# Synthesis of Tertiary Enamides by $\mathrm{Ag}_{2} \mathrm{CO}_{3}$-promoted Pd-Catalyzed Alkenylation of Acyclic Secondary Amides 

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## 1. General Methods, Chemicals and Technical Equipment

Thin layer chromatography (TLC) was conducted on pre-coated aluminum sheets with 0.20 mm Machevery-Nagel Alugram SIL G/UV254 with fluorescent indicator UV254. Column chromatography was carried out using Merck Gerduran silica gel 60 (particle size 63-200 $\mu \mathrm{m}$ ). Microwave reactions were performed on a Biotage $A B$ Initiator microwave instrument producing controlled irradiation at 2.450 GHz . Melting points (M.p.) were measured on a Büchi Melting Point B-545 in open capillary tubes and have not been corrected. Nuclear magnetic resonance (NMR) ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ spectra were obtained on a 400 MHz NMR (Jeol JNM EX-400), 270 MHz (Jeol JNM EX-270) or a Brucker Fourier 300 MHz at rt otherwise stated. Chemical shifts were reported in ppm according to trimethylsilane using the solvent residual signal as an internal reference $\left(\mathrm{CDCl}_{3}: \delta_{\mathrm{H}}=7.26 \mathrm{ppm}, \delta_{\mathrm{C}}=77.16 \mathrm{ppm} ; \mathrm{DMSO}-\mathrm{d}_{6}: \delta_{\mathrm{H}}=2.50 \mathrm{ppm}\right.$, $\delta_{\mathrm{C}}=39.52 \mathrm{ppm} ; \mathrm{CD}_{2} \mathrm{Cl}_{2}: \delta_{\mathrm{H}}=5.32 \mathrm{ppm}, \delta_{\mathrm{C}}=53.84 \mathrm{ppm} ;$ ). Coupling constants $(\mathcal{J})$ were given in Hz. Resonance multiplicity was described as $s$ (singlet), $d$ (doublet), $t$ (triplet), $d d$ (doublet of doublets), $d t$ (doublet of triplets), td (triplet of doublets), $q$ (quartet), $m$ (multiplet) and broad (broad signal). Carbon spectra were acquired with a complete decoupling for the proton. Infrared spectra (IR) were recorded on (i) a BIO-RAD FTS-165 apparatus between 4000 and $600 \mathrm{~cm}^{-1}$. Liquid samples have been prepared as film between two sodium chloride cells ( NaCl ) and solid samples were spread out in potassium bromide ( KBr ) before being pressed as a transparency 0.2 mm tablet or (ii) on a Perkin-Elmer Spectrum II FT-IR System with Specac Silver Gate Evolution single-reflection ATR mounted with a diamond mono-crystal. Liquid chromatography mass spectrometry (LC-MS) measurements were conducted on an Agilent 6200 series TOF mass spectrometer equipped with ESI and APCI ionization sources and a Time Of Flight (TOF) detector, operating in positive mode. The analyte solutions were delivered to the ESI or APCI source by an Agilent 1200 series LC system at a flow rate of $0.25 \mathrm{~mL} / \mathrm{min}$. Typical elution gradient start from $\mathrm{H}_{2} \mathrm{O}(90 \%)$ to $\mathrm{CH}_{3} \mathrm{CN}(100 \%)$ for 20 minutes. ESI mode: Typical ESI conditions were capillary voltage 2.0 kV ; cone voltage 65 V ; source temperature $150^{\circ} \mathrm{C}$; desolvation temperature $250{ }^{\circ} \mathrm{C}$; drying gas $5 \mathrm{~L} / \mathrm{min}$, nebulizer 60 psig. APCI: Typical APCI conditions were, capillary voltage 2.0 kV ; cone voltage 65 V ; source temperature 250 ${ }^{\circ} \mathrm{C}$; desolvation temperature $350^{\circ} \mathrm{C}$; drying gas $5 \mathrm{~L} / \mathrm{min}$; nebuliser 60 psig. Dry nitrogen was used as the ESI and APCI gas. Mass spectrometry was generally performed by the Centre de spectrométrie de masse at (i) the Université de Mons in Belgium were they performed ESI-MS and MALDI-MS, on using the following
instrumentation. ESI-MS measurements were performed on a Waters QToF2 mass spectrometer operating in positive mode. The analyte solutions were delivered to the ESI source by a Harvard Apparatus syringe pump at a flow rate of $5 \mu \mathrm{~L} / \mathrm{min}$. Typical ESI conditions were, capillary voltage 3.1 kV ; cone voltage 20-50 V; source temperature $80^{\circ} \mathrm{C}$; desolvation temperature $120^{\circ} \mathrm{C}$. Dry nitrogen was used as the ESI gas. For the recording of the single-stage ESI-MS spectra, the quadrupole (rfonly mode) was set to pass ions from 50 to 1000 Th, and all ions were transmitted into the pusher region of the time-of-flight analyzer where they were mass analyzed with 1 s integration time. MALDI-MS were recorded using a Waters QToF Premier mass spectrometer equipped with a nitrogen laser, operating at 337 nm with a maximum output of 500 mW delivered to the sample in 4 ns pulses at 20 Hz repeating rate. Time-of-flight analyses were performed in the reflectron mode at a resolution of about 10,000 . The matrix solution ( $1 \mu \mathrm{~L}$ ) was applied to a stainless steel target and air-dried. Analyte samples were dissolved in a suitable solvent to obtain 1 $\mathrm{mg} / \mathrm{mL}$ solutions. $1 \mu \mathrm{~L}$ aliquots of those solutions were applied onto the target area already bearing the matrix crystals, and air-dried. For the recording of the singlestage MS spectra, the quadrupole (rf-only mode) was set to pass ions from 100 to 1000 Th, and all ions were transmitted into the pusher region of the time-of-flight analyzer where they were analyzed with 1 s integration time or (ii) The "Fédération de Recherche" ICOA/CBM (FR2708) platform of Orléans in France. High-resolution ESI mass spectra (HRMS) were performed on a Bruker maXis Q-TOF in the positive ion mode. The analytes were dissolved in a suitable solvent at a concentration of 1 $\mathrm{mg} / \mathrm{mL}$ and diluted 200 times in methanol ( $\approx 5 \mathrm{ng} / \mathrm{mL}$ ). The diluted solutions $(1 \mu \mathrm{~L})$ were delivered to the ESI source by a Dionex Ultimate 3000 RSLC chain used in FIA (Flow Injection Analysis) mode at a flow rate of $200 \mu \mathrm{~L} / \mathrm{min}$ with a mixture of $\mathrm{CH}_{3} \mathrm{CN} / \mathrm{H}_{2} \mathrm{O}+0.1 \%$ of $\mathrm{HCO}_{2} \mathrm{H}$ (65/35). ESI conditions were as follows: capillary voltage was set at 4.5 kV ; dry nitrogen was used as nebulizing gas at 0.6 bars and as drying gas set at $200^{\circ} \mathrm{C}$ and $7.0 \mathrm{~L} / \mathrm{min}$. ESI-MS spectra were recorded at 1 Hz in the range of 50-3000 m/z. Calibration was performed with ESI-TOF Tuning mix from Agilent and corrected using lock masses at $m / z 299.294457$ (methyl stearate) and 1221.990638 (HP-1221). Data were processed using Bruker DataAnalysis 4.1 software. X-ray measurements for compound 20 and 21 were performed on a Gemini Ultra R system (4-circle kappa platform, Ruby CCD detector) using Mo K $\alpha$ radiation ( $\lambda=0.71073 \AA$ ) or $\mathrm{Cu} \mathrm{K} \alpha$ radiation ( $\lambda=1.54178 \AA \AA$ ) at Université F.U.N.D.P. de Namur in Belgium. After mounting and centering of the single crystal on the diffractometer, cell parameters were estimated from a pre-experiment run and full
data sets collected at room temperature. Structures were solved by direct methods with SHELXS-86 program and then refined on $\mathrm{F}^{2}$ using SHELXL-97 software. ${ }^{[1]}$ Nonhydrogen atoms were anisotropically refined and the hydrogen atoms (not implicated in H -bonds) in the riding mode with isotropic temperature factors fixed at 1.2 times $\mathrm{U}(\mathrm{eq})$ of the parent atoms. In addition for compound S1, data collections were performed at the X-ray diffraction beamline (XRD1) of the Elettra Synchrotron, Trieste (Italy), with a Pilatus 2M image plate detector. Complete datasets were collected at 100 K (nitrogen stream supplied through an Oxford Cryostream 700) with a monochromatic wavelength of $0.700 \AA$ through the rotating crystal method. The crystals of compound S1 were dipped in N-paratone and mounted on the goniometer head with a nylon loop. The diffraction data were indexed, integrated and scaled using XDS. ${ }^{[2]}$ The structures were solved by direct methods using SIR2014, ${ }^{[3]}$ Fourier analyzed and refined by the full-matrix least-squares based on $F^{2}$ implemented in SHELXL-2014. ${ }^{[4]}$ The Coot program was used for modeling. ${ }^{[5]}$ Anisotropic thermal motion modeling was then applied to atoms with full occupancy. Hydrogen atoms were included (except for disordered water molecules) at calculated positions with isotropic $U_{\text {factors }}=1.2 \mathrm{U}_{\text {eq }}$ or $\mathrm{U}_{\text {factors }}=1.5 \mathrm{U}_{\text {eq }}$ for methyl groups.

