1,4-Additions to γ-Aminoalkyl-Substituted α-Methylene γ-Butyrolactones: Synthesis of Highly Functionalized Amino Acid Derivatives

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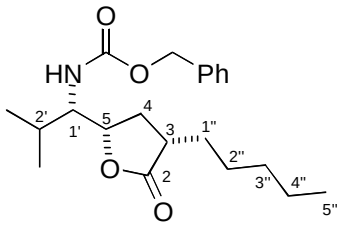
Supporting Information

Contents:

- Full characterization for compounds **4** – **10**.
- X-Ray data for compounds **7a, 7b** and **8**.

Characterization for Compounds 4 – 10

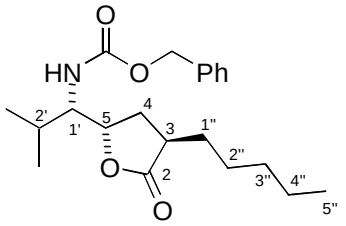
(3S,5S,1'S)- and (3R,5S,1'S)-5-[1-(Benzyloxycarbonylamino)-2-methylpropyl]-3-pentyltetrahydrofuran-2-one (4a/b)



Lactone **4a**: Colourless oil. — $[\alpha]^{20}_{D}$ = –25.6 (*c* = 1.04, $CHCl_3$). — IR (neat) $\tilde{\nu}$ = 3315 cm^{-1} (N-H), 3010, 2930, 2850 (C-H), 1769 (C=O, lactone), 1714 (C=O, carbamate), 1531 (C=C). — ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 6.5 Hz, 3 H, 5"-H), 0.98 (d, ^3J = 6.7 Hz, 3 H, -CH_3), 1.02 (d, ^3J = 6.7 Hz, 3 H, -CH_3), 1.22 – 1.37 (m, 7 H, 1"-H_A, 2"-H, 3"-H, 4"-H), 1.65 (ddd, ^2J = 12.3 Hz, ^3J = 12.3 Hz, ^3J = 10.4 Hz, 1 H, 4-H_B), 1.86 (m_c, 1 H, 1"-H_B), 1.89 (dsept, ^3J = 7.9 Hz, ^3J = 6.8 Hz, 1 H, 2'-H), 2.31 (ddd, ^2J = 12.7 Hz, ^3J = 8.9 Hz, ^3J = 5.9 Hz, 1 H, 4-H_A), 2.57 (dddd, ^3J = 11.9 Hz, ^3J = ^3J = 8.9 Hz, ^3J = 4.3 Hz, 1 H, 3-H), 3.54 (ddd, ^3J = 9.7 Hz, ^3J = 7.9 Hz, ^3J = 1.5 Hz, 1 H, 1'-H), 4.59 (ddd, ^3J = 10.4 Hz, ^3J = 5.9 Hz, ^3J = 1.5 Hz, 1 H, 5-H), 4.83 (d, ^3J = 10.3 Hz, 1 H, -NH), 5.11 (d, ^2J =

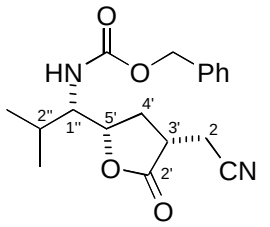
12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 5.13 (d, ^2J = 12.3 Hz, 1 H, -OCH$_A$$H_B$Ph), 7.29 – 7.39 (m, 5 H, -C_6H_5). — ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 14.0 (C-5”), 19.3, 19.7 [-CH(*C*H$_3$)$_2$], 22.5 (C-4”), 26.9 (C-3”), 30.1 (C-2”), 31.4 (C-2’), 31.5 (C-1”, C-4), 40.3 (C-3), 58.2 (C-1’), 67.0 (-O*C*H$_2$Ph), 77.4 (C-5), 127.9, 128.2, 128.6 (-C_6H_5), 136.3 (-C_6H_5 *ipso*), 157.0 (C=O, carbamate), 178.8 (C-2). — MS (FAB, pos.) *m/z* (%): 723 (3, [2 M + H]$^+$), 384 (6, [M + Na]$^+$), 362 (54, [M + H]$^+$), 91 (100, $C_7H_7^+$). — $C_{21}H_{31}NO_4$ (361.48): calcd. C 69.78, H 8.64, N 3.87; found C 69.68, H 8.71, N 3.81.

Lactone **4b**: Colourless oil. — $[\alpha]^{20}_D$ = –23.6 (*c* = 1.25, $CHCl_3$). — IR (neat) $\tilde{\nu}$ = 3308 cm^{-1} (N-H), 3010, 2960, 2850 (C-H), 1767 (C=O, lactone), 1713 (C=O, carbamate), 1531 (C=C). — ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 6.8 Hz, 3 H, 5”-H), 0.97 (d, ^3J = 6.7 Hz, 3 H, -CH_3), 1.02 (d, ^3J = 6.8 Hz, 3 H, -CH_3), 1.22 – 1.38 (m, 6 H, 2”-H, 3”-H, 4”-H), 1.43 (m$_c$, 1 H, 1”-H$_A$), 1.75 (m$_c$, 1 H, 1”-H$_B$), 1.86 (dsept, ^3J = 8.2 Hz, ^3J = 6.7 Hz, 1 H, 2’-H), 1.97 (ddd, ^2J = 13.7 Hz, ^3J = 8.0 Hz, ^3J = 6.0 Hz, 1 H, 4-H$_A$), 2.24 (ddd, ^2J = 13.2 Hz, ^3J = 9.9 Hz, ^3J = 6.2 Hz, 1 H, 4-H$_B$), 2.51 (dddd, ^3J = 11.2 Hz, ^3J = 9.7 Hz, ^3J = ^3J = 5.7 Hz, 1 H, 3-H), 3.51 (ddd, ^3J = 10.1 Hz, ^3J = 8.2 Hz, ^3J = 1.7 Hz, 1 H, 1’-H), 4.71 (ddd, ^3J = 8.0 Hz, ^3J = 6.2 Hz, ^3J = 1.7 Hz, 1 H, 5-H), 4.79 (d, ^3J = 10.2 Hz, 1 H, -NH), 5.11 (d, ^2J = 12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 5.13 (d, ^2J = 12.3 Hz, 1 H, -OCH$_A$$H_B$Ph), 7.30 – 7.38 (m, 5 H, -C_6H_5). — ^{13}C- NMR (125 MHz, $CDCl_3$): δ = 14.0 (C-5”), 19.3, 19.8 [-CH(*C*H$_3$)$_2$], 22.4 (C-4”), 26.9 (C-3”), 30.8 (C-4), 31.1 (C-2’), 31.4 (C-1”, C-2”), 39.5 (C-3), 59.7 (C-1’), 67.1 (-O*C*H$_2$Ph), 77.7 (C-5), 128.0, 128.2, 128.6 (-C_6H_5), 136.3 (-C_6H_5 *ipso*), 157.0 (C=O, carbamate), 179.7 (C-2). — MS (FAB, pos.) *m/z* (%): 723 (4, [2 M + H]$^+$), 384 (3, [M + Na]$^+$), 362 (28, [M + H]$^+$), 91 (100, $C_7H_7^+$). — $C_{21}H_{31}NO_4$ (361.48): calcd. C 69.78, H 8.64, N 3.87; found C 69.92, H 8.64, N 3.89.



