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Supporting Information

# Formamide Synthesis through Borinic Acid-Catalysed Transamidation under Mild Conditions

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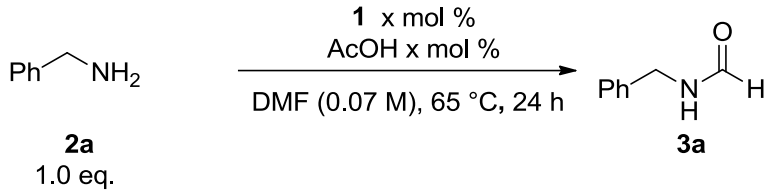
Contents:

## 1. General Information

Unless otherwise stated, all reactions were performed under argon atmosphere using flame-dried glassware. Commercially available compounds were used without further purification. DMF was distilled from $CaH_2$. NMR experiments were performed in deuterated solvents. $^{1}H$ NMR, $^{13}C$ NMR, $^{11}B$ NMR and $^{19}F$ spectra were recorded on 400 and 500 MHz spectrometers. Chemical shifts are reported in parts per million (ppm) relative to the residual protium in the solvents ($^{1}H$) or the solvent carbon ($^{13}C$) as internal standards. $^{1}H$ NMR spectral data features are tabulated in the following order: chemical shift in ppm (δ) (multiplicity, coupling constant, integration, type of H). The following abbreviations were used in reporting NMR data: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplet; td, triplet of doublet; ddd, doublet of doublet of doublet; m, multiplet; sept, septet; quin, quintet. Because of their low intensity (resulting from quadruple coupling), $^{13}C$ signals arising from the quaternary carbon bearing the borinic acid group were not always observed and therefore were not always listed. Chromatographic separations were achieved on silica gel columns (Kieselgel 60, 40-63 μm). Detection was accomplished by irradiation with a UV lamp or staining with $KMnO_4$. IR Spectra were recorded on a FTIR spectrometer with frequencies expressed in $cm^{-1}$. HSQCETGP (2D H-1/X correlation via double inept transfer phase sensitive using Echo/Antiecho-TPPI gradient selection with decoupling during acquisition using trim pulses in inept transfer). HMBCGPLPNDQF (2D H-1/X correlation via heteronuclear zero and double quantum coherence optimized on long range couplings with low-pass J-filter to suppress one-bond correlations no decoupling during acquisition using gradient pulses for selection). DEPT135 (dept polarization transfer with 135 degree read pulse to give XH, $XH_3$ positive and $XH_2$ negative with decoupling during acquisition) were used to assign the NMR peaks. Mass Spectra and high-resolution mass spectra (HRMS) were obtained on a Q-Tof instrument were recorded using either electron impact (EI) or electrospray ionization (ESI) techniques. Powdered molecular sieves were dried for 3 hours under high vacuum (<1 mbar) at 250 °C using a Kugelrohr instrument.

## 2. Optimization Experiments

Table 1. Optimization of **1** loading and ratio AcOH:**1**[a]

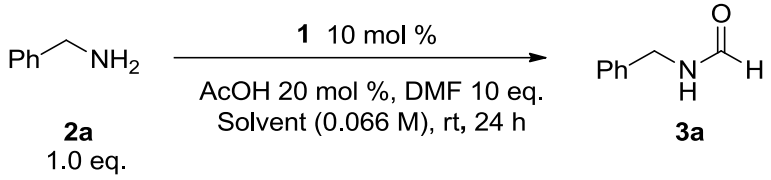



| Entry | AcOH (mol %) | 1 (mol %) | Isolated Yield (%) |
|---|---|---|---|
| 1 | 40 | 10 | 98 |
| 2 | 20 | 10 | 98 |
| 3 | | 5 | 93 |
| 4 | 10 | 10 | 80 |

[a] Reaction conditions: Borinic acid **1** (5-10 mol %) and AcOH (10-40 mol %) in DMF (7 mL) were stirred at 65 °C for 15 min before the addition of benzylamine **2a** (55.5 μL, 0.50 mmol) and stirring was maintained for further 24 h.

As shown by Table 1, a catalyst loading of 10 mol % along with 40 mol % of AcOH provided the corresponding benzyl formamide **3a** in an excellent yield of 98% (Entry 1). Decreasing the amount of AcOH 20 mol % had no impact on the yield (Entry 2). Whereas, upon decreasing the catalyst loading to 5 mol % with 20 mol % AcOH, a slight decrease in the yield of **3a** was observed (93%, Entry 3). A further decrease for AcOH to 10 mol % greatly lowered the yield (80%, Entry 4). As a result, the optimal conditions appeared to involve a ratio of 2 : 1 AcOH/Borinic acid rather than a ratio of 1 : 1.

Table 2. Solvent screening using **1**[a]



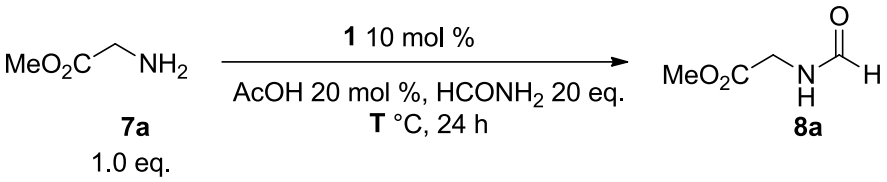

| Entry | Solvent | Yield (%) |
|---|---|---|
| 1 | THF | 15 |
| 2 | $CH_2Cl_2$ | 8 |
| 3 | MeCN | 7 |
| 4 | Toluene | 5 |
| 5 | AcOH | 0 |
| 6 | DMF | 73 |

[a] Reaction conditions: Borinic acid **1** (10 mol %), AcOH (20 mol %) and DMF (10 eq.) in the chosen solvent (6.6 mL) were stirred at room temperature for 15 min before the addition of benzylamine **2a** (55.5 μL, 0.50 mmol) and stirring was maintained for further 24 h.

The results described in Table 2 showed that using DMF only as a reactant in the presence of another co-solvent significantly hindered the *N*-formylation of benzylamine **2a** (Entries1-4). However, using AcOH as a solvent completely inhibited the reaction (Entry 5). As a result, DMF was chosen as a solvent and reactant at the same time (Entry 6).

## Optimization of *N*-formylation of glycine amino ester using $HCONH_2$

Table 3. Optimisation of temperature using **1**[a]

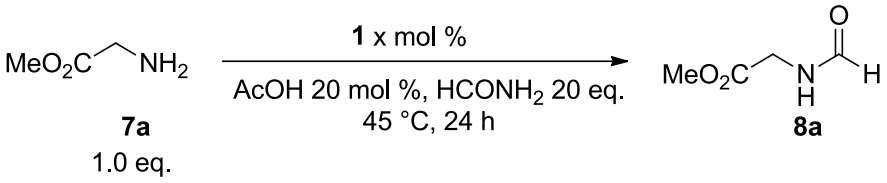



| Entry | T (°C) | Isolated Yield (%) |
|---|---|---|
| 1 | 65 | 99 |
| 2 | 45 | 99 |
| 3 | 20 | 80 |

[a] Reaction conditions: Borinic acid **1** (10 mol %) and AcOH (20 mol %) in $HCONH_2$ (20 eq.) were stirred at the specified temperature for 15 min before the addition of glycine methyl ester amine **7a** (40.0 μL, 0.50 mmol) and stirring was maintained for further 24 h.

Taking into account the previous optimal conditions used for the transamidation using DMF (Entry 1), we were able to reduce the temperature to 45 °C without affecting the yield of **8a** (Entry 2). Running the reaction at room temperature provided a lower yield of 80% (Entry 3).

Table 4. Optimisation of catalyst loading of **1**[a]

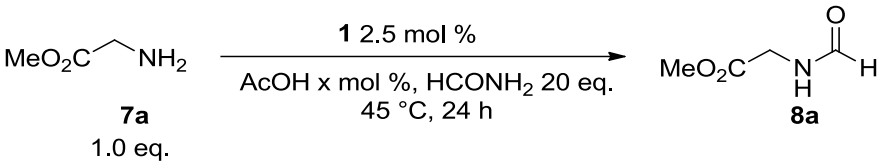



| Entry | 1 (mol %) | Isolated Yield (%) |
|---|---|---|
| 1 | 10 | 99 |
| 2 | 5 | 99 |
| 3 | 2.5 | 99 |

[a] Reaction conditions: Borinic acid **1** (2.5-10 mol %) and AcOH (20 mol %) in $HCONH_2$ (20 eq.) were stirred at 45 °C for 15 min before the addition of glycine methyl ester amine **7a** (40.0 μL, 0.50 mmol) and stirring was maintained for further 24 h.

As shown by Table 4, a catalyst loading of 10 mol % provided **8a** in an excellent yield (Entry 1). Decreasing the loading of **1** to 5 mol % and even 2.5 mol % had no effect on the yield which remained quantitative (Entries 2 and 3). Thus, 2.5 mol% was chosen as the optimal catalyst loading for the *N*-formylation of α-amino esters using $HCONH_2$.

Table 5. Optimisation of **1**:AcOH ratio[a]

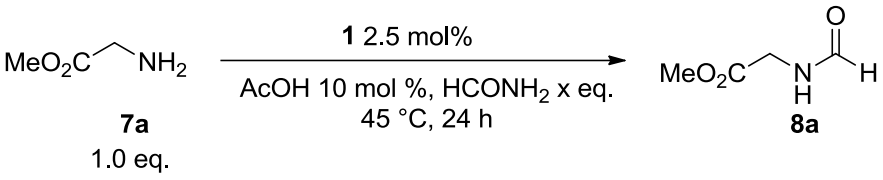



| Entry | AcOH (mol %) | Ratio 1 : AcOH | Isolated Yield (%) |
|---|---|---|---|
| 1 | 20 | 8 : 1 | 99 |
| 2 | 10 | 4 : 1 | 99 |
| 3 | 5 | 2 : 1 | 60 |

[a] Reaction conditions: Borinic acid **1** (2.5 mol %) and AcOH (5-20 mol %) in $HCONH_2$ (20 eq.) were stirred at 45 °C for 15 min before the addition of glycine methyl ester amine **7a** (40.0 μL, 0.50 mmol) and stirring was maintained for further 24 h.

As shown by Table 5, using 10 mol % or 20 mol % of AcOH provided **8a** in quantitative yield (Entries 1 and 2). Decreasing the loading of AcOH down to 05 mol % greatly lowered the yield of the reaction to 60% (Entry 3). Thus, the optimal ratio between AcOH and borinic acid was chosen to be 4 : 1.

Table 6. Optimisation of $HCONH_2$ equivalents using **1**[a]



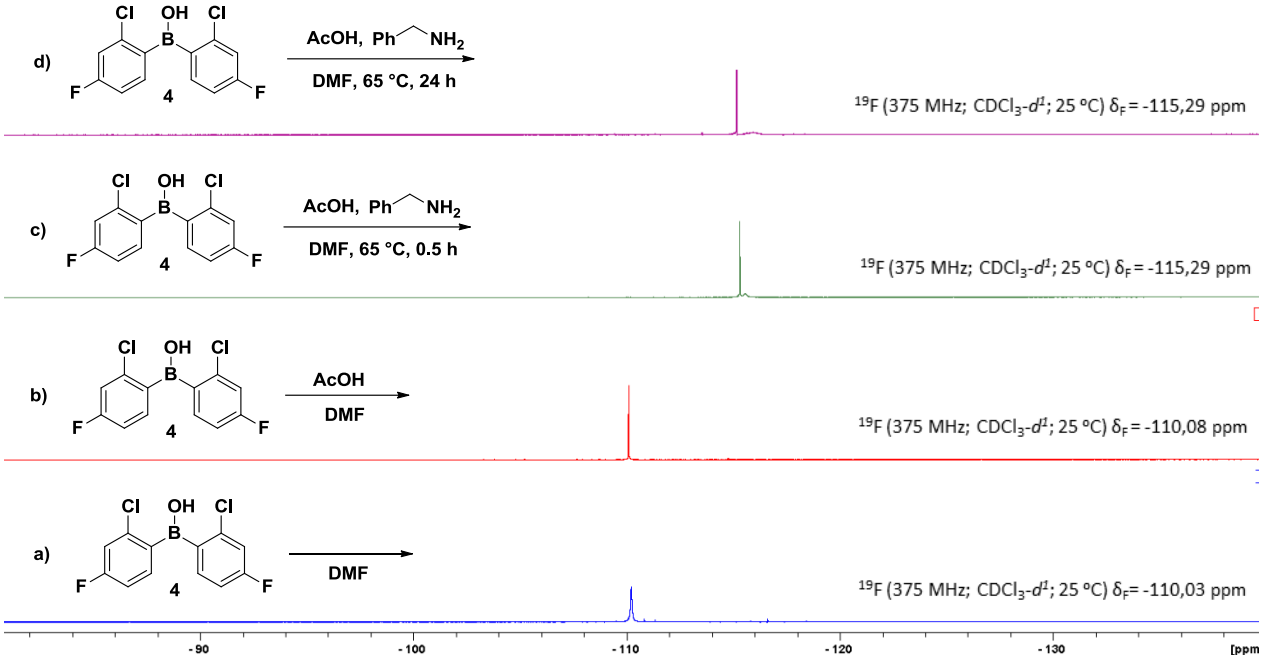

| Entry | # eq of $HCONH_2$ | Isolated Yield (%) |
|---|---|---|
| 1 | 20 | 99 |
| 2 | 10 | 99 |
| 3 | 5 | 99 |

[a] Reaction conditions: Borinic acid **1** (2.5 mol %) and AcOH (10 mol %) in $HCONH_2$ (x eq.) were stirred at 45 °C for 15 min before the addition of glycine methyl ester amine **7a** (40.0 μL, 0.50 mmol) and stirring was maintained for further 24 h.

As shown by Table 6, the number of $HCONH_2$ equivalents can be decreased down to 5 eq. while providing the same quantitative yield of **8a** (Entries 1-3).

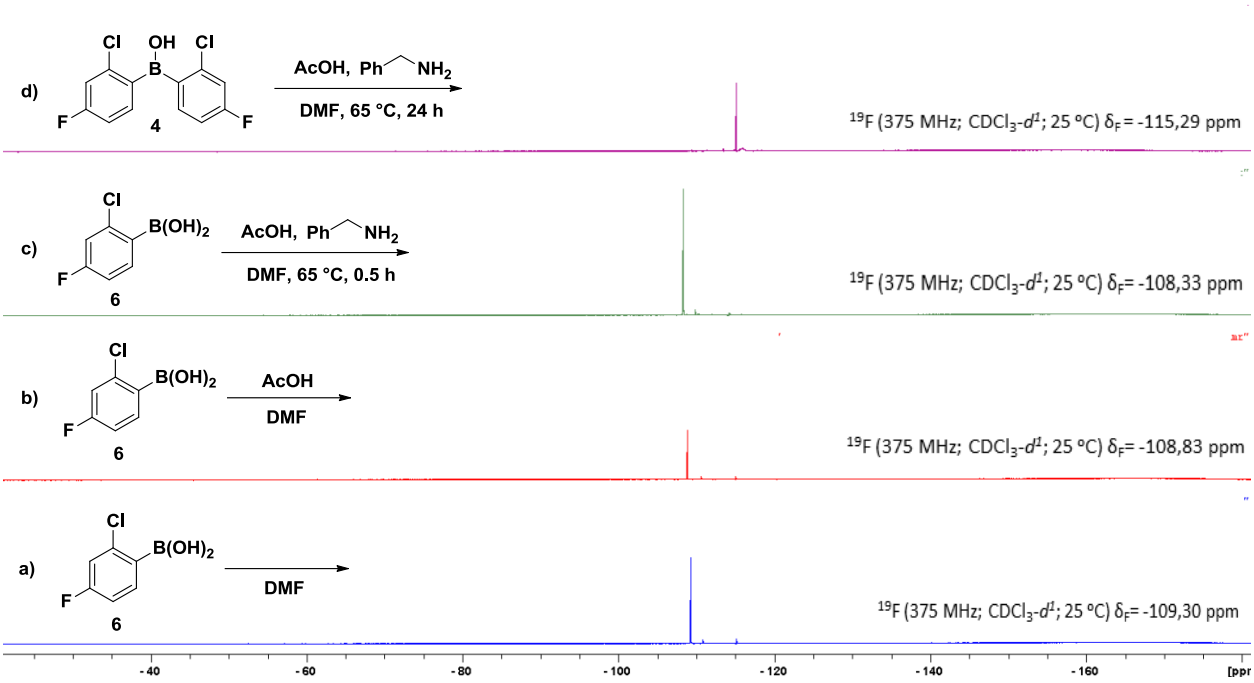
## 3. Mechanistic Studies

Scheme 1. Monitoring the progress of the reaction using **4** as a $^{19}F$ probe



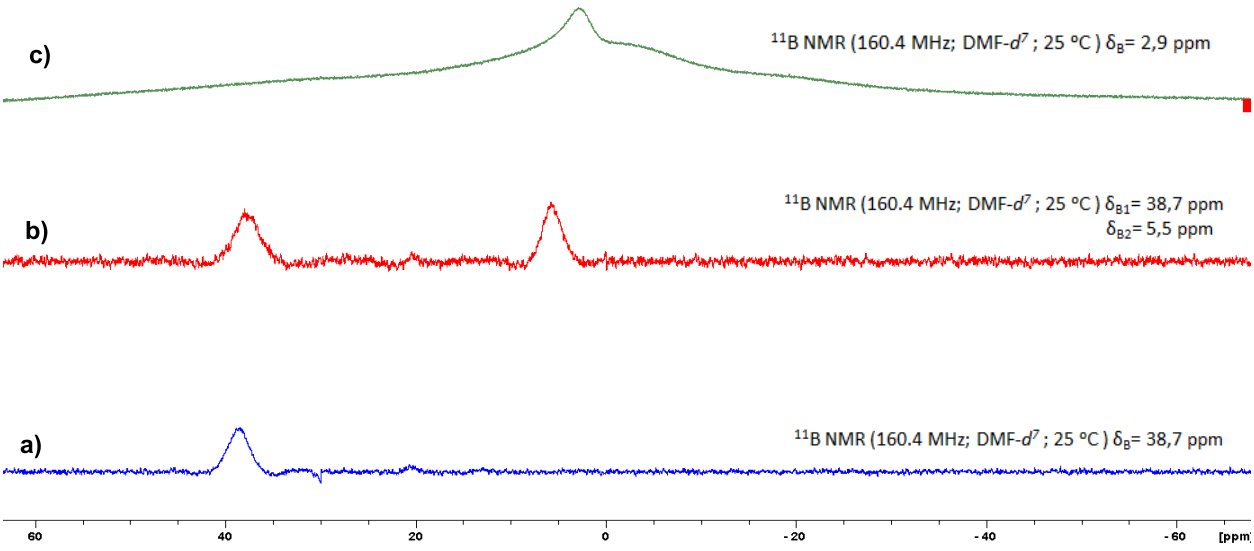

All the reactions were carried out at 65 °C in DMF (1 mL) the presence of 1,3,5-trimethoxybenzene as an internal standard (20 mol %). **(a) 4** (10 mol %). **(b) 4** (10 mol %) with AcOH (20 mol %). **(c) 4** (10 mol %) with AcOH (20 mol %) and benzylamine **2a** (50 mol %) after 30 min. **(d) 4** (10 mol %) with AcOH (20 mol %) and benzylamine **2a** (50 mol %) after 24 h.

Scheme 2. Studying the stability of **4** compared to boronic acid analogue **6**



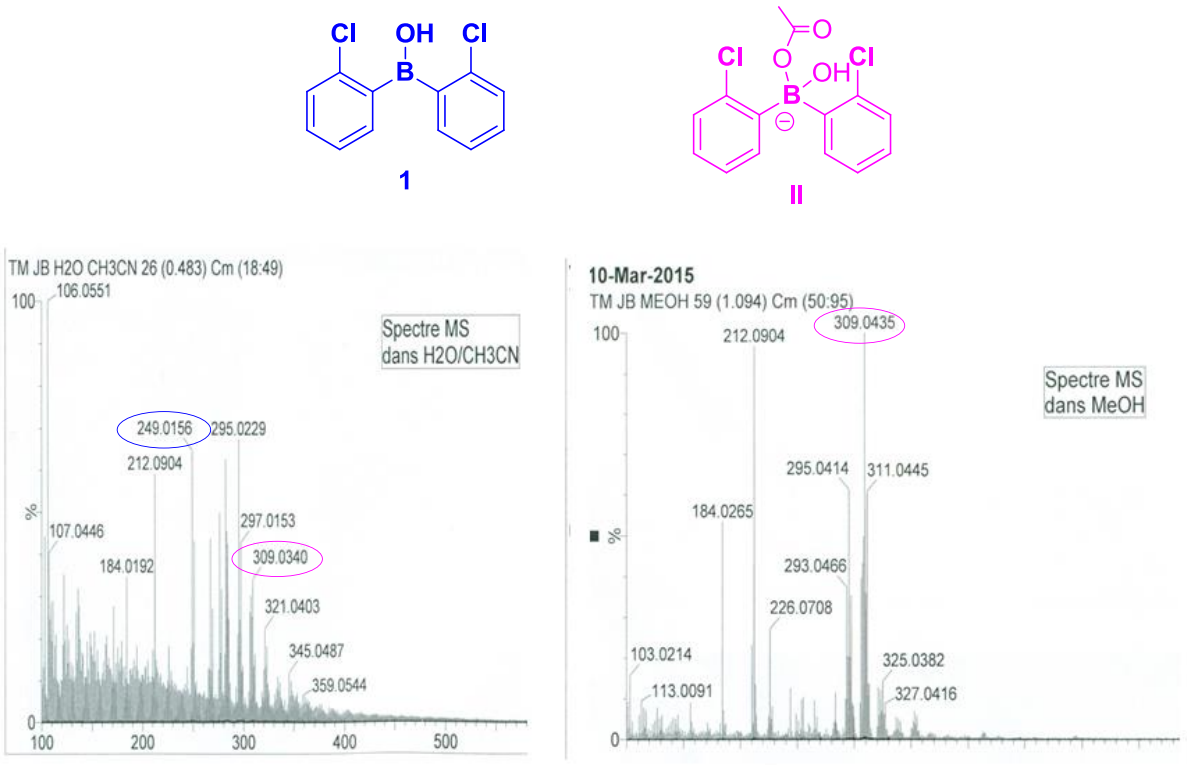

All the reactions were carried out at 65 °C in DMF (1 mL) the presence of 1,3,5-trimethoxybenzene as an internal standard (20 mol %). **(a) 6** (10 mol %). **(b) 6** (10 mol %) with AcOH (20 mol %). **(c) 6** (10 mol %) with AcOH (20 mol %) and benzylamine **2a** (50 mol %) after 24 h. **(d) 4** (10 mol %) with AcOH (20 mol %) and benzylamine **2a** (50 mol %) after 24 h.

Scheme 3. Monitoring the progress of the reaction using $^{11}$B NMR of the borinic acid catalyst **1**




All the reactions were carried out in deuterated DMF-$d^7$ at RT. **(a) 1** alone. **(b) 1** with AcOH (20-40 mol %). **(c) 1** with AcOH (40 mol %) and benzylamine **2a** (50 mol %).

Scheme 4. Monitoring the progress of the reaction using mass spectroscopy

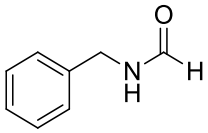



An equimolar mixture of **1** : **II** observed using LRMS (ESI-TOF) m/z: $[M - H]^-$

## 4. General Procedure A: *N*-Formylation of Amines using DMF

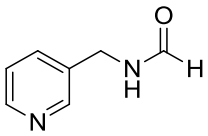
To a round-bottom flask under an argon atmosphere were added 2-chlorophenylborinic acid **1** (12.5 mg, 0.05 mmol, 0.1 equiv.), dry DMF (5 equiv. unless otherwise mentioned) and acetic acid (6 mg, 0.10 mmol, 6 µL, 0.2 equiv.). The mixture was vigorously stirred for 15 min at the given temperature (Table 2 main article) and the amine (0.50 mmol, 1 equiv.) was then slowly added using a gastight syringe. The resulting mixture was stirred for the given time. DMF was removed using Kugelrohr distillation apparatus (55 °C) and the residue was purified by column chromatography to give the title compounds. A sealed-pressure tube was used for the reactions involving low boiling points amines. When diluted conditions were required, 7 mL of dry DMF were used.

**Benzylformamide (3a)**. Known and described.[1] The title compound was prepared according to the general procedure **A** at room temperature for 72 h using benzylamine (55.5 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (70/30) as the eluent and isolated in the form of a colourless solid (58.2 mg, 0.43 mmol, 86%). Using a temperature of 65 °C provided a higher yield of **3a** within 12 h (67 mg, 0.50 mmol, 99%).



M.p: 62 – 64 °C (*lit*: 63-64).[2] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.37. The product was obtained in the form of 2 rotamers with a ratio of 9:1. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.15 (br s, 0.9$H_{CHO}$), 8.07 (d, *J* = 12.0 Hz, 0.1$H_{CHO}$), 7.37 – 7.22 (m, 5$H_{Ar}$), 6.68 (br s, 0.9 $H_{NH}$), 6.39 (br s, 0.1$H_{NH}$), 4.41 (d, *J* = 6.0 Hz, 1.8$H_{CH2}$), 4.34 (d, *J* = 6.5 Hz, 0.2$H_{CH2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 164.7 (C=O $_{minor}$), 161.1 (C=O $_{major}$) 137.6 ($Cq_{Ar}$), 129.0 ($CH_{Ar\ minor}$), 128.8 ($CH_{Ar\ major}$), 128.0 ($CH_{Ar\ minor}$) 127.8 ($CH_{Ar\ major}$), 127.7 ($CH_{Ar\ major}$), 127.0 ($CH_{Ar\ minor}$), 45.7 ($CH_{2\ minor}$) 42.2 ($CH_{2\ major}$).

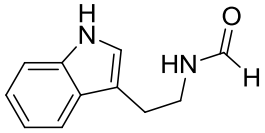
***N*-(Pyridine-2-yl)methylformamide (3b).** The title compound was prepared according to the general procedure **A** at room temperature for 72 h using 2-picolylamine (52 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (60/40 to 50/50) as the eluent and isolated in the form of a yellow oil (52.4 mg, 0.385 mmol, 77%). Using a temperature of 65 °C provided a higher yield of **3b** within 12 h (67.3 mg, 0.49 mmol, 99%).



[1] R. Fu, Y. Yang, Z. Chen, W. Lai, Y. Ma, R. Yuan, Q. Wang, *Tetrahedron* **2014**, *70*, 9492–9499.
[2] R. Lanigan, R. Starkov, T. Sheppard, *J. Org. Chem.* **2013**, *78*, 4521–4523.

$R_f$ ($CH_2Cl_2$/EtOAc: 60/40) = 0.10. The product was obtained in the form of 2 rotamers with a ratio of 9:1. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.54 (d, *J* = 4.8 Hz, 0.1$H_{NH}$), 8.50 (d, *J* = 4.3 Hz, 0.9$H_{NH}$), 8.29 (br s, 1$H_{CHO}$), 7.65 (td, *J* = 7.6, 1.5 Hz, 1$H_{Ar}$), 7.27-7.25 (m, 2$H_{Ar}$), 7.20-7.17 (m, 1$H_{Ar}$), 4.58 (d, *J* = 5.3 Hz, 1.8$H_{CH_2}$), 4.51 (d, *J* = 6.3 Hz, 0.2$H_{CH_2}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 161.2 (C=O), 155.8 ($Cq_{Ar}$), 148.8 ($CH_{Ar}$), 136.9 ($CH_{Ar}$), 122.4 ($CH_{Ar}$), 122.0 ($CH_{Ar}$), 42.9 ($CH_{2\ major}$), 29.6 ($CH_{2\ minor}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3284, 3012, 2929, 2863, 1663, 1593, 1572, 1531, 1477, 1437, 1385, 1242, 1216. HRMS (ESI$^+$ TOF) m/z: [M + H]$^+$ Calcd for $C_7H_9N_2O^+$ : 137.0715; Found: 137.0714.

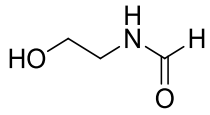
***N*-(2-(1*H*-Indol-3-yl)ethyl)formamide (3c).** The title compound was prepared according to the general procedure **A** at room temperature for 72 h using 2–(1*H*-indol-3-yl)ethanamine (94.1 mg, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (70/30) as the eluent and isolated in the form of a brown oil (81.0 mg, 0.43 mmol, 86%). Using a temperature of 65 °C provided the same yield of **3c** within 24 h (94.1 mg, 0.50 mmol, 99%).




$R_f$ ($CH_2Cl_2$/EtOAc: 70/43) = 0.22. The product was obtained in the form of 2 rotamers with a ratio of 8:2. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.65 (br s, 1$H_{NHAr}$), 7.90 (br s, 0.8$H_{CHO}$), 7.69 (br d, *J* = 12.0 Hz, 0.2$H_{CHO}$), 7.51 (d, *J* = 7.8 Hz, 0.8$H_{Ar}$), 7.50-7.47 (m, 0.2$H_{Ar}$), 7.27 (d, *J* = 7.8 Hz, 1$H_{Ar}$), 7.13 (t, *J* = 7.2 Hz, 1$H_{Ar}$), 7.06-7.02 (m, 1$H_{Ar}$), 6.87 (s, 0.8$H_{Ar}$), 6.83 (s, 0.2$H_{Ar}$), 5.92 (br s, 1$H_{NH}$), 3.51 (q, *J* = 6.1 Hz, 1.5$H_{CH_2\text{-}NH}$), 3.34 (q, *J* = 6.0 Hz, 0.5$H_{CH_2\text{-}NH}$), 2.87 (t, *J* = 6.6 Hz, 1.5$H_{CH_2\text{-}CH_2\text{-}NH}$), 2.81 (t, *J* = 6.8 Hz, 0.5$H_{CH_2\text{-}CH_2\text{-}NH}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 164.7 (C=O $_{minor}$), 161.5 (C=O $_{major}$), 136.4 ($Cq_{Ar\ minor}$), 136.3 ($Cq_{Ar\ major}$), 127.1 ($Cq_{Ar\ major}$), 126.7 ($Cq_{Ar\ minor}$), 122.8 ($CH_{Ar\ minor}$), 122.3 ($CH_{Ar\ major}$), 122.0 ($CH_{Ar\ minor}$), 121.9 ($CH_{Ar\ major}$), 119.3 ($CH_{Ar\ minor}$), 119.2 ($CH_{Ar\ major}$), 118.4 ($CH_{Ar\ major}$), 118.2 ($CH_{Ar\ minor}$), 112.0 ($Cq_{Ar\ major}$), 111.5 ($CH_{Ar\ minor}$), 111.3 ($CH_{Ar\ major}$), 111.1 (s, $Cq_{Ar\ minor}$), 42.0 ($CH_{2\ minor}$), 38.3 ($CH_{2\ major}$), 27.1 ($CH_{2\ minor}$), 24.9 ($CH_{2\ major}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3289, 3059, 3010, 2928, 2872, 1660, 1515, 1457, 1435,

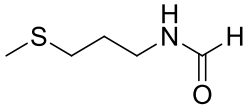
1385, 1339, 1216. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_{11}H_{12}ON_2Na^+$ : 211.0847; Found: 211.0849.

***N*-(2-Hydroxyethyl)formamide (3d).** The title compound was prepared according to the general procedure **A** at room temperature for 72 h using 2-amino-ethan-1-ol (30 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/MeOH (90/10 to 80/20) as the eluent and isolated in the form of a yellow oil (43.8 mg, 0.49 mmol, 98%).




$R_f$ ($CH_2Cl_2$/MeOH: 80/20) = 0.18. The product was obtained in the form of 2 rotamers with a ratio of 9:1. $^1$H NMR (400.0 MHz; MeOD-*d*$^4$) $\delta_H$ = 8.09 (br s, 0.9H$_{CHO}$), 8.01 (br s, 0.1H$_{CHO}$), 3.62 (t, *J* = 5.7 Hz, 1.6H$_{CH_2\text{-}OH}$), 3.59-3.58 (m, 0.4H$_{CH_2\text{-}OH}$), 3.35 (t, *J* = 5.6 Hz, 1.6H$_{CH_2\text{-}NH}$), 3.30 (t, *J* = 5.5 Hz, 0.4H$_{CH_2\text{-}NH}$). $^{13}$C NMR (101.6 MHz; MeOD-*d*$^4$) $\delta_C$ = 167.9 (C=O $_{minor}$), 164.2 (C=O $_{major}$), 62.5 ($CH_2$ $_{minor}$), 61.5 ($CH_2$ $_{major}$), 45.4 ($CH_2$ $_{minor}$), 41.6 ($CH_2$ $_{major}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3313, 2940, 2879, 2468, 2387, 1737, 1643, 1536, 1427, 1380, 1228, 1064. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_3H_7NO_2Na^+$ : 112.0374; Found: 112.0380.