### 1.1. Materials and methods

Chemicals were purchased from Sigma Aldrich, Acros Organics, TCI and ABCR and were used as received. Solvents were purchased from Sigma Aldrich, while deuterated solvents from Eurisotop. THF was distilled from Na-benzophenone ketyl. Sulfuric acid ( $\mathrm{H}_{2} \mathrm{SO}_{4} 95 \%$ ) and hydrochloridic acid ( $\mathrm{HCl} 32 \%$ ) were purchased from Fischer Scientific. The following vinyl halides trans-3-bromo-methylacrylate, trans-3-iodo-methylacrylate, trans-3-chloro-methylacrylate and 1:1 mixture of cis and trans-3-bromo-2-methylacrylonitrile were purchased, whereas cis-3-bromo-ethylacrylate ${ }^{[6]}$, cis-3-fluoro-ethylacrylate ${ }^{[7]}$, methyl-3-bromo-methylacrylate ${ }^{[8]}$ and methyl-3-bromo-2methoxyacrylate ${ }^{[9]}$ were synthesized according to the reported procedures. Anhydrous conditions were achieved by drying Schlenk tubes or 2-neck flasks by flaming with a heat gun under vacuum and then purging with Argon. The inert atmosphere was maintained using Argon-filled balloons equipped with a syringe and needle that was used to penetrate the silicon stoppers used to close the flasks necks. Additions of liquid reagents were performed using dried plastic or glass syringes.

## 2. Synthetic procedures

## Optimisation of reaction conditions for the synthesis of enamide: General method

A Schlenk tube under argon, was charged with the Pd-based catalyst ( 0.0125 mmol ), the ligand ( 0.019 mmol ), N-methylpropionamide ( $26 \mathrm{mg}, 0.3 \mathrm{mmol}$ ), the base ( 0.35 mmol ) and $3 \AA$ molecular sieves ( 20 mg ). After the addition of the solids, the Schlenk tube was evacuated and back filled with argon. This was followed by the addition of a solution of methyl-(E)-3bromoacrylate ( $41 \mathrm{mg}, 0.25 \mathrm{mmol}$ ) in THF ( 3 mL ) at room temperature. After 1 h , the mixture was heated at $65^{\circ} \mathrm{C}$ for additional 16 h . The reaction mixture was then cooled down to room temperature, diluted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, filtered on silica gel and concentrated in vacuo. The crude materials were purified using silica gel preparative TLC plates (cyclohexane/EtOAc, 8:2).

## Methyl ( $E$ )-3-(N-methylpropionamido)acrylate 1


M.F. : $\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{NO}_{3}$
M.W. : 171.19600
$36 \mathrm{mg}, 83 \%$; yellow powder; m.p. $79-51^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(270 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.09$ (brs, 1 H , $\left.H_{e}\right), 5.27\left(\mathrm{~d}, J=13.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right), 3.74\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 3.12\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 2.62(\mathrm{q}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{b}}\right), 1.20\left(\mathrm{t}, \mathrm{J}=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(68 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 173.5,168.0,142,6,98.6$, 51.6, 29.8, 27.2, 9.1; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1711,1695,1622,1244,1217,1187,1172,1114$, 1067, 755 ; HR-EI-MS: $\left[\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 171.0895; found 171.0903.

## Synthesis of enamide: general method

A Schlenk tube under argon, was charged with $\left[\mathrm{Pd}_{2}(\mathrm{dba})_{3}\right]$ ( $\left.11 \mathrm{mg}, 0.0125 \mathrm{mmol}\right)$, Xantphos $(22 \mathrm{mg}, 0.019 \mathrm{mmol})$, the relevant amide ( 0.3 mmol ), $\mathrm{Ag}_{2} \mathrm{CO}_{3}(96.5 \mathrm{mg}, 0.35 \mathrm{mmol})$ and $3 \AA$ molecular sieves $(20 \mathrm{mg})$. After the addition of the solids, the Schlenk tube was evacuated and back filled with argon. This was followed by the addition of a solution of the relevant vinyl bromide ( 0.25 mmol ) in THF ( 3 mL ) at room temperature. After 1 h , the mixture was heated at $65{ }^{\circ} \mathrm{C}$ for additional 16 h . The reaction mixture was then cooled down to room temperature, diluted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, filtered on silica gel and concentrated in vacuo. The crude materials were purified using silica gel preparative TLC plates (cyclohexane/EtOAc, 8:2).

## Ethyl (Z)-3-( $N$-methylpropionamido) acrylate 2


$30 \mathrm{mg}, 70 \% ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right) \delta(\mathrm{ppm}) 7.10\left(\mathrm{~d}, J=9.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 5.16(\mathrm{~d}, J=9.9$ $\left.\mathrm{Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right), 4.13\left(\mathrm{q}, J=7.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 3.20\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 2.47\left(\mathrm{q}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.26(\mathrm{t}$, $\left.J=7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 1.24\left(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right) \delta(\mathrm{ppm}) 176.4$, 167.3, 142.1, 104.5, 62.5, 38.2, 29.8, 16.4, 11.1; IR (neat, $\mathrm{cm}^{-1}$ ) $u_{\max } 2981,2941,1708,1690$, 1620, 1460, 1371, 1339, 1267, 1161, 1107, 1058, 1032, 947, 800; HR-EI-MS: [C ${ }_{9} \mathrm{H}_{15} \mathrm{NO}_{3}$ ] $\left(\mathrm{M}^{+}\right)$requires 185.1052; found 185.1053.

## Ethyl (Z)-3-(2-oxopiperidin-1-yl)acrylate 3


M.F. : $\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}$
M.W. : 197.23100
$33 \mathrm{mg}, 67 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.35(\mathrm{~d}, J=10.4 \mathrm{~Hz}, 1 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{f}}\right), 5.24\left(\mathrm{~d}, J=10.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 4.14\left(\mathrm{q}, J=7.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 3.71\left(\mathrm{t}, J=5.8 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.54$ $\left(\mathrm{t}, J=6.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.87-1.81\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{c}-\mathrm{d}}\right), 1.27\left(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{j}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(75 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.8,165.5,138.9,103.1,60.4,49.8,32.7,23.3,20.7,14.4$; IR (neat, $\mathrm{cm}^{-1}$ ) $u_{\max }$ 2953, 1707, 1678, 1622, 1460, 1389, 1331, 1292, 1271, 1145, 1083, 1028; HR-EI-MS: $\left[\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}\right]\left(\mathrm{M}^{+}\right)$requires 197.1052; found 197.1053.

## Methyl (E)-3-(2-oxopiperidin-1-yl)acrylate 4


$32 \mathrm{mg}, 69 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.61\left(\mathrm{~d}, \mathrm{~J}=14.7 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right), 5.26$ $\left(\mathrm{d}, J=14.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.73\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 3.43\left(\mathrm{t}, J=6.2 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.56(\mathrm{t}, J=6.6 \mathrm{~Hz}, 2 \mathrm{H}$, $\mathrm{H}_{\mathrm{b}}$ ), 1.97-1.90 (m, 2H, $\mathrm{H}_{\mathrm{c}}$ ), 1.87-1.81 (m, 2H, $\mathrm{H}_{\mathrm{d}}$ ) ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 169.4$, $168.0,141.1,99.6,51.5,45.7,33.3,22.5,20.4$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2956,1707,1683,1614$, 1410, 1329, 1294, 1257, 1155, 1092; HR-EI-MS: $\left[\mathrm{C}_{9} \mathrm{H}_{13} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 183.0895; found 183.0888.

## Methyl (E)-2-methyl-3-( $N$-phenylacetamido)acrylate 5


$34 \mathrm{mg}, 63 \%$; white solid; m.p. $116-118^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.69(\mathrm{~d}, J=$ $14.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{g}}$ ), 7.54-7.46 (m, 3H, $\mathrm{H}_{\mathrm{Ar}}$ ), 7.18-7.15 (m, 2H, Har $), 4.68\left(\mathrm{~d}, J=14.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right)$, $3.69\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{j}}\right), 1.96\left(\mathrm{br} \mathrm{s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 169.7,167.9,142.3$, $138.5,130.6,129.6,128.4,102.2,51.5,23,5$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1720,1696,1642,1598$, 1495, 1370, 1288, 1256, 1169,1128; HR-EI-MS: $\left[\mathrm{C}_{12} \mathrm{H}_{13} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 219.0895; found 219.0900.

