

Supplementary Material

General Methods. ^1H and ^{13}C NMR spectra were recorded at 250 or 400 MHz using CDCl_3 as internal standard. MS experiments were done in the EI mode (70 eV). Flash chromatography was performed using Merck silica gel 60 (0.004-0.063 mm). TLC monitoring was done on Merck plates (silica gel F₂₅₄), compounds were visualized by treatment with a solution of 48 g $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$ and 2 g $\text{Ce}(\text{SO}_4)_2$ in 1 l of 10 % H_2SO_4 , followed by heating. Solvents were distilled, if necessary, before use. *tert*-Butyl- α -bromomethylacrylate (**1**) was prepared following literature procedures¹⁵. ^{13}C -Methyl iodide was purchased from Cambridge Isotope Laboratories.

4- ^{13}C -*tert*-Butyl-2-oxobutanoate (**2**).

^{13}C -Methyl iodide (5.19 mmol, 0.74 g) was added to 5.19 mmol (126 mg) dry magnesia in 3 ml of Et_2O under an argon - atmosphere. The mixture was heated to 40 °C until no solid magnesia could be observed in the solution. After cooling to 0 °C, 4.55 mmol (1 g) of *tert*-Butyl- α -bromomethylacrylate (**1**) were added dropwise. The reaction mixture was stirred for 15 min. at 0 °C and for additionally 2 h at room temperature. After the solution was cooled to 0 °C, 3 g of ice and 2 ml saturated NH_4Cl solution were added. The aqueous phase was extracted 3 times with Et_2O (5 ml each). The organic layers were washed with NaHCO_3 solution and water, dried over MgSO_4 and evaporated. Kugelrohrdestillation of the crude product yielded 608 mg (3.9 mmol, 85%) of 4- ^{13}C -*tert*-Butyl-2-ethylacrylate. ^1H NMR (250 MHz, CDCl_3) δ 6.00 (s, 1H), 5.41 (s, 1H), 2.24-2.29 (m, 2H), 1.47 (s, 9H), 1.29 and 0.79 (two t, J = 126.5, 7.3 Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 167.0, 144.3, 122.7, 80.7, 28.5, 25.2 (d, J = 34.4 Hz), 13.11; EI-MS m/z = 157.0 (M^+), 101.1 ($\text{M}^+ - \text{C}_4\text{H}_9$), 57.1 (C_4H_9).

Ozone was bubbled through a solution of 3.9 mmol (608 mg) [4- ^{13}C]-*tert*-Butyl-2-ethylacrylate in 60 ml CH_2Cl_2 at -78°C until the mixture turned blue. Dry air was bubbled through the solution until the blue colour disappeared. After addition of 5.4 mmol (1.4 g) of triphenylphosphine, the mixture was brought to room temperature by stirring overnight. The solution was then evaporated, and the product purified by Kugelrohrdestillation, which afforded 462 mg (2.9 mmol, 75%) of 4- ^{13}C -*tert*-Butyl-2-oxobutanoate (**2**). ^1H NMR (250 MHz, CDCl_3) δ 2.72-2.82 (m, 2H), 1.52 (s, 9H), 1.34 and 0.83 (two t, J = 128.4, 7.3 Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 194.2, 158.8, 81.8, 30.5 (d, J = 35.9 Hz), 25.8, 5.0.

2-Keto-4- ^{13}C -butyrate (**3**).

Anhydrous HCl gas was bubbled through a solution of 3 mmol (480 mg) [4- ^{13}C]-*tert*-Butyl-2-oxobutanoate (**2**) in 10 ml $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ (1:1) for 15 minutes at a temperature of 0 °C. The

solution was stirred for 2 h at room temperature until TLC showed completion of the reaction. The solution was dried over MgSO_4 and evaporated to give a clear oil. Silica gel column chromatography (hexanes/ Et_2O = 1:1) yielded 250 mg (2.43 mmol, 81%) of product **3**. ^1H NMR (250 MHz, CDCl_3) δ 5.34 (s, 1H), 2.89-2.99 (m, 2H), 1.40 and 0.88 (two t, J = 129.1, 7.3 Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 4.9, 29.1 (d, J = 35.8 Hz), 157.6, 194.3; EI-MS m/z = 102.9 (M^+), 58.9 ($\text{M}^+ - \text{CO}_2$), 58.0 ($\text{M}^+ - \text{HCO}_2$).

2-Keto-3-methyl-d₃-4- ^{13}C -butyrate (4).