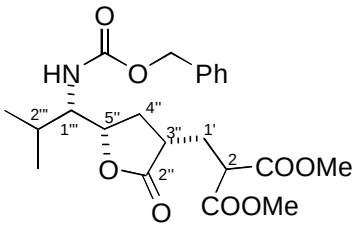
(3’S,5’S,1”S)-2-{5-[1-(Benzyloxycarbonylamino)-2-methylpropyl]-2-oxotetrahydro-3-furanyl}-acetonitrile (5)

Colourless oil. — $[\alpha]^{20}_D$ = –15.9 (*c* = 0.80, $CHCl_3$). — IR (Film) $\tilde{\nu}$ = 3320 cm^{-1} (N-H), 3020, 2960, 2880 (C-H), 2250 (CN), 1770 (C=O, lactone), 1695 (C=O, carbamate), 1540 (C=C). — ^{1}H- NMR (500 MHz, $CDCl_3$): δ = 0.93 [d, ^3J = 6.8 Hz, 3 H, -CH(CH_3)$_2$], 1.03 [d, ^3J = 6.6 Hz, 3 H, -CH(CH_3)$_2$], 1.85 (dsept, ^3J = 8.4 Hz, ^3J = 6.8 Hz, 1 H, 2”-H), 2.25 (ddd, ^2J = 13.6 Hz, ^3J = 11.9 Hz, ^3J = 11.9 Hz, 1 H, 4’-H$_A$), 2.50 (ddd, ^2J = 13.7 Hz, ^3J = 10.2 Hz, ^3J = 3.7 Hz, 1 H, 4’-H$_B$), 2.61 (dd, ^2J = 17.0 Hz, ^3J = 7.1 Hz, 1 H, 2-H$_A$), 2.64 (dd, ^2J = 16.9 Hz, ^3J = 5.4 Hz, 1 H, 2-H$_B$), 2.79 (dddd, ^3J = 12.3 Hz, ^3J = 10.2 Hz, ^3J = 7.1 Hz, ^3J = 5.4 Hz, 1 H, 3’-H), 3.56 (ddd, ^3J = 10.1 Hz, ^3J = 8.5 Hz, ^3J = 1.9 Hz, 1 H, 1”-H),

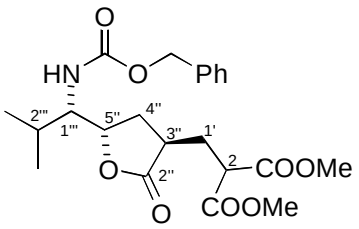


4.78 – 4.85 (2m, 2 H, 5'-H, -NH), 5.09 (d, ^2J = 12.2 Hz, 1 H, -OCH_AH$_B$Ph), 5.15 (d, ^2J = 12.2 Hz, 1 H, -OCH$_A$$H_B$Ph), 7.32 – 7.39 (m, % H, -C_6H_5). — ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 19.2, 19.8 [-CH(CH_3)$_2$], 19.3 (C-2), 29.8 (C-4'), 30.7 (C-2"), 36.0 (C-3'), 60.2 (C-1"), 67.3 (-OCH_2Ph), 78.1 (C-5'), 116.7 (-CN), 128.2, 128.4, 128.6 (-C_6H_5), 136.2 (-C_6H_5 *ipso*), 157.0 (-*C*=O, carbamate), 176.0 (C-2'). — MS (FAB, pos.) *m/z* (%): 661 (7, [2 M + H]$^+$), 353 (5, [M + Na]$^+$), 331 (51, [M + H]$^+$), 91 (100, $C_7H_7^+$). — $C_{18}H_{22}N_2O_4$ (330.38): calcd. C 65.44, H 6.71, N 8.48; found C 65.21, H 6.74, N 8.24.

(3"S,5"S,1'"S)- and (3"R,5"S,1'"S) Dimethyl 2-{[5-(1-benzyloxycarbonylamino)-2-methylpropyl]-2-oxotetrahydro-3-furanyl}methylmalonate (6a/b)



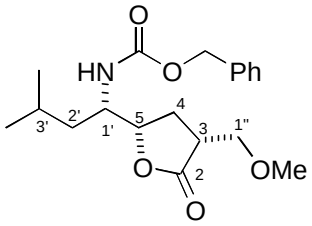
Malonate **6a**: Colourless oil. — $[\alpha]^{20}_D$ = –23.8 (*c* = 1.16, $CHCl_3$). — IR (neat) $\tilde{\nu}$ = 3327 cm^{-1} (N-H), 3014, 2957 (C-H), 1731 (br, C=O), 1539 (C=C). — ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, ^3J = 6.8 Hz, 3 H, -CHCH_3), 1.01 (d, ^3J = 6.8 Hz, 3 H, -CHCH_3), 1.70 (ddd, ^2J = 12.5 Hz, ^3J = 12.5 Hz, ^3J = 10.4 Hz, 1 H, 4"-H$_A$), 1.85 (dsept, ^3J = 7.9 Hz, ^3J = 6.8 Hz, 1 H, 2'"-H), 2.03 (ddd, ^2J = 14.2 Hz, ^3J = 8.0 Hz, ^3J = 8.0 Hz, 1 H, 1'-H$_A$), 2.33 (ddd, ^2J = 12.6 Hz, ^3J = 8.9 Hz, ^3J = 5.7 Hz, 1 H, 4"-H$_B$), 2.35 (ddd, ^2J = 14.1 Hz, ^3J = 10.2 Hz, ^3J = 7.0 Hz, 1 H, 1'-H$_B$), 2.69 (dddd, ^3J = 12.2 Hz, ^3J = 8.7 Hz, ^3J = 7.9 Hz, ^3J = 6.9 Hz, 1 H, 3"-H), 3.52 (ddd, ^3J = 9.9 Hz, ^3J = 8.0 Hz, ^3J = 1.6 Hz, 1 H, 1'"-H), 3.74 (m$_c$, 1 H, 2-H), 3.74 (s, 3 H, -OCH$_3$), 3.75 (s, 3 H, -OCH$_3$), 4.59 (ddd, ^3J = 10.4 Hz, ^3J = 5.7 Hz, ^3J = 1.6 Hz, 1 H, 5"-H), 4.84 (d, ^3J = 10.3 Hz, 1 H, -NH), 5.12 (d, ^2J = 12.3 Hz, 1 H, -OCH_AH$_B$Ph), 5.13 (d, ^2J = 12.3 Hz, 1 H, -OCH$_A$$H_B$Ph), 7.30 – 7.38 (m, 5 H, -C$_6H_5$). — ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.3, 19.7 [-CH(CH_3)$_2$], 29.2 (C-1'), 31.4 (C-2'"), 31.8 (C-4"), 37.9 (C-3"), 49.1 (C-2), 52.7 (2 -OCH$_3$), 57.9 (C-1'"), 67.1 (-OCH_2Ph), 77.5 (C-5"), 128.0, 128.2, 128.6 (-C_6H_5), 136.3 (-C_6H_5 *ipso*), 156.9 (-*C*=O, carbamate), 169.1, 169.3 (C-1, C-3), 177.5 (C-2"). — MS (FAB, pos.) *m/z* (%): 458 (8, [M + Na]$^+$), 436 (81, [M + H]$^+$), 392 (14, [M – C_3H_8 + H]$^+$), 91 (100, $C_7H_7^+$). — $C_{22}H_{29}NO_8$ (435.47): calcd. C 60.68, H 6.71, N 3.22; found C 60.63, H 6.76, N 3.14.