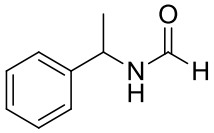
***N*-(3-(Methylthio)propyl)formamide (3e).** The title compound was prepared according to the general procedure **A** at room temperature for 72 h using 3-methylthiopropanamine (56 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (80/20 to 70/30) as the eluent and isolated in the form of an orange oil (66.3 mg, 0.50 mmol, 99%).




$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.15. The product was obtained in the form of 2 rotamers with a ratio of 9:1. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.07 (br s, 0.9H$_{CHO}$), 7.97 (d, *J* = 12.0 Hz, 0.1H$_{CHO}$), 6.67 (br s, 0.9H$_{NH}$), 6.51 (br s, 0.1H$_{NH}$), 3.31 (q, *J* = 6.3Hz, 1.8H$_{CH_2\text{-}NH}$), 3.25-3.23 (m,

0.2H$_{CH_2\text{-NH}}$), 2.46 (t, *J* = 7.0 Hz, 2H$_{CH_2\text{-SMe}}$), 2.02 (s, 3H$_{CH_3}$), 1.79-1.72 (m, 2H$_{CH_2\text{-}CH_2\text{-}CH_2\text{-NH}}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 164.8 (C=O $_{minor}$), 161.5 (C=O $_{major}$), 40.1 ($CH_{2\ minor}$), 36.9 ($CH_{2\ major}$), 31.2 ($CH_{2\ major}$), 30.5 ($CH_{2\ minor}$), 29.5 ($CH_{2\ minor}$), 28.3 ($CH_{2\ major}$), 15.2 ($CH_{3\ major}$), 15.1 ($CH_{3\ minor}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3283, 3055, 2918, 2860, 1658, 1533, 1437, 1384, 1265, 1238, 1174, 1073. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_5H_{11}NONaS^+$ : 156.0459; Found: 156.0458.

***N*-(1-Phenylethyl)formamide (3f)**. Known and described.[3] The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using 1-phenylethan-1-amine (65 µL, 0.50 mmol). It was purified by column chromatography using Pentane/EtOAc (90/10 to 60/40) as the eluent and isolated in the form of a yellow oil (73.9 mg, 0.50 mmol, 99%).

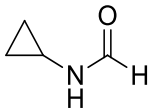



$R_f$ ($CH_2Cl_2$/EtOAc: 80/20) = 0.68. The product was obtained in the form of 2 rotamers with a ratio of 8:2. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.10 (br s, 0.8H$_{CHO}$), 8.08 (br s, 0.2H$_{CHO}$), 7.31-7.26 (m, 3H$_{Ar}$), 7.25-7.20 (m, 2H$_{Ar}$), 6.00 (br s, 0.2H$_{NH}$), 5.86 (br s, 0.8H$_{NH}$), 5.15 (quin, *J* = 7.3 Hz, 0.8H$_{CH}$), 4.63 (quin, *J* = 7.2 Hz, 0.2H$_{CH}$), 1.50 (d, *J* = 7.0 Hz, 0.6H$_{CH3}$), 1.46 (d, *J* = 6.9 Hz, 2.4H$_{CH3}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 164.1 (C=O $_{minor}$), 160.2 (C=O $_{major}$), 142.7 (Cq$_{Ar\ minor}$), 142.5 (Cq$_{Ar\ major}$), 128.9 (CH$_{Ar\ minor}$), 128.7 (CH$_{Ar\ major}$), 127.7 (CH$_{Ar\ minor}$), 127.5 (CH$_{Ar\ major}$), 126.1 (CH$_{Ar\ major}$), 125.7 (CH$_{Ar\ minor}$), 51.6 (CH $_{minor}$), 47.6 (CH $_{major}$), 23.6 ($CH_{3\ minor}$), 21.7 ($CH_{3\ major}$).

***N*-Cyclopropylformamide (3g)**. The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using cyclopropylamine (35 µL, 0.50 mmol) in a

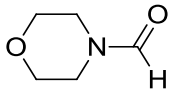
[3] T. Nakamura, K. Tateshi, S. Tsukagoshi, S. Hasimoto, S. Watanabe, V. A. Soloshonok, J. L. Acena, O. Kitagawa, *Tetrahedron* **2012**, *68*, 4013–4017.

sealed-pressure tube. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (80/20 to 70/30) as the eluent and isolated in the form of a yellow oil (42.2 mg, 0.50 mmol, 99%).



$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.28. The product was obtained in the form of 2 rotamers with a ratio of 7:3. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.12 (d, *J* = 11.9 Hz, 0.3$H_{CHO}$), 8.00 (br s, 0.7$H_{CHO}$), 6.97 (br s, 0.7$H_{NH}$), 6.75 (br s, 0.3$H_{NH}$), 2.65-2.59 (m, 0.7$H_{CH\text{-}NH}$), 2.58-2.52 (m, 0.3$H_{CH\text{-}NH}$), 0.71-0.62 (m, 2$H_{CH_2}$), 0.56-0.52 (m, 0.6$H_{CH_2}$), 0.48-0.44 (m, 1.4$H_{CH_2}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 166.8 (C=O $_{minor}$), 162.8 (C=O $_{major}$), 22.7 (CH $_{minor}$), 21.2 (CH $_{major}$), 6.2 ($CH_{2\ minor}$), 6.0 ($CH_{2\ major}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3266, 3016, 2867, 1737, 1651, 1526, 1455, 1385, 1360, 1262, 1200. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_4H_7NONa^+$ : 108.0425; Found: 108.0428.

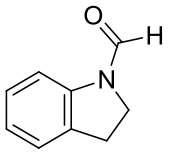
**Morpholine-4-carbaldehyde (3h)**. Known and described.[4] The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 24 h using morpholine (43 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (80/20 to 70/30) as the eluent and isolated in the form of a yellow oil (51.2 mg, 0.44 mmol, 89%).



$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.23. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ 8.02 (br s, 1$H_{CHO}$), 3.67 (t, *J* = 4.7 Hz, 2$H_{O\text{-}CH_2\text{-}CH_2\text{-}N}$), 3.63 (t, *J* = 4.6 Hz, 2$H_{O\text{-}CH_2\text{-}CH_2\text{-}N}$), 3.54 (t, *J* = 5.1 Hz, 2$H_{O\text{-}CH_2\text{-}CH_2\text{-}N}$), 3.37 (t, *J* = 5.0 Hz, 2$H_{O\text{-}CH_2\text{-}CH_2\text{-}N}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 160.6 (C=O), 67.0 ($CH_2$), 66.2 ($CH_2$), 45.6 ($CH_2$), 40.4 ($CH_2$).

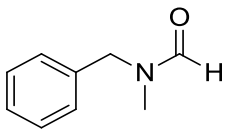
[4] Y. Zhao, S. Cai, J. Li, D. Zhigang, *Tetrahedron* **2013**, *69*, 8129–8131.

**1-*H*-Indole-1-carbaldehyde (3i).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 24 h using indole (56 µL, 0.50 mmol). It was purified by column chromatography using $CH_2Cl_2$/EtOAc (90/10) as the eluent and isolated in the form of a brown oil (70.6 mg, 0.48 mmol, 96%).



$R_f$ ($CH_2Cl_2$/EtOAc: 90/10) = 0.26. The product was obtained in the form of 2 rotamers with a ratio of 8:2. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 9.03 (br s, 0.8H$_{CHO}$), 8.61 (br s, 0.2H$_{CHO}$), 7.36-7.25 (m, 3H$_{Ar}$), 7.17-7.13 (m, 1H$_{Ar}$), 4.21 (t, *J* = 8.4 Hz, 0.5H$_{CH_2\text{-}CH_2\text{-}N}$), 4.16 (td, *J* = 8.5, 0.9 Hz, 1.5H$_{CH_2\text{-}CH_2\text{-}N}$), 3.31-3.29 (m, 0.4H$_{CH_2\text{-}CH_2\text{-}N}$), 3.25 (m, 1.6H$_{CH_2\text{-}CH_2\text{-}N}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 159.3 (C=O $_{minor}$), 157.6 (C=O $_{major}$), 141.0 (Cq$_{Ar}$), 131.9 (Cq$_{Ar}$), 127.58 (CH$_{Ar\ minor}$), 127.57 (CH$_{Ar\ major}$), 126.0 (CH$_{Ar\ major}$), 124.8 (CH$_{Ar\ minor}$), 124.6 (CH$_{Ar\ minor}$), 124.3 (CH$_{Ar\ major}$), 116.7 (CH$_{Ar\ minor}$), 109.4 (CH$_{Ar\ major}$), 47.0 (CH$_{2\ minor}$), 44.6 (CH$_{2\ major}$), 27.7 (CH$_{2\ major}$), 27.2 (CH$_{2\ minor}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 2918, 2851, 1668, 1595, 1494, 1463, 1405, 1363, 1338, 1293, 1267, 1173. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_9H_9NONa^+$ : 170.0590; Found: 170.0582.

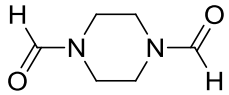
***N*-Benzyl-*N*-methylformamide (3j).** Known and described.[5] The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using *N*-methyl-1-phenylmethanamine (65 µL, 0.50 mmol). It was purified by column chromatography using pentane/EtOAc (80/20) as the eluent and isolated in the form of a yellow oil (74.4 mg, 0.50 mmol, 99%).



[5] L. Zhang, Z. Han, X. Zhao, Z. Wang, K. Ding, *Angew. Chem. Int. Ed*. **2015**, *54*, 6186–6189.

$R_f$ (Pentane/EtOAc: 80/20) = 0.13. The product was obtained in the form of 2 rotamers with a ratio of 6:4. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.21 (br s, 0.6$H_{CHO}$), 8.08 (br s, 0.4$H_{CHO}$), 7.32-7.22 (m, 3$H_{Ar}$), 7.20-7.12 (m, 2$H_{Ar}$), 4.44 (s, 0.8$H_{CH_2}$), 4.31 (s, 1.2$H_{CH_2}$), 2.76 (s, 1.2H, $CH_3$), 2.70 (s, 1.8H, $CH_3$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 162.6 ($C{=}O_{\text{major}}$), 162.4 ($C{=}O_{\text{minor}}$), 135.8 ($Cq_{Ar\ \text{minor}}$), 135.5 ($Cq_{Ar\ \text{major}}$), 128.6 ($CH_{Ar\ \text{major}}$), 128.4 ($CH_{Ar\ \text{minor}}$), 128.0 ($CH_{Ar\ \text{major}}$), 127.8 ($CH_{Ar\ \text{minor}}$), 127.4 ($CH_{Ar\ \text{minor}}$), 127.2 ($CH_{Ar\ \text{major}}$), 53.2 ($CH_{2\ \text{major}}$), 47.5 ($CH_{2\ \text{minor}}$), 33.8 ($CH_{3\ \text{major}}$), 29.2 ($CH_{3\ \text{minor}}$).

**Piperazine-1,4-carbaldehyde (3k).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using piperazine (43.1 mg, 0.50 mmol) under the diluted conditions, purified by column chromatography using $CH_2Cl_2$/MeOH (90/10) and isolated in the form of a yellow oil (68.0 mg, 0.48 mmol, 96%).

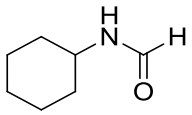



$R_f$ ($CH_2Cl_2$/MeOH: 90/10) = 0.49. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.03 (br s, 2$H_{CHO}$), 3.54-3.52 (m, 2$H_{CH_2}$), 3.47 (s, 2$H_{CH_2}$), 3.37 (s, 2$H_{CH_2}$), 3.34-3.31 (m, 2$H_{CH_2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 160.8 (C=O), 160.6 (C=O), 45.8 ($CH_2$), 44.7 ($CH_2$), 40.2 ($CH_2$), 39.2 ($CH_2$). $\upsilon_{max}$ (neat)/$cm^{-1}$ 3569, 2927, 2871, 2244, 1651, 1432, 1396, 1357, 1277, 1253, 1208, 1182, 1167. HRMS ($ESI^+$ TOF) m/z: $[M + Na]^+$ Calcd for $C_6H_{10}N_2O_2Na^+$ : 165.0640; Found: 165.0647.

***N*-Cyclohexylformamide (3l).** Known and described.[6] The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using cyclohexylamine (57 µL, 0.50 mmol) under the diluted conditions. It was purified by column chromatography

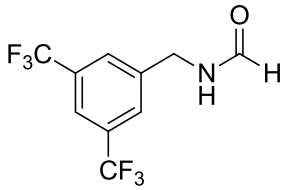
[6] O. Saidi, M. J. Bamford, A. J. Blacker, J. Lynch, S. P. Marsden, P. Plucinski, R. J. Watson, J. M. J. Williams, *Tetrahedron Lett.* **2010**, *51*, 5804–5806.

using $CH_2Cl_2$/EtOAc (90/10 to 80/20) as the eluent and isolated in the form of a yellow oil (61.3 mg, 0.48 mmol, 97%).



$R_f$ ($CH_2Cl_2$/EtOAc: 80/20) = 0.26. The product was obtained in the form of 2 rotamers with a ratio of 8:2. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.06 (br s, 0.2$H_{CHO}$), 8.02 (br s, 0.8$H_{CHO}$), 6.24 (br s, 0.2$H_{NH}$), 6.11 (br s, 0.8$H_{NH}$), 3.82-3.73 (m, 0.8$H_{CH}$), 3.25-3.23 (m, 0.2$H_{CH}$), 1.89-1.81 (m, 2$H_{CH_2}$), 1.68-1.63 (m, 2$H_{CH_2}$), 1.57-1.54 (m, 1$H_{CH_2}$), 1.34-1.24 (m, 2$H_{CH_2}$), 1.21-1.08 (m, 3$H_{CH_2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 160.5 (C=O), 51.0 (CH), 47.0 ($CH_2$), 34.6 ($CH_2$), 32.9 ($CH_2$), 25.4 ($CH_2$), 24.7 ($CH_2$).

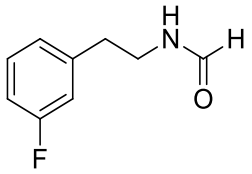
***N*-(3,5-bis(Trifluoromethyl)benzyl)formamide (3m).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using 3,5-bis(trifluoromethyl)-phenylmethanamine (122 mg, 0.50 mmol) under the diluted conditions. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (70/30) as the eluent and isolated in the form of a colorless oil (135.4 mg, 0.50 mmol, 99%).



$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.42. The product was obtained in the form of 2 rotamers with a ratio of 9.5:0.5. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.25 (br s, 1$H_{CHO}$), 7.76 (s, 1$H_{Ar}$), 7.72 (s, 2$H_{Ar}$), 7.09 (br s, 1$H_{NH}$), 4.54 (d, *J* = 6.3 Hz, 2$H_{CH_2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 164.8 (C=O $_{minor}$) 161.6 (C=O $_{major}$) 140.4 ($Cq_{Ar}$) 131.9 (q, $J_{C-F}$ = 33.4 Hz, $Cq_{CF_3}$) 127.6 (d, $J_{C-F}$ = 2.6 Hz, $CH_{Ar}$) 123.1 (d, $J_{C-F}$ = 272.8 Hz, $Cq_F$) 121.4 (quin, $J_{C-F}$ = 15.2 Hz, $CH_{Ar\ major}$) 119.0 ($CH_{Ar\ minor}$) 44.8 ($CH_{2\ minor}$) 41.1 ($CH_{2\ major}$). $^{19}F$ NMR (375 MHz; $CDCl_3$-d[1]) $\delta_F$ = -62.9 (s). $\upsilon_{max}$

(neat)/cm$^{-1}$ 3287, 3054, 2877, 1662, 1529, 1381, 1351, 1274, 1167, 1120. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_{10}H_7NONa\ F_6^+$ : 294.0330; Found: 294.0343.

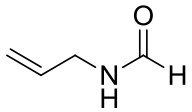
***N*-(3-Fluorophenethyl)formamide (3n).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using 2-(3-fluorophenyl)ethan-1-amine (65 µL, 0.50 mmol) under the diluted conditions. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (70/30) as the eluent and isolated in the form of a colorless oil (82.1 mg, 0.49 mmol, 98%).




$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.25. The product was obtained in the form of 2 rotamers with a ratio of 9:1. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.05 (br s, 0.9H$_{CHO}$), 7.82 (d, *J* = 11.8 Hz, 0.1H$_{CHO}$), 7.23 (dd, *J* = 12.2, 5.5 Hz, 1H$_{Ar}$), 6.94 (d, *J* = 5.5 Hz, 1H$_{Ar}$), 6.90-6.86 (m, 2H$_{Ar}$), 6.20 (br s, 1H$_{NH}$), 3.50 (q, *J* = 6.8 Hz, 1.7H$_{CH_2\text{-}CH_2\text{-}NH}$), 3.42 (q, *J* = 6.7 Hz, 0.3H$_{CH_2\text{-}CH_2\text{-}NH}$), 2.79 (t, *J* = 7.0 Hz, 2H$_{CH_2\text{-}CH_2\text{-}NH}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 164.5 (C=O $_{minor}$), 162.8 (*d*, $J_{C\text{-}F}$ = 246.0 Hz, Cq$_{ArF}$), 161.3 (C=O $_{major}$), 141.0 (d, $J_{C\text{-}F}$ = 7.4 Hz, Cq$_{Ar\ major}$), 140.1 (d, $J_{C\text{-}F}$ = 7.2 Hz, Cq$_{Ar\ minor}$), 130.2 (d, $J_{C\text{-}F}$ = 8.3 Hz, CH$_{Ar\ minor}$), 130.0 (d, $J_{C\text{-}F}$ = 8.3 Hz, CH$_{Ar\ major}$), 124.5 (d, $J_{C\text{-}F}$ = 2.8 Hz, CH$_{Ar\ minor}$), 124.3 (d, $J_{C\text{-}F}$ = 2.8 Hz, CH$_{Ar\ major}$), 115.6 (d, $J_{C\text{-}F}$ = 21.1 Hz, CH$_{Ar\ minor}$), 115.48 (d, $J_{C\text{-}F}$ = 21.1 Hz, CH$_{Ar\ major}$), 113.7 (d, $J_{C\text{-}F}$ = 20.9 Hz, CH$_{Ar\ minor}$), 113.4 (d, $J_{C\text{-}F}$ = 21.1 Hz, CH$_{Ar\ major}$), 42.8 (CH$_{2\ minor}$), 38.9 (CH$_{2\ major}$), 37.2 (d, $J_{C\text{-}F}$ = 1.6 Hz, CH$_{2\ minor}$), 35.1 (d, $J_{C\text{-}F}$ = 1.6 Hz, CH$_{2\ major}$). $^{19}$F NMR (375 MHz; $CDCl_3$-d$^1$) $\delta_F$ = -113.0 (s). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3281, 3056, 2936, 2866, 1657, 1616, 1588, 1488, 1449, 1383, 1250, 1140. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_9H_{10}NOFNa^+$: 190.0644; Found: 190.0654.

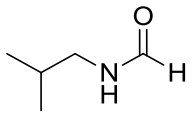
***N*-Allylformamide (3o).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 24 h using allylamine (96 µL, 0.50 mmol) under the diluted

conditions in a sealed-pressure tube. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (90/10 to 70/30) as the eluent and isolated in the form of a colorless oil (42.6 mg, 0.50 mmol, 99%).



$R_f$ ($CH_2Cl_2$/EtOAc: 90/10) = 0.11. The product was obtained in the form of 2 rotamers with a ratio of 9:1. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.12 (br s, 0.9H$_{CHO}$), 7.95 (d, *J* = 12.0 Hz, 0.1H$_{CHO}$), 6.68 (br s, 0.9H$_{NH}$), 6.38 (br s, 0.1H$_{NH}$), 5.83-5.70 (m, 1H$_{CH\text{-}CH_2\text{-}NH}$), 5.20-5.14 (m, 0.2H$_{(CH)_2\text{-}C=CH}$), 5.17-5.07 (m, 1.8H$_{(CH)_2\text{-}C=CH}$), 3.83 (t, *J* = 5.7 Hz, 1.8H$_{CH_2\text{-}NH}$), 3.79-3.76 (m, 0.2H$_{CH_2\text{-}NH}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 164.9 (C=O $_{minor}$), 161.3 (C=O $_{major}$), 134.2 (CH $_{minor}$), 133.4 (CH $_{major}$), 116.6 (CH $_{minor}$), 116.3 (CH $_{major}$), 43.8 ($CH_2$ $_{minor}$), 40.2 ($CH_2$ $_{major}$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3284, 3055, 2924, 2867, 1658, 1644, 1532, 1421, 1383, 1338, 1232, 1145. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_4H_7NONa^+$ : 108.0425; Found: 108.0429.

***N*-Isobutylformamide (3p).** Known and described.[7] The title compound was prepared according to the general procedure **B** at a temperature of 65 °C for 12 h using isobutylamine (50 µL, 0.50 mmol) under the diluted conditions in a sealed-pressure tube. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (80/20) as the eluent and isolated in the form of a colorless oil (49.9 mg, 0.49 mmol, 99%).

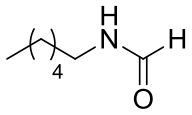


$R_f$ ($CH_2Cl_2$/EtOAc: 80/20) = 0.21. The product was obtained in the form of 2 rotamers with a ratio of 9:1. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.01 (br s, 0.9H$_{CHO}$), 7.84 (d, *J* = 11.9 Hz, 0.1H$_{CHO}$), 7.05 (br s,

[7] A. P. Johnson, R. W. A. Luke, A. N. Boa, *J. Chem. Soc., Perkin Trans.1* **1996**, *1*, 895–905.

1$H_{NH}$), 2.94 (t, *J* = 6.5 Hz, 1.6$H_{CH2}$), 2.87 (t, *J* = 6.5 Hz, 0.4$H_{CH2}$), 1.70-1.56 (m, 1$H_{CH}$), 0.79 (d, *J* = 6.8 Hz, 2 x 3$H_{CH3}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 165.0 (C=O $_{minor}$), 161.5 (C=O $_{major}$), 49.1 ($CH_{2\ minor}$), 45.1 ($CH_{2\ major}$), 29.2 (CH $_{minor}$), 28.0 (CH $_{major}$), 19.7 ($CH_{3\ major}$), 19.2 ($CH_{3\ minor}$).

***N*-Hexylformamide (3q).** Known and described.[8] The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 12 h using hexylamine (66 µL, 0.50 mmol) under the diluted conditions. It was purified by column chromatography using $CH_2Cl_2$/EtOAc (70/30) as the eluent and isolated in the form of a yellow oil (63.2 mg, 0.49 mmol, 98%).




$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.42. The product was obtained in the form of 2 rotamers with a ratio of 8:2. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.16 (br s, 0.8$H_{CHO}$), 8.04 (d, *J* = 12.0 Hz, 0.2 $H_{CHO}$), 5.60 (br s, 1$H_{NH}$), 3.30 (q, *J* = 6.9 Hz, 1.5$H_{CH2\text{-}NH}$), 3.21 (q, *J* = 6.8 Hz, 0.5$H_{CH2\text{-}NH}$), 1.52 (qiun, *J* = 7.2 Hz, 2$H_{CH2\text{-}CH2\text{-}NH}$), 1.30 (s, 3 x 2$H_{CH2}$), 0.89 (t, *J* = 6.7 Hz, 3$H_{CH3}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 164.8 (C=O $_{minor}$), 161.3 (C=O $_{major}$), 41.8 ($CH_{2\ minor}$), 38.1 ($CH_{2\ major}$), 31.3 ($CH_{2\ major}$), 31.2 ($CH_{2\ minor}$), 31.0 ($CH_{2\ minor}$), 29.3 ($CH_{2\ major}$), 26.4 ($CH_{2\ major}$), 25.9 ($CH_{2\ minor}$), 22.41 ($CH_{2\ major}$), 22.38 ($CH_{2\ minor}$), 13.9 ($CH_{3\ major}$), 13.8 ($CH_{3\ minor}$).

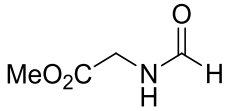
## 6. General Procedure B: *N*-formylation of α-amino esters using $HCONH_2$

To a sealed tube was added 2-chlorophenylborinic acid **1** (3 mg, 0.0125 mmol, 0.025 equiv.), $HCONH_2$ (0.10 mL, 2.5 mmol, 5 equiv.) and acetic acid (3 mg, 0.05 mmol, 3 µL, 0.1 equiv.). The mixture was vigorously stirred for 15 min at 45 °C and the α-amino ester amine (0.50 mmol, 1 equiv.) was then slowly added using a gastight syringe. The resulting mixture was stirred for a

[8] N. Ortega, C. Richter, F. Glorius, *Org. Lett.* **2013**, *15*, 1776–1779.

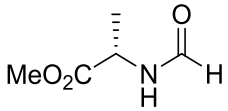
further 24 h. The reaction mixture was directly purified using column chromatography using $CH_2Cl_2$/EtOAc (90/10 to 80/20 and 70/30) as the eluent, unless otherwise stated, to yield the corresponding title compounds in good to excellent yields. It should be noted that the density of each free amine was determined prior to its addition and the volume was accordingly calculated.

**Methyl-*N*-formyl-glycinate (8a).** The title compound was prepared according to the general procedure **B** using glycine methyl ester (40 µL, 0.50 mmol) and isolated in the form of a yellow oil (58.2 mg, 0.50 mmol, 99%).



$R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.26. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*$^1$) $\delta_H$ = 8.23 (s, $1H_{CHO}$), 6.45 (br s, $1H_{NH}$), 4.08 (d, *J* = 5.4 Hz, $2H_{CH2}$), 3.75 (s, $3H_{OCH3}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*$^1$) $\delta_C$ = 169.9 ($C{=}O_{ester}$), 161.2 (C=O), 52.4 ($CH_3$), 39.7 ($CH_2$). $\upsilon_{max}$ (neat)/cm$^{-1}$ 3316, 3054, 2957, 2251, 1745, 1662, 1521, 1439, 1385, 1370, 1207, 1183, 1008. HRMS (ESI$^+$ TOF) m/z: [M + Na]$^+$ Calcd for $C_4H_7NO_3Na^+$ : 140.0324; Found: 140.0327.

**(*S*)-Methyl-*N*-formyl-alinate (8b)**. Known and described.[9] The title compound was prepared according to the general procedure **B** using of (*S*)-alanine methyl ester (54 µL, 0.50 mmol) and isolated in the form of a brown oil (65.6 mg, 0.50 mmol, 99%, *ee*: 94%).

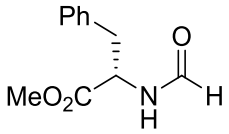


$[\alpha]_D^{25}$ - 53.1° (*c* 0.6, EtOH), $[\alpha]_D^{25}$ (*lit*) - 54.4° (*c* 0.6, EtOH).[10] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.21. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz;

[9] M. Suchý, A. A. H. Elmehriki, R. H. E. Hudson, *Org. Lett.* **2011**, *13*, 3952–3955.
[10] T. V. Q. Nguyen, W.-J. Yoo, S. Kobayashi, *Angew. Chem.* **2015**, *127*, 9341 – 9344.

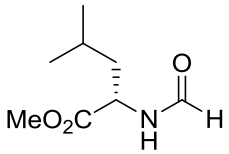
$CDCl_3$-*d*[1]) $\delta_H$ = 8.14 (br s, $1H_{CHO}$), 6.63 (br s, $1H_{NH}$), 4.63 (q, *J* = 7.2 Hz, $1H_{CH}$), 3.72 (s, $3H_{OCH_3}$), 1.40 (d, *J* = 7.2 Hz, $3H_{CH_3}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 172.9 (C=O), 160.5 (C=O), 52.4 ($CH_3$), 46.6 (CH), 18.2 ($CH_3$).

**(*S*)-Methyl-*N*-formyl-phenylalinate (8c).** Known and described.[11] The title compound was prepared according to the general procedure **B** using of (*S*)-phenylalanine methyl ester (82 µL, 0.50 mmol) and isolated in the form of a colorless oil (101.9 mg, 0.49 mmol, 98%, *ee*: 92%).




$[\alpha]_D^{25}$ + 82.3° (*c* 2.0, EtOH), $[\alpha]_D^{25}$ (*lit*) + 86.1° (*c* 2.0, EtOH).[12] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.38. The $^1$H and $^{13}$C data were consistent with those reported in the literature. $^1$H NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.11 (br s, $1H_{CHO}$), 7.30-7.22 (m, $3H_{Ar}$), 7.11-7.09 (m, $2H_{Ar}$), 6.39 (d, *J* = 6.3 Hz, $1H_{NH}$), 4.94 (q, *J* = 7.6 Hz, $1H_{CH\text{-}CH_2}$), 3.72 (s, $3H_{OCH_3}$), 3.15 (dd, *J* = 13.9, 6.6 Hz, $1H_{CH\text{-}CH_2}$), 3.09 (dd, *J* = 13.9, 5.6 Hz, $1H_{CH\text{-}CH_2}$). $^{13}$C NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 171.5 ($C{=}O_{ester}$), 160.6 (C=O), 135.4 ($Cq_{Ar}$), 129.1, ($CH_{Ar}$), 128.5 ($CH_{Ar}$), 127.1 ($CH_{Ar}$), 52.3 ($CH_3$), 51.7 (CH), 37.5 ($CH_2$).

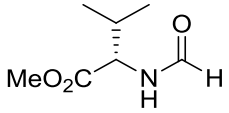
**(*S*)-Methyl-*N*-formyl-leucinate (8d).** The title compound was prepared according to the general procedure **B** using of (*S*)-leucine methyl ester (72 µL, 0.50 mmol) and isolated in the form of a yellow oil (83.9 mg, 0.484 mmol, 97%).




[11] D. W. Carney, J. V. Truong, J. K. Sello, *J. Org. Chem.*, **2011**, *76*, 10278–10285.
[12] J.-G. Kim, D. O. Jang, *Synlett* **2010**, 1231–1234

$[\alpha]_D^{25}$ + 4.2° (*c* 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) + 4.1° (*c* 1.0, $CHCl_3$).[13] $R_f$ ($CH_2Cl_2$/EtOAc: 90/10) = 0.26. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.18 (br s, $1H_{CHO}$), 6.46 (br s, $1H_{NH}$), 4.69 (td, *J* = 8.8, 4.5 Hz, $1H_{CH_2\text{-}CH\text{-}NH}$), 3.71 (s, $3H_{OCH_3}$), 1.66-1.58 (m, $2H_{CH_2\text{-}CH\text{-}NH}$), 1.56-1.51 (m, $1H_{(CH_3)_2CH}$), 0.92 (m, 2 x $3H_{CH_3}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 173.1 ($C{=}O_{ester}$), 160.8 (C=O), 52.3 ($CH_3$), 49.2 (CH), 41.4 ($CH_2$), 24.7 (CH), 22.6 ($CH_3$), 21.7 ($CH_3$). $\upsilon_{max}$ (neat)/$cm^{-1}$ 2924, 2957, 1744, 1661, 1531, 1437, 1384, 1076. HRMS ($ESI^+$ TOF) m/z: $[M + Na]^+$ Calcd for $C_8H_{15}NO_3Na^+$ : 196.0950; Found: 196.0954.

**(*S*)-Methyl-*N*-formyl-valinate (8e).** The title compound was prepared according to the general procedure **B** using of (*S*)-valine methyl ester (70 µL, 0.50 mmol) and isolated in the form of a yellow oil (76.7 mg, 0.48 mmol, 96%, *ee*> 99%).




$[\alpha]_D^{25}$ + 22.2° (*c* 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) + 28.2° (*c* 1.0, $CHCl_3$).[14] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.33. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.21 (br s, $1H_{CHO}$), 6.64 (d, *J* = 5.5 Hz, $1H_{NH}$), 4.60 (dd, *J* = 9.0, 4.9 Hz, $1H_{CH_2\text{-}CH\text{-}NH}$), 3.70 (s, $3H_{OCH_3}$), 2.19-2.11- (m, $1H_{(CH_3)_2CH}$), 0.92 (d, *J* = 6.8 Hz, $3H_{CH_3}$), 0.87 (d, *J* = 6.8 Hz, $3H_{CH_3}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 172.1 ($C{=}O_{ester}$), 161.1 (C=O), 55.5 (CH), 52.1 ($CH_3$), 31.0 (CH), 18.8 ($CH_3$), 17.5 ($CH_3$). $\upsilon_{max}$ (neat)/$cm^{-1}$ 3303, 2968, 2877, 2251, 1739, 1662, 1520, 1466, 1437, 1384, 1372, 1268, 1182, 1138. HRMS ($ESI^+$ TOF) m/z: $[M + Na]^+$ Calcd for $C_7H_{14}NO_3Na^+$ : 182.0793; Found: 182.0803.