## Methyl (E)-3-(N-pentyl-2-phenylacetamido)acrylate 6


$24 \mathrm{mg}, 33 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.64\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{I}}\right), 7.37-7.25(\mathrm{~m}, 5 \mathrm{H}$, $\mathrm{H}_{\mathrm{Ar}}$ ), $3.98\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.78\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{o}}\right), 3.61-3.60\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 5.26\left(\mathrm{~d}, \mathrm{~J}=14 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{m}}\right)$, 1.57-1.47 (m, 2H, $\mathrm{H}_{\mathrm{d}}$ ), 1.36-1.21 (m, 4H, $\left.\mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}\right), 0.88\left(\mathrm{t}, \mathrm{J}=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(66$ $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}): 170.7,168.0,142.2,134.8,133.6,129.0,127.5,98.5,52.8,51.6,41.3$, 29.1, 26.2, 22.5, 14.1; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2955,1715,1692,1619,1309,1282,1257,1167$, 1114; HR-EI-MS: $\left[\mathrm{C}_{17} \mathrm{H}_{23} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 289.1678; found 289.1676.

## Methyl (E)-3-acetamido-2-methylacrylate 7


$8 \mathrm{mg}, 19 \%$; yellow powder; m.p.: $122-123^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.01$ (d, $J=$ $12.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{c}}$ ), $7.22(\mathrm{brs}, 1 \mathrm{H},-\mathrm{NH}), 3.74\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 2.17\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 1.82(\mathrm{~d}, J=1.4 \mathrm{~Hz}$, $\left.3 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 168.7,167.6,131.8,107.6,51.9,23.8,10.8 ; \mathrm{IR}$ (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 3307,1711,1685,1650,1510,1425,1255,1204,1182,1124 ; H R-E I-M S$ : $\left[\mathrm{C}_{7} \mathrm{H}_{11} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 157.0739; found 157.0747.

## Methyl (E)-2-methyl-3-(2-oxopiperidin-1-yl)acrylate 8


M.F. : $\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}$ M.W. : 197.23400
$38 \mathrm{mg}, 78 \%$; yellow solid; m.p. $51-53^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.77\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right)$, $3.74\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{j}}\right), 3.59-3.62\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.55-2.51\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.90\left(\mathrm{~d}, \mathrm{~J}=1.4 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right)$, 1.88-1.84 (m, 4H, $\left.\mathrm{H}_{\mathrm{c}}+\mathrm{H}_{\mathrm{d}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.4,169.0,138.9,117.6$, 52.1, 49.8, 32.6, 23.4, 20.8, 13.5; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1701,1669,1630,1404,1296,1239$, 1188, 1160, 1119, 1093; HR-EI-MS: $\left[\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 197.1052; found 197.1049.

## Methyl (E)-2-methyl-3-( N -methylpropionamido)acrylate 9


M.F. : $\mathrm{C}_{9} \mathrm{H}_{15} \mathrm{NO}_{3}$ M.W. : 185.22300
$37 \mathrm{mg}, 81 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(270 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.65$ (brs, $1 \mathrm{H}, \mathrm{H}_{\mathrm{e}}$ ), 3.76 (s, $\left.3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 3.18\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 2.41\left(\mathrm{q}, J=7.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.92\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 1.16(\mathrm{t}, J=7.6 \mathrm{~Hz}, 3 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(66 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 174.5,168.8,139.7,52.7,52.2,35.1,27.9,13.2,9.2 ;$ IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1712,1688,1634,1436,1377,1295,1233,1132,1104,1068$; HR-EI-MS: $\left[\mathrm{C}_{9} \mathrm{H}_{15} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 185.1052; found 185.1043.

## Methyl (E)-2-methyl-3-(N-phenylacetamido)acrylate 10


$46 \mathrm{mg}, 79 \%$; white solid; m.p. $70^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 8.26\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right)$, 7.46-7.35 (m, 3H, $\mathrm{H}_{\text {Ar }}$ ), 7.21-7.18 (m, 2H, $\mathrm{H}_{\text {Ar }}$ ), $3.72\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{k}}\right), 2.01\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 1.16(\mathrm{~s}, 3 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 171.0,169.6,140.9,136.5,129.8,128.5,128.5$, 113.5, 52.0, 23.2, 11.7; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1687,1636,1594,1493,1366,1316,1295,1221$, 1114, 700 ; HR-EI-MS: $\left[\mathrm{C}_{13} \mathrm{H}_{15} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 233.1052; found 233.1045 .

## Methyl (E)-2-methyl-3-(N-pentyl-2-phenylacetamido)acrylate 11


M.F. : $\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{3}$
M.W. : 303.40200
$24 \mathrm{mg}, 31 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.40\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{1}\right), 7.32-7.20(\mathrm{~m}, 5 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{Ar}}\right), 3.79\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{p}}\right), 3.67\left(\mathrm{brs}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.54\left(\mathrm{t}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 1.82\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{n}}\right), 1.49(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 1.31-1.19\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}\right), 0.84\left(\mathrm{t}, \mathrm{J}=7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ (ppm) 170.9, 168.2, 138.7, 134.4, 129.2, 128.7, 127.1, 123.0, 52.3, 47.2, 41.9, 29.1, 27.9 , 22.5, 14.1, 13.1; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max }$ 2954, 2929, 1714, 1673, 1631, 1435, 1352, 1272, 1187, 1107; HR-EI-MS: $\left[\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 303.1834; found 303.1844.

## Methyl (Z)-3-acetamido-2-methoxyacrylate 12


$32 \mathrm{mg}, 75 \%$; yellow powder; m.p. $67-69^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.75$ (br s, $1 \mathrm{H},-\mathrm{NH}$ ), $7.66\left(\mathrm{~d}, \mathrm{~J}=11.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{c}}\right), 3.75\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.73\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.14\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right)$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 167.6,164.1,131.6,121.9,60.1,51.8,23.5$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1686,1651,1492,1433,1332,1225,1107,1040,993,772 ;$ HR-EI-MS: $\left[\mathrm{C}_{7} \mathrm{H}_{11} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 173.0688; found 173.0690.

## Methyl (Z)-2-methoxy-3-(N-methylpropionamido)acrylate 13


M. F. : $\mathrm{C}_{9} \mathrm{H}_{15} \mathrm{NO}_{4}$
M.W. : 201.22200
$43 \mathrm{mg}, 85 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(270 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.48$ (brs, $\left.1 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 3.79$ (s, $3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}$ ), $3.67\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.36\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 2.51\left(\mathrm{q}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.19(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(66 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 173.9,165.4,132.0,125.6,60.9,52.2,32.8,27.5$, 9.2; IR (neat, $\mathrm{cm}^{-1}$ ) v1714, 1687, 1634, 1376, 1290, 1217, 1120, 1097, 1062, 1034; HR-EIMS: $\left[\mathrm{C}_{9} \mathrm{H}_{15} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 201.10001; found 201.0995.

## Methyl (Z)-2-methoxy-3-(2-oxopiperidin-1-yl)acrylate 14


$39 \mathrm{mg}, 74 \%$; yellow solid; m.p. $46-49{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.85\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right)$, $3.78\left(\mathrm{t}, \mathrm{J}=4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 3.76\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{j}}\right), 3.65\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 2.53\left(\mathrm{t}, \mathrm{J}=4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.86-$
$1.84\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{c}}+\mathrm{H}_{\mathrm{d}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.0,165.3,133.3,124.2,60.8$, 52.0, 48.1, 32.9, 23.2, 20.5; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1712,1671,1641,1288,1231,1194,1177$, 1158, 1094, 1027; HR-EI-MS: $\left[\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 213.1001; found 213.1008.

## Methyl (Z)-2-methoxy-3-(N-phenylacetamido)acrylate 15


$23 \mathrm{mg}, 37 \%$; yellow powder; m.p.: $55-57^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.99(\mathrm{~s}, 1 \mathrm{H}$, $\mathrm{H}_{\mathrm{g}}$ ), 7.44-7.39 (m, 3H, $\mathrm{H}_{\text {Ar }}$ ), 7.27-7.24 (m, $2 \mathrm{H}, \mathrm{H}_{\mathrm{Ar}}$ ), $3.76\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{k}}\right), 2.93\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{i}}\right), 1.93(\mathrm{~s}$, $\left.3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(66 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.5,165.3,141.3,133.1,129.4,128.6,128.1$, 124.5, 59.4, 52.0, 23.0; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1718,1693,1649,1372,1300,1231,1138,1106$, 1050, 700; HR-EI-MS: $\left[\mathrm{C}_{13} \mathrm{H}_{15} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 249.1001; found 249.0991.