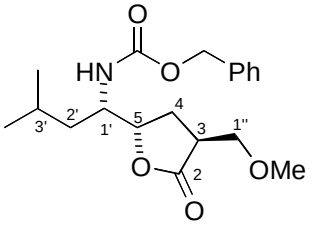
Malonate **6b**: Colourless oil. — $[\alpha]^{20}_D$ = –14.1 (*c* = 0.57, $CHCl_3$). — IR (neat) $\tilde{\nu}$ = 3324 cm^{-1} (N-H), 3010, 2958 (C-H), 1715 (br, C=O), 1539 (C=C). — ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (d, ^3J = 6.7 Hz, 3 H, -CHCH_3), 1.02 (d, ^3J = 6.7 Hz, 3 H, -CHCH_3), 1.85 (dsept, ^3J = 8.2 Hz, ^3J = 6.8 Hz, 1 H, 2'"-H), 1.98 (ddd, ^2J = 13.3 Hz, ^3J = 8.1 Hz, ^3J = 6.5 Hz, 1 H, 4"-H$_A$), 2.11 (ddd, ^2J = 16.2 Hz, ^3J = 8.5 Hz, ^3J = 7.6 Hz, 1 H, 1'-H$_A$), 2.29 (ddd, ^2J = 16.0 Hz, ^3J = 8.2 Hz, ^3J = 6.4 Hz, 1 H, 1'-H$_B$), 2.34 (ddd, ^2J = 13.3 Hz, ^3J = 9.9 Hz, ^3J = 5.9 Hz, 1 H, 4"-H$_B$), 2.65

(dddd, ^3J = 9.8 Hz, ^3J = ^3J = 7.9 Hz, ^3J = 6.4 Hz, 1 H, 3”-H), 3.52 (ddd, ^3J = 10.1 Hz, ^3J = 8.2 Hz, ^3J = 1.8 Hz, 1 H, 1’”-H), 3.69 (dd, ^3J = 8.6 Hz, ^3J = 6.4 Hz, 1 H, 2-H), 3.73 (s, 3 H, -OCH_3), 3.74 (s, 3 H, -OCH_3), 4.71 (d, ^3J = 10.2 Hz, 1 H, -NH), 4.75 (ddd, ^3J = 7.9 Hz, ^3J = 5.8 Hz, ^3J = 1.8 Hz, 1 H, 5”-H), 5.10 (d, ^2J = 12.2 Hz, 1 H, -OC$H_A$$H_B$Ph), 5.13 (d, ^2J = 12.2 Hz, 1 H, -OC$H_A$$H_B$Ph), 7.30 – 7.39 (m, 5 H, -C_6H_5). — ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 19.8 [-CH(*C*H_3)$_2$], 30.3 (C-1’), 31.0 (C-2’”), 31.2 (C-4”), 37.2 (C-3”), 49.1 (C-2), 52.8 (2 -OCH_3), 59.6 (C-1’”), 67.2 (-O*C*H_2Ph), 77.8 (C-5”), 128.0, 128.3, 128.6 (-*C*$_6$$H_5$), 136.2 (-*C*$_6$$H_5$ *ipso*), 157.0 (-*C*=O, carbamate), 169.0, 169.2 (C-1, C-3), 178.2 (C-2”). — MS (FAB, pos.) *m/z* (%): 458 (8, $[M + Na]^+$), 436 (76, $[M + H]^+$), 392 (8, $[M – C_3H_8 + H]^+$), 91 (100, $C_7H_7^+$). — $C_{22}H_{29}NO_8$ (435.47): calcd. C 60.68, H 6.71, N 3.22; found C 60.51, H 6.69, N 3.16.

(3*R*,5*S*,1’*S*)- and (3*S*,5*S*,1’*S*)-5-[1-(Benzyloxycarbonylamino)-3-methylbutyl]-3-methoxymethyltetrahydrofuran-2-one (7a/b)