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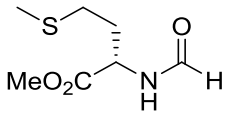
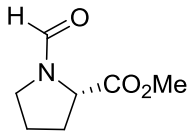
[13] A. Karim, A. Mortreux, F. Petit, G. Buono, G. Pfeiffer, C. Siv, *J. Organomet. Chem*. **1986**, *317*, 93–104.
[14] M. Aitali, S. Allaoud, A. Karim, C. Meliet, A. Mortreux, *Tetrahedron: Asymmetry* **2000**, *11*, 1367–1374.

**(*S*)-Methyl-*N*-formylmethioninate (8f).** Known and described.[9] The title compound was prepared according to the general procedure **B** using of (*S*)-methionine methyl ester (75 µL, 0.50 mmol) and isolated in the form of a yellow oil (87.1 mg, 0.456 mmol, 91%, *ee*: 90%).



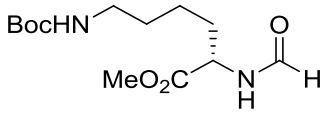
$[\alpha]_D^{25}$ + 39.4° (*c* 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) + 38.8° (*c* 1.0, $CHCl_3$).[9] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.54. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.17 (s, $1H_{CHO}$), 6.85 (d, *J* = 6.4 Hz, $1H_{NH}$), 4.76-4.71 (m, $1H_{CH_2\text{-}CH\text{-}NH}$), 3.71 (s, $3H_{OCH_3}$), 2.47 (t, *J* = 7.5 Hz, $2H_{SMe\text{-}CH_2\text{-}CH_2\text{-}CH}$), 2.17-2.08 (m, $1H_{SMe\text{-}CH_2\text{-}CH_2\text{-}CH}$), 2.04 (s, $3H_{SCH_3}$), 2.0-1.93 (m, $1H_{CH_2\text{-}CH_2\text{-}CH}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 172.0 ($C{=}O_{ester}$), 161.0 (C=O), 52.5 ($CH_3$), 49.9 (CH), 31.3 ($CH_2$), 29.7 ($CH_2$), 15.2 ($CH_3$).

**(*S*)-Methyl-*N*-formylprolinate (8g).** Known and described.[9] The title compound was prepared according to the general procedure **B** using of (*S*)-proline methyl ester (60 µL, 0.50 mmol) and isolated in the form of a yellow oil (78.2 mg, 0.50 mmol, 99%).



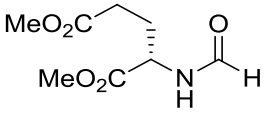
$[\alpha]_D^{25}$ – 109.7° (*c* 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) -89.5° (*c* 1.0, $CHCl_3$).[9] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.32. The product was obtained in the form of 2 rotamers with a ratio of 6:4. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.22 (br s, $0.6H_{CHO}$), 8.18 (br s, $0.4H_{CHO}$), 4.40-4.38 (m, $1H_{CH}$) 3.70 (s, $1.2H_{OCH_3}$), 3.67 (s, $1.8H_{OCH_3}$) 3.63-3.53 (m, $1H_{CH_2\text{-}N}$), 3.48-3.45 (m, $1H_{CH_2\text{-}N}$), 2.24-2.13 (m, $2H_{CH_2\text{-}CH_2\text{-}CH}$), 2.00-1.85 (m, $2H_{CH_2\text{-}CH_2\text{-}CH}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 172.0 ($C{=}O_{ester\ minor}$), 171.9 ($C{=}O_{ester\ major}$), 161.4 ($C{=}O_{\ minor}$), 160.6 (s, $C{=}O_{\ major}$), 58.4 ($CH_{\ major}$), 56.2 ($CH_{\ minor}$), 52.5 ($CH_{3\ minor}$), 52.1 ($CH_{3\ major}$), 46.1 ($CH_{2\ major}$), 43.7 ($CH_{2\ minor}$), 29.4 ($CH_{2\ minor}$), 29.2 ($CH_{2\ major}$), 23.8 ($CH_{2\ major}$), 22.6 ($CH_{2\ minor}$).

**(*S*)-Methyl-$N^6$-Boc-*N*-formyllysinate (8h).** Known and described.[9] The title compound was prepared according to the general procedure **B** using of (*S*)-lysine methyl ester (130.2 mg, 0.50 mmol) and isolated in the form of a yellow oil (143.8 mg, 0.50 mmol, 99%).




$[\alpha]_D^{25}$ + 10.2° (*c* 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) + 12.6° (*c* 1.0, $CHCl_3$).[9] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.20. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.18 (br s, $1H_{CHO}$), 6.70 (d, *J* = 6.1 Hz, $1H_{NH}$), 4.72 (t, *J* = 5.3 Hz, $1H_{Boc\text{-}NH}$), 4.63-4.58 (m, $1H_{CH_2\text{-}CH\text{-}NH}$), 3.72 (s, $3H_{OCH_3}$), 3.08-3.06 (m, $2H_{BocNH\text{-}CH_2\text{-}CH_2}$), 1.90-1.82 (m, $1H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 1.75-1.65 (m, $1H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 1.52-1.44 (m, $2H_{BocNH\text{-}\ CH_2\text{-}CH_2\text{-}CH_2}$), 1.40 (s, $9H_{(CH_3)_3C=O}$), 1.36-1.30 (m, $2H_{BocNH\text{-}CH_2\text{-}CH_2\text{-}CH_2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ =172.4 ($C{=}O_{ester}$), 160.9 (C=O), 156.2 ($C{=}O_{Boc}$), 79.1 (Cq), 52.4 ($CH_3$), 50.6 (CH), 39.6 ($CH_2$), 31.4 ($CH_2$), 29.4 ($CH_2$), 28.3 ($CH_3$), 22.1 ($CH_2$).

**(*S*)-Dimethyl-*N*-formylglutamate (8i).** The title compound was prepared according to the general procedure **B** using of (*S*)-glutamate dimethyl ester (87.6 µL, 0.50 mmol) and isolated in the form of a yellow oil (58.2 mg, 0.29 mmol, 57%).

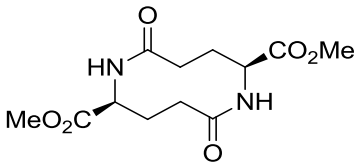



$[\alpha]_D^{25}$ + 66.9° (*c* 1.4, $CHCl_3$), $[\alpha]_D^{25}$ (*lit*) + 69.7° (*c* 1.4, $CHCl_3$).[15] $R_f$ ($CH_2Cl_2$/EtOAc: 70/30) = 0.24. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 8.21 (br s, $1H_{CHO}$), 6.55 (d, *J* = 4.6 Hz, $1H_{NH}$), 4.73-4.68 (m, $1H_{CH\text{-}NH}$), 3.75 (s, $3H_{OCH_3}$), 3.66 (s, $3H_{OCH_3}$), 2.48-2.35 (m, $2H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 2.27-2.19 (m, $1H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 2.06-1.97 (m, $1H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 173.1 ($C{=}O_{ester}$), 171.9 ($C{=}O_{\text{ester next to (CH)}}$), 160.8 (C=O), 52.6 ($CH_3$), 51.8 ($CH_3$), 50.2 (CH), 29.8

[15] A. G. Avent, H. M. E. Duggan, D. W. Young, *Org. Biomol. Chem.* **2005**, *3*, 2327-2332.

($CH_2$), 27.2 ($CH_2$). $\upsilon_{max}$ (neat)/$cm^{-1}$ 3322, 2956, 2927, 2857, 2254, 1733, 1668, 1525, 1437, 1384, 1335, 1260, 1204, 1172. HRMS ($ESI^+$ TOF) m/z: $[M + Na]^+$ Calcd for $C_8H_{13}NO_5Na^+$ : 226.0691; Found: 226.0699.

**(*S*,*S*)-Dimethyl-5,10-dioxo-1,6-diazecane-2,7-dicarboxylate (9).** The title compound was prepared according to the general procedure **A** at a temperature of 65 °C for 48 h using of (*S*)-glutamate dimethyl ester (87.6 µL, 0.50 mmol) under the diluted conditions, purified by column chromatography using $CH_2Cl_2$/EtOAc (80/20) and isolated in the form of a yellow oil (65.1 mg, 0.23 mmol, 91%).



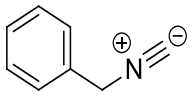

$[\alpha]_D^{25}$ + 0.69 ° (*c* 1.0, $CHCl_3$), (no reported $[\alpha]_D^{25}$ in *lit*). $R_f$ ($CH_2Cl_2$/EtOAc: 80/20) = 0.26. $^1H$ NMR (400.0 MHz; $CDCl_3$-$d^1$) $\delta_H$ = 6.82 (br s, $2H_{NH}$), 4.27-4.24 (m, 2 x $1H_{CH\text{-}NH}$), 3.76 (s, 2 x $3H_{CH_3}$), 2.51-2.41 (m, $2H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 2.39-2.28 (m, 2 x $2H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$), 2.25-2.18 (m, $2H_{CH_2\text{-}CH_2\text{-}CH\text{-}NH}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-$d^1$) $\delta_C$ =178.2 (C=O), 172.6 (C=O), 55.4 (CH), 52.6 ($CH_3$), 29.2 ($CH_2$), 24.8 ($CH_2$). $\upsilon_{max}$ (neat)/$cm^{-1}$ 3231, 2956, 1739, 1694, 1437, 1378, 1205, 1152, 1113, 1042, 1023. HRMS ($ESI^+$ TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{18}N_2O_6Na^+$ : 309.1064; Found: 309.1076.

## 7. Procedure C: One-Pot Synthesis of an Isocyanide from Benzylamine

To a round-bottom flask under an argon atmosphere were added 2-chlorophenylborinic acid **1** (12.5 mg, 0.05 mmol, 0.1 equiv.), dry DMF (7 mL) and acetic acid (6 mg, 0.10 mmol, 6 µL, 0.2 equiv.) at 65 °C. The mixture was vigorously stirred for 15 mins and the amine (0.50 mmol, 1 equiv.) was then slowly added using a gastight 100 µL syringe. The resulting mixture was stirred for 12 h at 65 °C. After 12 h, Burgess reagent (360 mg, 1.5 mmol, 3 equiv.), trimethylamine (418 µL, 3 mmol, 6 equiv.) and 5 Å powdered molecular sieves (1 g) were added and stirring was maintained for further 48 h. The reaction mixture was extracted five times with $Et_2O$ and $H_2O$ in order to remove DMF, washed with brine, dried over anhydrous $MgSO_4$ and concentrated under

vacuum. The crude mixture was purified by column chromatography using Pentane/EtOAc as the eluent to give the desired isocyanides.

**Benzyl isocyanide (10)**. Known and described.[16] The title compound was prepared according to the procedure **C** using benzylamine (55 µL, 0.50 mmol). It was purified by column chromatography using Pentane /EtOAc (80/20 to 50/50) as the eluent to yield the title compound as an orange oil (43.9 mg, 0.33 mmol, 65%).

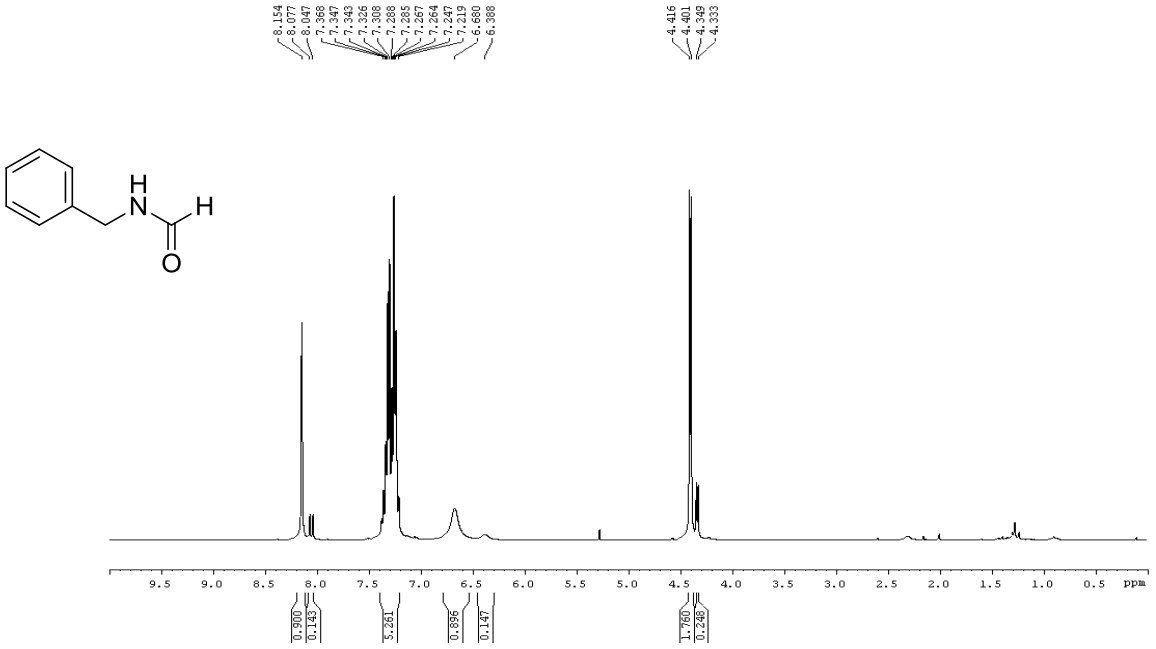


$R_f$ ($CH_2Cl_2$/EtOAc: 95/5) = 0.55. The $^1H$ and $^{13}C$ data were consistent with those reported in the literature. $^1H$ NMR (400.0 MHz; $CDCl_3$-*d*[1]) $\delta_H$ = 7.43-7.34 (m, $5H_{Ar}$), 4.55 (s, $2H_{CH_2}$). $^{13}C$ NMR (101.6 MHz; $CDCl_3$-*d*[1]) $\delta_C$ = 157.7 (t, *J* = 5.4 Hz, CN), 132.3 ($Cq_{Ar}$), 129.0 ($CH_{Ar}$), 128.4 ($CH_{Ar}$), 126.6 ($CH_{Ar}$), 45.5 (t, *J* = 7.3 Hz, $CH_2$).

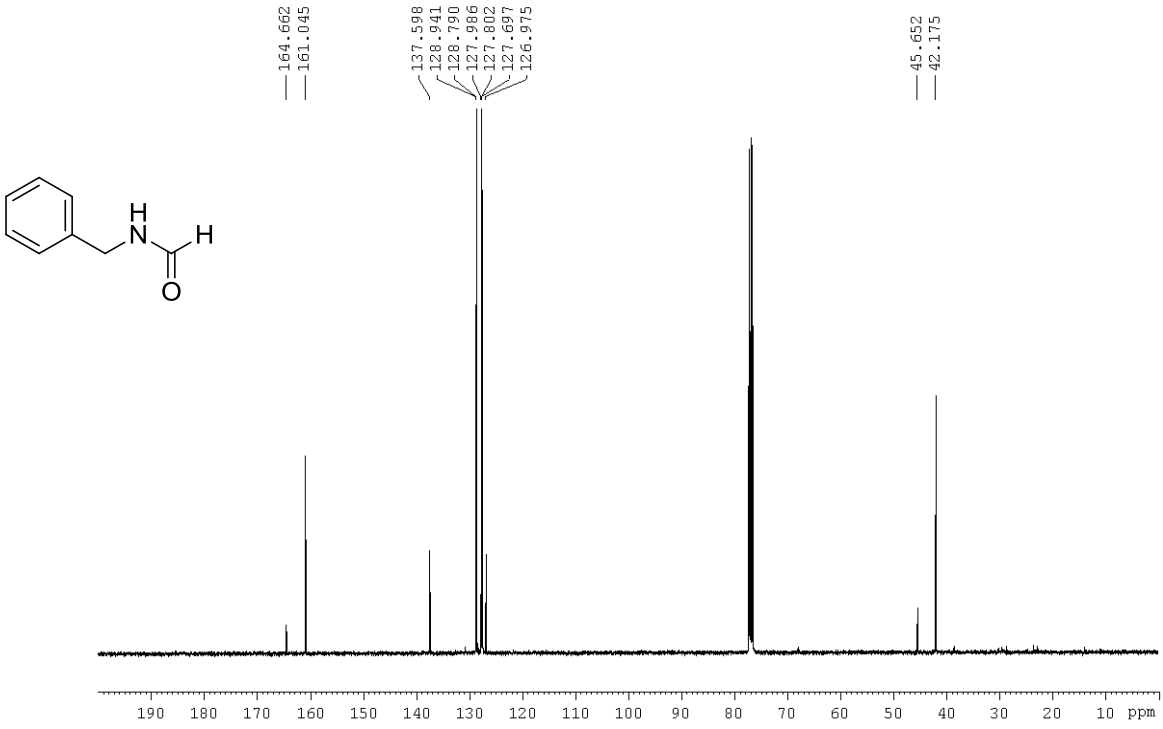
[16] M. Ketia, M. Vandamme, O. Mahé, J.-F. Paquin, *Tetrahedron Lett.* **2015**, *56*, 461–464.

## 8. $^{1}H$ and $^{13}C$ NMR Spectra of the Synthesised products

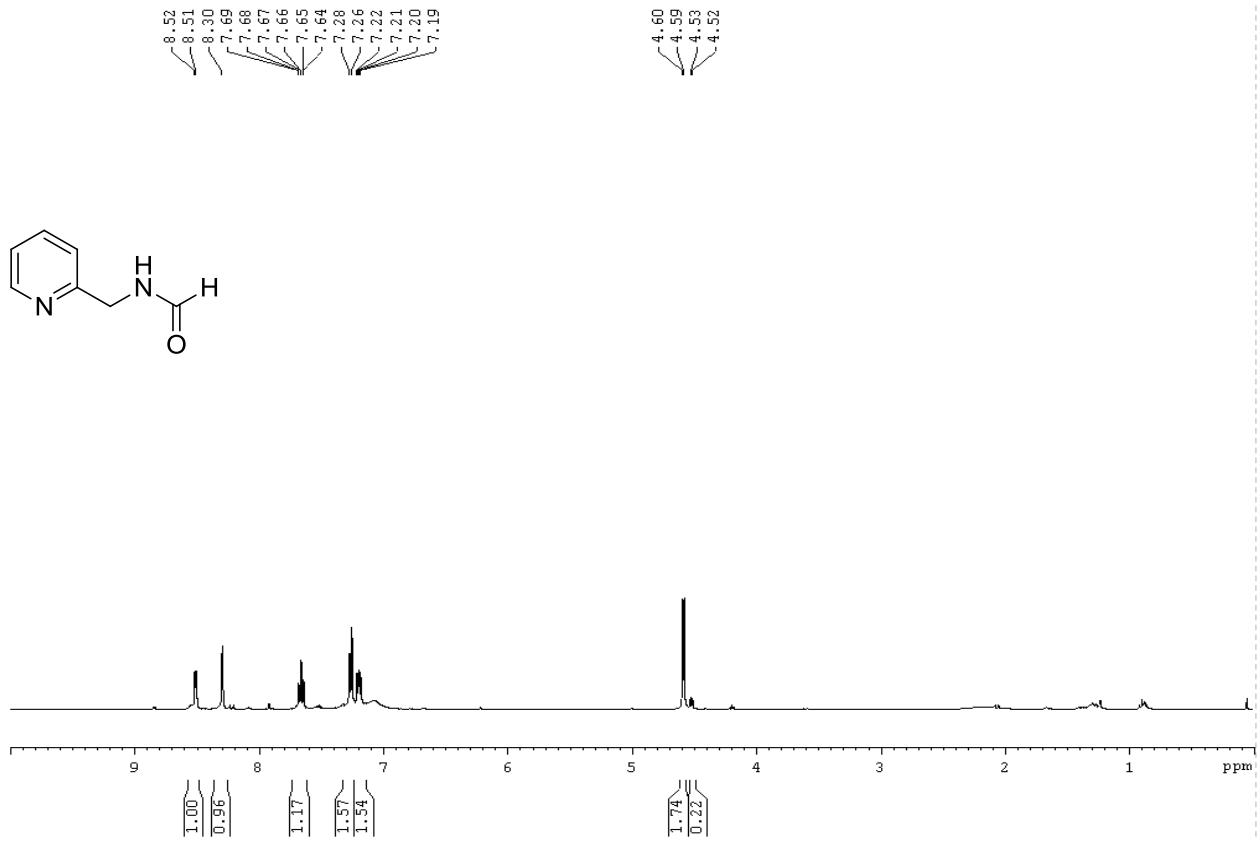
$^{1}H$ NMR (400.0 MHz; $CDCl_3$) of **3a**.



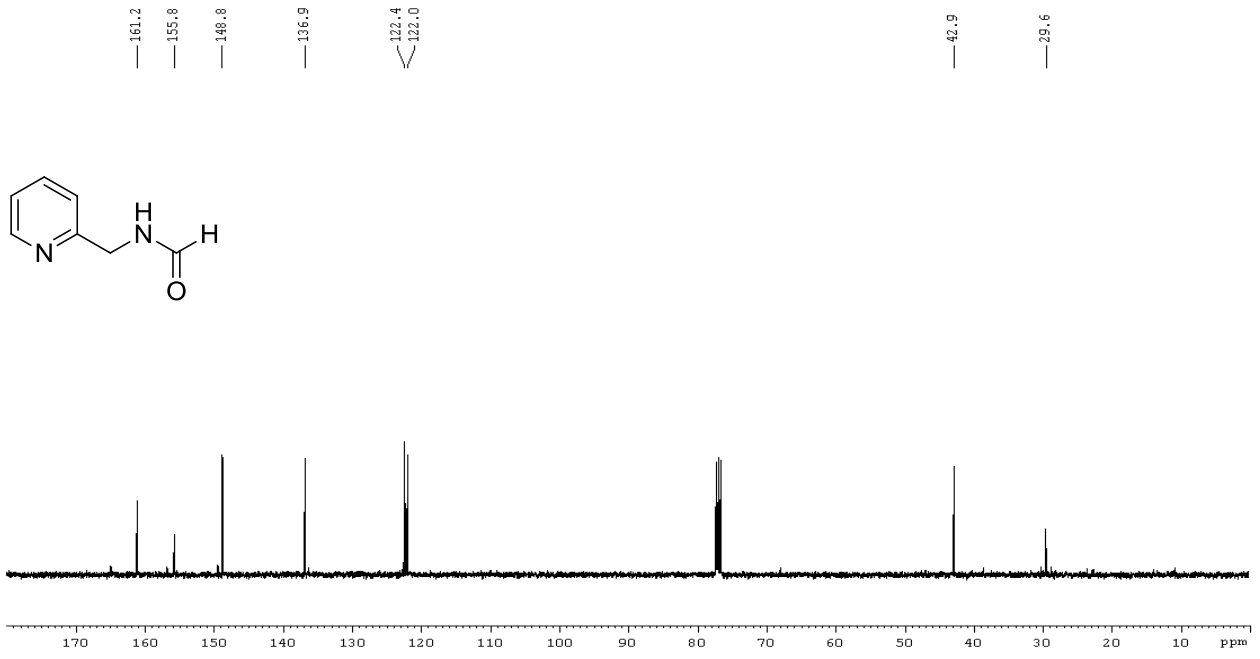

$^{13}C$ NMR (100.0 MHz; $CDCl_3$) of **3a**.



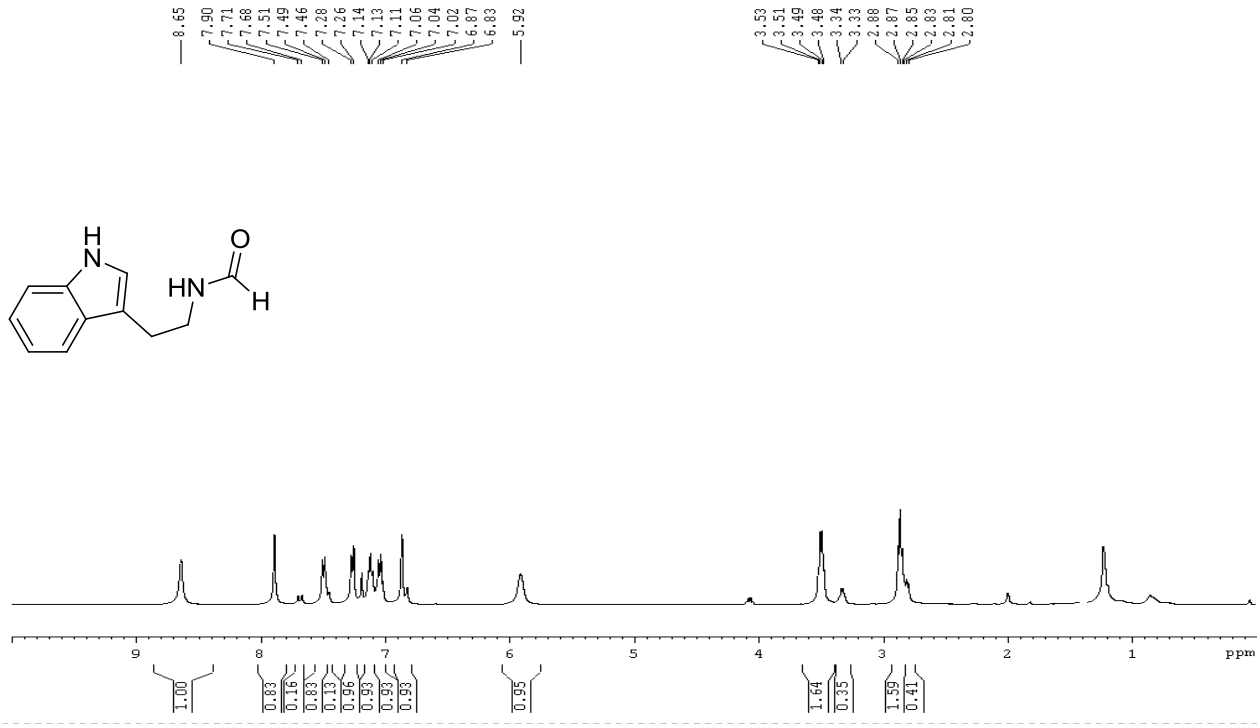
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3b**.



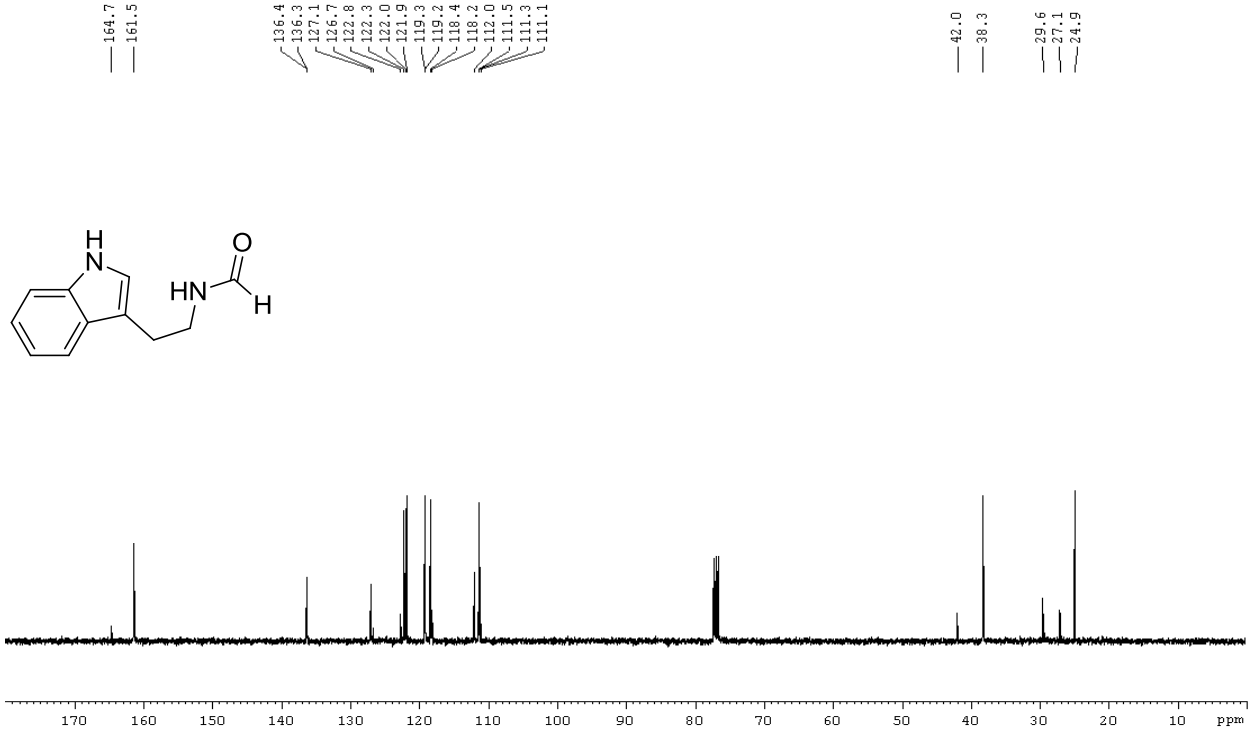

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3b**.



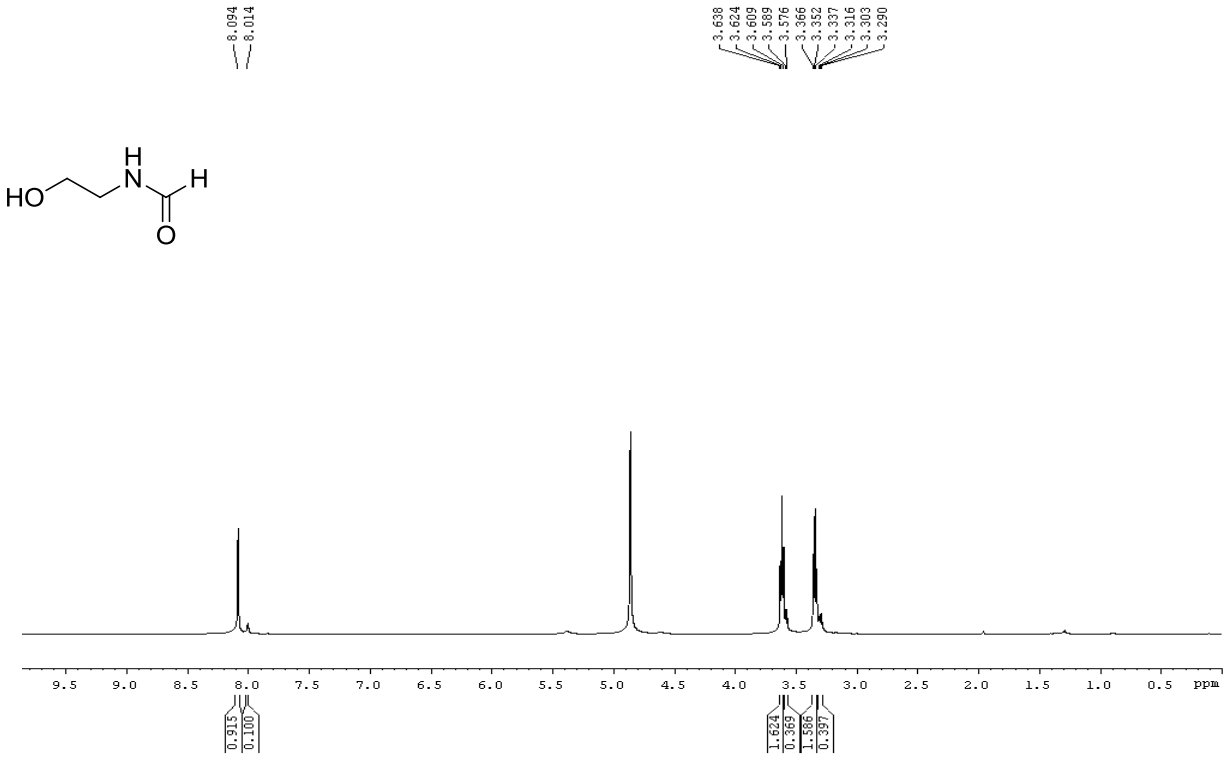
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3c**.