## Methyl (Z)-2-methoxy-3-( $N$-pentyl-2-phenylacetamido)acrylate 16


$24 \mathrm{mg}, 30 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.41$ (brs, $\left.1 \mathrm{H}, \mathrm{H}_{1}\right), 7.35-7.24(\mathrm{~m}$, $5 \mathrm{H}, \mathrm{H}_{\text {Ar }}$ ), $3.85\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.80-3.76\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 3.79\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{p}}\right), 3.63\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{n}}\right), 1.55-1.51$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 1.31-1.22\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}\right), 0.87\left(\mathrm{t}, \mathrm{J}=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(100 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 171.0,165.2,134.1,132.2,129.0,128.9,127.3,124.4,60.5,52.2,45.5,41.9$, 29.1, 28.4, 22.5, 14.2; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2954,1716,1682,1637,1434,1377,1237,1190$, 1100, 1031; HR-EI-MS: $\left[\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 319.1784; found 319.1774.

## N-(2-Cyanoprop-1-en-1-yl)-N-methylpropionamide 17


M.F. : $\mathrm{C}_{8} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$
M.W. : 152.19700

## Diastereoisomer A

$15 \mathrm{mg}, 39 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 3.48\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 2.48(\mathrm{q}, \mathrm{J}=7.3$ $\left.\mathrm{Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.98\left(\mathrm{~d}, J=1.2 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 1.17\left(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right)$ (the vinylic proton could not be observed on the spectra); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(66 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ (ppm) 173.2, 153.0, 139.8, 119.1, 87.1, 27.5, 19.8, 9.0; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2984,2201,1688,1633,1415,1375,1277$, 1064, 819, 599; HR-EI-MS: [ $\left.\mathrm{C}_{8} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 152.0950; found 152.0948.

## Diastereoisomer B

$13 \mathrm{mg}, 33 \%$; yellow oil; m.f.: $\mathrm{C}_{8} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 3.20\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right)$, 2.41 ( $\mathrm{q}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}$ ), $1.97\left(\mathrm{~d}, J=1.2 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.16\left(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right)$ (the vinylic proton could not be observed on the spectra); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(66 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm})$ 173.7, 142.3, 120.9, 96.5, 35.0, 27.7, 15.8, 9.0; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2983,2212,1688,1635$, 1420, 1412, 1322, 1295, 1067, 540; HR-EI-MS: $\left[\mathrm{C}_{8} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 152.0950; found 152.0954.

## 2-Methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18


M.F. : $\mathrm{C}_{9} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$ M.W. : 164.20800

## Diastereoisomer A

$11 \mathrm{mg}, 26 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.64\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right), 3.98(\mathrm{t}, \mathrm{J}=6.2$ $\left.\mathrm{Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.54\left(\mathrm{t}, J=6.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.98\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 1.94-1.81\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{c}}+\mathrm{H}_{\mathrm{d}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}$ (100 MHz, $\mathrm{CDCl}_{3}$ ) $\delta(\mathrm{ppm}) 169.6,138.9,119.3,87.3,47.8,32.9,22.9,20.3,20.0$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max }$ 2203, 1677, 1628, 1403, 1343, 1331, 1289, 1264, 1163, 1104; HR-EI-MS: $\left[\mathrm{C}_{9} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 164.0950; found 164.0956.

## Diastereoisomer B

$16 \mathrm{mg}, 39 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.33\left(\mathrm{~d}, \mathrm{~J}=1.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{f}}\right), 3.64-$ $3.60\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 2.55-2.52\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 1.94\left(\mathrm{~d}, J=1.4 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{h}}\right), 1.90-1.83(\mathrm{~m}, 4 \mathrm{H}$, $\mathrm{H}_{\mathrm{c}}+\mathrm{H}_{\mathrm{d}}$ ) ; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 169.8,141.4,121.1,97.2,49.7,32.6,23.2,20.6$, 16.2; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2210,1673,1626,1403,1344,1330,1299,1254,1160,1092$; HR-El-MS: $\left[\mathrm{C}_{9} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 164.0950; found 164.0956.

## Ethyl 3-(N-pentyl-2-phenylacetamido)prop-2-enoate 19


$17 \mathrm{mg}, 23 \%$; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.36-7.30\left(\mathrm{~m}, 5 \mathrm{H}, \mathrm{H}_{\mathrm{Ar}}\right), 6.91(\mathrm{~d}, \mathrm{~J}$ $\left.=10.5 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{l}}\right), 5.20\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 5.11\left(\mathrm{~d}, J=10.6 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{m}}\right), 4.12\left(\mathrm{q}, J=7.3 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{0}\right)$, $3.90\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 1.53\left(\mathrm{~m}, 2 \mathrm{H}_{\mathrm{d}}\right), 1.28-1.23\left(\mathrm{~m}, 7 \mathrm{H}, \mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}+\mathrm{H}_{\mathrm{p}}\right), 0.85\left(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right)$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 165.3,154.8,138.0,135.7,128.7,128.5,128.3,101.9$, 68.6, 60.3, 47.6, 28.8, 27.8, 22.5, 14.4, 14.1; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 1710,1628,1455,1389$, 1340, 1267, 1134, 1029, 956, 697; HR-EI-MS: $\left[\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 303.1834; found 303.1827.

## N-((2-(tert-Butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)-N-pentyl-2-phenylacetamide 20


$59 \mathrm{mg}, 66 \%$; white powder; m.p.: $65-64^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.33-7.25(\mathrm{~m}$, $5 \mathrm{H}, \mathrm{H}_{\text {Ar }}$ ), $6.78\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{l}}\right), 5.43\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{o}}\right), 3.87\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.78-3.74\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 1.65-1.52$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 1.42-1.25\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}\right), 0.97\left(\mathrm{~s}, 9 \mathrm{H}, \mathrm{H}_{\mathrm{q}}\right), 0.87\left(\mathrm{t}, \mathrm{J}=4 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}$ $\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.3,164.4,133.8,128.9,128.9,127.3,123.1,110.2,44.8,41.3$, $35.8,28.9,28.5,22.9,22.5,14.1$ (the sp2 carbon alpha to the amide couldn't be seen on the ${ }^{13} \mathrm{C}-\mathrm{NMR}$ ); IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2961,1783,1662,1395,1329,1220,1168,1115,1083,734$; HR-EI-MS: $\left[\mathrm{C}_{21} \mathrm{H}_{29} \mathrm{NO}_{4}\right]^{+}\left(\mathrm{M}^{+}\right)$requires 359.2096; found 359.2106 .

## 2-((2-Oxo-2-phenylethyl)(pentyl)amino)acetic acid S1


M.F. : $\mathrm{C}_{15} \mathrm{H}_{21} \mathrm{NO}_{3}$
M.W. : 263.3370

In a round bottom flask containing ( $0.300 \mathrm{~g}, 0.83 \mathrm{mmol}) \mathrm{N}$-( $(2$-(tert-Butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)- $N$-pentyl-2-phenylacetamide 20 in ( 10 mL ) THF, was added ( 1 mL ) 1 M aq. NaOH solution. The reaction mixture was stirred at rt for 5 h . This was followed by the dropwise addition of a 1 M aq. HCl solution, until the reaction mixture became neutral. The aqueous layer was extracted with $\mathrm{Et}_{2} \mathrm{O}$, and the combined organic layers were dried, filtrated and concentrated under vacuum. The crude material was purified using silica gel preparative

TLC plates (cyclohexane/EtOAc, 1:1). $160 \mathrm{mg}, 73 \%$; white powder; m.p.: $53^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}(400$ $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 7.35-7.22\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{Ar}}\right), 4.09\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{I}}\right), 3.80\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{g}}\right), 3.36-3.32(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right), 1.48-1.42\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{d}}\right), 1.30-1.17\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}_{\mathrm{b}}+\mathrm{H}_{\mathrm{c}}\right), 0.87\left(\mathrm{t}, \mathrm{J}=4 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}$ ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta(\mathrm{ppm}) 173.0,172.7,134.6,128.9,128.9,127.1,50.1,49.6,48.5,47.7$, $41.2,40.5,29.1,28.9,28.3,27.1,22.5,22.5,14.2,14.1$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 3253,2935$, 1734, 1370, 1289, 1115, 1083, 734; HR-EI-MS: $\left[\mathrm{C}_{15} \mathrm{H}_{22} \mathrm{NO}_{3}\right]^{+}\left(\mathrm{M}+\mathrm{H}^{+}\right)$requires 264.1594; found 264.1593.