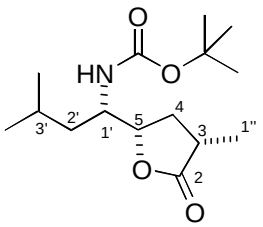
Lactone **7a**: Colourless solid, m.p. 91–93 °C. — $[\alpha]^{20}_D$ = –26.9 (*c* = 0.68, $CHCl_3$). — IR (KBr) $\tilde{\nu}$ = 3280 cm^{-1} (N-H), 3040, 2940, 2880 (C-H), 1770 (C=O, lactone), 1690 (C=O, carbamate), 1540 (C=C). — ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, ^3J = 5.0 Hz, 3 H, -CH_3), 0.94 (d, ^3J = 4.9 Hz, 3 H, -CH_3), 1.37 (ddd, ^2J = 13.7 Hz, ^3J = 8.7 Hz, ^3J = 4.8 Hz, 1 H, 2’-H_A), 1.58 (ddd, ^2J = 13.6 Hz, ^3J = 10.1 Hz, ^3J = 5.2 Hz, 1 H, 2’-H_B), 1.67 (m_c, 1 H, 3’-H), 2.09 (ddd, ^2J = 13.0 Hz, ^3J = 11.3 Hz, ^3J = 10.0 Hz, 1 H, 4-H_A), 2.33 (ddd, ^2J = 12.9 Hz, ^3J = 9.5 Hz, ^3J = 6.5 Hz, 1 H, 4-H_B), 2.85 (dddd, ^3J = 11.2 Hz, ^3J = 9.4 Hz, ^3J = 5.5 Hz, ^3J = 3.8 Hz, 1 H, 3-H), 3.28 (s, 3 H, -OMe), 3.56 (dd, ^2J = 9.4 Hz, ^3J = 5.4 Hz, 1 H, 1”-H_A), 3.59 (dd, ^2J = 9.4 Hz, ^3J = 3.8 Hz, 1 H, 1”-H_B), 3.92 (dddd, ^3J = ^3J = 10.0 Hz, ^3J = 5.0 Hz, ^3J = 2.1 Hz, 1 H, 1’-H), 4.45 (ddd, ^3J = 10.0 Hz, ^3J = 6.5 Hz, ^3J = 2.1 Hz, 1 H, 5-H), 4.77 (d, ^3J = 10.0 Hz, 1 H, -NH), 5.12 (d, ^2J = 12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 5.14 (d, ^2J = 12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 7.30 – 7.39 (m, 5 H, -C_6H_5). — ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.9, 23.1 [-CH(*C*H_3)$_2$], 24.7 (C-3’), 27.8 (C-4), 41.5 (C-3), 42.2 (C-2’), 51.0 (C-1’), 59.1 (-OCH_3), 66.9 (-O*C*H_2Ph), 70.6 (C-1”), 80.2 (C-5), 127.9, 128.1, 128.5 (-C_6H_5), 136.4 (-C_6H_5 *ipso*), 156.6 (C=O, carbamate), 176.7 (C-2). — MS (FAB, pos.) *m/z* (%): 372 (7, $[M + Na]^+$), 350 (47, $[M + H]^+$), 91 (100, $C_7H_7^+$). — $C_{19}H_{27}NO_5$ (349.42): calcd. C 65.31, H 7.79, N 4.01; found C 65.15, H 7.82, N 3.97.



Lactone **7b**: Colourless solid, m.p. 95–97 °C. — $[\alpha]^{20}_D$ = –12.7 (*c* = 0.30, $CHCl_3$). — IR (KBr) $\tilde{\nu}$ = 3300 cm^{-1} (N-H), 3040, 2940, 2880 (C-H), 1760 (C=O, lactone), 1680 (C=O, carbamate), 1535 (C=C). — ^{1}H NMR (500

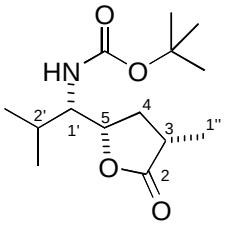
MHz, $CDCl_3$): δ = 0.92 [d, ^3J = 6.6 Hz, 6 H, -CH(CH_3)$_2$], 1.36 (ddd, ^2J = 13.8 Hz, ^3J = 8.9 Hz, ^3J = 4.7 Hz, 1 H, 2'-H_A), 1.58 (ddd, ^2J = 13.9 Hz, ^3J = 10.2 Hz, ^3J = 5.1 Hz, 1 H, 2'-H_B), 1.65 (m_c, 1 H, 3'-H), 2.21 – 2.29 (2 m, 2 H, 4-H), 2.69 (dddd, ^3J = 9.9 Hz, ^3J = 7.6 Hz, ^3J = 4.3 Hz, ^3J = 3.5 Hz, 1 H, 3-H), 3.33 (s, 3 H, -OMe), 3.50 (dd, ^2J = 9.2 Hz, ^3J = 3.4 Hz, 1 H, 1"-H_A), 3.66 (dd, ^2J = 9.2 Hz, ^3J = 4.3 Hz, 1 H, 1"-H_B), 3.90 (dddd, ^3J = ^3J = 10.1 Hz, ^3J = 4.9 Hz, ^3J = 1.9 Hz, 1 H, 1'-H), 4.54 (ddd, ^3J = 8.6 Hz, ^3J = 6.7 Hz, ^3J = 1.9 Hz, 1 H, 5-H), 4.62 (d, ^3J = 9.8 Hz, 1 H, -NH), 5.09 (d, ^2J = 12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 5.11 (d, ^2J = 12.3 Hz, 1 H, -OC$H_A$$H_B$Ph), 7.28 – 7.38 (m, 5 H, -C_6H_5). — ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.8, 23.1 [-CH(CH_3)$_2$], 24.7 (C-3'), 27.8 (C-4), 41.2 (C-3), 42.1 (C-2'), 52.1 (C-1'), 59.2 (-OCH_3), 67.1 (-OCH_2Ph), 71.9 (C-1"), 81.3 (C-5), 128.0, 128.2, 128.6 (-C_6H_5), 136.3 (-C_6H_5 *ipso*), 156.7 (C=O, carbamate), 178.0 (C-2). — MS (FAB, pos.) *m/z* (%): 372 (8, $[M + Na]^+$), 350 (66, $[M + H]^+$), 220 (6, $[M – C_6H_9O_3]^+$), 91 (100, $C_7H_7^+$). — $C_{19}H_{27}NO_5$ (349.42): calcd. C 65.31, H 7.79, N 4.01; found C 65.07, H 7.86, N 3.98.

(3*S*,5*S*,1'*S*)-5-[1-(*tert*-Butyloxycarbonylamino)-3-methylbutyl]-3-methyltetrahydrofuran-2-one (8)