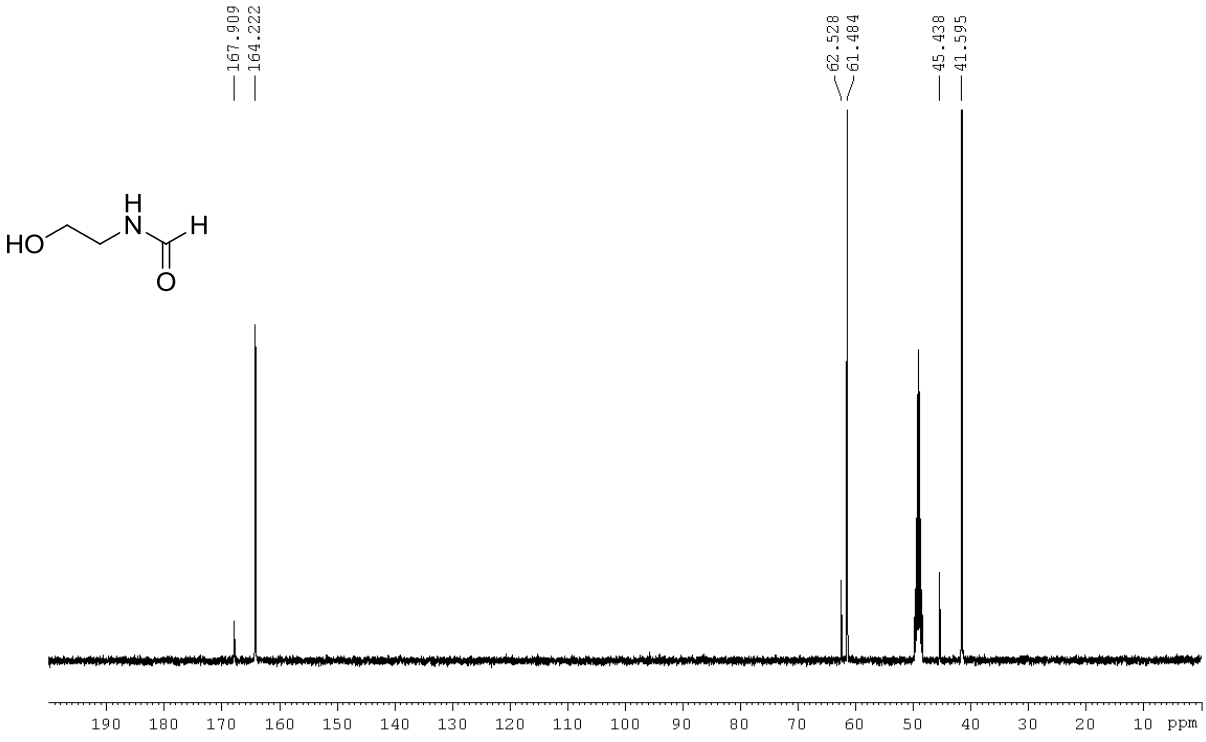

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3c**.



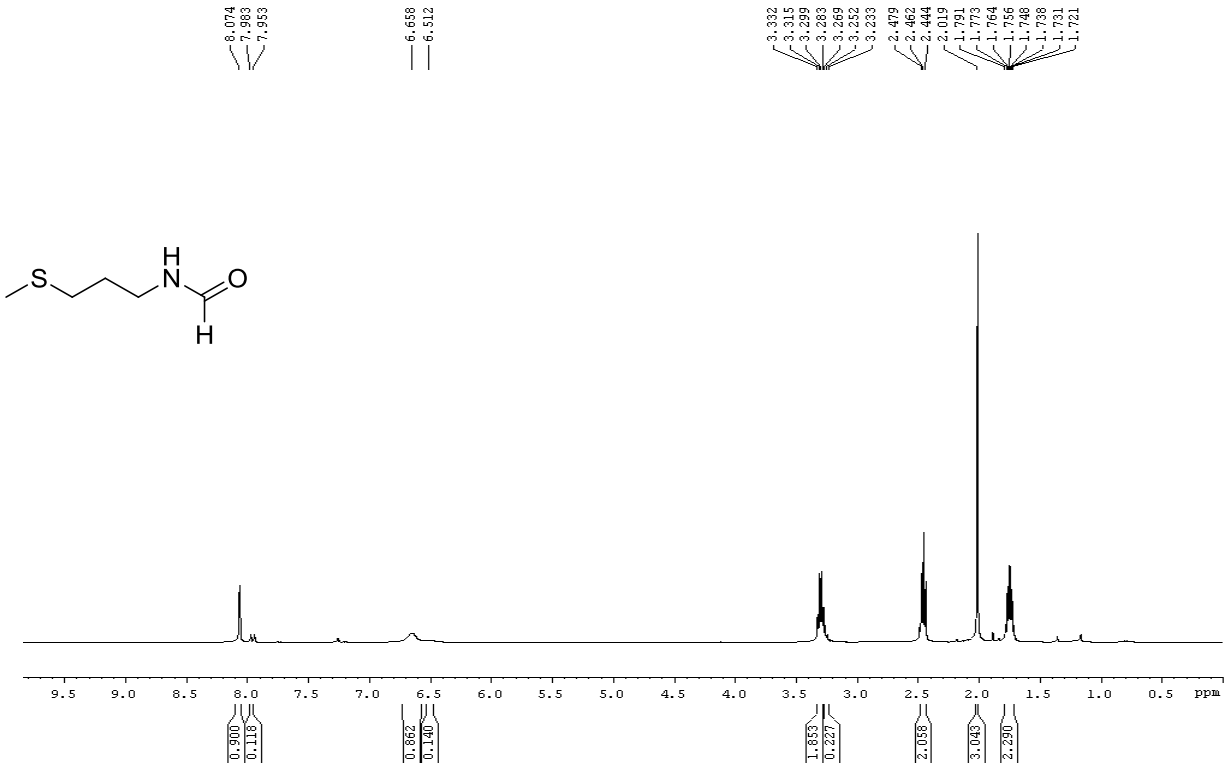
$^{1}$H NMR (400.0 MHz; MeOH-d$^{4}$) of **3d**.



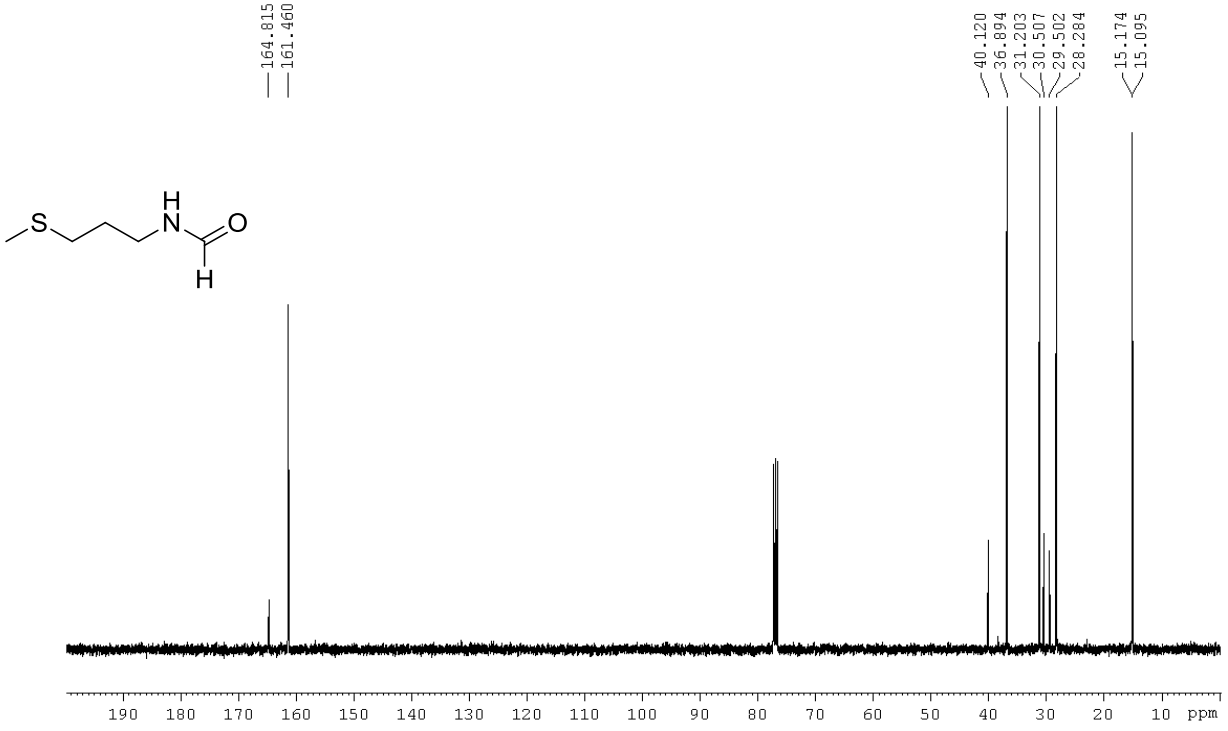

$^{13}$C NMR (100.0 MHz; MeOH-d$^{4}$) of **3d**.



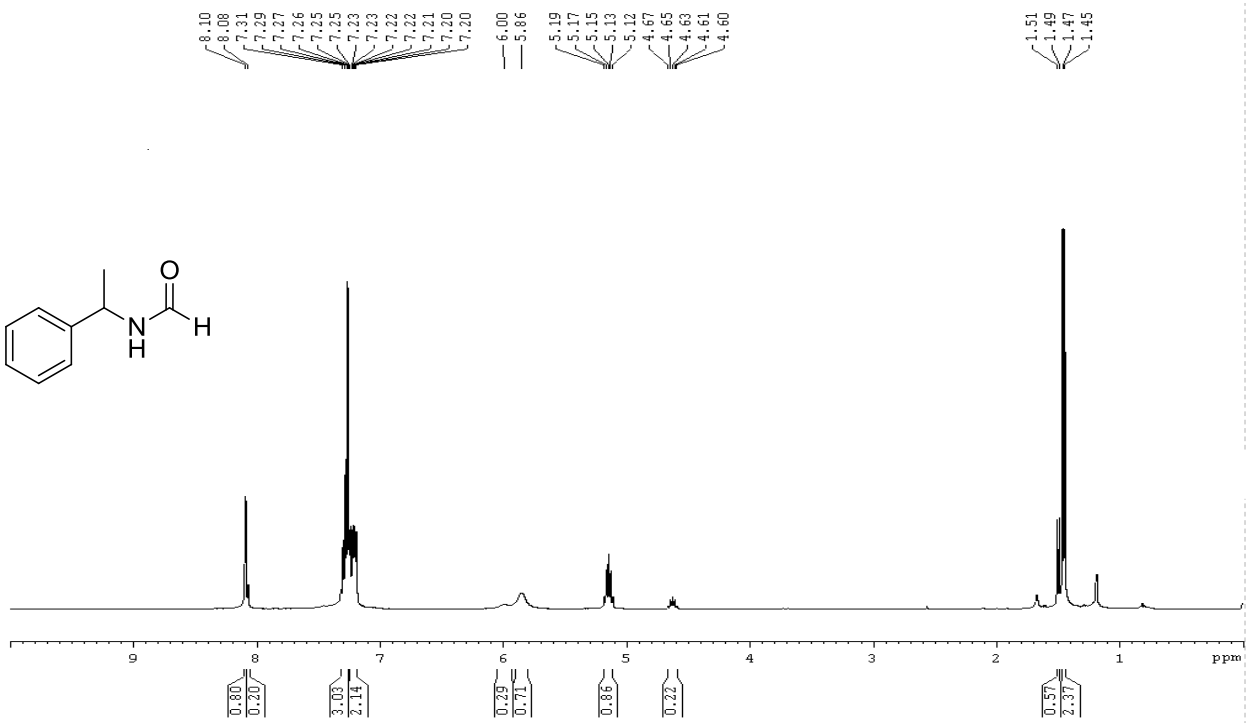
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3e**.



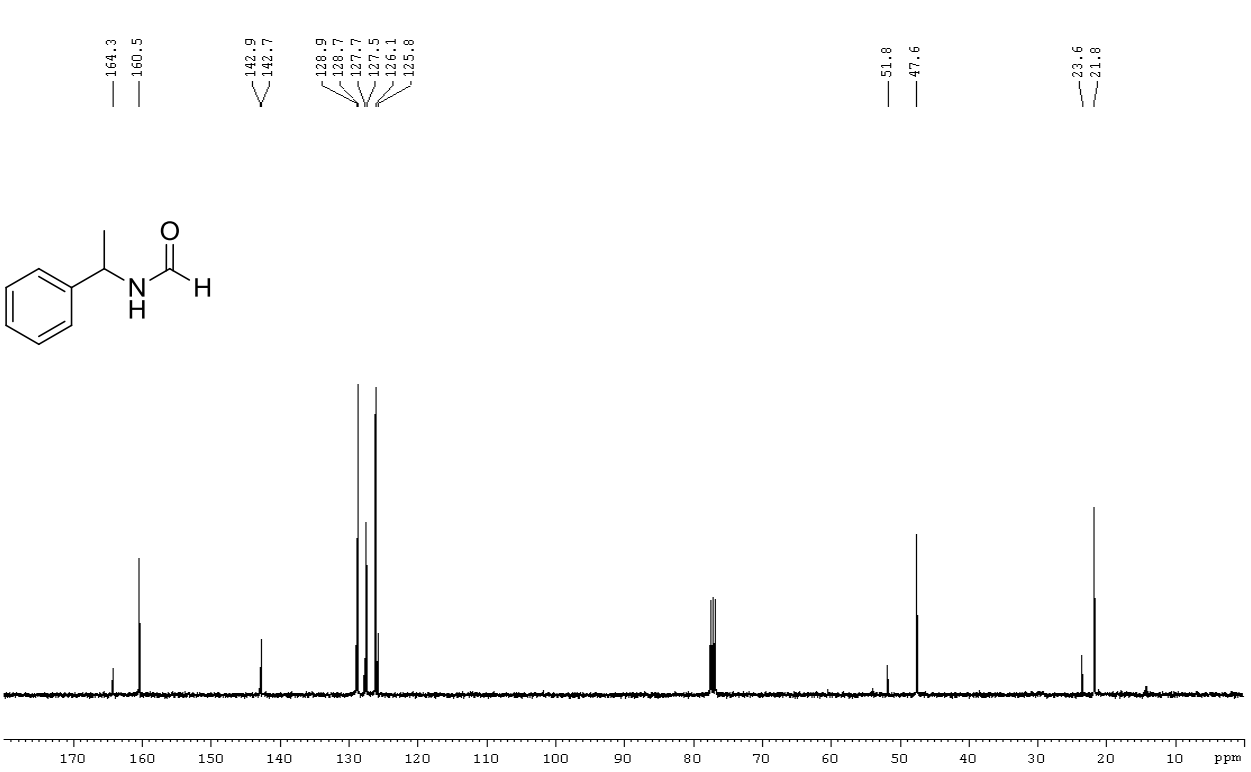

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3e**.



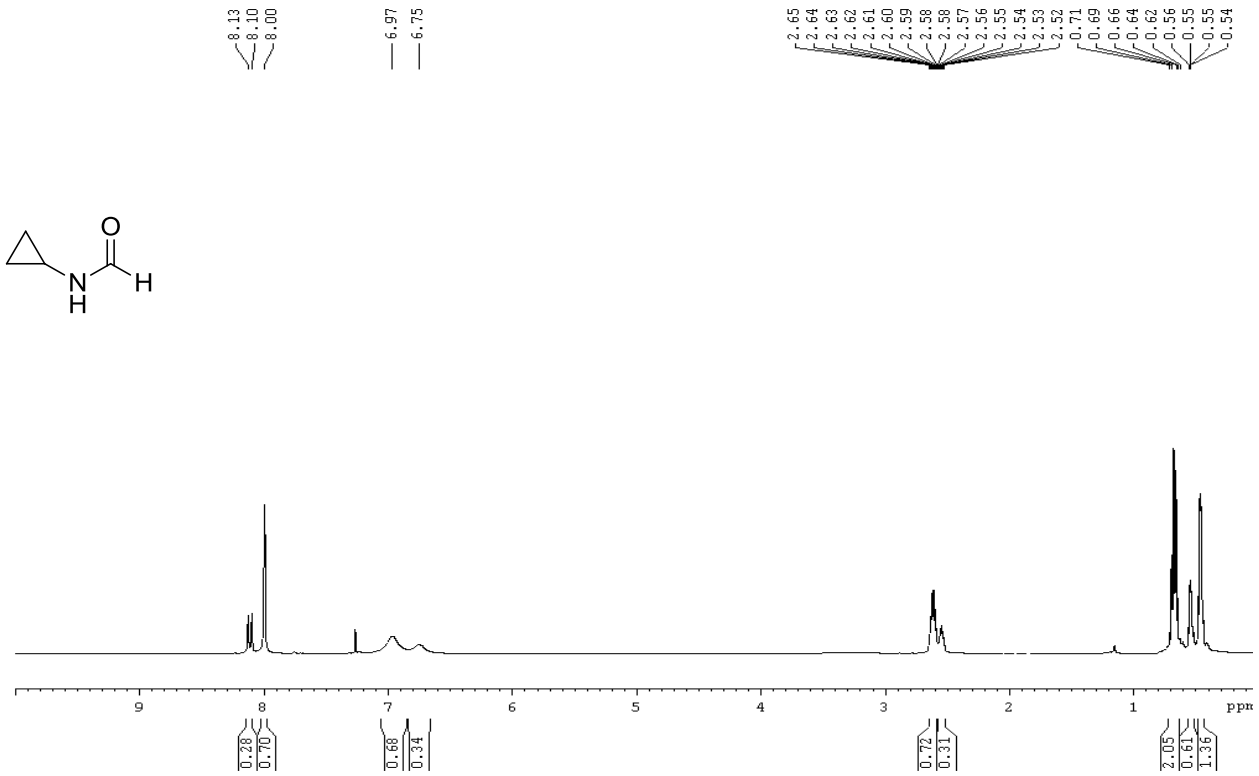
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3f**.



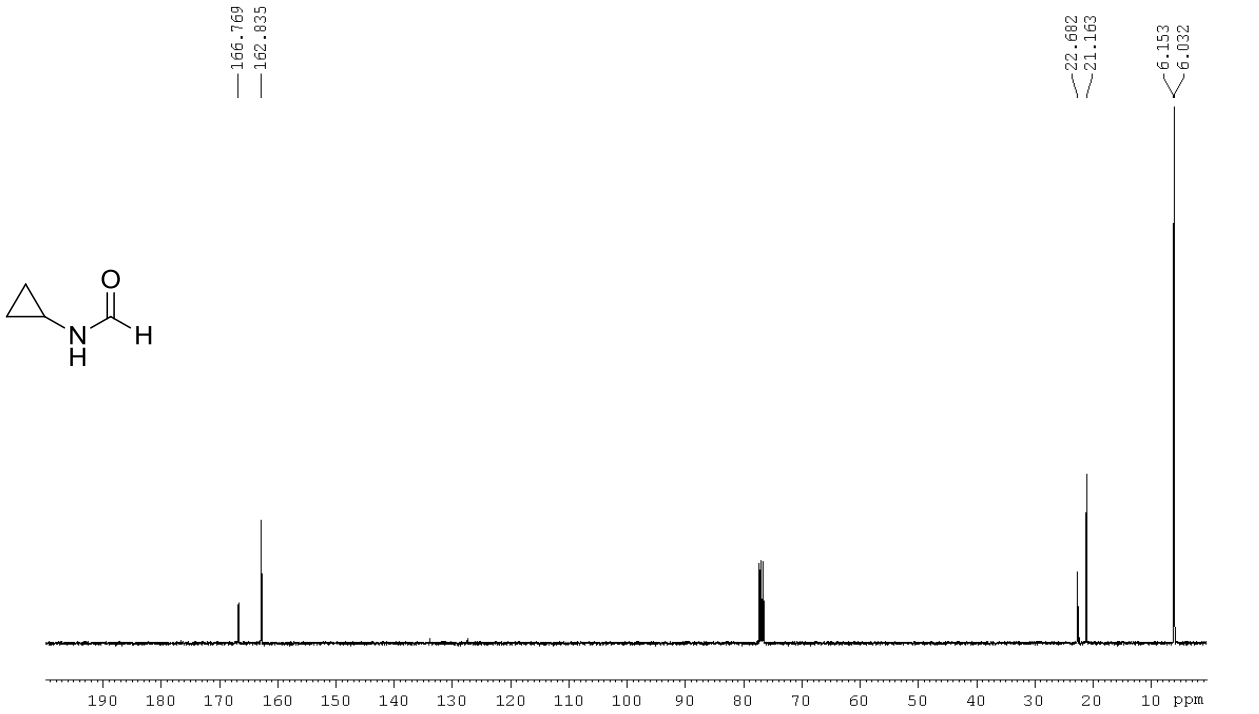

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3f**.



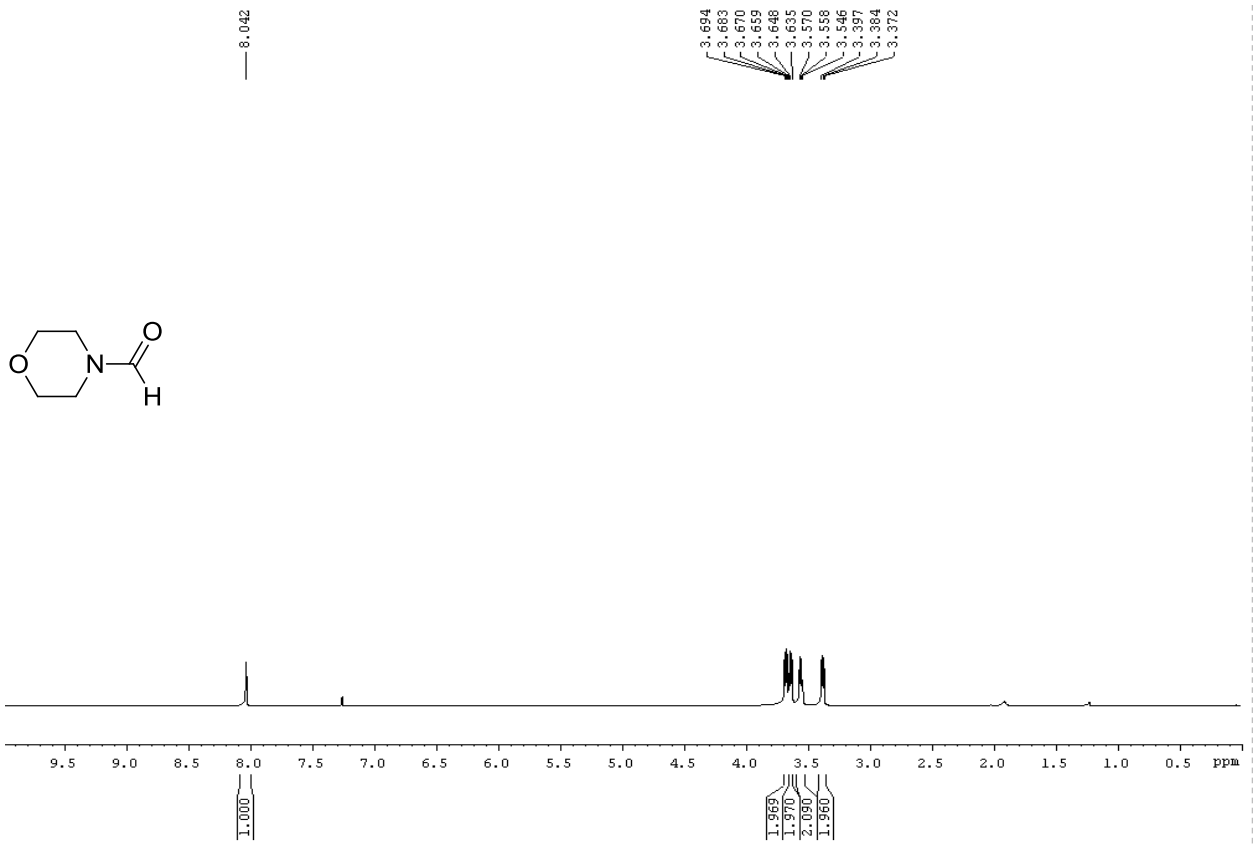
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3g**.



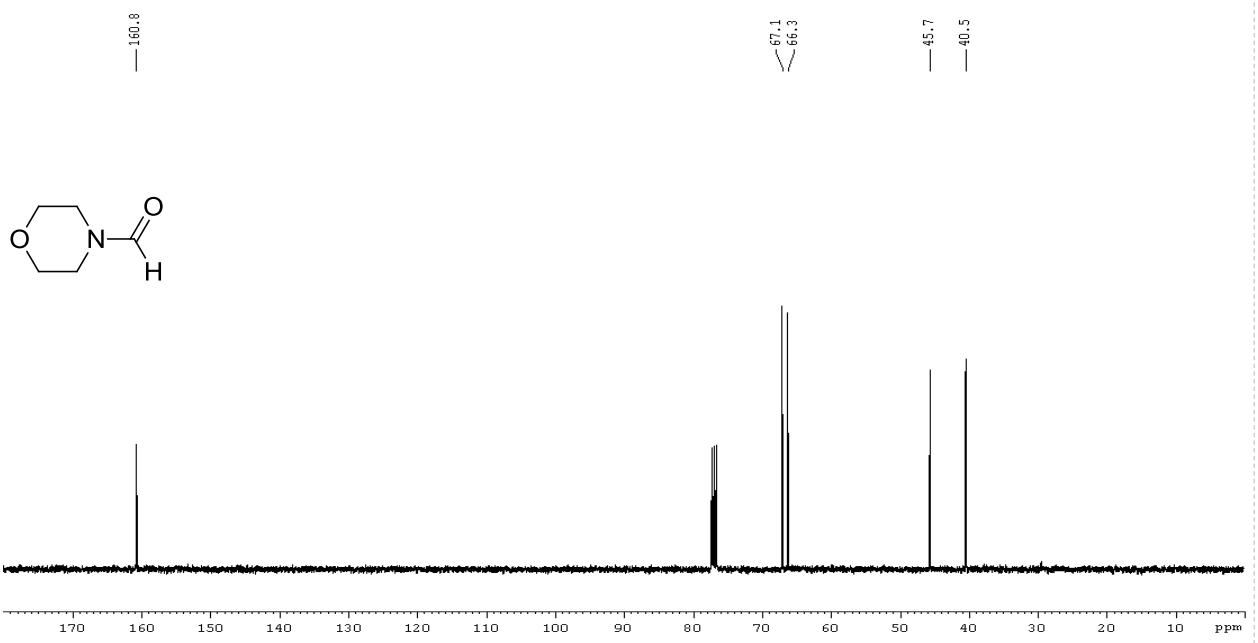

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3g**.



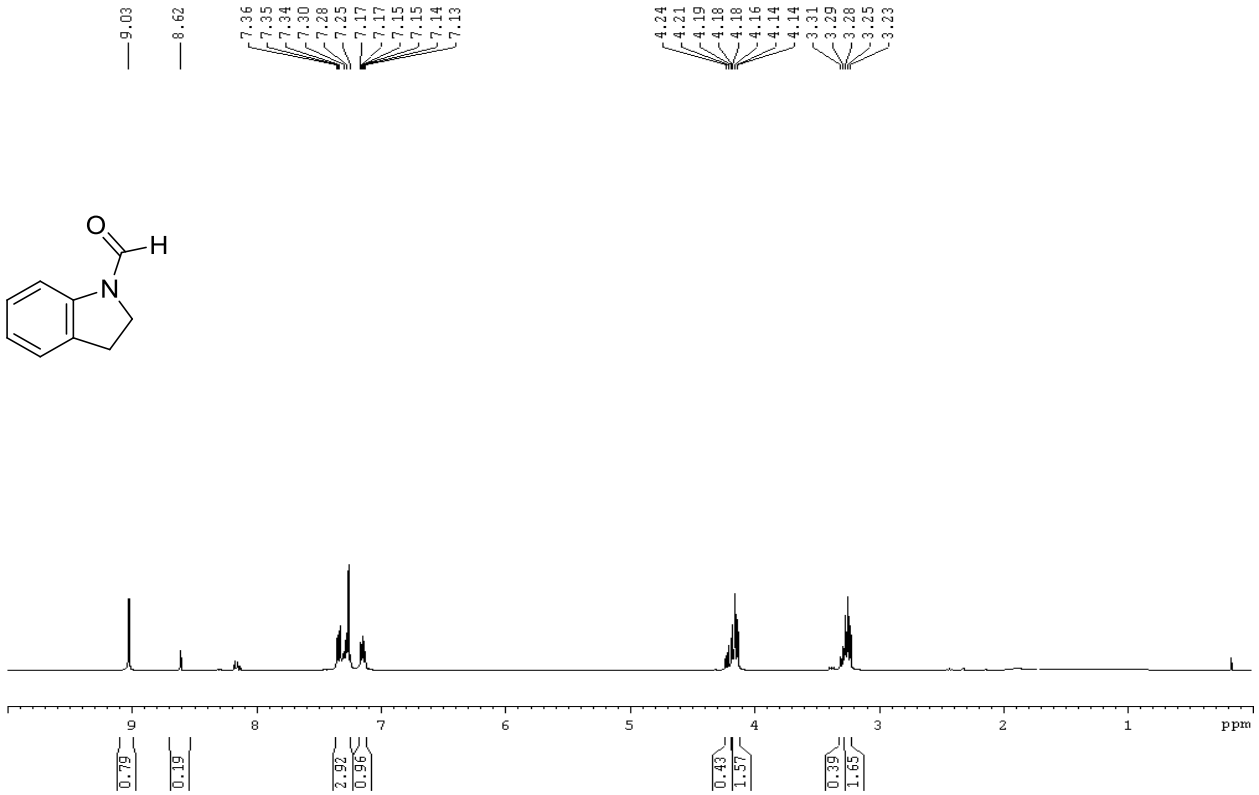
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3h**.



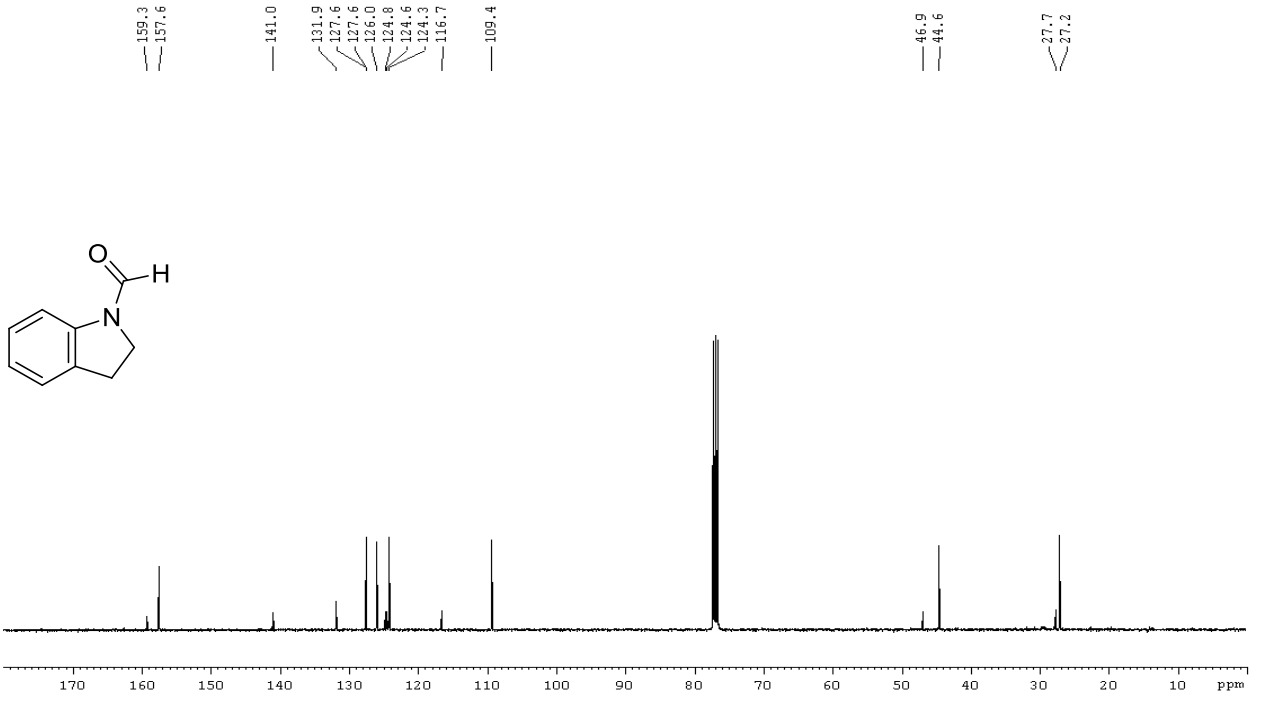

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3h**.