## 3-chloro-2-hydroxypropanoic acid S2


M.F. : $\mathrm{C}_{3} \mathrm{H}_{5} \mathrm{ClO}_{3}$
M.W.: 124.52000

In a two necked round bottom flask equipped with a condenser, a dropping funnel and containing 3 -chloro-1,2-propanediol ( $10 \mathrm{~g}, 90.5 \mathrm{mmol}$ ), $\mathrm{HNO}_{3}\left(65 \%\right.$ in $\mathrm{H}_{2} \mathrm{O}, 31 \mathrm{~mL}$ ) was added dropwise at $0^{\circ} \mathrm{C}$. The temperature was then raised slowly to $80^{\circ} \mathrm{C}$ after what an important evolution of gas began. After 20 min , the temperature was raised to $100^{\circ} \mathrm{C}$ and after 15 minutes the evolution of gas slowed down. The reaction was then quenched with (40 $\mathrm{mL}) \mathrm{H}_{2} \mathrm{O}$ and $\mathrm{NaHCO}_{3}(6.66 \mathrm{~g})$. The solution was then filtrated but any solid collected and the aqueous layer was extracted with $\mathrm{Et}_{2} \mathrm{O}(3 \times 100 \mathrm{~mL})$. After evaporation of the solvents in vacuo, the residue was freed from trace of $\mathrm{HNO}_{3}$ by distillation with a liquid nitrogen trap at $60^{\circ} \mathrm{C}$ and 1 mbar . The resulting solid was then recrystallized from boiling chloroform. The compound was then dissolved in $\mathrm{H}_{2} \mathrm{O}$ and the pH adjusted to 3 . The solution was extracted with $\mathrm{Et}_{2} \mathrm{O}$ and the combined organic extracts were dried over $\mathrm{MgSO}_{4}$. After evaporation of the solvents in vacuo, the solid was dried in vacuo over $\mathrm{P}_{2} \mathrm{O}_{5}$ to give 3-chloro-2-hydroxypropanoic acid ( $6.198 \mathrm{~g}, 49.77 \mathrm{mmol}$ ). $55 \%$; white powder; m.p.: $77-78^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}(400 \mathrm{MHz}$, DMSO$\left.d_{6}\right) \delta(\mathrm{ppm}) 5.72(\mathrm{brs}, 1 \mathrm{H},-\mathrm{OH}), 4.30\left(\mathrm{t}, J=4.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{b}}\right), 3.76\left(\mathrm{~d}, J=4.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right) ;{ }^{13} \mathrm{C}-$ NMR ( $100 \mathrm{MHz}, \mathrm{DMSO}-d_{6}$ ) $\delta(\mathrm{ppm})$ 172.5, 70.1, 47.2. All characterization data are in full agreement with the ones reported in the literature. ${ }^{[10]}$

## 2-tert-Butyl-5-(chloromethyl)-1,3-dioxolan-4-one S3


M.F. : $\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{ClO}_{3}$

MW. : 192.63900
3-Chloro-2-hydroxypropanoic acid ( $1.053 \mathrm{~g}, 8.46 \mathrm{mmol}$ ), trimethylacetaldehyde ( $1.457 \mathrm{~g}, 16.9$ mmol ) and $p$-toluenesulfonic acid monohydrate ( $10 \mathrm{mg}, 0.05 \mathrm{mmol}$ ) were refluxed under
argon at $100^{\circ} \mathrm{C}$ for 30 min in ( 10 mL ) cyclohexane with azeotropic removal of water. The solution was then washed with $\mathrm{H}_{2} \mathrm{O}(1 \mathrm{~mL})$, sat. aq. solution of $\mathrm{NaHCO}_{3}(1 \mathrm{~mL})$ and $\mathrm{H}_{2} \mathrm{O}(2$ mL ). The organic phase was then dried with $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated under vacuum. Purification of the resulting oil using silica gel column chromatography (pentane/Et ${ }_{2} \mathrm{O}, 4: 1$ ) afforded 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one (as a mixture of diastereisomers) ( $1.238 \mathrm{~g}, 6.43 \mathrm{mmol}$ ). 76\%; transparent oil.

## Diastereoisomer A

$684 \mathrm{mg}, 42 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 5.48(\mathrm{~d}, J=1.6 \mathrm{~Hz}, 1 \mathrm{H}$, $\left.\mathrm{H}_{\mathrm{d}}\right)$, 4.70-4.69 (m, 1H, $\left.\mathrm{H}_{\mathrm{b}}\right), 3.86\left(\mathrm{~d}, J=3.44 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 0.97\left(\mathrm{~s}, 9 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(100 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.4,112.5,75.1,43.7,36.0,23.3$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2964,1796,1355$, 1310, 1207, 1169, 1112, 1034, 983, 892; HR-EI-MS: $\left[\mathrm{C}_{4} \mathrm{H}_{4} \mathrm{ClO}_{3}\right]^{+}\left(\mathrm{M}^{+}-\mathrm{C}_{4} \mathrm{H}_{9}\right)$ requires 134.9849; found 134.9849 .

## Diastereoisomer B

$554 \mathrm{mg}, 34 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 5.21(\mathrm{~d}, J=1.1 \mathrm{~Hz}, 1 \mathrm{H}$, $\mathrm{H}_{\mathrm{d}}$ ), 4.58-4.57 (m, 1H, $\mathrm{H}_{\mathrm{b}}$ ), 3.89-3.84 (m, 2H, $\mathrm{H}_{\mathrm{a}}$ ), $1.02\left(\mathrm{~s}, 9 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(100 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 170.1,110.0,75.5,41.9,34.7,23.7$; IR (neat, $\mathrm{cm}^{-1}$ ) $v_{\max } 2965,1797,1484$, 1410, 1303, 1204, 1183, 1111, 1046, 965; HR-EI-MS: $\left[\mathrm{C}_{4} \mathrm{H}_{4} \mathrm{ClO}_{3}\right]^{+}\left(\mathrm{M}^{+}-\mathrm{C}_{4} \mathrm{H}_{9}\right)$ requires 134.9849; found 134.9849

## 2-tert-Butyl-5-methylidene-1,3-dioxolan-4-one S4



2-tert-Butyl-5-(chloromethyl)-1,3-dioxolan-4-one (320 mg, 1.66 mmol ) and 1,8-diazabicyclo[5.4.0]undec-7-ene ( $279 \mathrm{mg}, 1.83 \mathrm{mmol}$ ) were vigorously stirred under argon at r.t. for 1 h in dry $\mathrm{CH}_{2} \mathrm{Cl}_{2}(10 \mathrm{~mL})$. The solution was then diluted with $\mathrm{H}_{2} \mathrm{O}(10 \mathrm{~mL})$ and extracted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}(3 \times 10 \mathrm{~mL})$. The organic phase was washed with a sat. aq. solution of $\mathrm{NaHCO}_{3}(10 \mathrm{~mL})$, brine ( 10 mL ), dried with $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated under vacuum. Purification on silica gel column chromatography (pentane $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}: 7 / 3$ ) afforded 2-tert-butyl-5-methylidene-1,3-dioxolan-4-one ( 202 mg ). The compound has to be stored as a solution in $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ at $4^{\circ} \mathrm{C} .78 \%$; transparent oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 5.43\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{c}}\right), 5.13$ $\left(\mathrm{d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 4.86\left(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 0.98\left(\mathrm{~s}, 9 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) .{ }^{13} \mathrm{C}-\mathrm{NMR}(100 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ : $163.0,144.6,109.8,91.2,36.1,23.0$. All characterization data are in full agreement with the ones reported in the literature. ${ }^{[11]}$

## 5-Bromo-5-(bromomethyl)-2-tert-butyl-1,3-dioxolan-4-one S5



2-tert-Butyl-5-methylene-1,3-dioxolan-4-one ( $157 \mathrm{mg}, 1 \mathrm{mmol}$ ) and $\mathrm{Br}_{2}$ ( $321 \mathrm{mg}, 2 \mathrm{mmol}$ ) were refluxed in dry $\mathrm{CH}_{2} \mathrm{Cl}_{2}(7 \mathrm{~mL})$ for 2 h . The solution was then washed with a 0.4 M aq. solution of $\mathrm{Na}_{2} \mathrm{~S}_{2} \mathrm{O}_{3}(2 \times 5 \mathrm{~mL})$ and then $\mathrm{H}_{2} \mathrm{O}(2 \times 5 \mathrm{~mL})$. The organic phase was then dried with $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated under vacuum. Purification on silica gel column chromatography (cyclohexane/EtOAc, 9:1) afforded 5-bromo-5-(bromomethyl)-2-tert-butyl-1,3-dioxolan-4-one (as a mixture of diastereoisomers) ( 226 mg ). 72\%; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}$ $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 5.43\left(\mathrm{~s}, 0.2 \mathrm{H}, \mathrm{H}_{\mathrm{c}}\right), 5.24\left(\mathrm{~s}, 0.8 \mathrm{H}, \mathrm{H}_{\mathrm{c}}\right), 4.25-4.19\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 1.08$ (s, 7.2H, $\mathrm{H}_{\mathrm{e}}$ ), $1.06\left(\mathrm{~s}, 1.8 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(68 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 164.8,108.6,88.3,34.3$, 30.9, 23.8, 23.7. All characterization data are in full agreement with the ones reported in the literature. ${ }^{[12]}$