Lactone **8**: Colourless solid, m.p. 110 – 112 °C. — $[\alpha]^{20}_D$ = –40.7 (*c* = 0.77, $CHCl_3$). — IR (KBr) $\tilde{\nu}$ = 3320 cm^{-1} (N-H), 2950, 2920, 2850 (C-H), 1765 (C=O, lactone), 1675 (C=O, carbamate), 1520 (N-H bending), 1360 (*tert.*-butyl). — ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 [d, ^3J = 6.3 Hz, 6 H, -CH(CH_3)$_2$], 1.26 (d, ^3J = 7.1 Hz, 3 H, 1"-H), 1.36 (ddd, ^2J = 13.8 Hz, ^3J = 8.7 Hz, ^3J = 5.0 Hz, 1 H, 2'-H_A), 1.44 [s, 9 H, -C(CH_3)$_3$], 1.59 (ddd, ^2J = 13.9 Hz, ^3J = 9.4 Hz, ^3J = 5.5 Hz, 1 H, 4-H_B), 2'-H_B), 1.67 (m_c, 1 H, 3'-H), 1.71 (ddd, ^2J = 12.8 Hz, ^3J = 11.9 Hz, ^3J = 10.2 Hz, 1 H, 4-H_B), 2.39 (ddd, ^2J = 12.8 Hz, ^3J = 9.0 Hz, ^3J = 5.9 Hz, 1 H, 4-H_B), 2.68 (ddq, ^3J = 11.8 Hz, ^3J = 9.1 Hz, ^3J = 7.1 Hz, 1 H, 3-H), 3.82 (dddd, ^3J = ^3J = 10.1 Hz, ^3J = 5.1 Hz, ^3J = 1.7 Hz, 1 H, 1'-H), 4.39 (ddd, ^3J = 10.2 Hz, ^3J = 5.9 Hz, ^3J = 1.6 Hz, 1 H, 5-H), 4.45 (d, ^3J = 9.8 Hz, 1 H, -N*H*). — ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2 (C-1"), 21.9, 23.1 [-CH(CH_3)$_2$], 24.8 (C-3'), 28.3 [-C(CH_3)$_3$], 32.9 (C-4), 35.4 (C-3), 42.3 (C-2'), 50.1 (C-1'), 79.7 [-C(CH_3)$_3$], 80.2 (C-5), 156.0 (-C=O, carbamate), 179.6 (C-2). — MS (CI) *m/z* (%): 571 (34, $[2 M + H]^+$), 515 (23, $[2 M – C_4H_8 + H]^+$), 471 (81, $[2 M – C_5H_7O_2]^+$), 415 (16, $[2 M – C_5H_7O_2 – C_4H_8]^+$), 371 (74, $[2 M – 2 C_5H_7O_2]^+$), 286 (34, $[M + H]^+$), 230 (100, $[M – C_4H_8 + H]^+$), 186 (61, $[M – C_5H_7O_2]^+$), 130 (19, $[M – C_5H_7O_2 – C_4H_8]^+$). — $C_{15}H_{27}NO_4$ (285.30): calcd. C 63.13, H 9.54, N 4.91; found C 63.07, H 9.56, N 4.81.

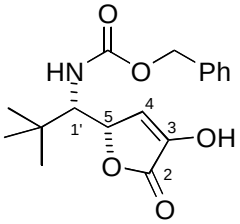
(3*S*,5*S*,1'*S*)- and (3*R*,5*S*,1'*S*)-5-[1-(*tert*-Butyloxycarbonylamino)-2-methylpropyl]-3-methyltetrahydrofuran-2-one (9a/b)



Lactone **9a**: Colourless solid, m.p. 98 – 100 °C (91:9-mixture). — $[\alpha]^{20}_D$ = –55.3 (c = 0.88, $CHCl_3$; 91:9-mixture). — IR (KBr) $\tilde{\nu}$ = 3320 cm^{-1} (N-H), 2960, 2910, 2860 (C-H), 1770 (C=O, Lacton), 1685 (C=O, carbamate), 1525 (N-H bending), 1360 (*tert.*-butyl). — ^{1}H NMR (500 MHz, $CDCl_3$); δ = 0.98 [d, ^3J = 6.8 Hz, 3 H, -CH(CH_3)$_2$], 1.01 [d, ^3J = 6.8 Hz, 3 H, -CH(CH_3)$_2$], 1.26 (d, ^3J = 7.1 Hz, 3 H, 1"-H), 1.44 [s, 9 H, -C(CH_3)$_3$], 1.71 (ddd, ^2J = 12.7 Hz, ^3J = 12.0 Hz, ^3J = 10.2 Hz, 1 H, 4-H_A), 1.86 (dsept, ^3J = 8.0 Hz, ^3J = 6.8 Hz, 1 H, 2'-H), 2.38 (ddd, ^2J = 12.8 Hz, ^3J = 9.0 Hz, ^3J = 6.0 Hz, 1 H, 4-H_B), 2.68 (ddq, ^3J = 11.9 Hz, ^3J = 9.0 Hz, ^3J = 7.1 Hz, 1 H, 3-H), 3.44 (ddd, ^3J = 10.3 Hz, ^3J = 8.0 Hz, ^3J = 1.4 Hz, 1 H, 1'-H), 4.57 (d, ^3J = 10.2 Hz, 1 H, -N*H*), 4.60 (ddd, ^3J = 10.2 Hz, ^3J = 6.0 Hz, ^3J = 1.4 Hz, 1 H, 5-H). — ^{13}C NMR (125 MHz, $CDCl_3$); δ = 15.2 (C-1"), 19.3, 19.7 [-CH(*C*H_3)$_2$], 28.4 [-C(*C*H_3)$_3$], 31.5 (C-2'), 33.6 (C-4), 35.2 (C-3), 57.5 (C-1'), 77.5 (C-5), 79.7 [-*C*(CH_3)$_3$], 156.4 (-*C*=O, carbamate), 179.6 (C-2). — MS (CI) *m/z* (%): 543 (3, [2 M + H]$^+$), 294 (8, [M + Na]$^+$), 272 (5, [M + H]$^+$), 216 (100, [M – C_4H_8 + H]$^+$), 172 (50, [M – $C_5H_7O_2$]$^+$), 57 (57, $C_4H_9^+$). — $C_{14}H_{25}NO_4$ (271.35): calcd. C 61.97, H 9.29, N 5.16; found C 61.95, H 9.38, N 5.12.

Lactone **9b**: ^{13}C NMR (125 MHz, $CDCl_3$; as determined from a mixture of **9a/b**); δ = 16.7 (C-1"), 19.3, 19.8 [-CH(*C*H_3)$_2$], 28.4 [-C(*C*H_3)$_3$], 31.2 (C-2'), 32.9 (C-4), 34.3 (C-3), 59.0 (C-1'), 77.7 (C-5), 79.8 [-*C*(CH_3)$_3$], 156.4 (-*C*=O, carbamate), 180.6 (C-2).