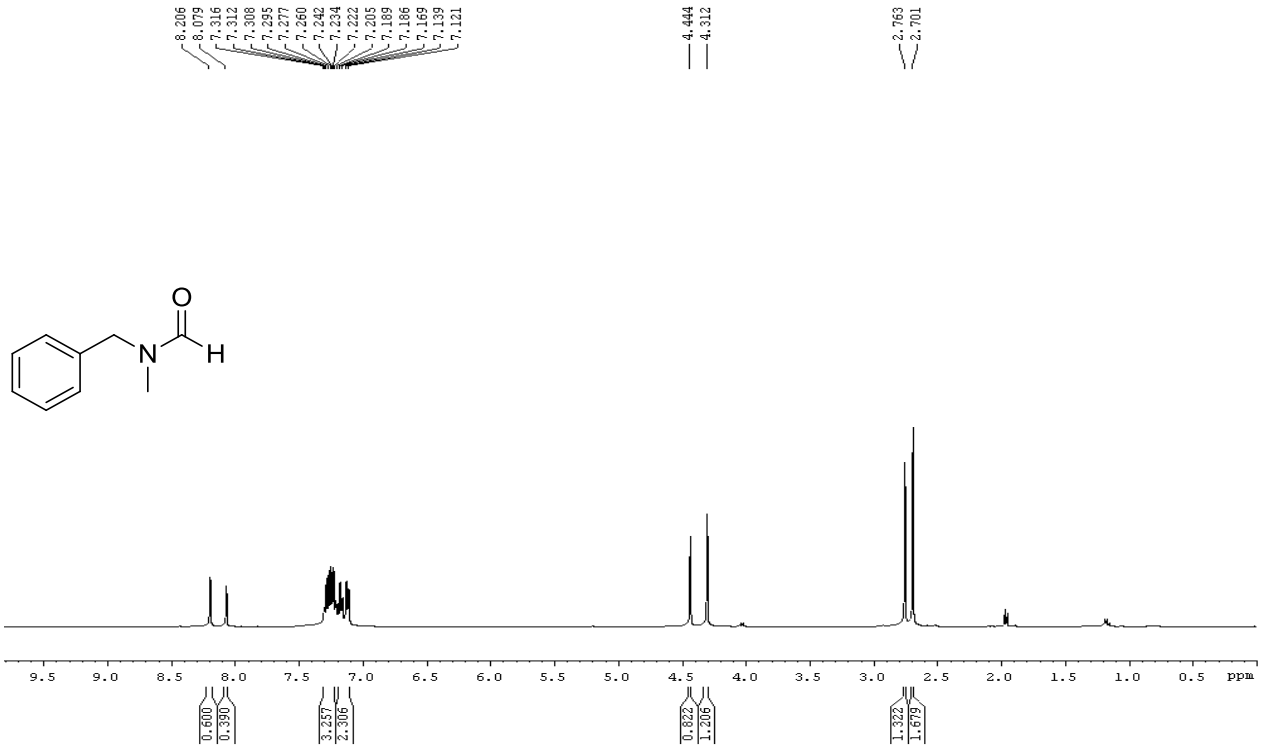
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3i**.



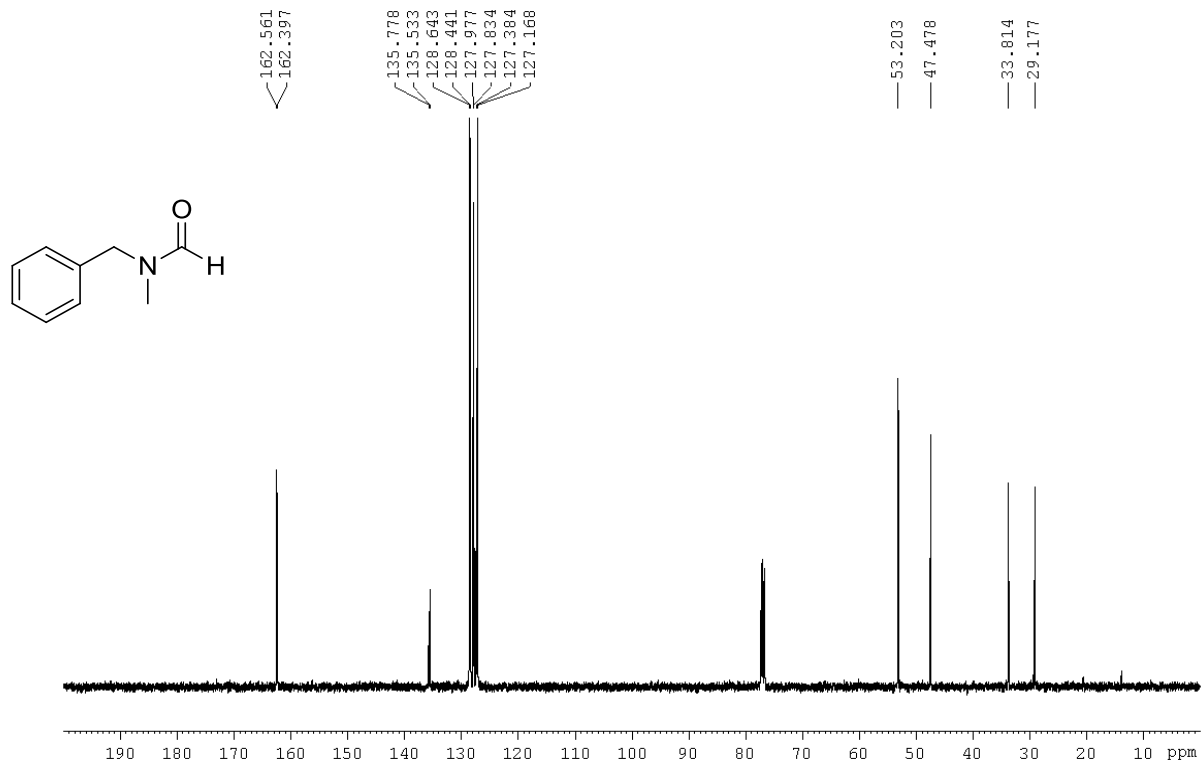

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3i**.



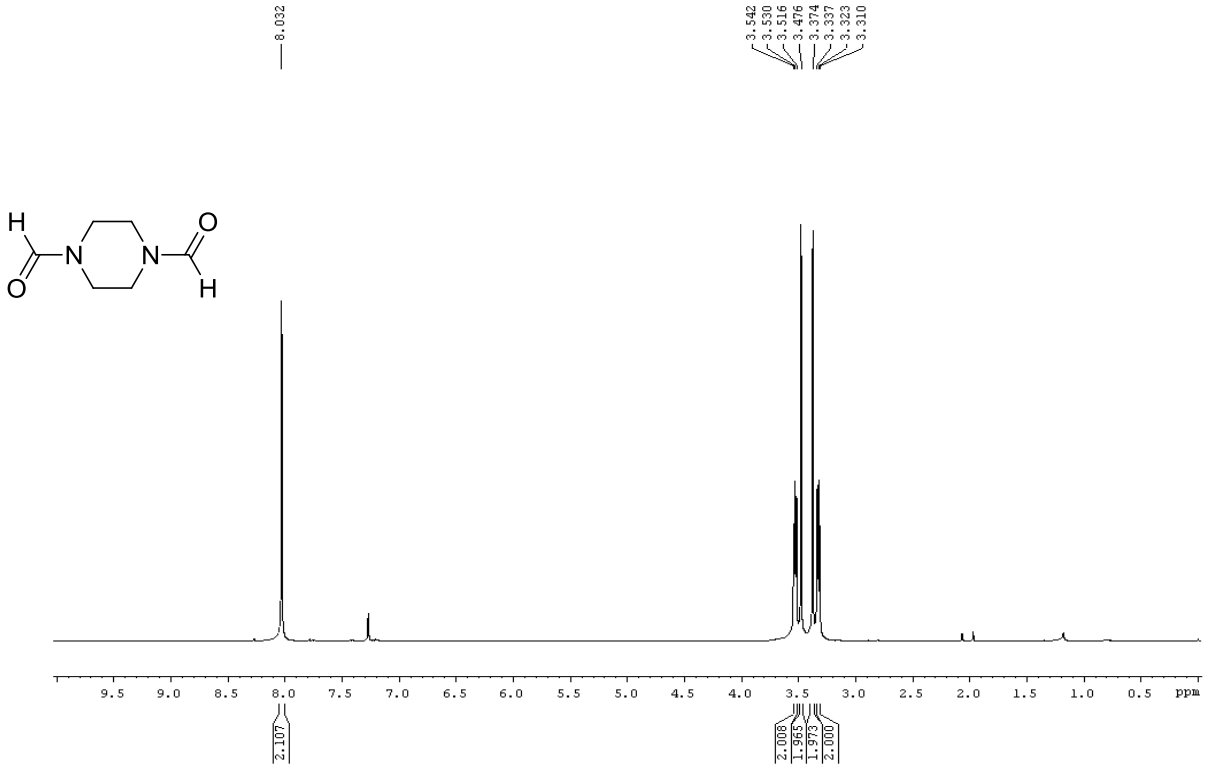
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3j**.



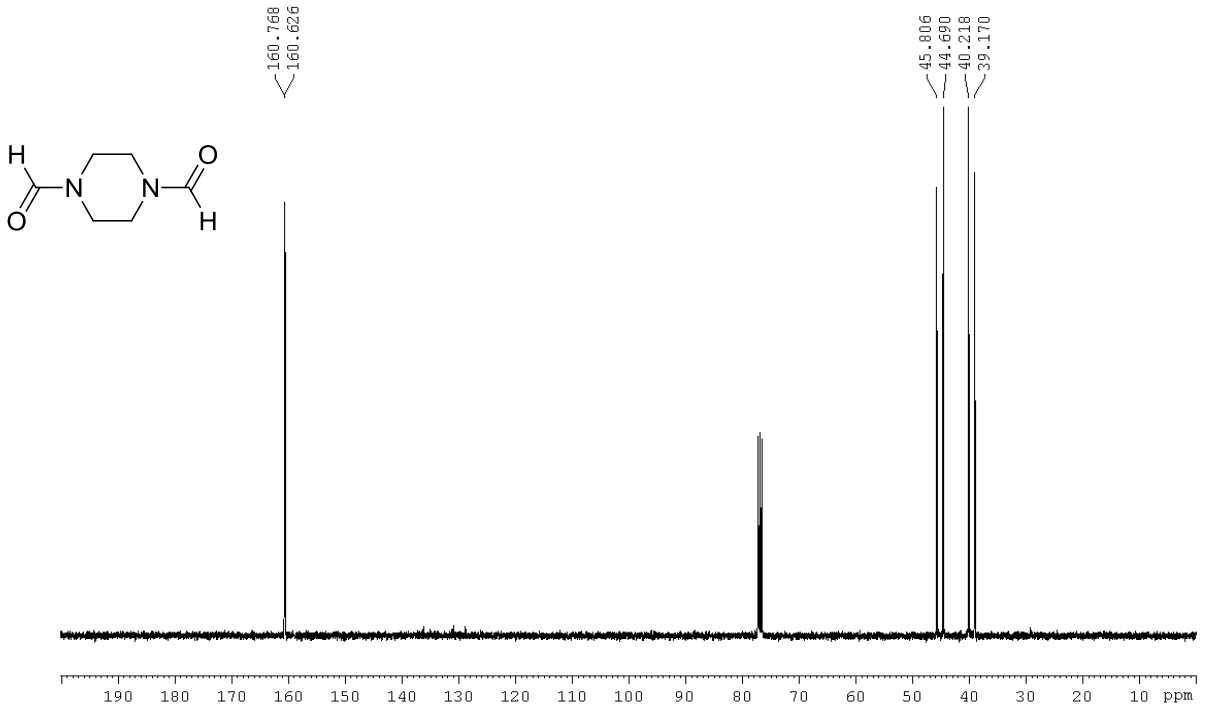

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3j**.



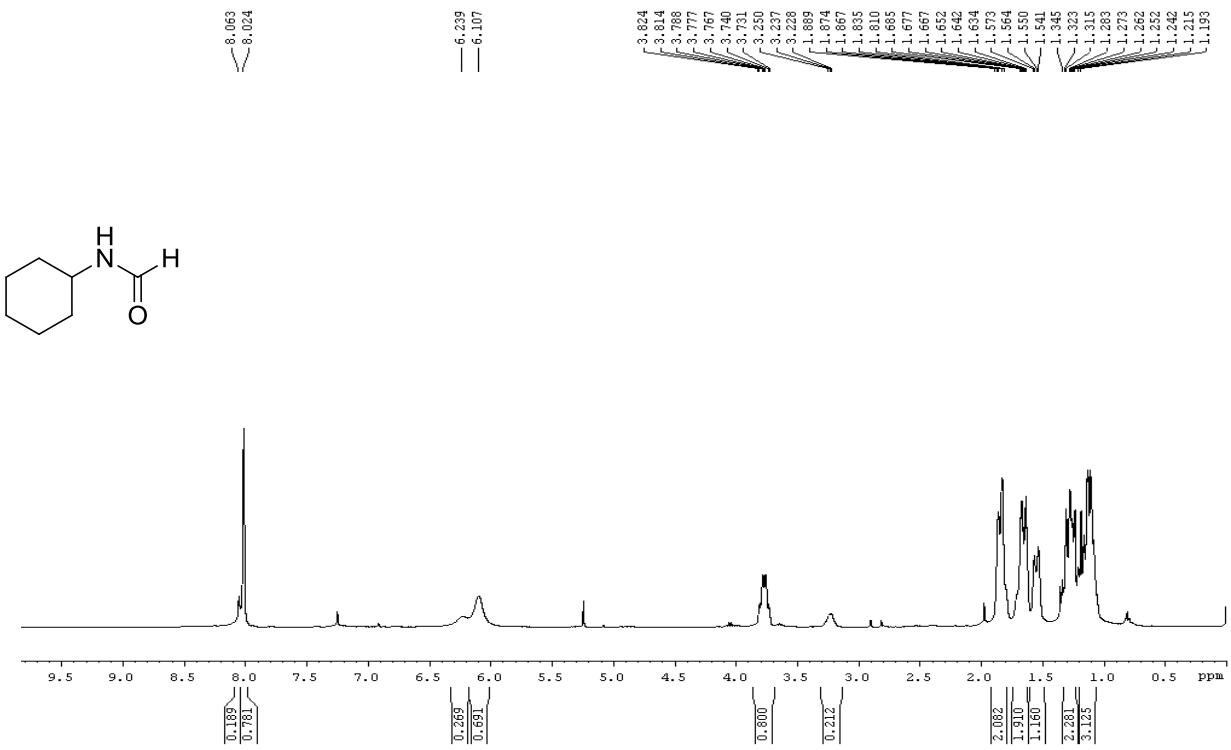
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3k**.



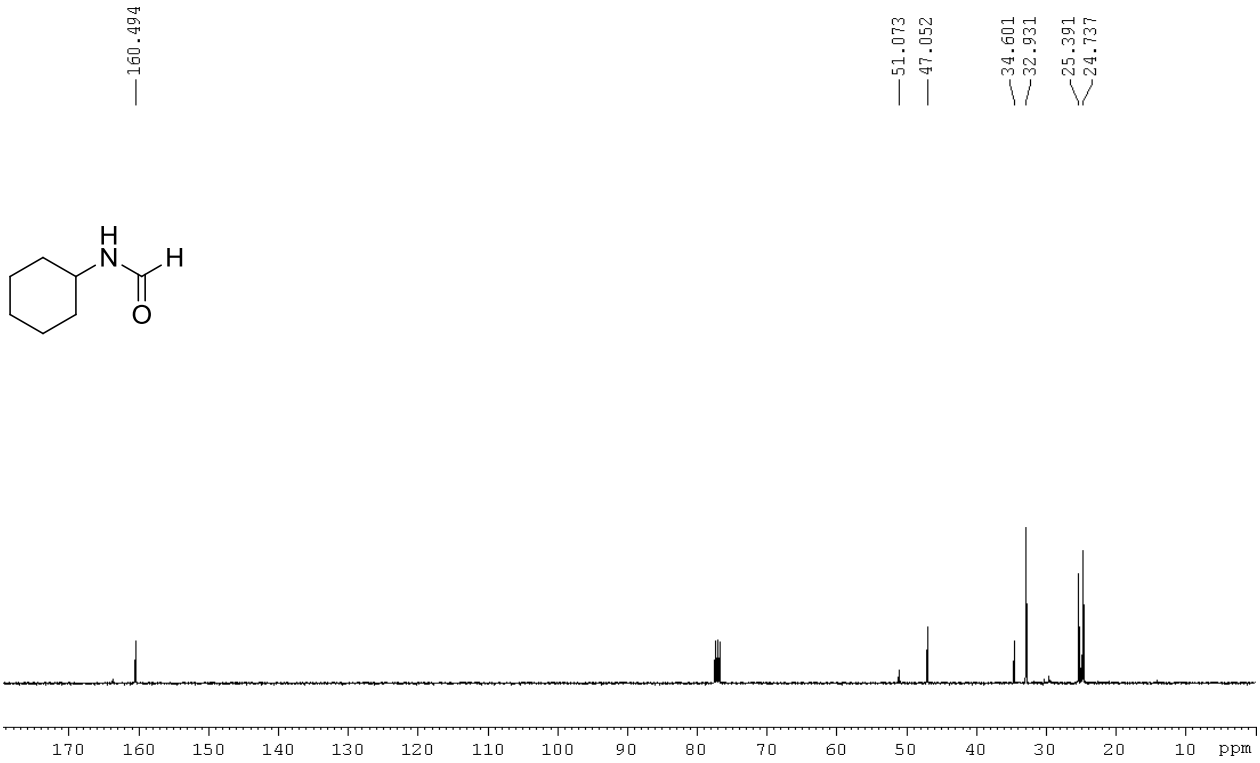

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3k**.



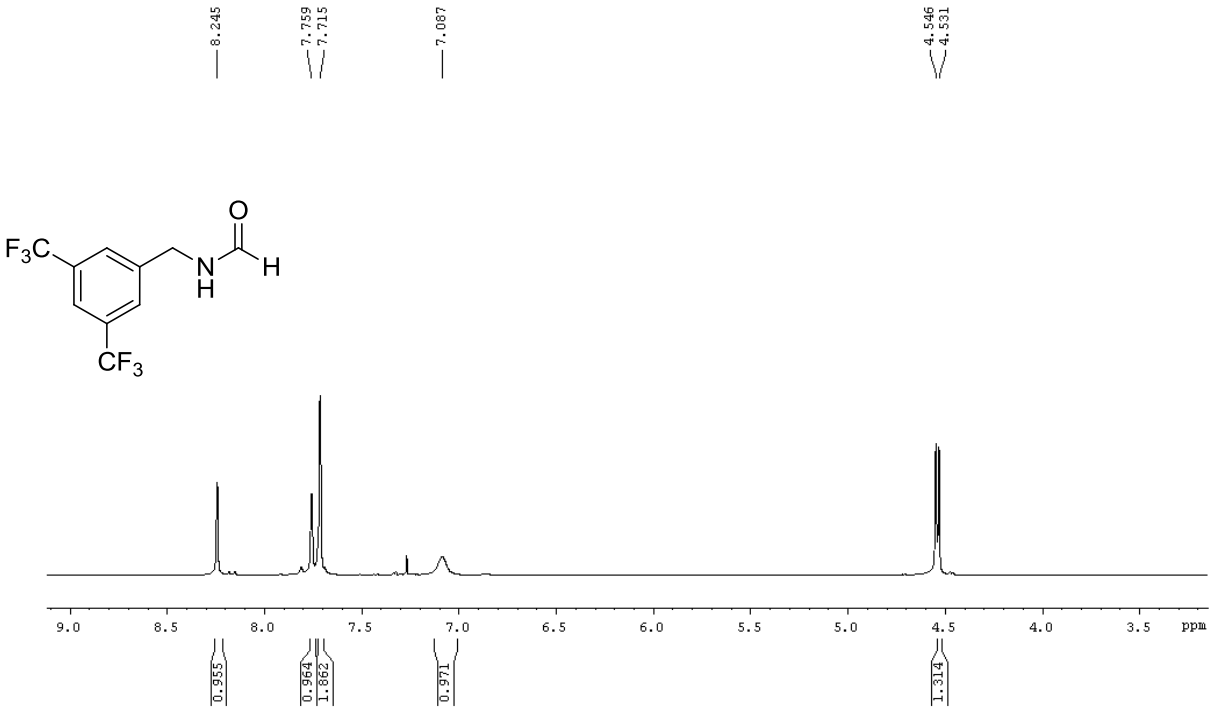
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3l**.



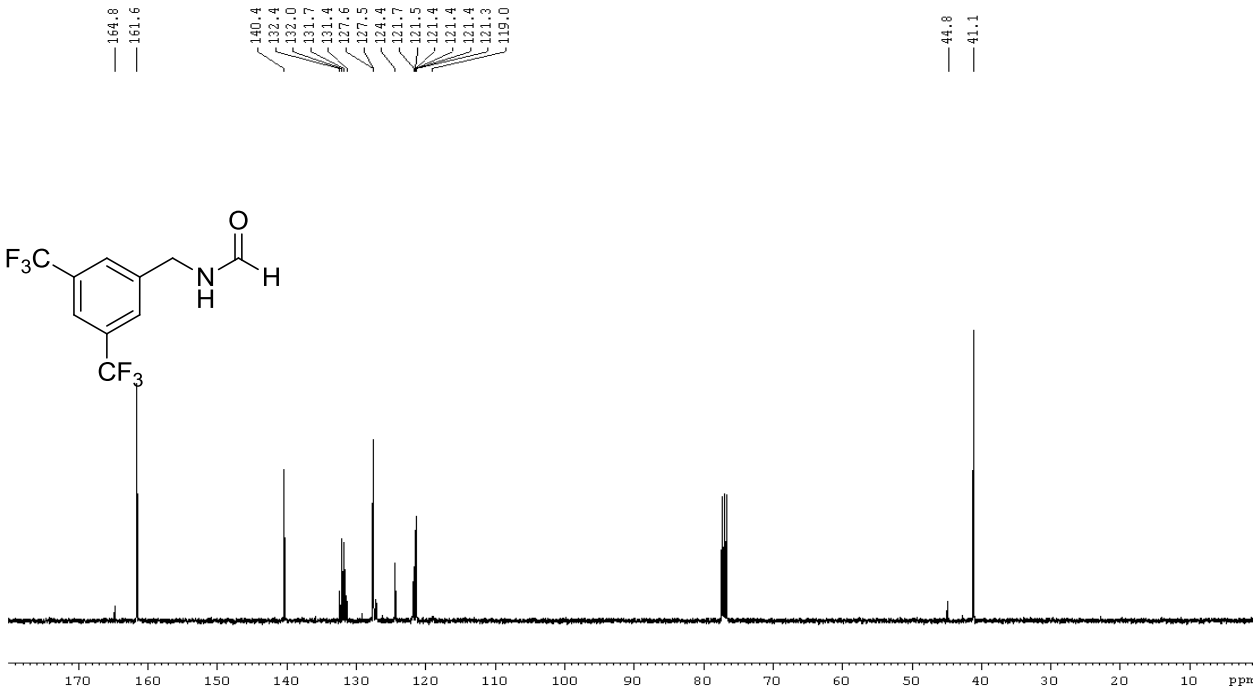

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3l**.



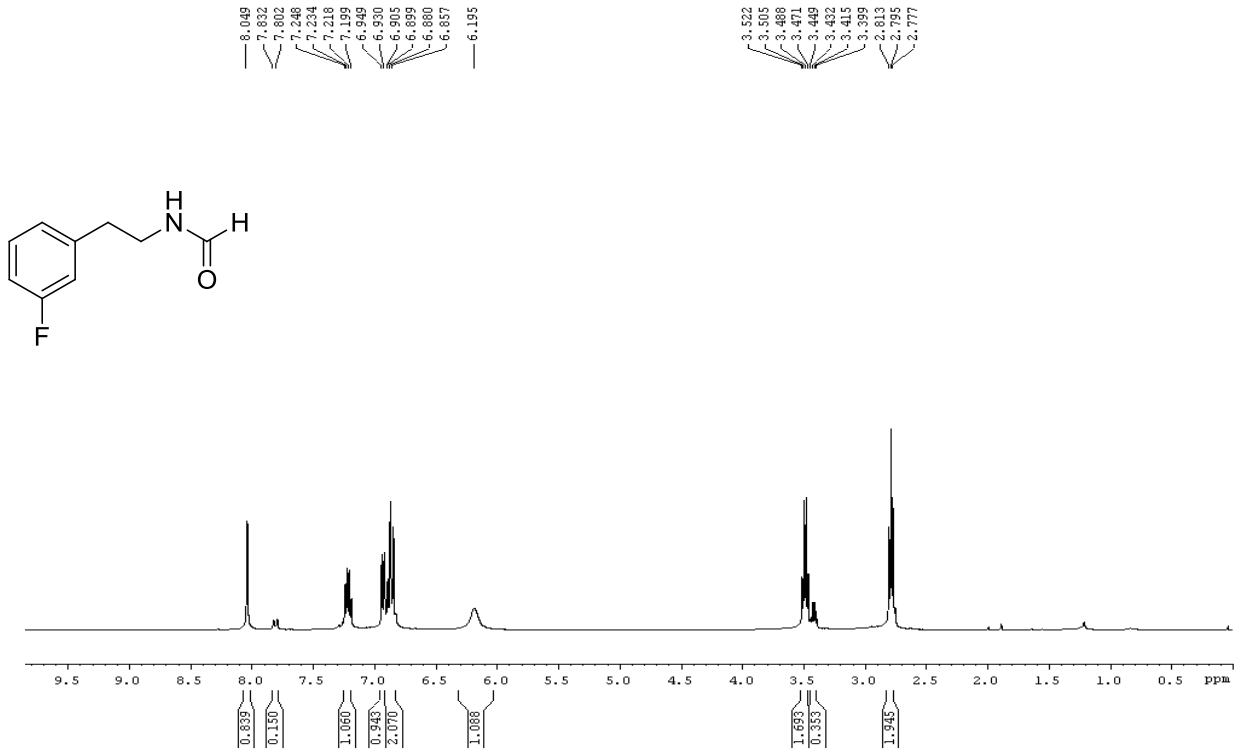
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3m**.



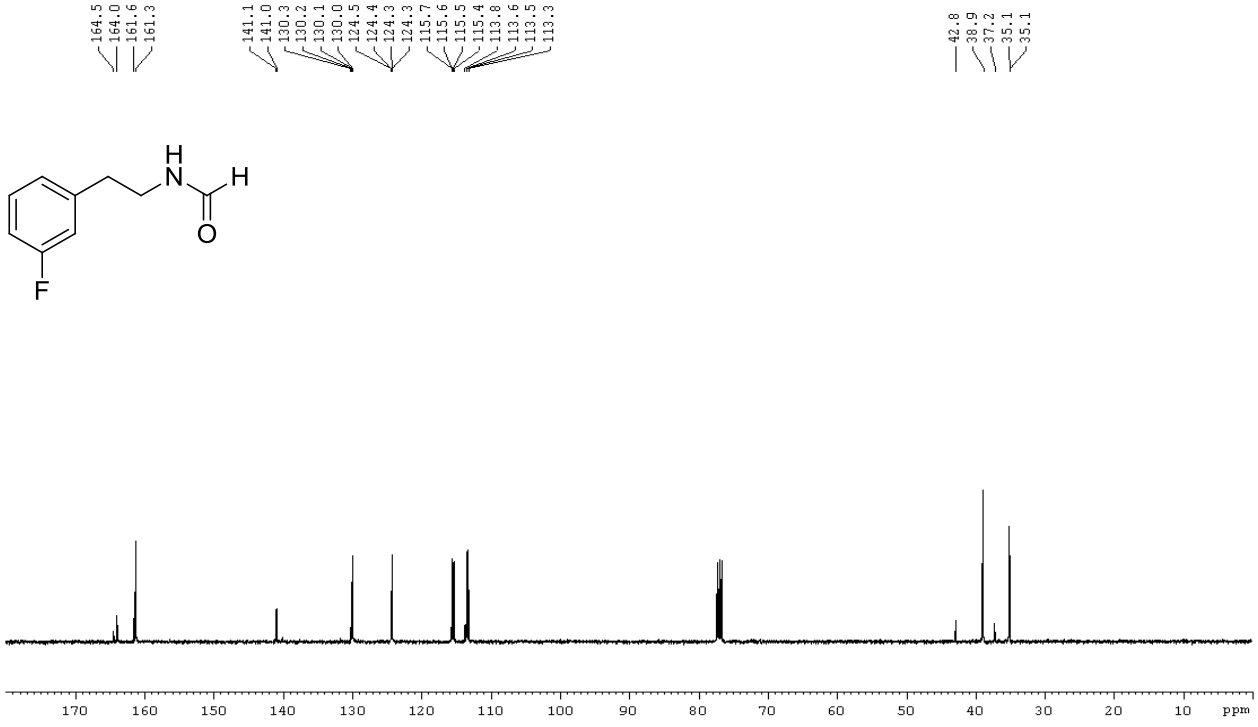

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3m**.



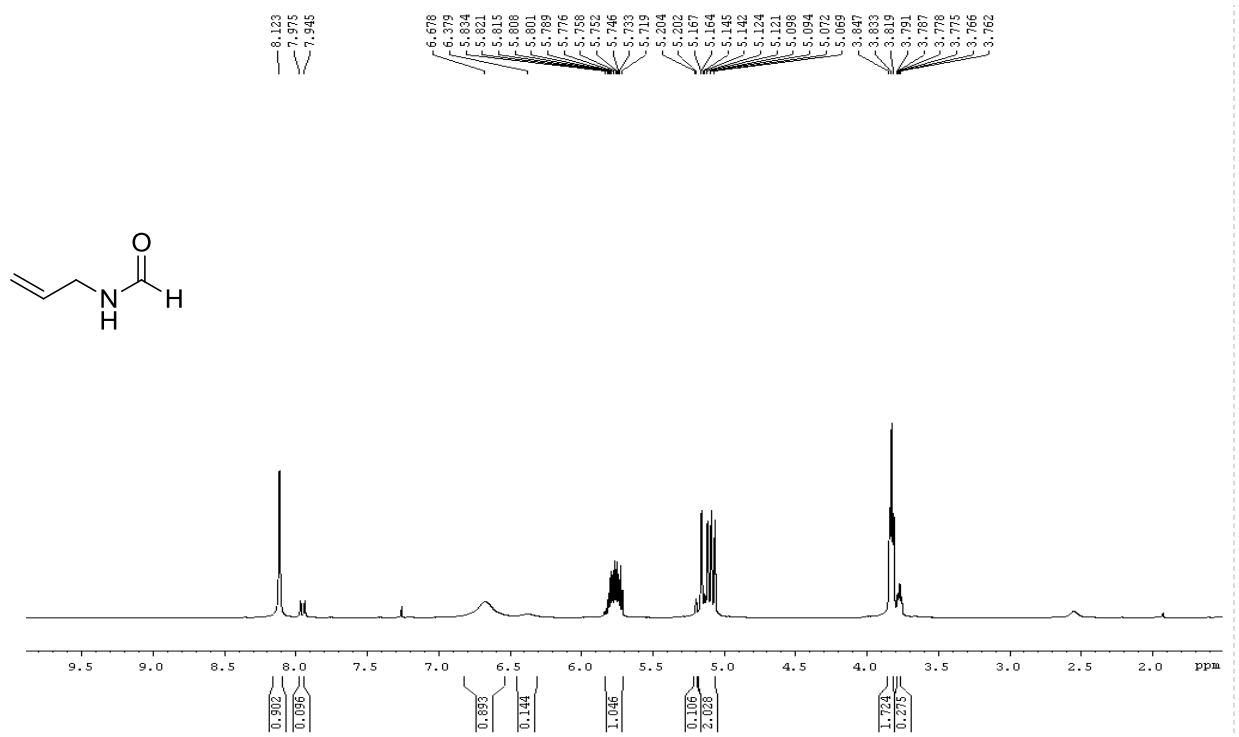
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3n**.



