$: (328.45) C 65.82, H 9.82, O 24.36; Found: C 65.94, H 9.60, O 24.50.
Attachment to the solid support (TentaGel S NH_2) was conducted in analogy to the reaction described above (**8**→**9**) yielding cyclohexyl-ether-photolinker-TentaGel **1b**: Loading: 0.15 mmol/g; Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 218.2, 172.8, 84.1, 77.9, 73.4, 44.6, 36.9, 36.4, 31.8, 27.2, 26.0, 25.7, 23.6, 23.4; IR (KBr) 3448 (OH), 1735 (CO), 1654 (CO); Anal. Found: C 65.35, H 8.85, N 0.42, O 25.16.



1c

Ether-Photolinker 1c. Coupling: Ether-Photolinker **1c** was prepared following the general procedure for base induced epoxide opening with polystyrene photolinker resin **9** (103 mg, ~0.13 mmol), Fmoc(L)-serine-methylester (275 mg, 804 μmol, 6 eq), $BF_3{\cdot}Et_2O$ (100 μl) and toluene (3 ml). **Amine Deprotection:** Piperidine (20%) in DMF (2 ml) was added, and the suspension was mixed for 7 min at room temperature. The supernatant was sucked off, and the resin was washed with DMF (loading: 0.05 mmol/g). **Coupling:** To a suspension of the resin (73 mg, ~ 95 μmol) in CH_2Cl_2 (1.5 ml) were added BocGlycine (166 mg, 950 μmol, 10eq), CMC (242 mg, 569 μmol, 6 eq) and DMAP (7.0 mg, 57 μmol, 0.6 eq) and the mixture was shaken for 2 days at room temperature. Washing (CH_2Cl_2, DMF, CH_2Cl_2) and drying afforded dipeptide-photolinker resin **1c**. Loading: 0.03 mmol/g; Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 216.1, 173.4, 169.4, 162.5, 156.7, 85.2, 84.0, 66.3, 63.8, 53.4, 50.8, 47.6, 37.2, 36.1, 35.5, 26.0, 24.7, 23.0, 22.9; IR (KBr) 3434 (OH), 1734 (CO), 1701 (CO), 1654 (CO) cm^{-1}.

General Photolysis Conditions. Photolyses in quartz glass cells (equipped with stir bar) were conducted with 4-10 mg of resin **1**, suspended in 1.5 – 3 ml of solvent in the beam of a 500 W Hg high-pressure arc lamp fitted with a water filter and a cut off filter (295nm) or a photochemical reactor from Rayonet with up to 16 x 21 W lamps of a spectral energy distribution from 370 to 250 nm, with the maximum at 300 nm. The cells were maintained at 20°C and irradiated horizontally with gentle mixing of the beads by means of a magnetic stirrer. After photolysis, a defined amount of standard (decane for GC analysis or naphtalene for RP-HPLC analysis) was added. After mixing, an aliquot was removed and analyzed by GC or reversed-phase HPLC with detection at 254 nm.



10

Resin-bound Methyl-Ketone (10). Cyclohexyl-ether-photolinker-TentaGel **1b** (60 mg) was suspended in two portions of CH_2Cl_2 (8 ml, quartz glass cells) and irradiated according to the general photolysis conditions (see below), followed by washing with THF and CH_2Cl_2 to

yield resin **10** (56 mg) and cyclohexanol: Gel phase ^{13}C-NMR (125.5 MHz, $CDCl_3$) δ 208.7, 172.7, 43.4, 36.2, 30.0, 25.1, 23.3; IR (KBr) 1718 (CO), 1654 (CO) cm^{-1}; Anal. Found: C 65.01, H 8.85, N 0.65, O 24.87.

Stability toward Treatment with Different Reagents. *ortho*-Bromophenetyl-ether-photolinker-Polystyrene **1a** (0.22 mmol/g, 3-6 mg each) was incubated for 2 h with 2 ml of (a) TFA (50% in CH_2Cl_2), rt (b) *p*-TsOH (1 % in toluene), 80°C, (c) $BF_3{\cdot}Et_2O$ (5% in CH_2Cl_2), rt, (d) $LiAlH_4$ (10eq, Et_2O) rt, (e) DIPEA (10% in THF), 60°C (f) DBU (5% in toluene), 80°C (g) hydrazine (10% in THF), rt and (h) KO^tBu (5% in THF), rt; washed (THF and CH_2Cl_2, in case of basic reagents first with 5% HOAc in MeOH) and dried, followed by photolysis. Yields were compared with the photolysis yield of untreated resin **1a**.