(5S,1'S)-5-[1-(Benzyloxycarbonylamino)-2,2-dimethylpropyl]-3-hydroxydihydrofuran-2-one (10)

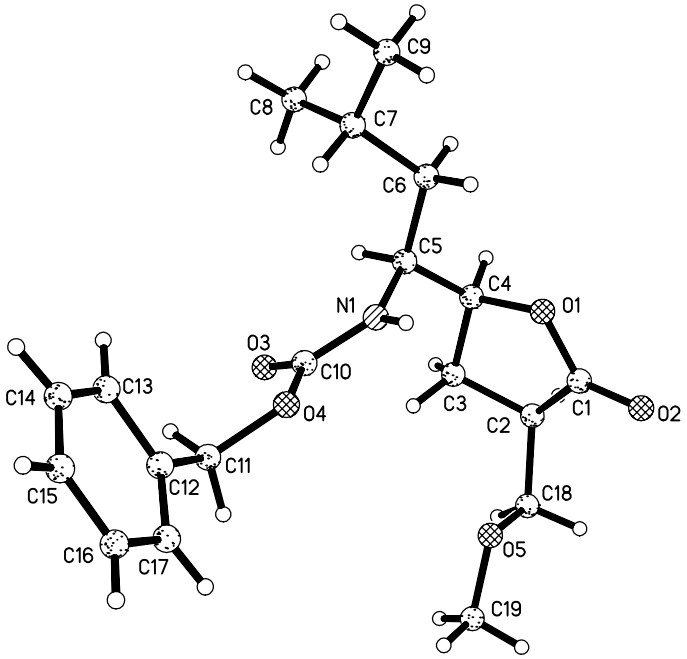


Lactone **10**: Colourless solid, m.p. 166 – 168 °C. — $[\alpha]^{20}_D$ = –116.5 (c = 1.07, $CHCl_3$). — IR (neat) $\tilde{\nu}$ = 3380, 3090 cm^{-1} (br N-H, O-H), 2940, 2850 (C-H), 1760 (C=O, lactone), 1670 (C=O, carbamate), 1530 (C=C). — ^{1}H NMR (500 MHz, $CDCl_3$); Mixture of 2 rotamers. δ = 0.98{1.00} (s, 9 H, -(CH_3)$_3$), 3.52{3.68} (dd, ^3J = 10.8{10.6} Hz, ^3J = 1.0{1.2} Hz, 1 H, 1'-H), 4.98{6.69} (d, ^3J = 10.7{10.8} Hz, 1 H, -N*H*), 5.01{5.08} (s, 2 H, -OCH_2Ph), 5.13{5.18} (dd, ^3J = 2.1{2.1} Hz, ^3J = 1.0{1.2} Hz, 1 H, 5-H), 5.76{6.06} (d, ^3J = 1.9{1.9} Hz, 1 H, 4-H), 6.21{8.96} (s, 1 H, -OH), 7.22 – 7.37 (m, 5 H, -C_6H_5). — ^{13}C NMR (125 MHz, $CDCl_3$); Mixture of 2 rotamers: δ = 26.2{26.3} [-(*C*H_3)$_3$], 33.7{33.8} (C-2'), 58.6{59.6} (C-1'), 66.0{66.7} (-O*C*H_2Ph), 76.4{76.6} (C-5), 116.4{117.0} (C-4), 126.8{127.1},

127.2{127.4}, 127.5{127.6} (-C_6H_5), 134.9{135.2} (-C_6H_5 *ipso*), 141.4{143.1} (C-3), 155.7{156.8} (-*C*=O, carbamate), 169.0{169.5} (C-2). — MS (FAB, pos.) *m/z* (%): 342 (2, $[M + Na]^+$), 320 (10, $[M + H]^+$), 91 (100, $C_7H_7^+$). — $C_{17}H_{21}NO_5$ (319.35): calcd. C 63.94, H 6.63, N 4.39; found C 63.78, H 6.65, N 4.31.

X-Ray data for Compounds 7a, 7b and 8

X-Ray Crystal Structure of (3*R*,5*S*,1'*S*)-5-[1-(Benzyloxycarbonylamino)-3-methylbutyl]-3-methoxy-methyltetrahydrofuran-2-one (7a).



Crystal data and structure refinement for **7a**.

Identification code	s656rm
Empirical formula	C19 H27 N O5
Formula weight	349.42
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 9.095(3) A alpha = 90 deg.
	b = 13.129(5) A beta = 90 deg.
	c = 17.174(6) A gamma = 90 deg.

Volume, Z	2050.8(13) A^3, 4
Density (calculated)	1.132 Mg/m^3
Absorption coefficient	0.081 mm^-1
F(000)	752
Crystal size	0.3 x 0.1 x 0.1 mm
Theta range for data collection	1.95 to 22.50 deg.
Limiting indices	0<=h<=10, 0<=k<=15, 0<=l<=20
Reflections collected	1561
Independent reflections	1561 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1324 / 0 / 226
Goodness-of-fit on F^2	1.224
Final R indices [I>2sigma(I)]	R1 = 0.1116, wR2 = 0.1499
R indices (all data)	R1 = 0.2112, wR2 = 0.2032
Absolute structure parameter	6(7)
Largest diff. peak and hole	0.184 and -0.184 e.A^-3

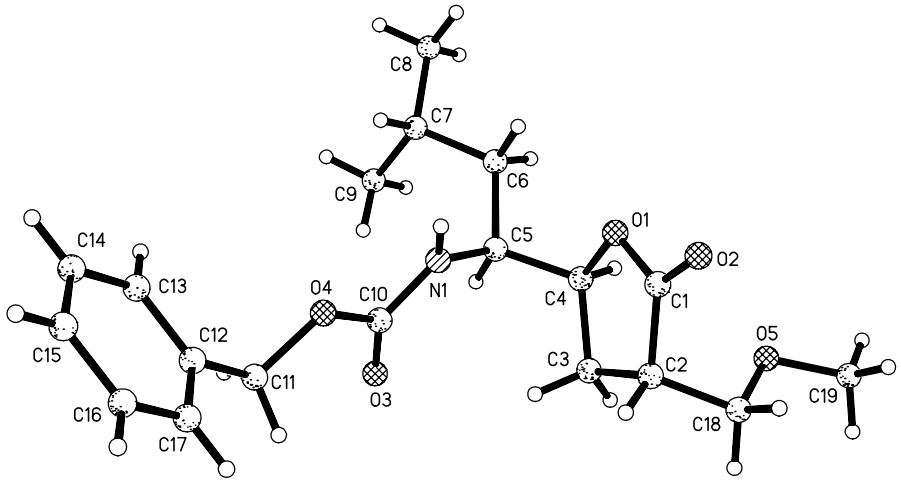
Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **7a**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	-75(10)	2941(7)	3161(5)	76(3)
N(1)	673(10)	2503(7)	4751(6)	61(3)
C(1)	-261(17)	3906(12)	2938(8)	72(4)
O(2)	-1393(13)	4250(8)	2721(7)	113(4)
C(2)	1210(17)	4463(12)	2995(9)	88(5)
O(3)	2675(9)	3032(11)	5418(6)	118(5)
C(3)	2132(14)	3789(11)	3508(9)	89(5)
O(4)	391(10)	3134(10)	5932(6)	112(4)
C(4)	1429(15)	2755(11)	3392(8)	72(4)
C(5)	1412(13)	2060(10)	4084(7)	59(4)
O(5)	624(16)	5635(10)	3928(9)	140(5)
C(6)	724(17)	1019(10)	3916(8)	80(4)
C(7)	903(22)	196(13)	4559(10)	101(6)
C(8)	2483(21)	-132(18)	4625(12)	183(10)
C(9)	-187(23)	-645(13)	4429(11)	163(9)
C(10)	1400(16)	2904(11)	5366(8)	74(4)
C(11)	1044(19)	3570(17)	6631(9)	188(12)
C(12)	199(22)	3310(18)	7326(12)	104(7)
C(13)	492(34)	2327(30)	7609(17)	207(20)
C(14)	-285(33)	2112(19)	8238(19)	199(18)
C(15)	-1340(39)	2686(22)	8597(14)	184(15)
C(16)	-1588(22)	3621(22)	8323(13)	148(11)
C(17)	-826(20)	3925(13)	7664(11)	104(7)
C(18)	1241(24)	5600(14)	3220(10)	139(8)
C(19)	864(34)	6659(16)	4213(12)	282(18)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **7a**.