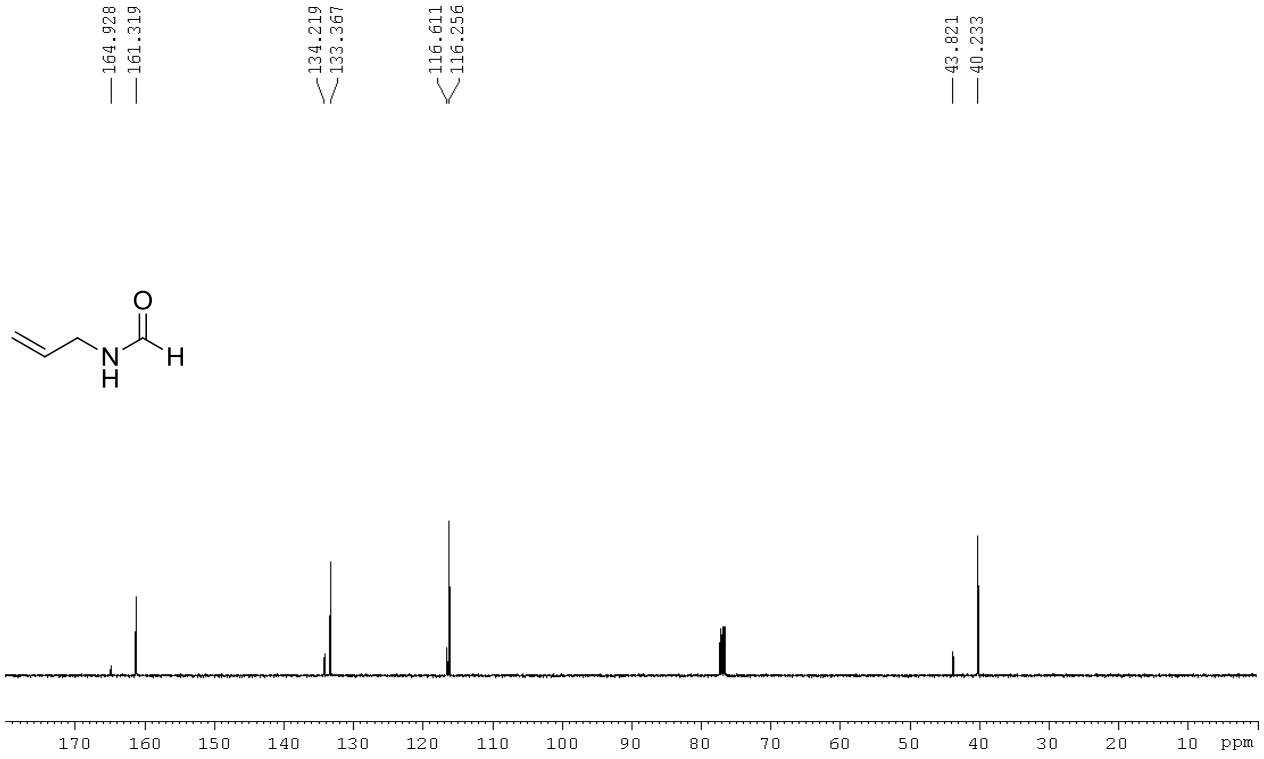

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3n**.



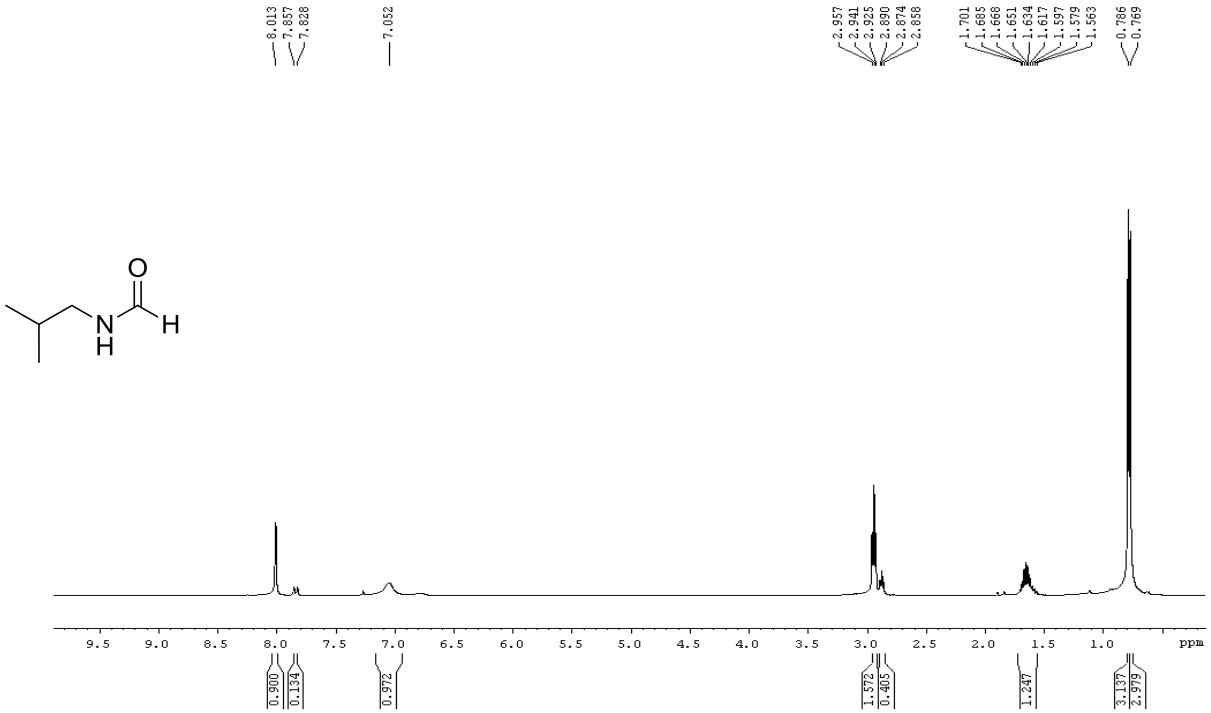
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3o**.



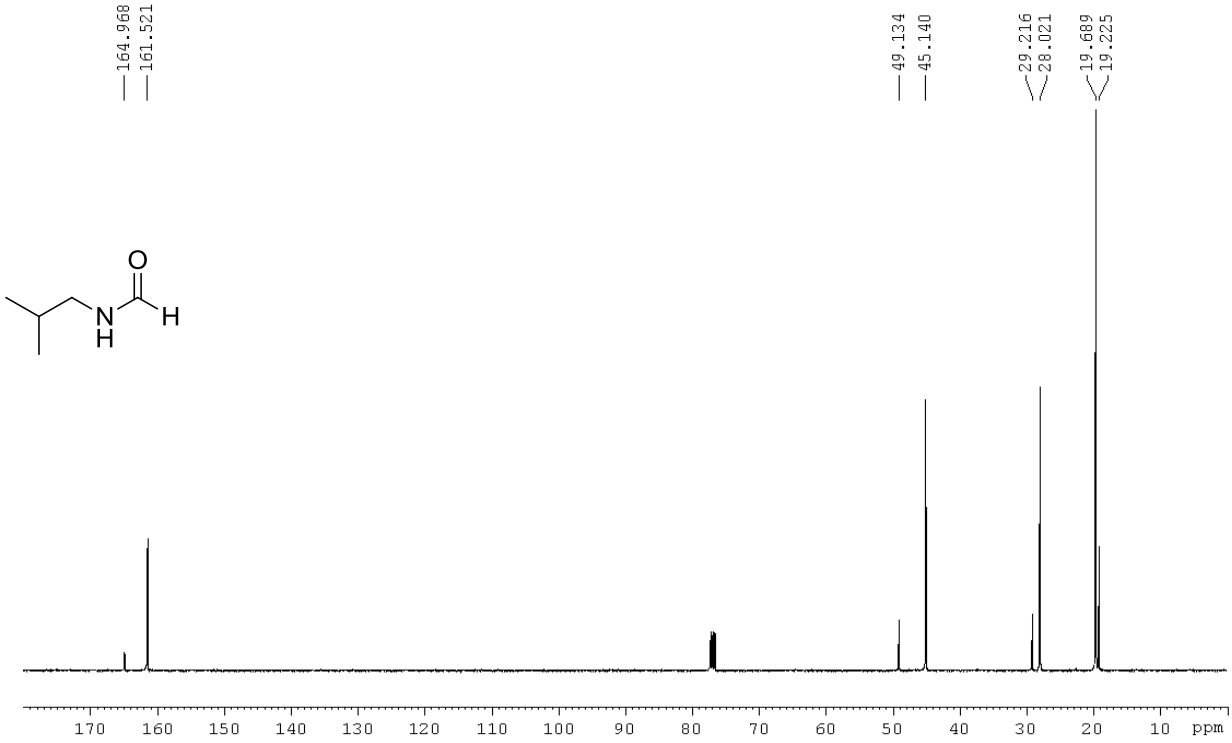

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3o**.



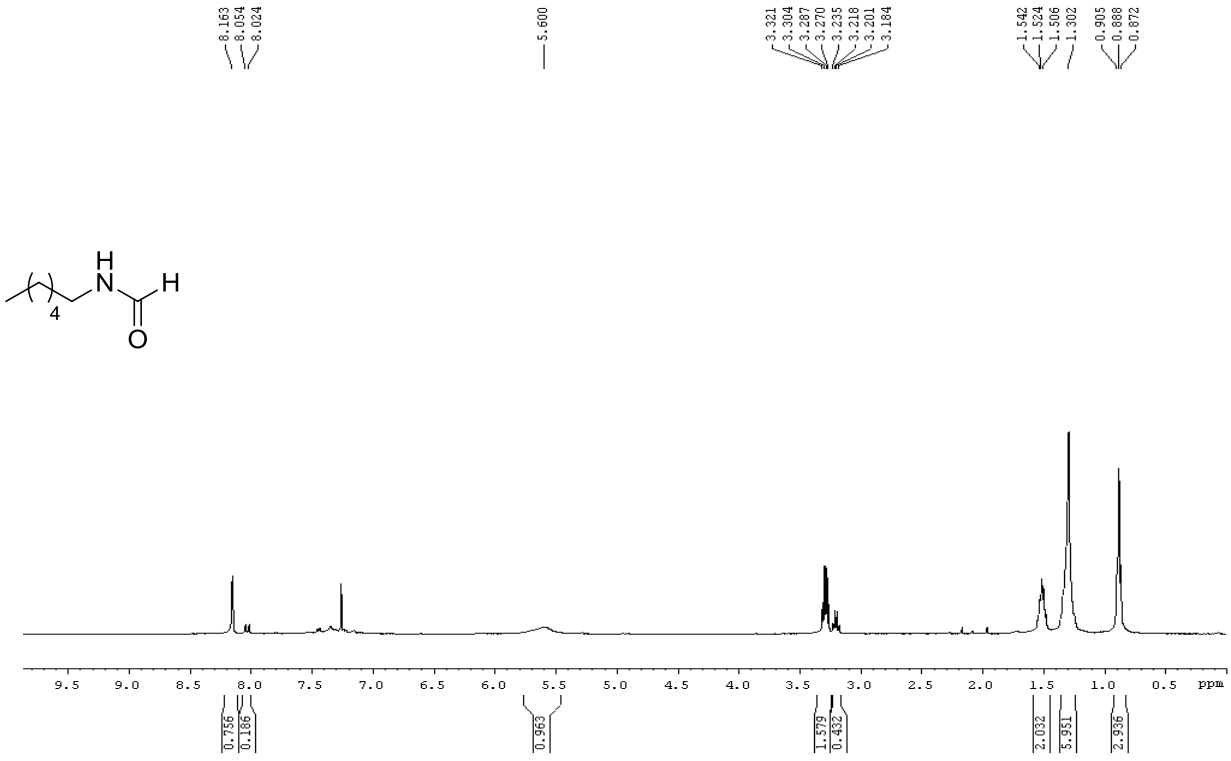
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3p**.



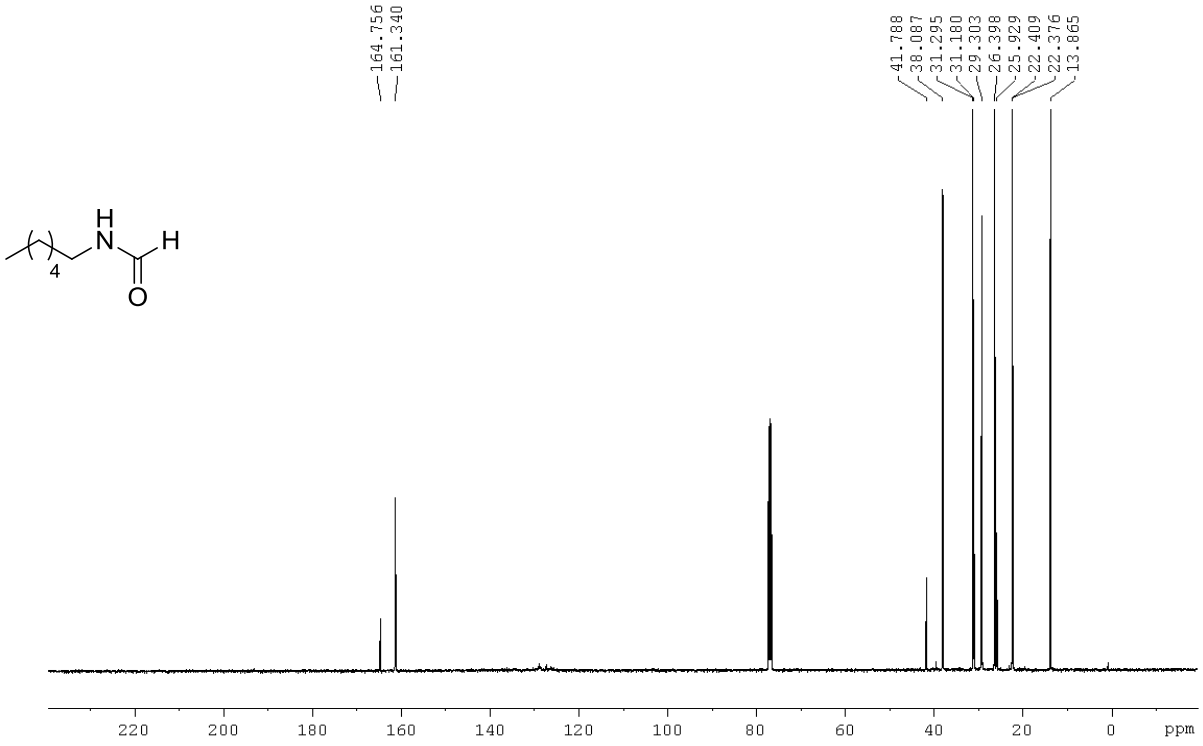

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3p**.



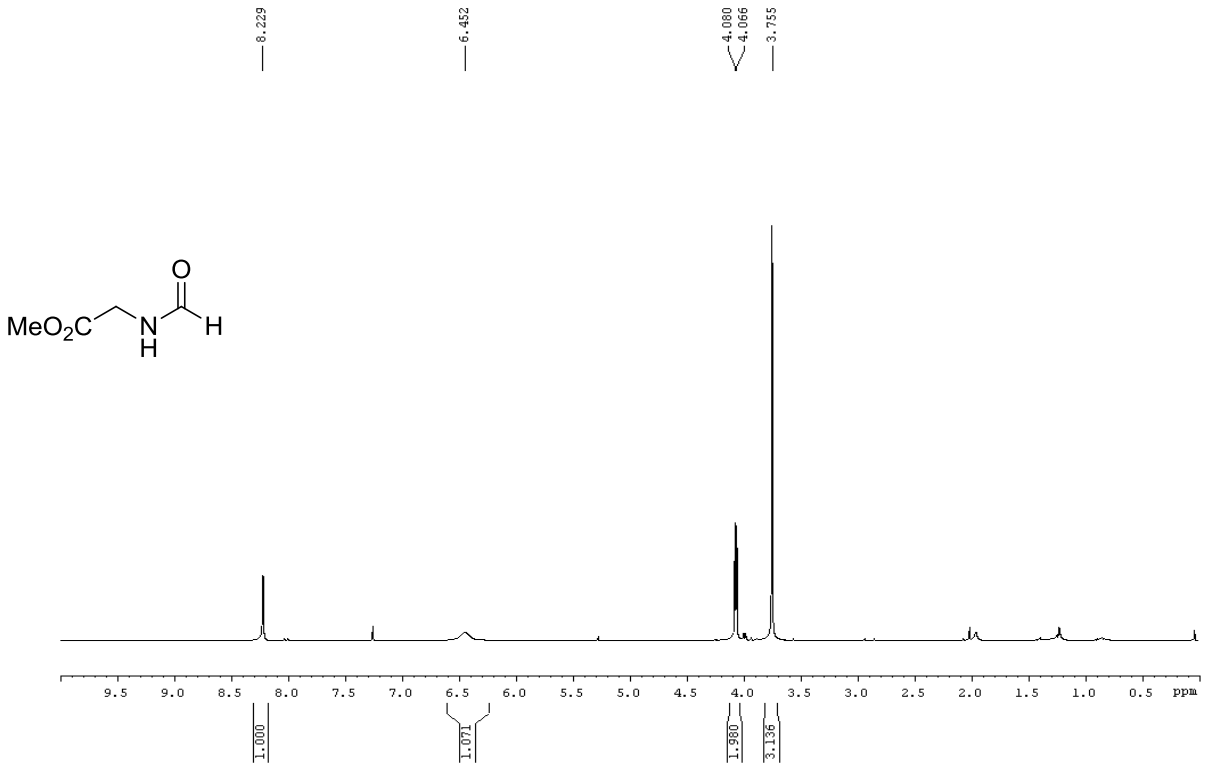
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **3q**.



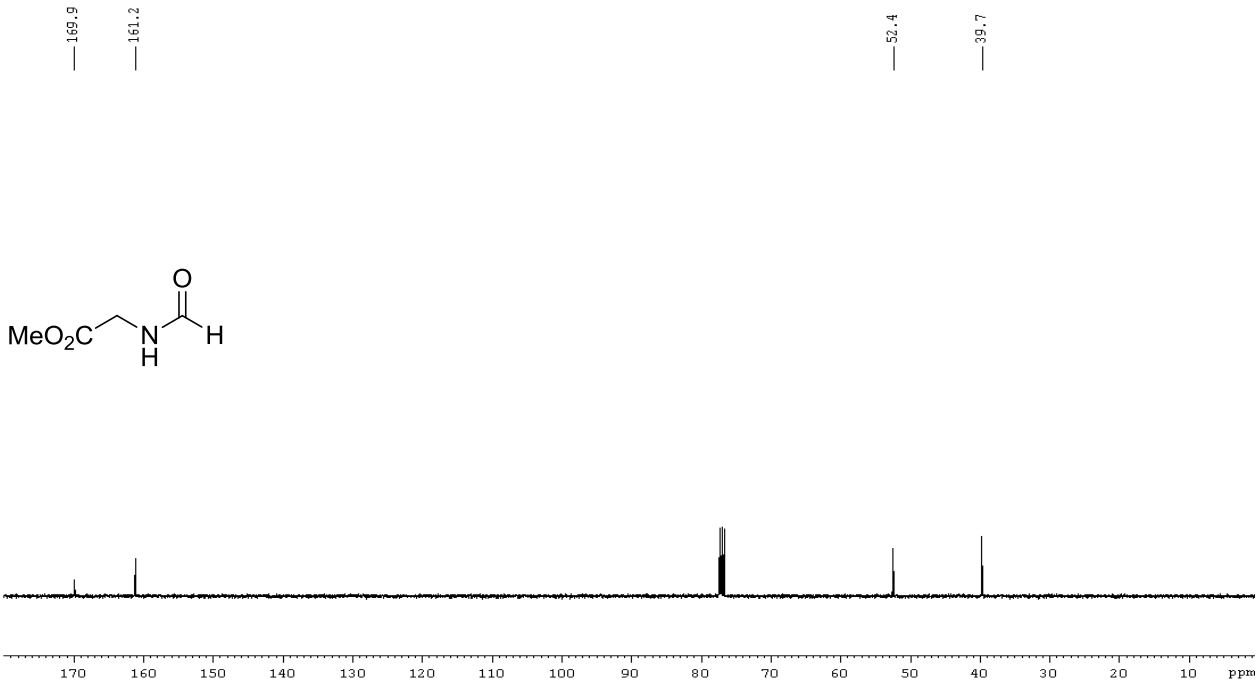

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **3q**.



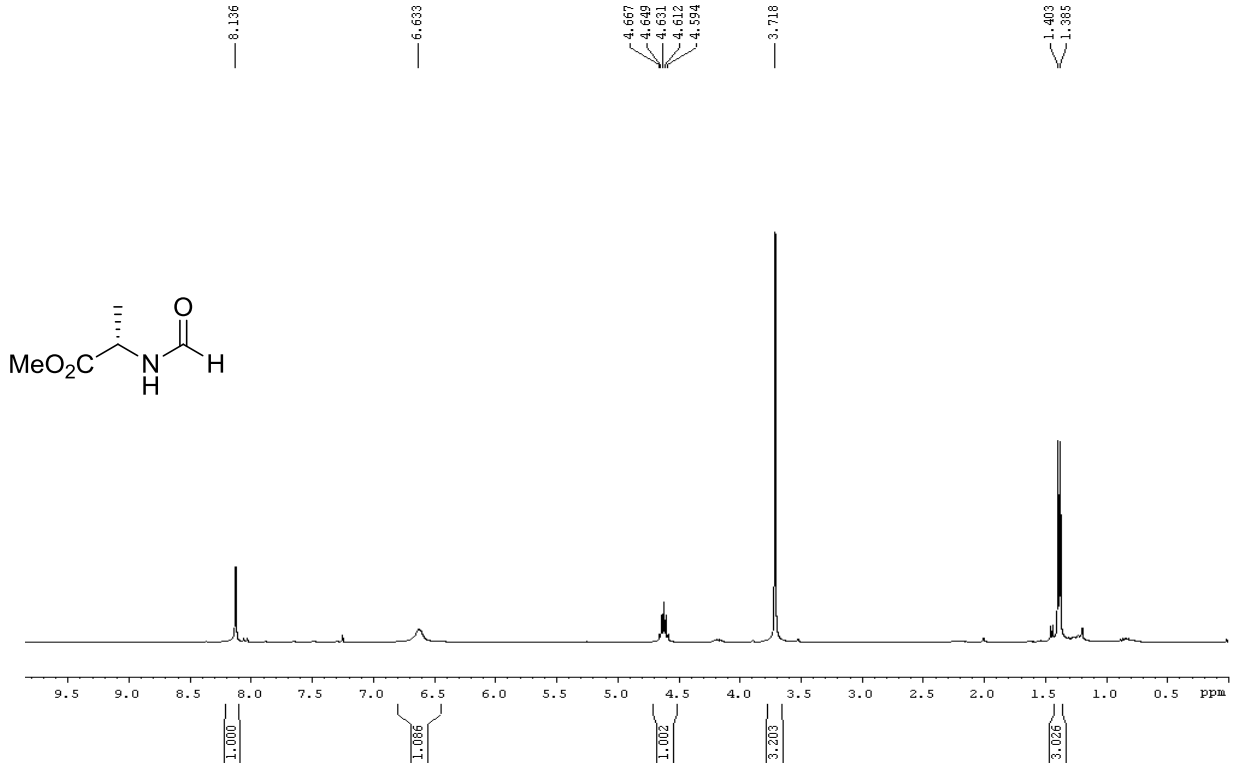
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8a**.



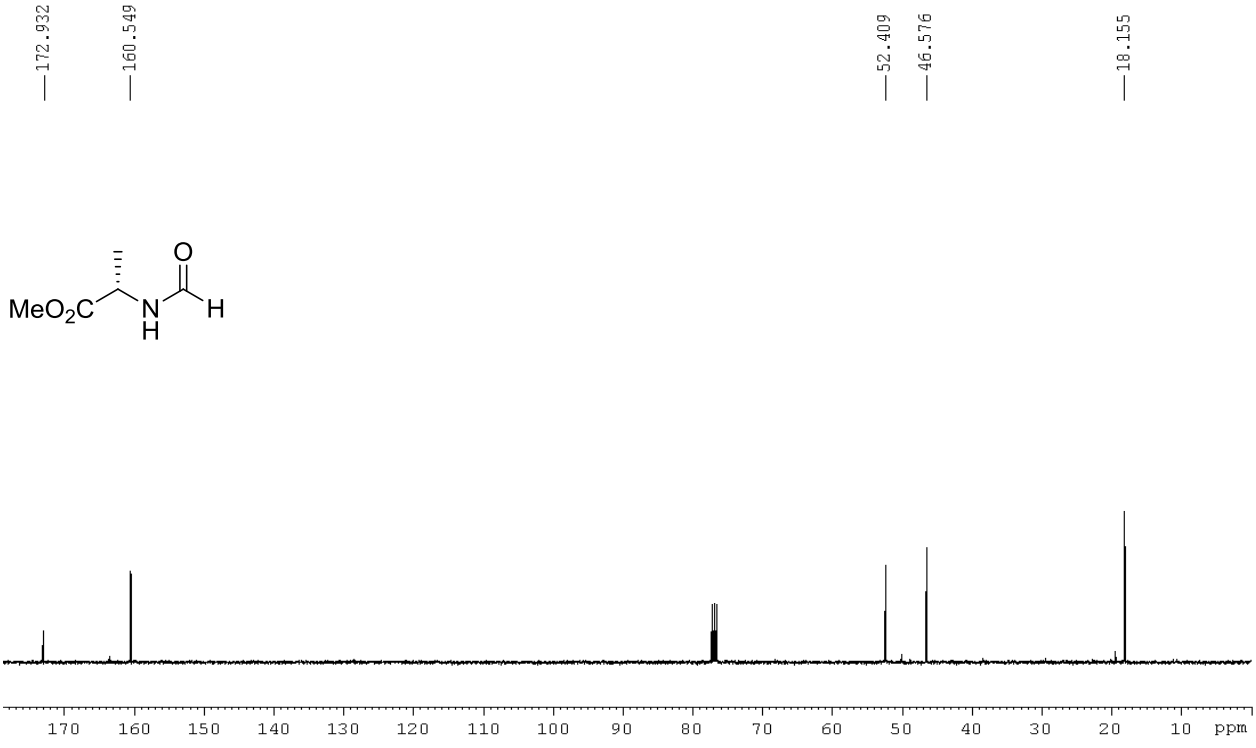

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8a**.



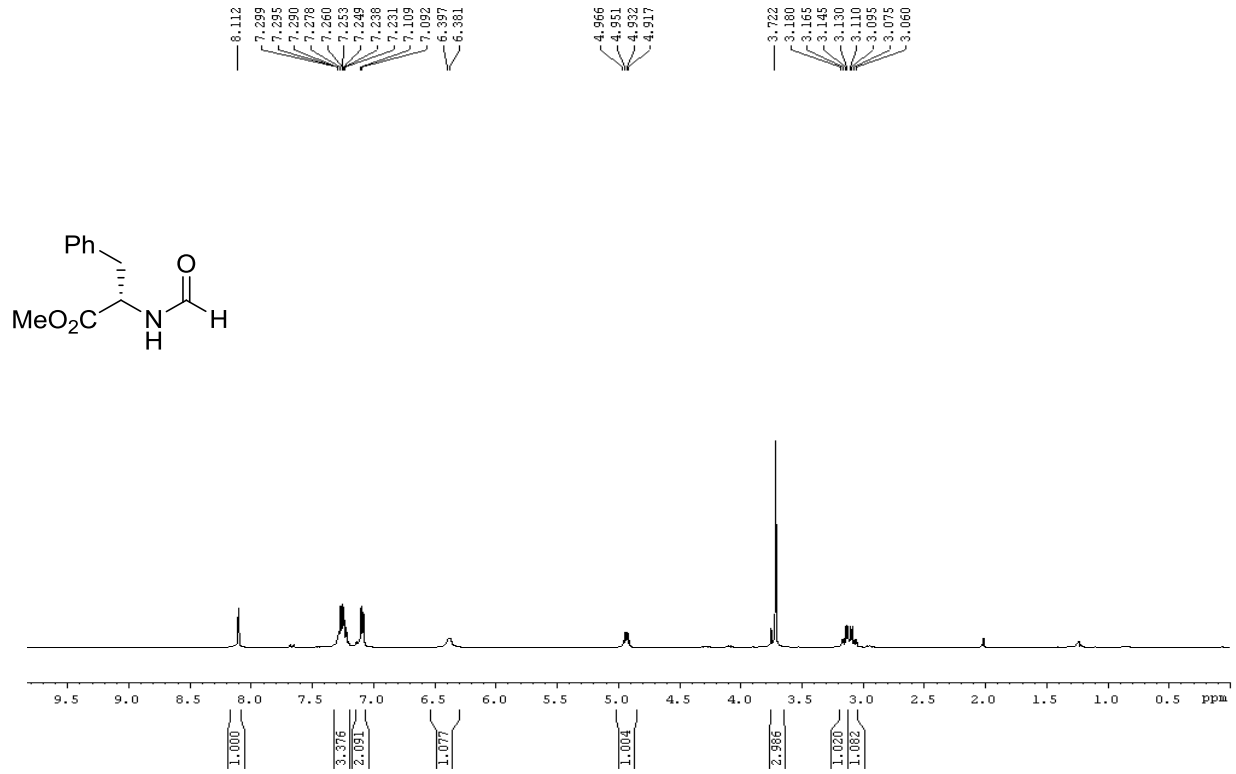
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8b**.



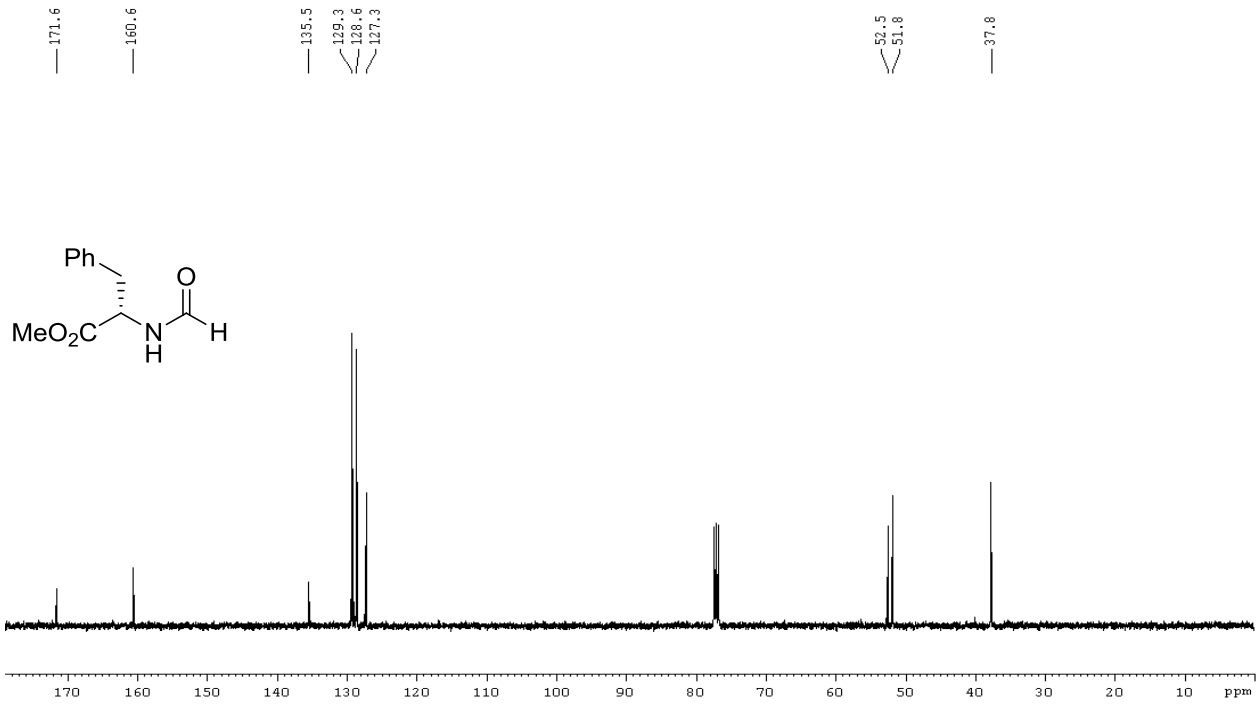

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8b**.