## 5-(Bromomethylidene)-2-tert-butyl-1,3-dioxolan-4-one S6


M.F. : $\mathrm{C}_{8} \mathrm{H}_{11} \mathrm{BrO}_{3}$

MW. : 235.08

5-Bromo-5-(bromomethyl)-2-tert-butyl-1,3-dioxolan-4-one ( $226 \mathrm{mg}, 0.71 \mathrm{mmol}$ ) and 1,8-diazabicyclo[5.4.0]undec-7-ene ( $120 \mathrm{mg}, 0.79 \mathrm{mmol}$ ) were vigorously stirred under argon at r.t. for 1 h in dry $\mathrm{CH}_{2} \mathrm{Cl}_{2}(10 \mathrm{~mL})$. The solution was then diluted with $\mathrm{H}_{2} \mathrm{O}(10 \mathrm{~mL})$ and extracted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}(3 \times 10 \mathrm{~mL})$. The organic phase was washed with a sat. aq. solution of $\mathrm{NaHCO}_{3}(10 \mathrm{~mL})$, brine ( 10 mL ), dried with $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated under vacuum. Purification on silica gel column chromatography (cyclohexane/EtOAc, 9:1) afforded 5-(bromomethylidene)-2-tert-butyl-1,3-dioxolan-4-one ( 130 mg ). 78\%; yellow oil; ${ }^{1} \mathrm{H}-\mathrm{NMR}$ ( 400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 6.35\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{a}}\right), 5.53\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}_{\mathrm{c}}\right), 1.01\left(\mathrm{~s}, 9 \mathrm{H}, \mathrm{H}_{\mathrm{e}}\right) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(68 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta(\mathrm{ppm}) 160.2,142.0,110.6,88.4,30.1,23.0$. All characterization data are in full agreement with the ones reported in the literature. ${ }^{[12]}$

## 3. Additional Experimental Studies

## VT ${ }^{1} \mathrm{H}$ NMR Studies

In order to further investigate the outcome (i.e. formation of two polymorphs belonging to two different compounds 20 and 21) when the crystallization of 20 was attempted, further studies were carried out. The initial aim was to examine by ${ }^{1} \mathrm{H}$ NMR at variable temperatures if $\mathbf{2 0}$ and 21 are in equilibrium in solution. Due to the fact that the ${ }^{1} \mathrm{H}$ NMR spectrum of 20 is complicated, with peaks present in the aromatic region it was not easy to examine and draw a definite conclusion from the changes of the chemical shits and more specific the hydrogen atom corresponding to the double bond. As a result the same study was performed with a simpler analogue, enamide 13. In particular, the ${ }^{1} \mathrm{H}$ NMR of 13 was obtained at different temperatures starting from $70^{\circ} \mathrm{C}$ and going down to $-40^{\circ} \mathrm{C}$. As shown in Figure SI .1 at $70^{\circ} \mathrm{C}$ there is one peak at 7.45 ppm corresponding to vinyl hydrogen, and as the temperature lowers the peak is slightly shielded reaching 7.27 ppm at rt . But as the temperature is reduced even more, at $-40^{\circ} \mathrm{C}$ to two peaks at 7.19 and 6.72 ppm are clearly observed, leading us believe that in solution only a cis/trans isomerization of the enamide can be observed and most likely the formation of the cyclobutane analogue is only favored at the solid state.

 temperatures.


Figure SI. $2{ }^{1} \mathrm{H}$-NMR spectrum of N -((2-(tert-butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)acetamide in $\mathrm{CD}_{2} \mathrm{Cl}_{2}$ at variable temperatures.



Figure $\mathrm{SI} .3{ }^{1} \mathrm{H}$-NMR spectrum of methyl-(E)-3-bromo-methylacrylate in $\mathrm{CDCl}_{3}$ at variable temperatures.


Figure SI. $4{ }^{1} \mathrm{H}$-NMR spectrum of 5-(bromomethylene)-2-(tert-butyl)-1,3-dioxolan-4-one in $\mathrm{CDCl}_{3}$ at variable temperatures.


Figure SI. $5{ }^{1} \mathrm{H}$-NMR spectrum of N -((2-(tert-Butyl)-5-oxo-1,3-dioxalan-4-ylidene)methyl)-N-pentyl-2-phenylacetamide 20 in $\mathrm{CD}_{3} \mathrm{CN}$ at variable temperatures.


Figure SI. $6{ }^{1} \mathrm{H}$-NMR spectrum of methyl (E)-2-methyl-3-(N-methylpropionamido)acrylate 9 in $\mathrm{CD}_{2} \mathrm{Cl}_{2}$ at variable temperatures


Figure SI. $7{ }^{1} \mathrm{H}-\mathrm{NMR}$ spectrum of methyl (E)-2-methyl-3-( N -phenylacetamido) acrylate $\mathbf{5}$ in $\mathrm{CDCl}_{3}$ at variable temperatures

## 4. Analytical Data

Methyl (E)-3-(N-methylpropionamido)acrylate 1

M.F. : $\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{NO}_{3}$ M.W. : 171.19600


Figure SI. $8{ }^{1} \mathrm{H}$-NMR spectrum of methyl ( $E$ )-3-( N -methylpropionamido)acrylate $\mathbf{1}$ in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .9{ }^{13} \mathrm{C}$-NMR spectrum of methyl ( $E$ )-3-( $N$-methylpropionamido) acrylate $\mathbf{1}$ in $\mathrm{CDCl}_{3}$.


Figure SI. 10 EI-HRMS spectrum of methyl (E)-3-( $N$-methylpropionamido)acrylate 1.

## Ethyl (Z)-3-(N-methylpropionamido)acrylate 2




Figure SI. $11^{1} \mathrm{H}-\mathrm{NMR}$ spectrum of Ethyl ( $Z$ )-3-( $N$-methylpropionamido)acrylate $\mathbf{2}$ in $\mathrm{CD}_{2} \mathrm{Cl}_{2}$.


Figure SI. $12{ }^{13} \mathrm{C}$-NMR spectrum of Ethyl (Z)-3-( $N$-methylpropionamido) acrylate $\mathbf{2}$ in $\mathrm{CD}_{2} \mathrm{Cl}_{2}$.


Figure SI. 13 EI-HRMS spectrum of Ethyl ( $Z$ )-3-( $N$-methylpropionamido)acrylate 2.

## Ethyl (Z)-3-(2-oxopiperidin-1-yl)acrylate 3


M.F. : $\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}$ M.W. : 197.23100


Figure SI. $14{ }^{1} \mathrm{H}$-NMR spectrum of Ethyl (Z)-3-(2-oxopiperidin-1-yl)acrylate $\mathbf{3}$ in $\mathrm{CDCl}_{3}$.


Figure SI. $15{ }^{13} \mathrm{C}$-NMR spectrum of Ethyl (Z)-3-(2-oxopiperidin-1-yl)acrylate 3 in $\mathrm{CDCl}_{3}$.

Monoisotopic Mass, Odd and Even Electron Ions
6 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
$\begin{array}{llll}\text { C: 0-10 } & \mathrm{H}: 0-15 & \mathrm{~N}: 0-1 & \mathrm{O}: 0-3\end{array}$
30-Aug-2016
DB_MS13139 17 ( 0.283 ( $\mathrm{Cm}(17-1)$

Figure SI. 16 El-HRMS spectrum of Ethyl (Z)-3-(2-oxopiperidin-1-yl)acrylate 3.

## Methyl (E)-3-(2-oxopiperidin-1-yl)acrylate 4



Figure $\mathrm{SI} .17{ }^{1} \mathrm{H}$-NMR spectrum of methyl $(E)$-3-(2-oxopiperidin-1-yl)acrylate 4 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .18{ }^{13} \mathrm{C}-\mathrm{NMR}$ spectrum of methyl $(E)$-3-(2-oxopiperidin-1-yl)acrylate $\mathbf{4}$ in $\mathrm{CDCl}_{3}$.

Monoisotopic Mass, Odd and Even Electron Ions
131 formula(e) evaluated with 86 results within limits (up to 50 best isotopic matches for each mass) Elements Used:
C: 0-50 $\quad \mathrm{H}: 0-100 \quad \mathrm{~N}: 0-10 \quad \mathrm{O}: 0-5$
100 ul ds eppendorf puls dilution $10000 \times 25000.00000000$
GCT_09-01-13_COMS-FUNDP_BAD361-1_BAD376_BAD397_004 769 (16.761) AM (Cen,4, 80.00, Ht,8600.0,218.99,0+70) ©


Figure SI. 19 El-HRMS spectrum of methyl $(E)$-3-(2-oxopiperidin-1-yl)acrylate 4.

## Methyl (E)-2-methyl-3-( $N$-phenylacetamido)acrylate 5



Figure SI. $20{ }^{1} \mathrm{H}$-NMR spectrum of methyl $(E)$-2-methyl-3-( $N$-phenylacetamido)acrylate 5 in $\mathrm{CDCl}_{3}$.


Figure $\mathbf{S I . 2 1}{ }^{13} \mathrm{C}$-NMR spectrum of methyl $(E)$-2-methyl-3-( $N$-phenylacetamido)acrylate 5 in $\mathrm{CDCl}_{3}$.


Figure SI. 22 EI-HRMS spectrum of methyl ( $\Xi$ )-2-methyl-3-( $N$-phenylacetamido)acrylate 5.