To a solution of 4- ^{13}C -*tert*-Butyl-2-oxobutanoate (**2**) (2.87 mmol, 462 mg) in 1 ml Et_2O , dimethyl hydrazine (2.81 mmol, 0.21 ml) was added dropwise. The mixture was stirred at room temperature overnight, then diluted with 25 ml ether and washed with H_2O . The organic layer was dried over MgSO_4 and evaporated to yield 3- ^{13}C -Methyl-2-oxo-*tert*-butylpropionate, N,N-dimethylhydrazone (554 mg, 2.75 mmol, 96%). ^1H NMR (250 MHz, CDCl_3) δ 2.49 (s, 6H), 2.30-2.40 (m, 2H), 1.51 (s, 9H), 1.34 and 0.83 (two t, J = 127.9, 7.5 Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 164.5, 153.6, 81.9, 47.8, 28.5, 22.4 (d, J = 33.7), 11.0; EI-MS m/z = 201.3 (M^+), 145.2 ($\text{M}^+ - \text{C}_4\text{H}_9$), 57.1 (C_4H_9).

3- ^{13}C -Methyl-2-oxo-*tert*-butylpropionate, N,N-dimethylhydrazone 2.75 mmol (554 mg) was dissolved in 9 ml of THF and cooled to -78°C . To this solution 3.5 mmol LDA were added dropwise under an argon – atmosphere. The enolate was allowed to generate over 1 h at -78°C , followed by the slow addition of a solution of 4 mmol CD_3I in 3 ml THF. Stirring was continued for 2 h at -78°C . The reaction was quenched by adding 0.8 ml H_2O . Then the reaction-mixture was brought to room temperature, evaporated, and the residue redissolved in 15 ml EtOAc . The solution was washed with H_2O , dried over MgSO_4 and evaporated to yield a yellow oil. Silica gel column chromatography (hexanes/ Et_2O = 7:3) yielded 476 mg (2.18 mmol, 80%) of 3- ^{13}C , 3- CD_3 -Dimethyl-2-oxo-*tert*-butylpropionate, N,N-dimethylhydrazone. ^1H NMR (250 MHz, CDCl_3) δ 2.59 (m, 1H), 2.45 (s, 6H), 1.50 (s, 9H), 1.38 and 0.87 (two d, J = 127.2, 6.8 Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 167.1, 165.3, 82.6, 47.6, 28.4, 19.9; EI-MS m/z = 218.1 (M^+), 162.1 ($\text{M}^+ - \text{C}_4\text{H}_9$), 57.0 (C_4H_9).

To a solution of 3- ^{13}C , 3- CD_3 -Dimethyl-2-oxo-*tert*-butylpropionate, N,N-dimethylhydrazone (2.18 mmol, 476 mg) in 9 ml THF 2.6 ml 1N HCl were added and the mixture was stirred for 1 h at room temperature. The solution was diluted with 30 ml Et_2O , the organic layer was separated and the aqueous phase was extracted 2 times with Et_2O (15 ml each). The combined organic phases were washed with brine (5 ml), dried over MgSO_4 , and evaporated to give an oil. Chromatography over silica gel (hexanes/ Et_2O = 7:3) yielded 353 mg (2 mmol, 92%) of 3- ^{13}C , 3- CD_3 -Dimethyl-2-oxo-*tert*-butylpropionate. ^1H NMR (250 MHz, CDCl_3) δ 3.11-3.15 (m,

1H), 1.53 (s, 9H), 1.38 and 0.87 (two d, $J = 128.2, 6.8$ Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3) δ 199.6, 162.1, 84.3, 37.1 (d, $J = 33.7$ Hz), 28.3, 17.4; EI-MS $m/z = 176.0$ (M^+), 118.0 ($\text{M}^+ - \text{C}_4\text{H}_9$), 75.0 ($\text{M}^+ - \text{C}_4\text{H}_9 - \text{CO}_2$), 57.0 (C_4H_9).

Anhydrous HCl gas was bubbled through a solution of 2 mmol (353 mg) 3- ^{13}C , 3- CD_3 -Dimethyl-2-oxo-*tert*-butylpropionate in 10 ml $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ (1:1) for 15 minutes at a temperature of 0 °C. The solution was stirred for 2 h at room temperature until TLC showed completion of the reaction. The reaction mixture was dried over MgSO_4 and evaporated to give a colorless oil. Silica gel column chromatography (hexanes/ $\text{Et}_2\text{O} = 7.3$) yielded 200 mg (1.66 mmol, 83%) of product **4**. ^1H NMR (250 MHz, CDCl_3) δ 3.44 (m, 1H), 1.46 and 0.94 (two d, $J = 128.8, 6.8$ Hz, 3H). EI-MS $m/z = 120.0$ (M^+), 75.0 ($\text{M}^+ - \text{HCO}_2$).