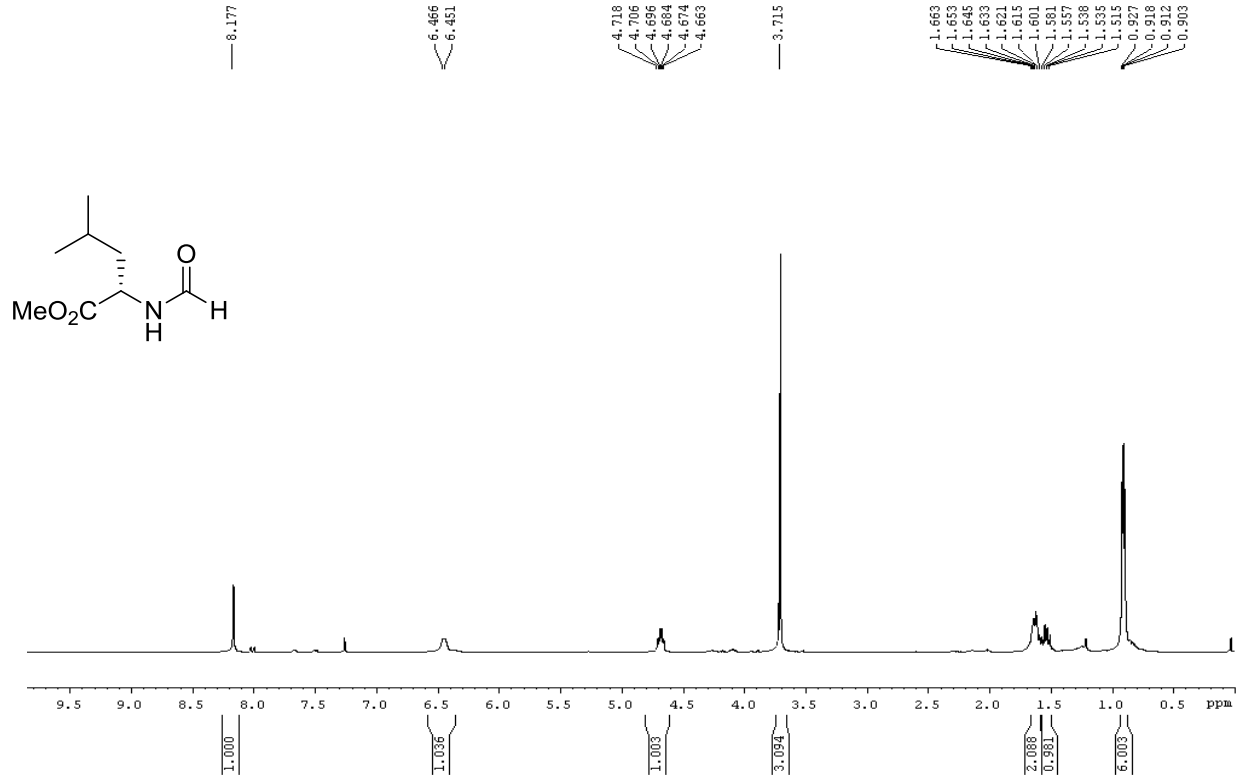
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8c**.



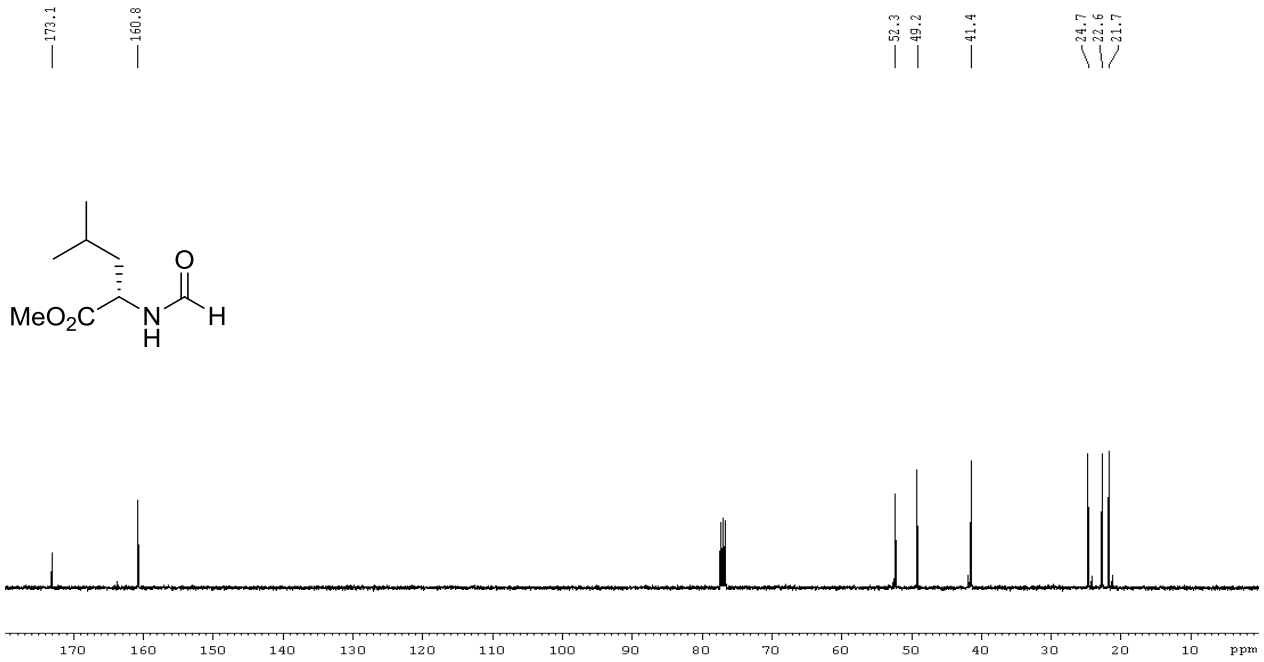

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8c**.



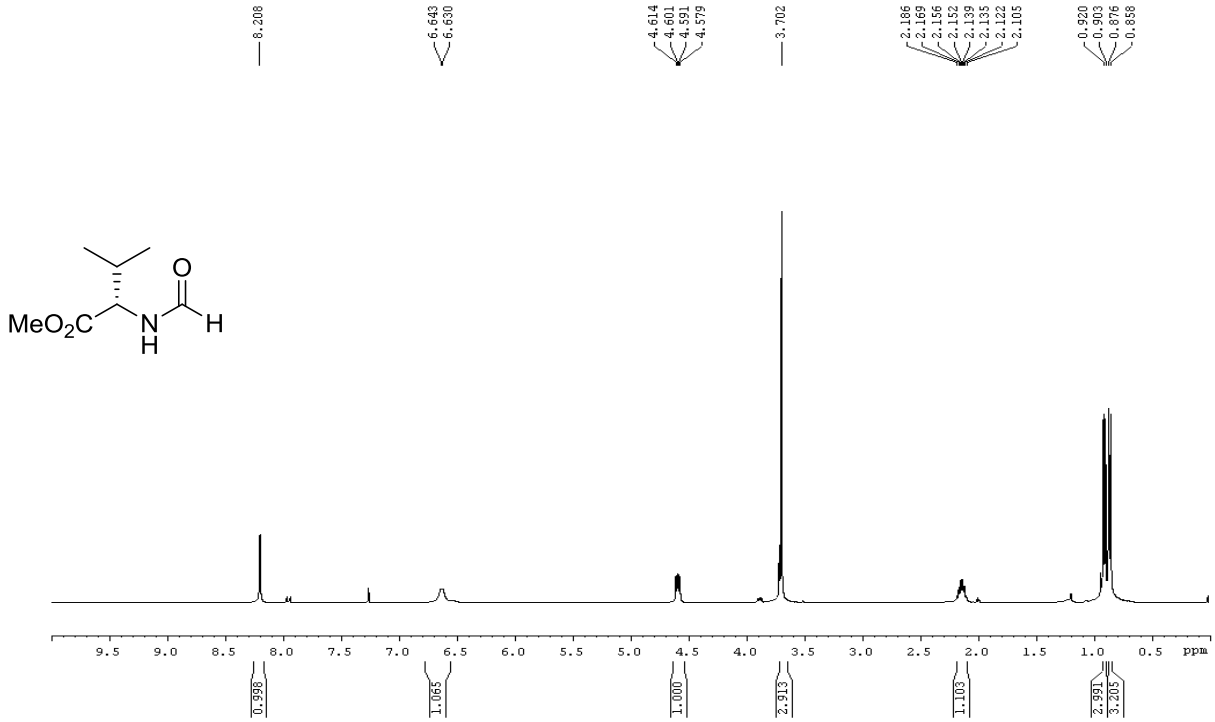
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8d**.



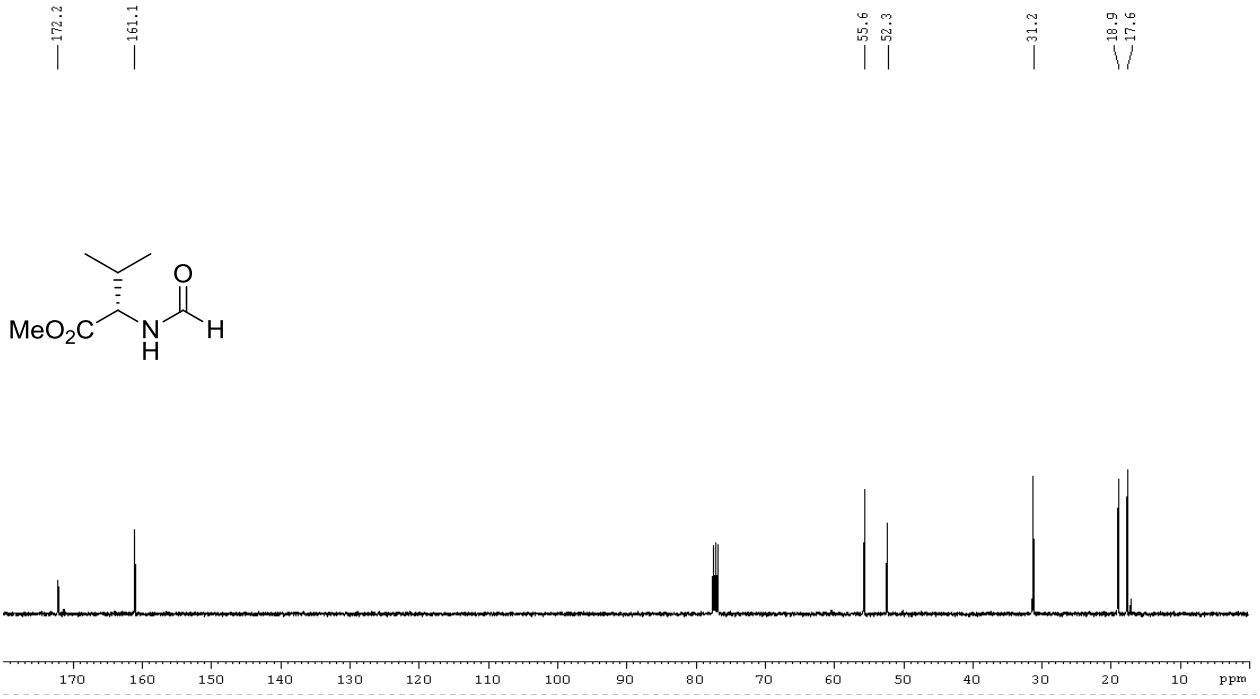

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8d**.



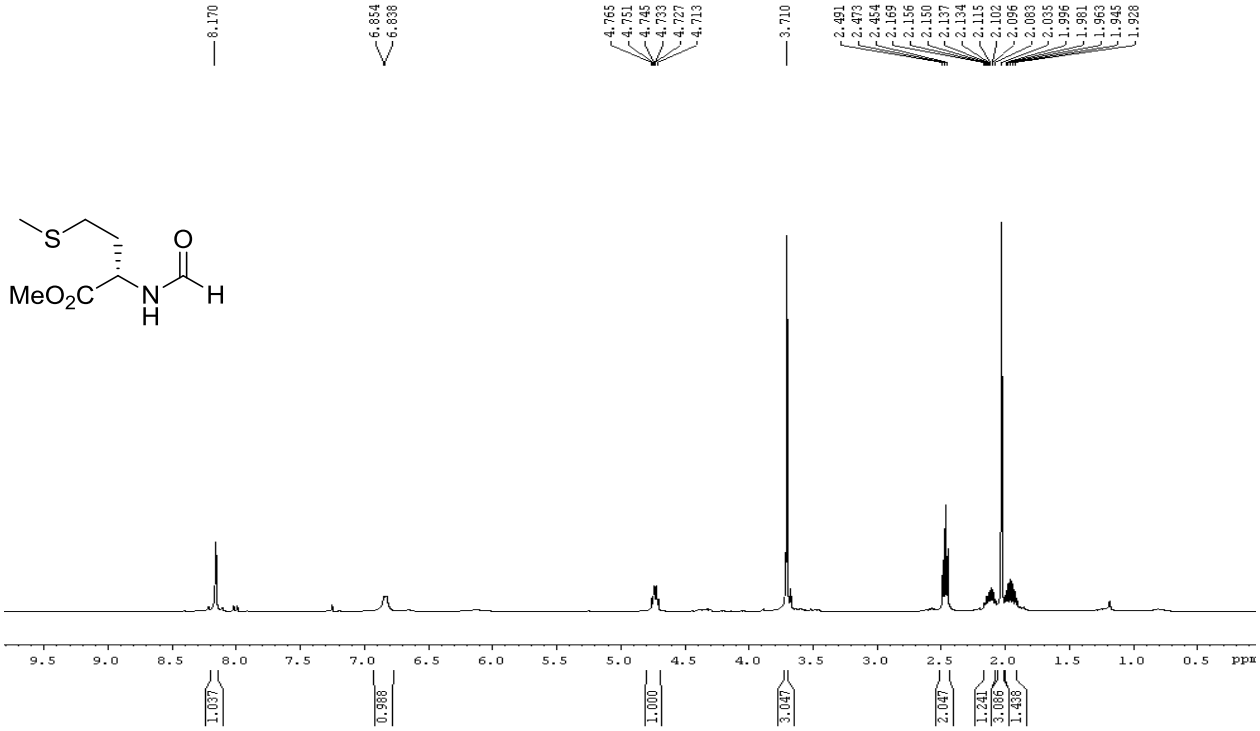
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8e**.



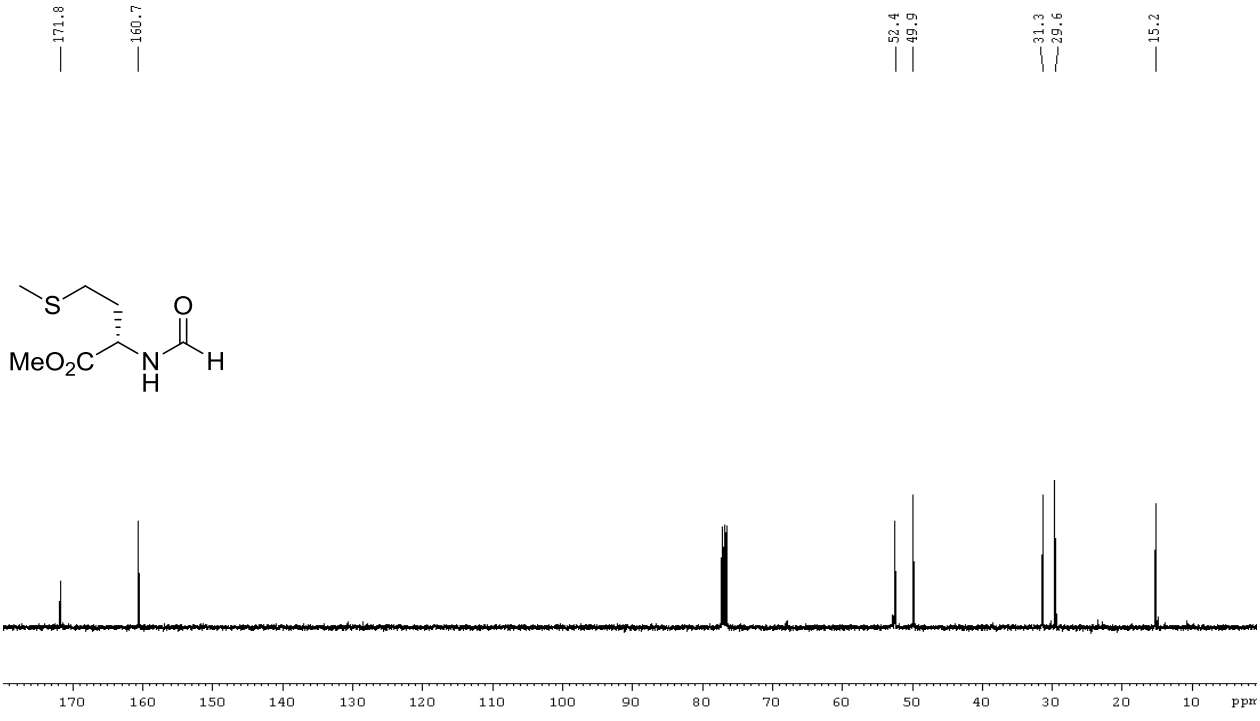

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8e**.



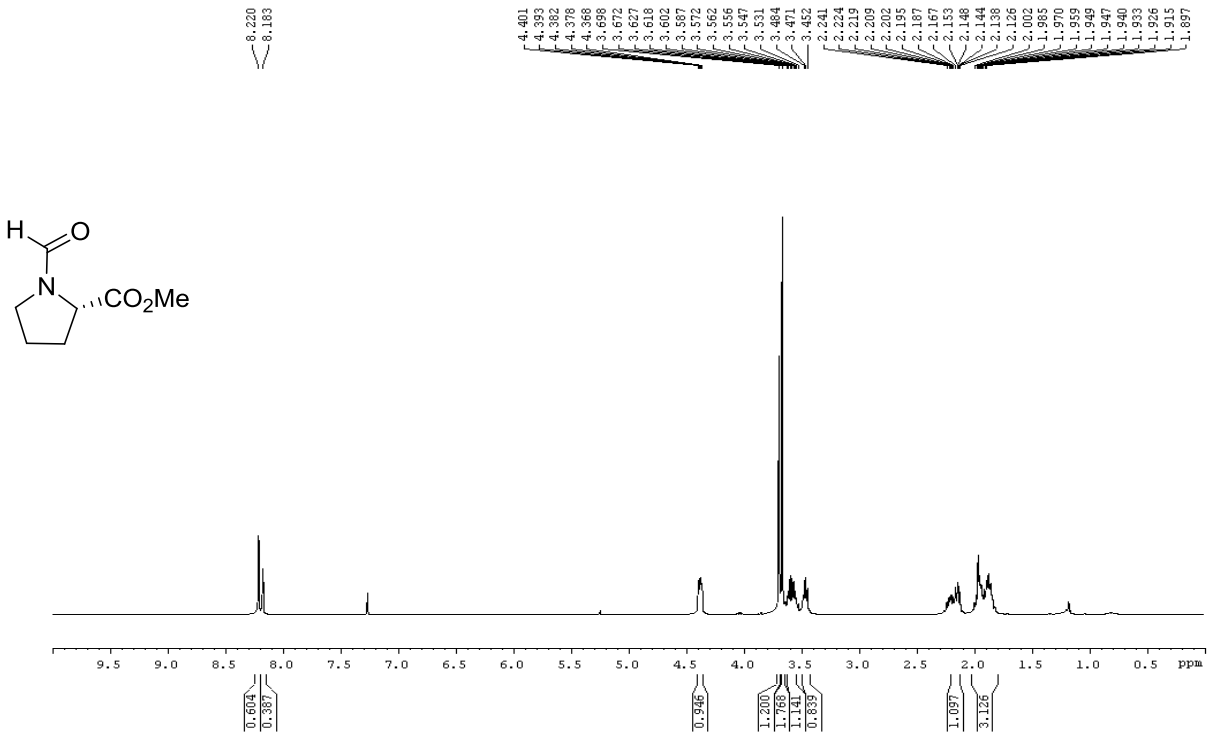
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8f**.



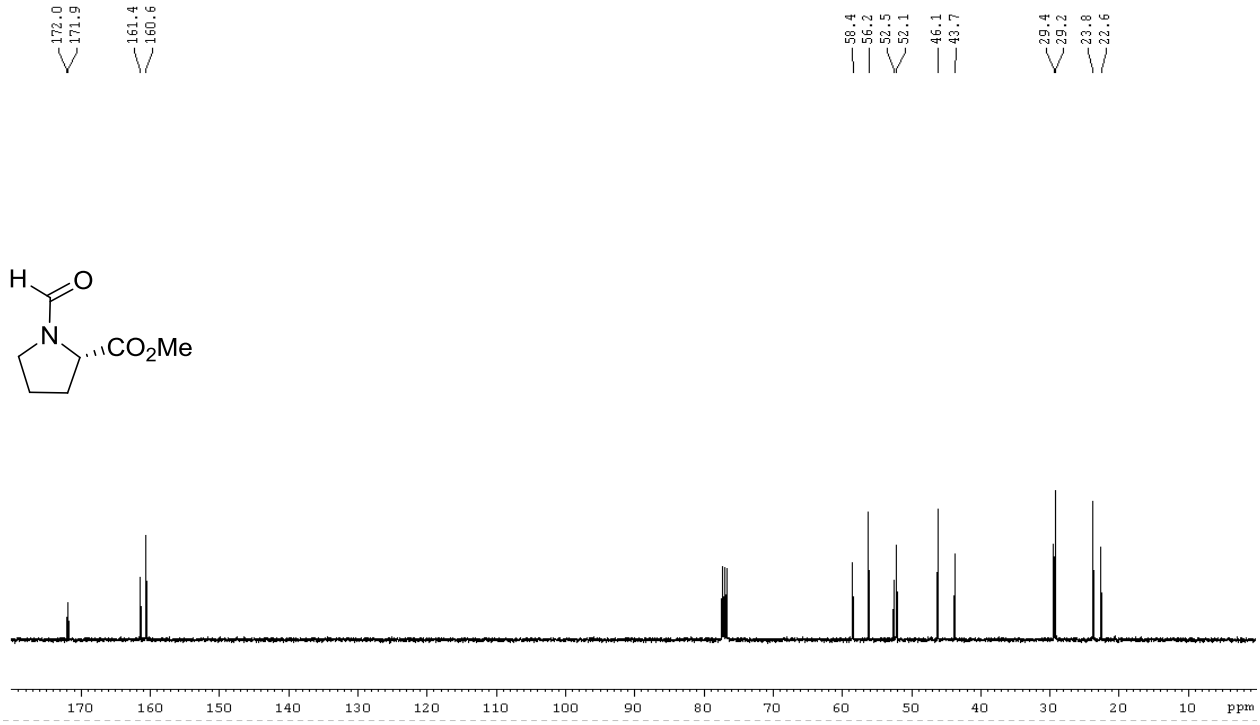

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8f**.



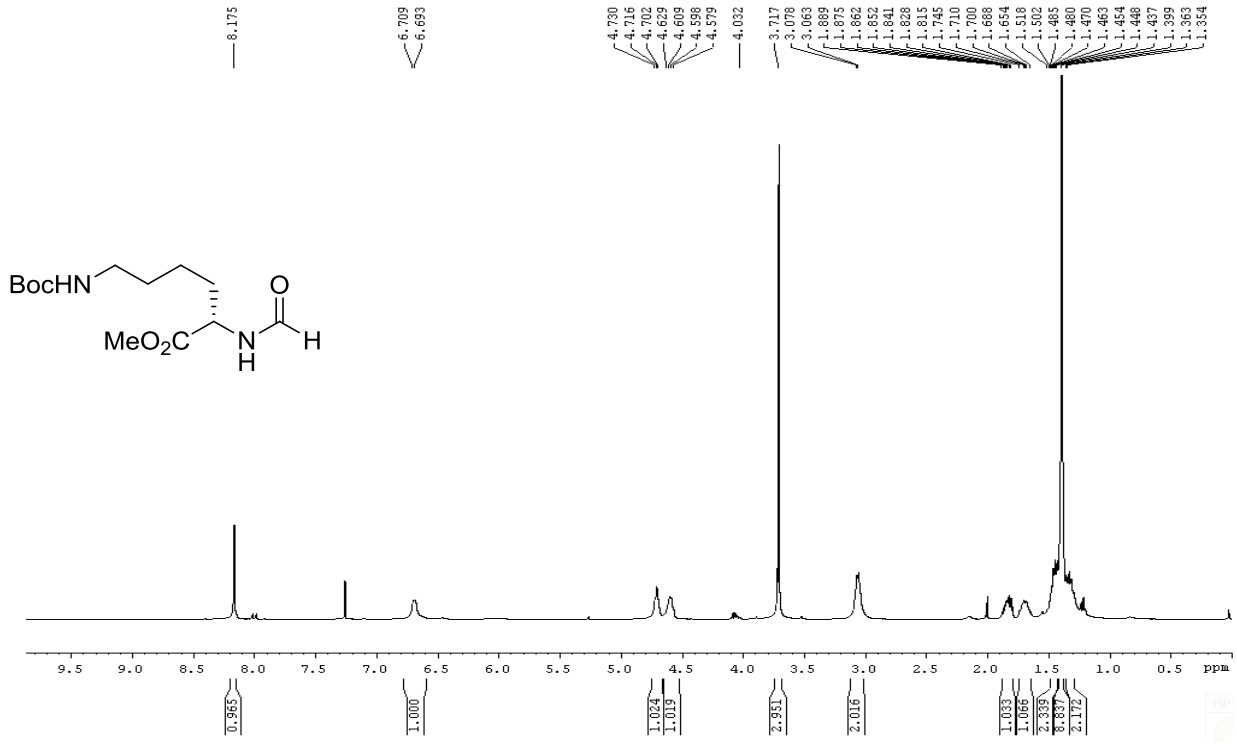
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8g**.



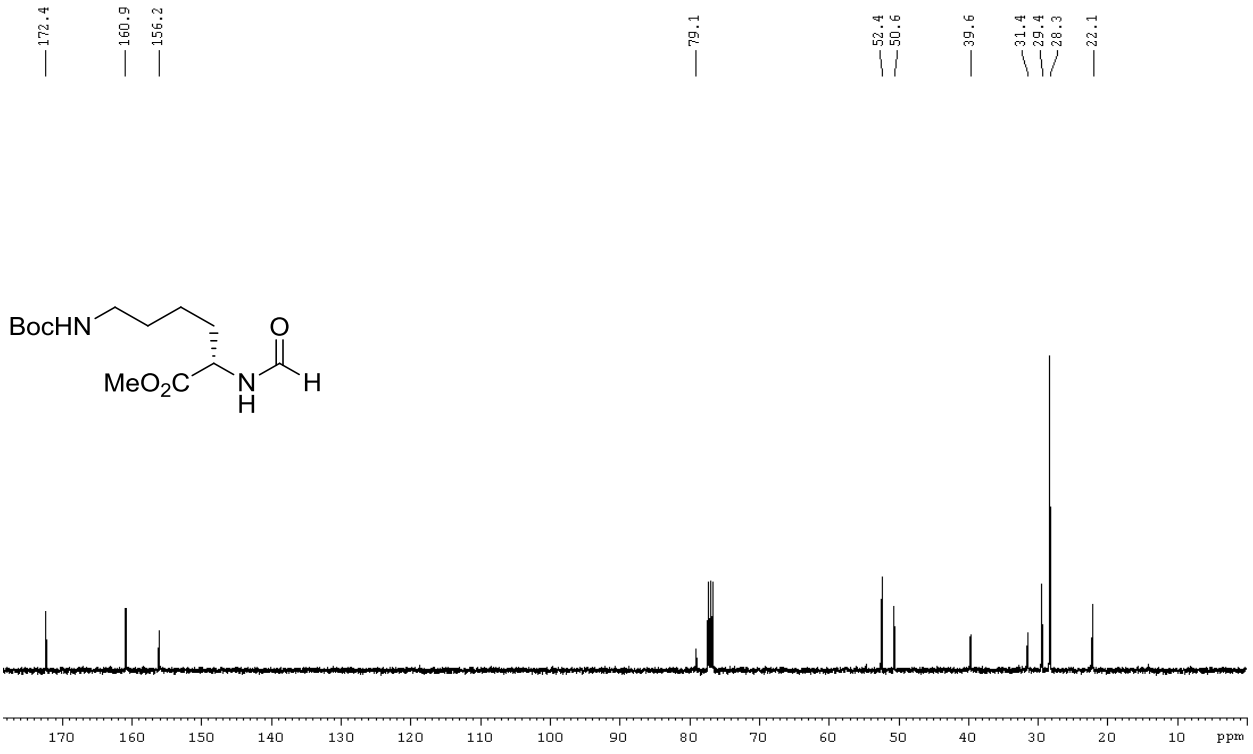

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8g**.



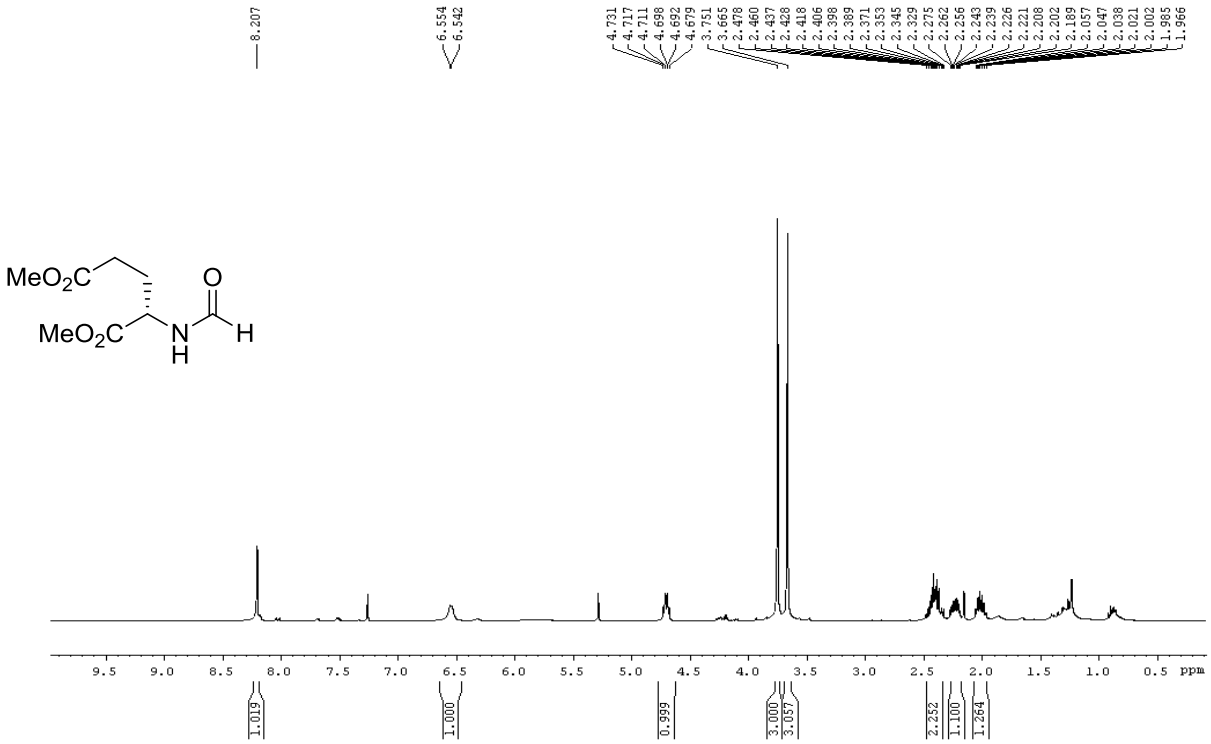
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8h**.