Methyl (E)-3-(N-pentyl-2-phenylacetamido)acrylate 6

M.F. : $\mathrm{C}_{17} \mathrm{H}_{23} \mathrm{NO}_{3}$
M.W. : 289.37500


Figure SI. $23{ }^{1} \mathrm{H}$-NMR spectrum of methyl ( $E$ )-3-( $N$-pentyl-2-phenylacetamido) acrylate 6 in $\mathrm{CDCl}_{3}$.


Figure SI. $24{ }^{13} \mathrm{C}$-NMR spectrum of methyl ( $E$ ( $)-3-\left(N\right.$-pentyl-2-phenylacetamido)acrylate $\mathbf{6}$ in $\mathrm{CDCl}_{3}$.


Figure SI. 25 EI-HRMS spectrum of methyl (E)-3-(N-pentyl-2-phenylacetamido)acrylate 6.

## Methyl (E)-3-acetamido-2-methylacrylate 7


M. W. : 157.16900


Figure SI. $26{ }^{1} \mathrm{H}$-NMR spectrum of methyl (E)-3-acetamido-2-methylacrylate 7 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .27{ }^{13} \mathrm{C}-\mathrm{NMR}$ spectrum of methyl (E)-3-acetamido-2-methylacrylate 7 in $\mathrm{CDCl}_{3}$.


Figure SI. 28 EI-HRMS spectrum of methyl 3-acetamido-2-methylacrylate 7.

## Methyl (E)-2-methyl-3-(2-oxopiperidin-1-yl)acrylate 8


M.F. : $\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{3}$ M.W. : 197.23400


Figure SI. $29{ }^{1} \mathrm{H}$-NMR spectrum of methyl (E)-2-methyl-3-(2-oxopiperidin-1-yl)acrylate 8 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .30{ }^{13} \mathrm{C}$-NMR spectrum of methyl (E)-2-methyl-3-(2-oxopiperidin-1-yl)acrylate 8 in $\mathrm{CDCl}_{3}$.


Figure SI. 31 EI-HRMS spectrum of methyl (E)-2-methyl-3-(2-oxopiperidin-1-yl)acrylate 8.

## Methyl (E)-2-methyl-3-(N-methylpropionamido)acrylate 9


M.F. : $\mathrm{C}_{9} \mathrm{H}_{15} \mathrm{NO}_{3}$ M.W. : 185.22300


Figure $\mathrm{SI} .32{ }^{1} \mathrm{H}$-NMR spectrum of methyl (E)-2-methyl-3-( N -methylpropionamido)acrylate 9 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .33{ }^{13} \mathrm{C}-\mathrm{NMR}$ spectrum of methyl (E)-2-methyl-3-( $N$-methylpropionamido) acrylate 9 in $\mathrm{CDCl}_{3}$.


Figure SI. 34 EI-HRMS spectrum of methyl (E)-2-methyl-3-( $N$-methylpropionamido)acrylate 9.

Methyl (E)-2-methyl-3-(N-phenylacetamido)acrylate 10



Figure $\mathrm{SI} .35{ }^{1} \mathrm{H}-\mathrm{NMR}$ spectrum of methyl (E)-2-methyl-3-(N-phenylacetamido)acrylate 10 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .36{ }^{13} \mathrm{C}-\mathrm{NMR}$ spectrum of methyl (E)-2-methyl-3-(N-phenylacetamido)acrylate 10 in $\mathrm{CDCl}_{3}$.


Figure SI. 37 EI-HRMS spectrum of methyl (E)-2-methyl-3-(N-phenylacetamido)acrylate $\mathbf{1 0}$ in $\mathrm{CDCl}_{3}$.

Methyl (E)-2-methyl-3-(N-pentyl-2-phenylacetamido)acrylate 11

M.F. : $\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{3}$ M.W. : 303.40200


Figure SI. $38{ }^{1} \mathrm{H}$-NMR spectrum of methyl (E)-2-methyl-3-( $N$-pentyl-2-phenylacetamido)acrylate 11 in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .39{ }^{13} \mathrm{C}$-NMR spectrum of methyl (E)-2-methyl-3-(N-pentyl-2-phenylacetamido)acrylate 11 in $\mathrm{CDCl}_{3}$.


Figure SI. 40 EI-HRMS spectrum of methyl (E)-2-methyl-3-(N-pentyl-2-phenylacetamido)acrylate 11.

M.F. : $\mathrm{C}_{7} \mathrm{H}_{11} \mathrm{NO}_{4}$
M.W. : 173.16800


Figure SI. $41{ }^{1} \mathrm{H}$-NMR spectrum of methyl (Z)-3-acetamido-2-methoxyacrylate 12 in $\mathrm{CDCl}_{3}$.


Figure SI. $42{ }^{13} \mathrm{C}$-NMR spectrum of methyl (Z)-3-acetamido-2-methoxyacrylate 12 in $\mathrm{CDCl}_{3}$.

Monoisotopic Mass, Odd and Even Electron lons
118 formula(o) ovaluatod with 79 roculte within limite (up to 50 best isotopic matches for each mass) Elements Used:
C: 0-50 $\quad \mathrm{H}: \mathbf{0 - 1 0 0} \quad \mathrm{N}: ~ 0-10 \quad \mathrm{O}: 0-5$
100ul ds eppendorf puls dilution 10000x25000.00000000 $1.950+003$ GCT_09-01-13_COMS-FUNDP_BAD361-1_BAD376_BAD397_004 508 (12.411) AM (Cen,4, 80.00, Ht,8600.0,218.99,0.70); $\varsigma$


Figure SI. 43 EI-HRMS spectrum of methyl (Z)-3-acetamido-2-methoxyacrylate 12.

## Methyl (Z)-2-methoxy-3-(N-methylpropionamido)acrylate 13



Figure SI. $44{ }^{1} \mathrm{H}$-NMR spectrum of methyl (Z)-2-methoxy-3-( N -methylpropionamido)acrylate 13 in $\mathrm{CDCl}_{3}$


Figure $\mathrm{SI} .45{ }^{13} \mathrm{C}$-NMR spectrum of methyl (Z)-2-methoxy-3-( $N$-methylpropionamido) acrylate 13 in $\mathrm{CDCl}_{3}$.


Figure SI. 46 EI-HRMS spectrum of methyl (Z)-2-methoxy-3-(N-methylpropionamido)acrylate 13.

Methyl (Z)-2-methoxy-3-(2-oxopiperidin-1-yl)acrylate 14

M.F. : $\mathrm{C}_{10} \mathrm{H}_{15} \mathrm{NO}_{4}$ M.W. : 213.23300


Figure SI. $47{ }^{1} \mathrm{H}$-NMR spectrum of methyl (Z)-2-methoxy-3-(2-oxopiperidin-1-yl)acrylate 14 in $\mathrm{CDCl}_{3}$


Figure $\mathrm{SI} .48{ }^{13} \mathrm{C}$-NMR spectrum of methyl (Z)-2-methoxy-3-(2-oxopiperidin-1-yl)acrylate 14 in $\mathrm{CDCl}_{3}$.

File:GP Ident: $4655+46$ PKD ( $3,3,3,0.50 \%, 0.0,0.00 \%$, F, F) SPEC(Hei> AutoSpec EI+ Voltage BpM:219 BpI:1909531 TIC:5850643 Flags:NOR> File Text:coms bad398 ei hrms dip



Figure SI. 49 El-HRMS spectrum of methyl (Z)-2-methoxy-3-(2-oxopiperidin-1-yl)acrylate 14.

Methyl (Z)-2-methoxy-3-(N-phenylacetamido)acrylate 15

M.F. : $\mathrm{C}_{13} \mathrm{H}_{15} \mathrm{NO}_{4}$
M.W. : 249.26600


Figure SI. $50{ }^{1} \mathrm{H}$-NMR spectrum of methyl (Z)-2-methoxy-3-( $N$-phenylacetamido)acrylate 15 in $\mathrm{CDCl}_{3}$


Figure SI. $51{ }^{13} \mathrm{C}$-NMR spectrum of methyl (Z)-2-methoxy-3-( $N$-phenylacetamido)acrylate 15 in $\mathrm{CDCl}_{3}$.

File:PG Ident: $42 \operatorname{SMO}(3,3) \operatorname{PKD}(7,3,7,0.50 \%, 0.0,0.00 \%, \mathrm{~F}, \mathrm{~F}) \mathrm{SPEC}(>$ AutoSpec EI+ Voltage BpM:243 BpI:26899 TIC: 45506 Flags:NORM File Text: COMS BAD404 EI HRMS DIP


Figure SI. 52 EI-HRMS spectrum of methyl (Z)-2-methoxy-3-( $N$-phenylacetamido)acrylate 15.