	x	y	z	U(eq)
H(1)	-272(10)	2512(7)	4755(6)	73
H(2)	1651(17)	4422(12)	2475(9)	105
H(3A)	2079(14)	4002(11)	4048(9)	107
H(3B)	3152(14)	3788(11)	3343(9)	107
H(4)	1935(15)	2408(11)	2964(8)	87
H(5)	2437(13)	1941(10)	4235(7)	71
H(6A)	1150(17)	758(10)	3439(8)	96
H(6B)	-319(17)	1118(10)	3823(8)	96
H(7)	644(22)	520(13)	5054(10)	122
H(8A)	3094(21)	455(18)	4706(12)	274
H(8B)	2776(21)	-470(18)	4154(12)	274
H(8C)	2588(21)	-591(18)	5056(12)	274
H(9A)	-1158(23)	-363(13)	4395(11)	244
H(9B)	-143(23)	-1116(13)	4857(11)	244
H(9C)	44(23)	-995(13)	3954(11)	244
H(11A)	1088(19)	4305(17)	6578(9)	226
H(11B)	2042(19)	3319(17)	6688(9)	226
H(13)	1156(34)	1879(30)	7380(17)	249
H(14)	-87(33)	1485(19)	8468(19)	239
H(15)	-1869(39)	2432(22)	9018(14)	221
H(16)	-2252(22)	4055(22)	8567(13)	178
H(17)	-1018(20)	4561(13)	7448(11)	124
H(18A)	2243(24)	5853(14)	3237(10)	167
H(18B)	684(24)	6004(14)	2851(10)	167
H(19A)	440(34)	6726(16)	4722(12)	423
H(19B)	411(34)	7138(16)	3865(12)	423
H(19C)	1901(34)	6791(16)	4240(12)	423

X-Ray Crystal Structure of (3S,5S,1'S)-5-[1-(Benzyloxycarbonylamino)-3-methylbutyl]-3-methoxy-methyltetrahydrofuran-2-one (7b).



Crystal data and structure refinement for **7b**.

Identification code	s647rm
Empirical formula	C19 H27 N O5
Formula weight	349.42
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 9.260(2) A alpha = 90 deg. b = 11.978(3) A beta = 90 deg. c = 17.622(5) A gamma = 90 deg.
Volume, Z	1954.7(9) A^3, 4
Density (calculated)	1.187 Mg/m^3
Absorption coefficient	0.085 mm^-1
F(000)	752
Crystal size	0.75 x 0.25 x 0.25 mm
Theta range for data collection	2.06 to 27.00 deg.
Limiting indices	0<=h<=12, 0<=k<=15, 0<=l<=23
Reflections collected	2435
Independent reflections	2435 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2174 / 0 / 227
Goodness-of-fit on F^2	1.182
Final R indices [I>2sigma(I)]	R1 = 0.0667, wR2 = 0.1099
R indices (all data)	R1 = 0.1132, wR2 = 0.1356
Absolute structure parameter	-6(3)
Extinction coefficient	0.0129(13)
Largest diff. peak and hole	0.156 and -0.141 e.A^-3

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **7b**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

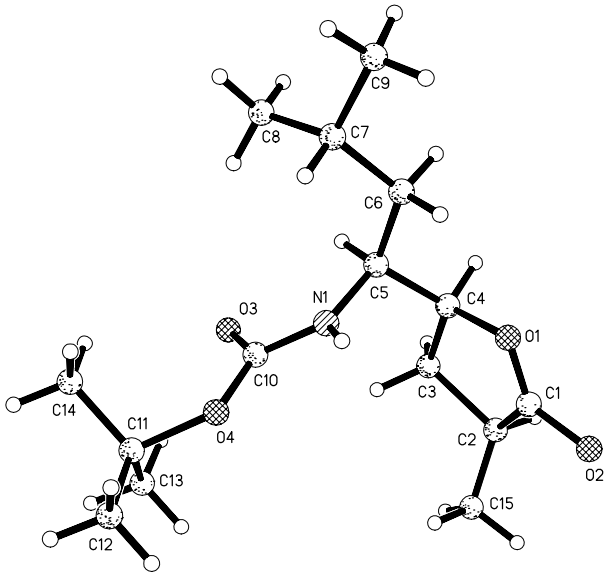
	x	y	z	U(eq)
O(1)	10562(3)	9669(2)	10923(2)	53(1)
N(1)	9375(4)	7734(3)	10199(2)	39(1)
C(1)	11079(6)	10463(4)	10468(3)	62(1)
O(2)	12325(4)	10728(3)	10483(3)	93(1)
C(2)	9901(6)	10925(4)	9969(3)	65(1)
O(3)	7424(3)	7628(3)	9411(2)	52(1)
C(3)	8616(6)	10194(4)	10125(3)	64(1)
O(4)	9552(3)	6793(2)	9120(2)	48(1)
C(4)	9005(4)	9526(3)	10842(3)	47(1)
C(5)	8647(4)	8300(3)	10821(2)	41(1)
O(5)	9281(6)	12242(3)	10898(3)	113(2)
C(6)	8993(5)	7721(4)	11578(2)	50(1)
C(7)	8646(5)	6478(4)	11627(3)	57(1)
C(8)	8922(6)	6075(5)	12439(3)	86(2)
C(9)	7114(5)	6207(4)	11385(3)	74(2)
C(10)	8673(4)	7406(3)	9572(2)	40(1)
C(11)	8898(5)	6390(4)	8425(2)	56(1)
C(12)	10003(5)	5729(5)	8010(3)	64(2)
C(13)	10383(7)	4697(6)	8274(4)	93(2)
C(14)	11398(9)	4079(8)	7884(5)	140(4)