Methyl (Z)-2-methoxy-3-(N-pentyl-2-phenylacetamido)acrylate 16

M.F. : $\mathrm{C}_{18} \mathrm{H}_{25} \mathrm{NO}_{4}$ M.W. : 319.40100


Figure SI. $53{ }^{1} \mathrm{H}$-NMR spectrum of methyl (Z)-2-methoxy-3-(N-pentyl-2-phenylacetamido)acrylate 16 in $\mathrm{CDCl}_{3}$


Figure SI. $54{ }^{13} \mathrm{C}-$ NMR spectrum of methyl (Z)-2-methoxy-3-(N-pentyl-2-phenylacetamido)acrylate 16 in $\mathrm{CDCl}_{3}$.


Figure SI. 55 El-HRMS spectrum of methyl (Z)-2-methoxy-3-(N-pentyl-2-phenylacetamido)acrylate 16.

## N-(2-Cyanoprop-1-en-1-yl)-N-methylpropionamide 17


M.F. : $\mathrm{C}_{8} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$
M.W. : 152.19700


Figure SI. $56{ }^{1} \mathrm{H}$-NMR spectrum of $N$-(2-cyanoprop-1-en-1-yl)- $N$-methylpropionamide 17 diastereoisomer A in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .57{ }^{13} \mathrm{C}$-NMR spectrum of N -(2-cyanoprop-1-en-1-yl)- N -methylpropionamide $\mathbf{1 7}$ diastereoisomer A in $\mathrm{CDCl}_{3}$.


Figure SI. 58 EI-HRMS spectrum of $N$-(2-cyanoprop-1-en-1-yl)- $N$-methylpropionamide 17 diastereoisomer A.


Figure SI. $59{ }^{1} \mathrm{H}$-NMR spectrum of N -(2-cyanoprop-1-en-1-yl)- N -methylpropionamide 17 diastereoisomer B in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .60{ }^{13} \mathrm{C}$-NMR spectrum of N -(2-cyanoprop-1-en-1-yl)- N -methylpropionamide $\mathbf{1 7}$ diastereoisomer B in $\mathrm{CDCl}_{3}$.


Figure SI. 61 EI-HRMS spectrum of $N$-(2-cyanoprop-1-en-1-yl)- $N$-methylpropionamide 17 diastereoisomer B.

## 2-Methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18



Figure $\mathbf{S I} .62{ }^{1} \mathrm{H}$-NMR spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile $\mathbf{1 8}$ diasteroisomer A in $\mathrm{CDCl}_{3}$.


Figure SI. $63{ }^{13} \mathrm{C}$-NMR spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18 diasteroisomer A in $\mathrm{CDCl}_{3}$.


Figure SI. 64 EI-MS spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18 diasteroisomer A .


Figure SI. $65{ }^{1} \mathrm{H}$-NMR spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18 diasteroisomer B in $\mathrm{CDCl}_{3}$.


Figure $\mathrm{SI} .66{ }^{13} \mathrm{C}$-NMR spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile $\mathbf{1 8}$ diasteroisomer B in $\mathrm{CDCl}_{3}$.


Figure SI. 67 EI-HRMS spectrum of 2-methyl-3-(2-oxopiperidin-1-yl)acrylonitrile 18 diasteroisomer B.

## Ethyl (Z)-3-(N-pentyl-2-phenylacetamido)acrylate 19



Figure SI. $68{ }^{1} \mathrm{H}$-NMR spectrum of ethyl (Z)-3-( $N$-pentyl-2-phenylacetamido)acrylate 19 in $\mathrm{CDCl}_{3}$.


Figure SI. $69{ }^{13} \mathrm{C}$-NMR spectrum of ethyl (Z)-3-( $N$-pentyl-2-phenylacetamido)acrylate 19 in $\mathrm{CDCl}_{3}$.


Figure SI. 70 EI-HRMS spectrum of ethyl (Z)-3-( $N$-pentyl-2-phenylacetamido)acrylate 19.

M.F. : $\mathrm{C}_{21} \mathrm{H}_{29} \mathrm{NO}_{4}$ M.W. : 359.46600


Figure SI. $71 \quad{ }^{1} \mathrm{H}-\mathrm{NMR}$ spectrum of $N$-((2-(tert-butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)- $N$-pentyl-2phenylacetamide 20 in $\mathrm{CDCl}_{3}$

Figure SI. $72{ }^{13} \mathrm{C}-\mathrm{NMR}$ spectrum of N -((2-(tert-butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)- N -pentyl-2phenylacetamide 20 in $\mathrm{CDCl}_{3}$.


Figure SI. 73 EI-HRMS spectrum of $N$-((2-(tert-butyl)-5-oxo-1,3-dioxolan-4-ylidene)methyl)- $N$-pentyl-2phenylacetamide 20.

## 2-tert-Butyl-5-(chloromethyl)-1,3-dioxolan-4-one S3


M.F. : $\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{ClO}_{3}$ MW. : 192.63900


Figure SI. $74{ }^{1} \mathrm{H}$-NMR spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer A in $\mathrm{CDCl}_{3}$


Figure SI. $75{ }^{13} \mathrm{C}$-NMR spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer A in $\mathrm{CDCl}_{3}$.


Figure SI. 76 EI-MS spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer A.


Figure $\mathrm{SI} .77{ }^{1} \mathrm{H}$-NMR spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer B in $\mathrm{CDCl}_{3}$


Figure $\mathrm{SI} .78{ }^{13} \mathrm{C}$-NMR spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer B in $\mathrm{CDCl}_{3}$.


Figure SI. 79 EI-HRMS spectrum of 2-tert-butyl-5-(chloromethyl)-1,3-dioxolan-4-one diastereoisomer B.


Figure SI. $80{ }^{1} \mathrm{H}$-NMR spectrum of 2-((2-oxo-2-phenylethyl)(pentyl)amino)acetic acid $\mathbf{S 1}$ in $\mathrm{CDCl}_{3}$


Figure $\mathbf{S I . 8 1}{ }^{13} \mathrm{C}$-NMR spectrum of 2-((2-oxo-2-phenylethyl)(pentyl)amino)acetic acid $\mathbf{S 1}$ in $\mathrm{CDCl}_{3}$


Figure SI. 82 EI-HRMS spectrum of 2-((2-oxo-2-phenylethyl)(pentyl)amino)acetic acid S1.


## Crystal Data

Formula
Molecular Weight
Crystal System
Space Group
Unit cell dimensions
$\mathrm{C}_{21} \mathrm{H}_{29} \mathrm{NO}_{4}$
359.45

Monoclinic
P2 ${ }_{1} / \mathrm{C}$
$a=16.041(2) \AA \quad \alpha=90^{\circ}$
$b=9.382(1) \AA \quad \beta=114.84(1)^{\circ}$
$\mathrm{c}=15.090$ (2) $\AA$
$\gamma=90^{\circ}$
2060.9(5) $\AA^{3}$

4
$1.158 \mathrm{~g} / \mathrm{cm}^{3}$
$0.640 \mathrm{~mm}^{-1}$
776
$0.25 \times 0.25 \times 0.50 \mathrm{~mm}$
Data Collection
Temperature
Wavelenght
Theta range for data collection Index range
Reflections collected Independent reflections
Observed data $[\$ 2 \sigma(I)]$

Data / parameters
R, wR2, S
$\mathrm{w}=1 /\left[\sigma^{2} \mathrm{~F}_{0}{ }^{2}\right)+(0.0612 \mathrm{P})^{2}$ +0.4074 P ]
Largest diff. peak and hole

293 K
$1.54184 \AA$
5.6 to $66.6^{\circ}$
$-19 \leq h \leq 19,-10 \leq k \leq 11,-11 \leq \leq \leq 17$
9337
$3609[\mathrm{R}$ (int) $=0.029]$
2929

## Refinement

3609 / 239
$0.0823,0.2750,1.08$
where $P=\left(F_{0}{ }^{2}+2 F_{c}^{2}\right) / 3$
0.58 and $-0.26 \mathrm{e} . \mathrm{A}^{-3}$


Data Collection

| Temperature | 293 K |
| :---: | :---: |
| Wavelenght | 0.71073 A |
| Theta range for data collection | 3.3 to $25.0^{\circ}$ |
| Index range | $\begin{aligned} & -32 \leq h \leq 33, \quad-10 \leq k \leq 10, \\ & 20 \leq \leq \leq 19 \end{aligned}$ |
| Reflections collected | 21159 |
| Independent reflections | $7199[\mathrm{R}$ (int) $=0.044]$ |
| Observed data | 4343 |

## [ $>2 \sigma(\mathrm{I})]$

## Refinement

| D | 7199 / 507 |
| :---: | :---: |
| R, wR2, S | 0.0744, 0.171 |
| w = |  |
| $\begin{aligned} & 1 /\left[\sigma^{2} F_{0}{ }^{2}\right)+(0.0568 \mathrm{P})^{2} \\ & +1.5352 \mathrm{P}] \end{aligned}$ | where $\mathrm{P}=$ |
| Largest diff. peak and hole | 0.17 and $-0.16 \mathrm{e} . \mathrm{A}^{-3}$ |

## 5. References

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