C(15)	12041(9)	4484(11)	7238(7)	172(7)
C(16)	11641(8)	5505(10)	6981(4)	149(5)
C(17)	10644(6)	6130(6)	7362(3)	93(2)
C(18)	9708(8)	12161(5)	10140(4)	95(2)
C(19)	9232(11)	13359(5)	11158(5)	168(4)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **7b**.

	x	y	z	U(eq)
H(1)	10286(4)	7605(3)	10235(2)	47
H(2)	10184(6)	10838(4)	9436(3)	77
H(3A)	8438(6)	9696(4)	9701(3)	76
H(3B)	7760(6)	10643(4)	10210(3)	76
H(4)	8523(4)	9866(3)	11279(3)	56
H(5)	7605(4)	8232(3)	10735(2)	50
H(6A)	10014(5)	7818(4)	11682(2)	60
H(6B)	8466(5)	8102(4)	11977(2)	60
H(7)	9308(5)	6079(4)	11289(3)	68
H(8A)	9895(6)	6253(5)	12583(3)	129
H(8B)	8783(6)	5281(5)	12464(3)	129
H(8C)	8261(6)	6437(5)	12779(3)	129
H(9A)	6955(5)	5418(4)	11427(3)	111
H(9B)	6973(5)	6437(4)	10869(3)	111
H(9C)	6446(5)	6596(4)	11707(3)	111
H(11A)	8580(5)	7014(4)	8117(2)	67
H(11B)	8067(5)	5927(4)	8540(2)	67
H(13)	9961(7)	4414(6)	8713(4)	111
H(14)	11652(9)	3375(8)	8062(5)	168
H(15)	12735(9)	4068(11)	6983(7)	207
H(16)	12052(8)	5784(10)	6538(4)	179
H(17)	10396(6)	6833(6)	7181(3)	112
H(18A)	10608(8)	12558(5)	10060(4)	114
H(18B)	8978(8)	12481(5)	9810(4)	114
H(19A)	8934(11)	13370(5)	11680(5)	252
H(19B)	8555(11)	13775(5)	10858(5)	252
H(19C)	10173(11)	13688(5)	11114(5)	252

(3*S*,5*S*,1'*S*)-5-[1-(*tert*-Butyloxycarbonylamino)-3-methylbutyl]-3-methyltetra-hydrofuran-2-one (8).



Crystal data and structure refinement for **8**.

Identification code	s663rm
Empirical formula	C15 H27 N O4
Formula weight	285.38
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	hexagonal
Space group	P6(5)
Unit cell dimensions	a = 10.4364(9) A alpha = 90 deg. b = 10.4364(9) A beta = 90 deg. c = 28.872(11) A gamma = 120 deg.
Volume, Z	2723.4(11) A^3, 6
Density (calculated)	1.044 Mg/m^3
Absorption coefficient	0.075 mm^-1
F(000)	936
Crystal size	1.0 x 0.2 x 0.15 mm
Theta range for data collection	2.25 to 22.48 deg.
Limiting indices	0<=h<=10, 0<=k<=10, 0<=l<=34
Reflections collected	1438
Independent reflections	1213 [R(int) = 0.0484]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1063 / 13 / 182
Goodness-of-fit on F^2	1.150
Final R indices [I>2sigma(I)]	R1 = 0.1119, wR2 = 0.1722
R indices (all data)	R1 = 0.2002, wR2 = 0.2246
Absolute structure parameter	0(7)
Extinction coefficient	0.0085(8)
Largest diff. peak and hole	0.170 and -0.152 e.A^-3

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **8**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	9733(13)	9395(11)	1468(4)	62(3)
O(1)	12861(13)	10975(16)	1263(4)	104(4)
C(1)	13528(20)	12411(19)	1229(9)	129(10)
C(2)	13544(28)	13137(37)	1719(7)	159(11)
O(2)	14199(16)	13040(18)	908(6)	181(8)
O(3)	8548(12)	9435(13)	2128(3)	88(4)
C(3)	12313(23)	11740(25)	1973(6)	121(7)
O(4)	7874(11)	9833(12)	1419(4)	86(3)
C(4)	12327(23)	10507(25)	1719(7)	103(6)
C(5)	10800(21)	9095(20)	1703(6)	83(5)
C(6)	10823(21)	7855(22)	1452(6)	106(7)
C(7)	9379(36)	6344(28)	1414(8)	157(11)
C(8)	8602(31)	5809(26)	1830(8)	186(12)
C(9)	9705(31)	5248(27)	1159(10)	208(12)
C(10)	8695(14)	9537(15)	1713(6)	61(4)
C(11)	6622(22)	9971(24)	1582(7)	91(5)
C(12)	6063(23)	10265(28)	1126(8)	169(11)
C(13)	7087(24)	11146(25)	1945(8)	165(10)
C(14)	5475(21)	8503(26)	1771(9)	163(10)
C(15)	13158(38)	14243(36)	1625(13)	244(18)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **8**.

	x	y	z	U(eq)
H(1)	9762(13)	9483(11)	1171(4)	75
H(2)	14505(28)	13546(37)	1874(7)	191
H(3A)	12551(23)	11740(25)	2298(6)	145
H(3B)	11359(23)	11682(25)	1947(6)	145
H(4)	13013(23)	10271(25)	1878(7)	123
H(5)	10461(21)	8778(20)	2021(6)	100
H(6A)	11557(21)	7684(22)	1601(6)	127
H(6B)	11171(21)	8194(22)	1140(6)	127
H(7)	8726(36)	6507(28)	1209(8)	188
H(8A)	8442(31)	6554(26)	1968(8)	280
H(8B)	9166(31)	5566(26)	2039(8)	280
H(8C)	7666(31)	4940(26)	1770(8)	280
H(9A)	10237(31)	5693(27)	879(10)	312
H(9B)	8790(31)	4370(27)	1085(10)	312
H(9C)	10290(31)	4995(27)	1354(10)	312
H(12A)	6795(23)	11205(28)	1004(8)	254
H(12B)	5162(23)	10276(28)	1182(8)	254
H(12C)	5882(23)	9499(28)	908(8)	254
H(13A)	7821(24)	12080(25)	1819(8)	247
H(13B)	7493(24)	10899(25)	2206(8)	247
H(13C)	6243(24)	11214(25)	2043(8)	247
H(14A)	5188(21)	7761(26)	1535(9)	244
H(14B)	4626(21)	8561(26)	1868(9)	244

H(14C)	5876(21)	8246(26)	2031(9)	244
H(15A)	13964(38)	15063(36)	1469(13)	366
H(15B)	12954(38)	14577(36)	1911(13)	366
H(15C)	12295(38)	13834(36)	1431(13)	366