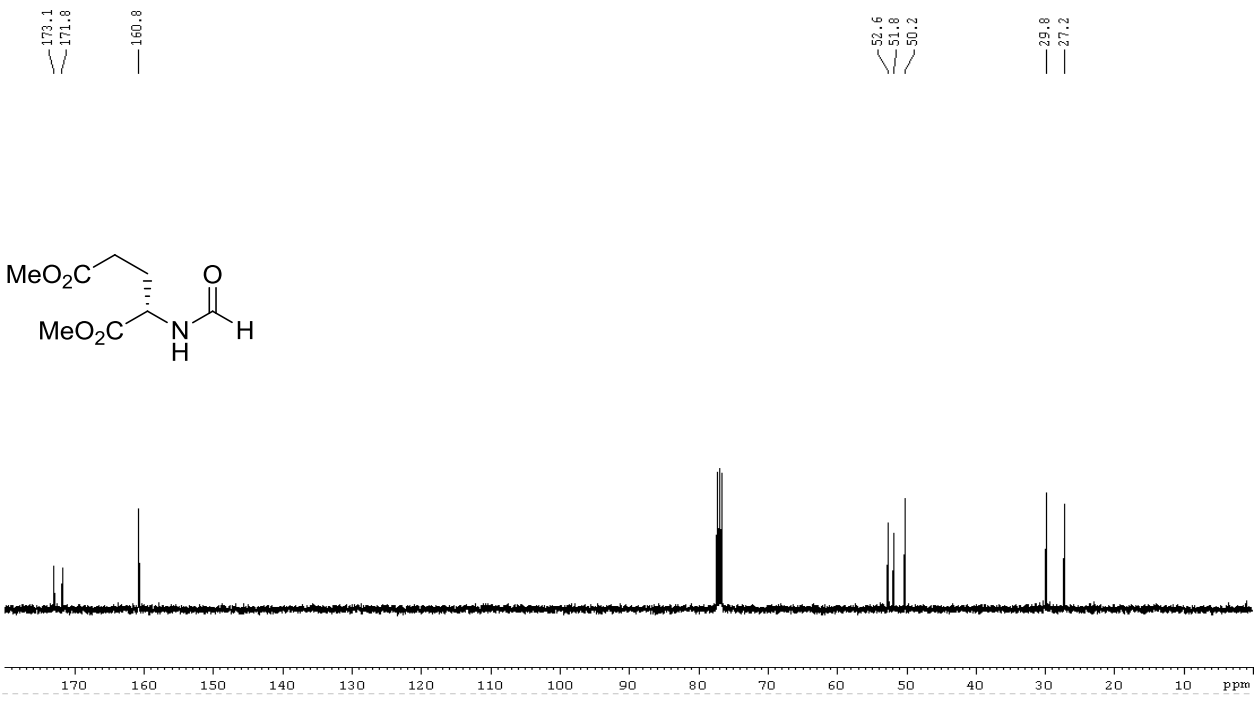

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8h**.



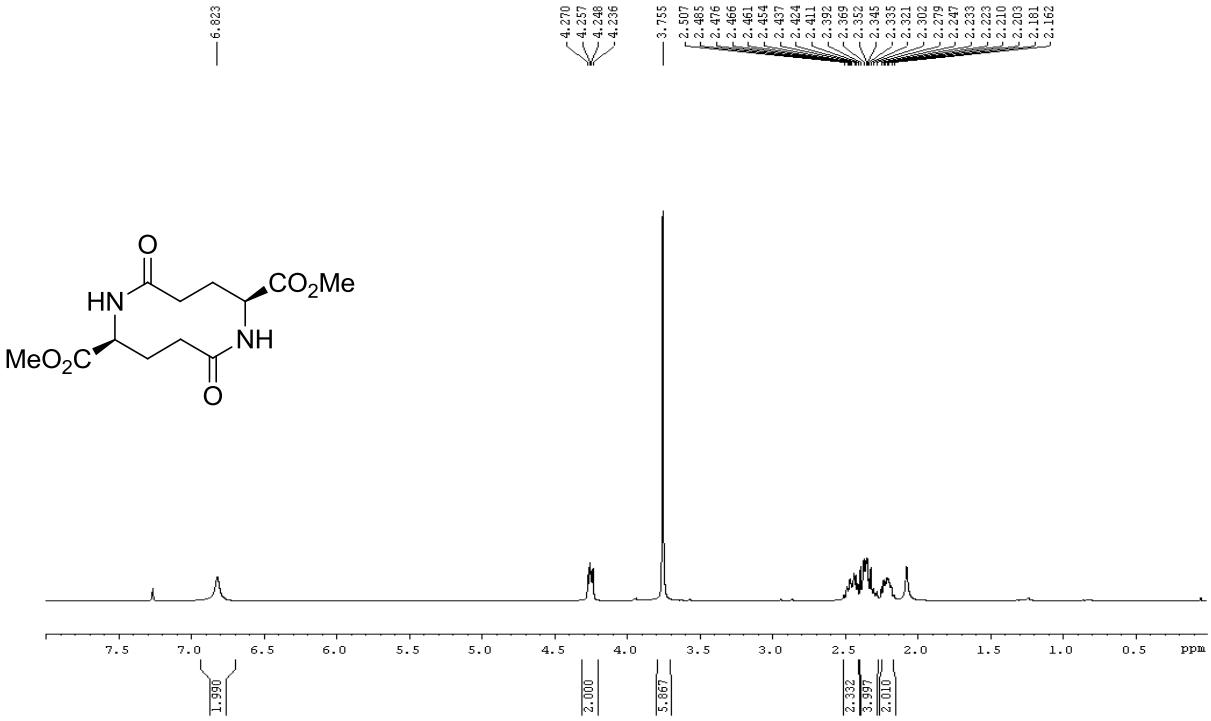
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **8i**.



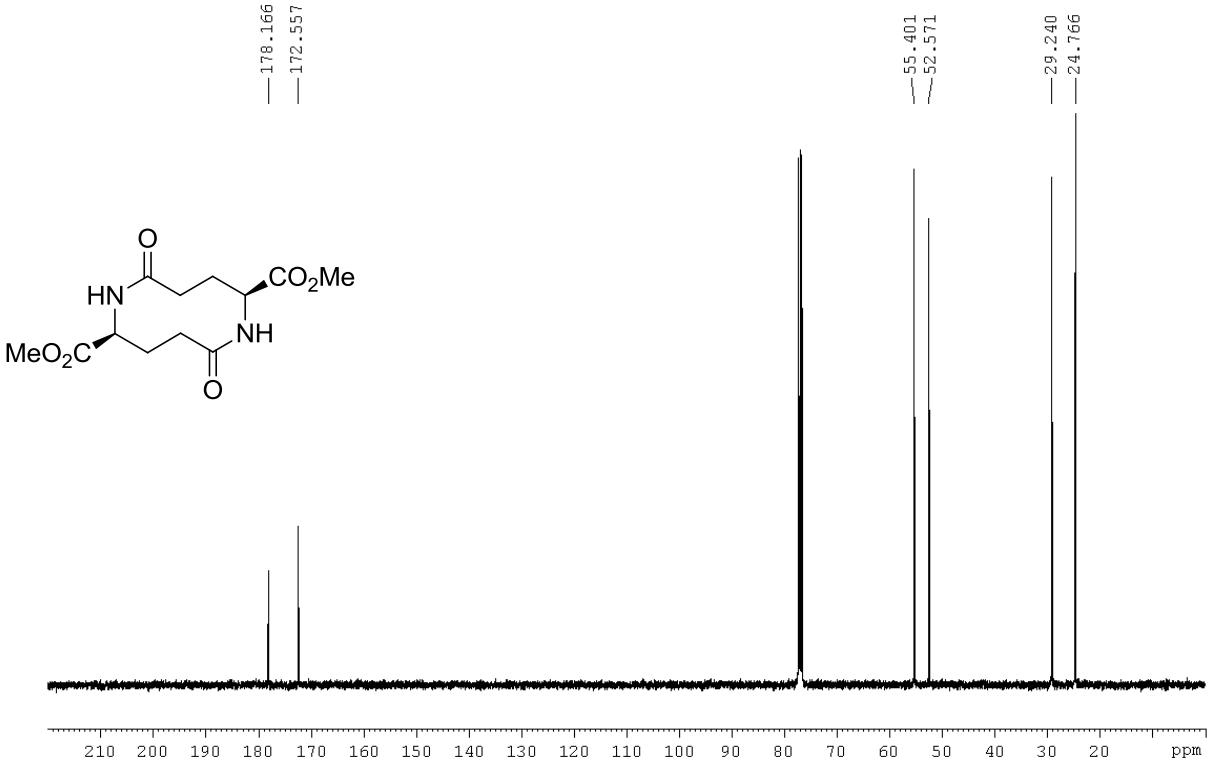

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **8i**.



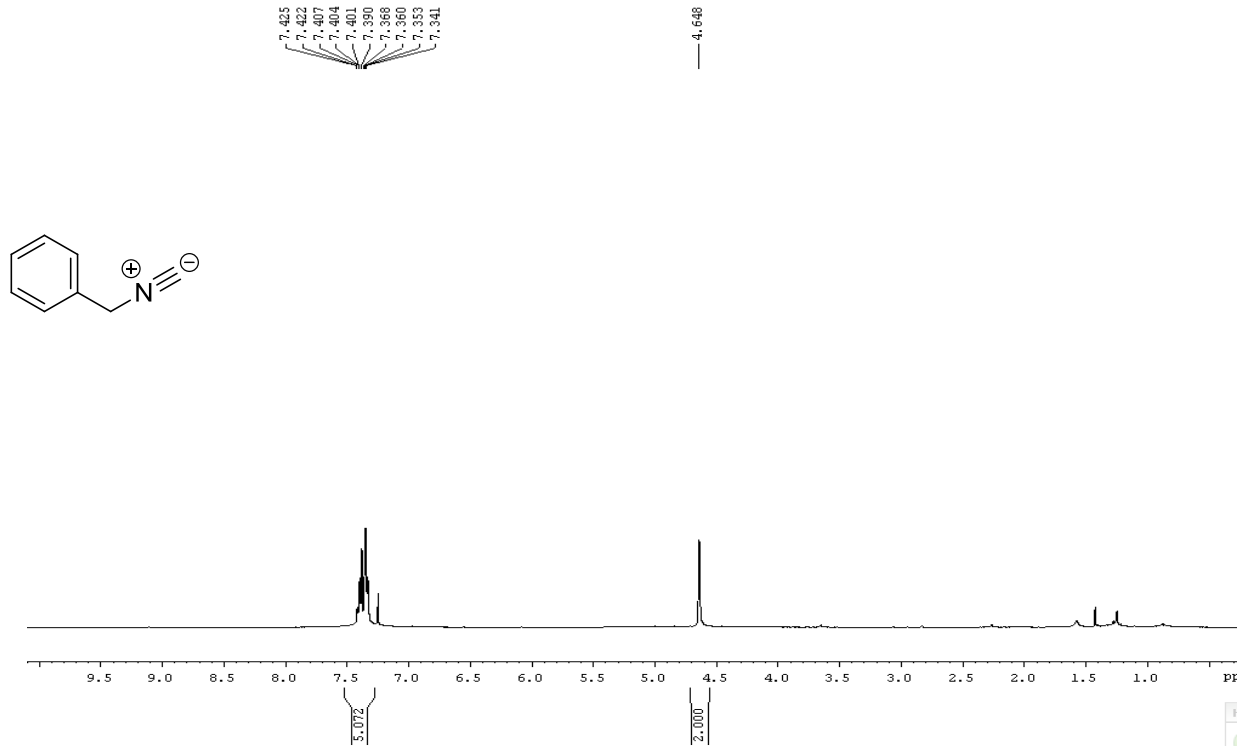
$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **9**



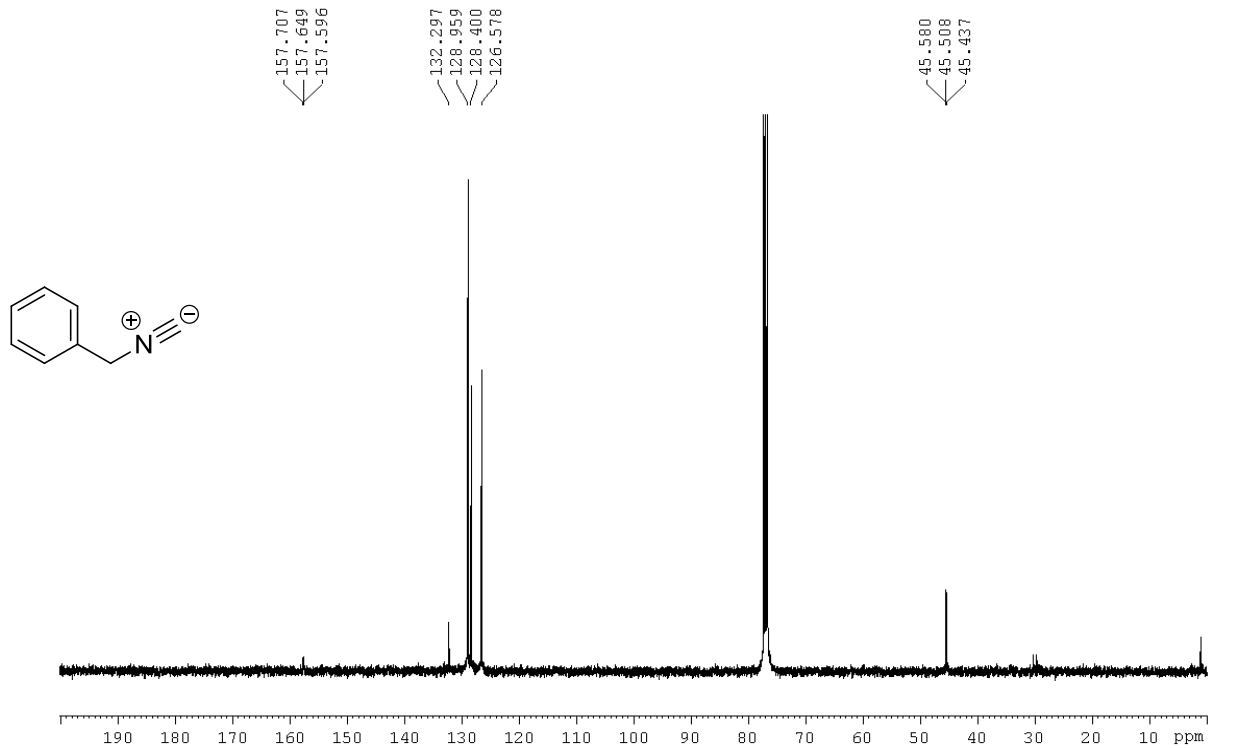

$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **7**.



$^{1}$H NMR (400.0 MHz; $CDCl_3$) of **10**

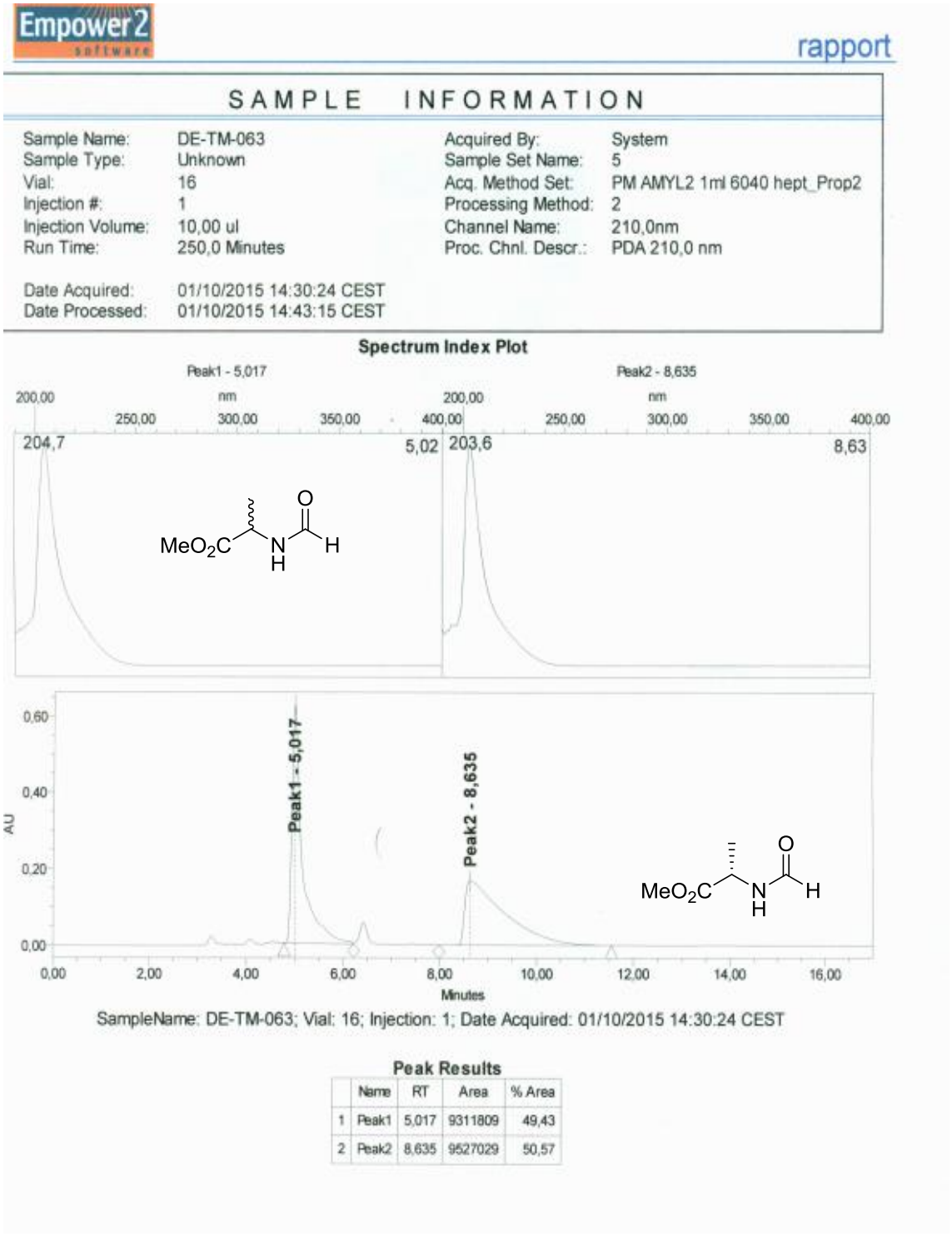



$^{13}$C NMR (100.0 MHz; $CDCl_3$) of **9**.

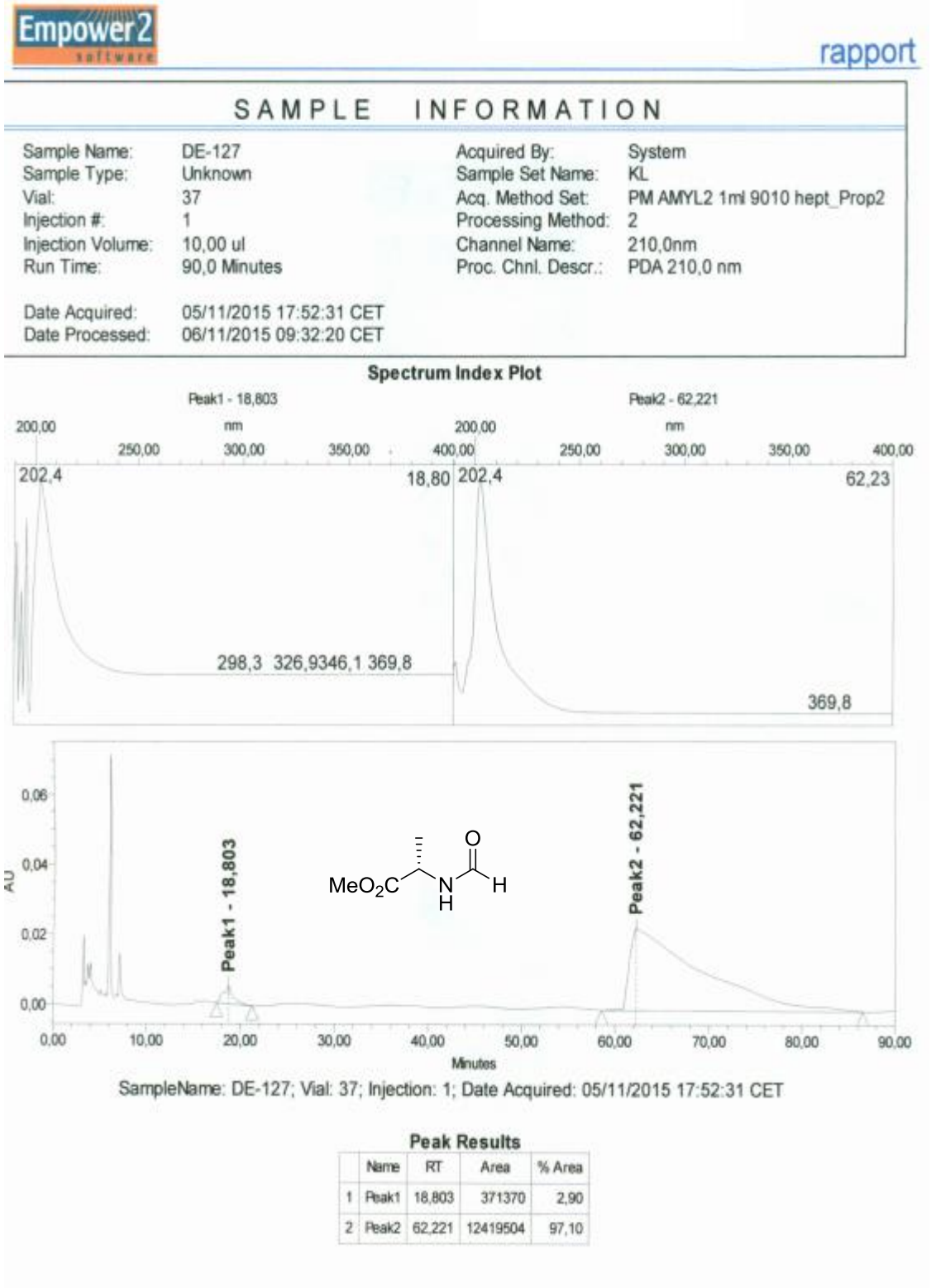


## 9. HPLC Spectra

*Racemic*-methyl-*N*-formyl-alinate **8b**



(*S*)-Methyl-*N*-formylalinate **8b** (Procedure **B**, $HCONH_2$ at 45 °C)



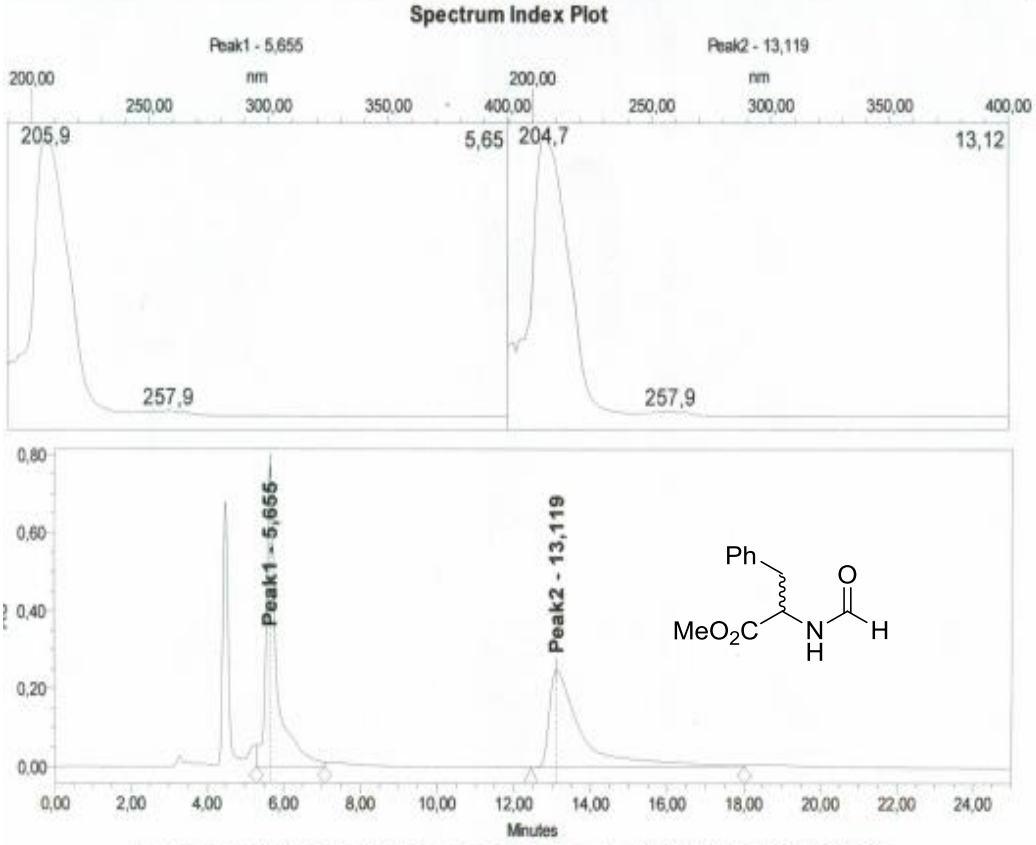
*Rac*-Methyl-*N*-formylphenylalinate

Empower 2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE-034 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 1 |
| Vial: | 9 | Acq. Method Set: | PM AMYL2 1ml 5050 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 10,00 ul | Channel Name: | 210,0nm |
| Run Time: | 240,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 02/09/2015 14:26:46 CEST | | |
| Date Processed: | 02/09/2015 15:29:13 CEST | | |




SampleName: DE-034; Vial: 9; Injection: 1; Date Acquired: 02/09/2015 14:26:46 CEST

**Peak Results**

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 5,655 | 14870677 | 50,49 |
| 2 | Peak2 | 13,119 | 14582701 | 49,51 |

(*S*)-Methyl-*N*-formylphenylalinate **8c** (Procedure **B**, $HCONH_2$ at 45 °C)

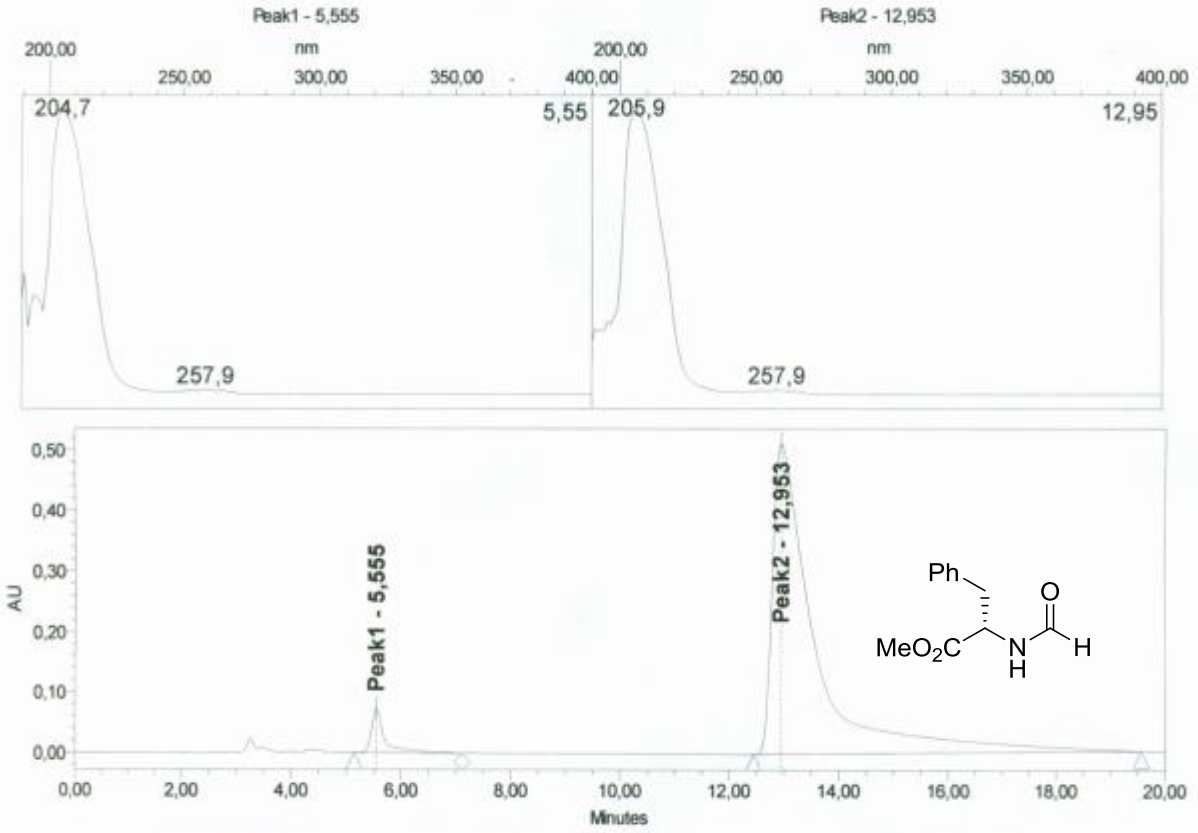
Empower 2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE-129 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | KL |
| Vial: | 36 | Acq. Method Set: | PM AMYL2 1ml 5050 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 10,00 ul | Channel Name: | 210,0nm |
| Run Time: | 20,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 05/11/2015 17:11:36 CET | | |
| Date Processed: | 06/11/2015 09:31:34 CET | | |

**Spectrum Index Plot**




SampleName: DE-129; Vial: 36; Injection: 1; Date Acquired: 05/11/2015 17:11:36 CET

**Peak Results**

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 5,555 | 1215756 | 4,21 |
| 2 | Peak2 | 12,953 | 27647722 | 95,79 |

*Rac*-Methyl-*N*-formylvalinate

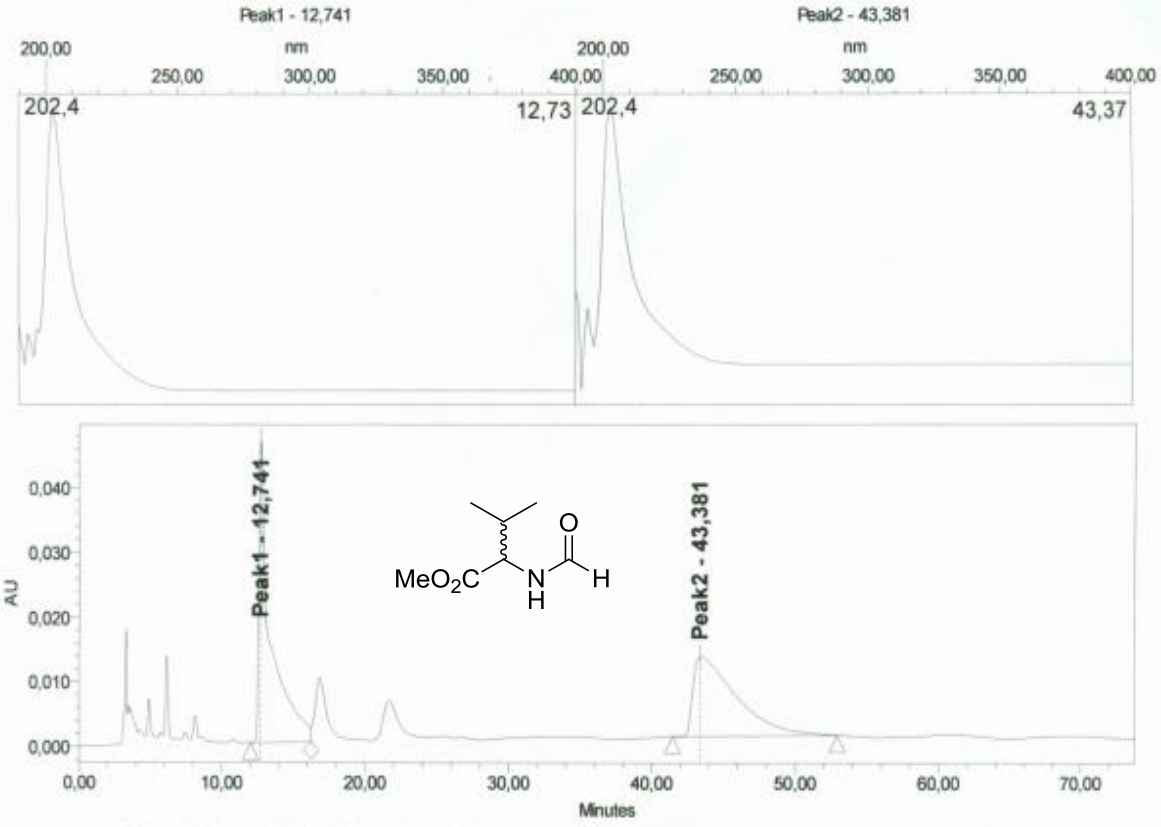
Empower 2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE-TM-067 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 1 |
| Vial: | 26 | Acq. Method Set: | PM AMYL2 1ml 9010 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 10,00 ul | Channel Name: | 210,0nm |
| Run Time: | 240,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 20/10/2015 14:37:54 CEST | | |
| Date Processed: | 21/10/2015 14:17:41 CEST | | |

**Spectrum Index Plot**




SampleName: DE-TM-067; Vial: 26; Injection: 1; Date Acquired: 20/10/2015 14:37:54 CEST

**Peak Results**

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 12,741 | 2616951 | 50,24 |
| 2 | Peak2 | 43,381 | 2591644 | 49,76 |

(*S*)-Methyl-*N*-formylvalinate **8e** (Procedure **B**, $HCONH_2$ at 45 °C)

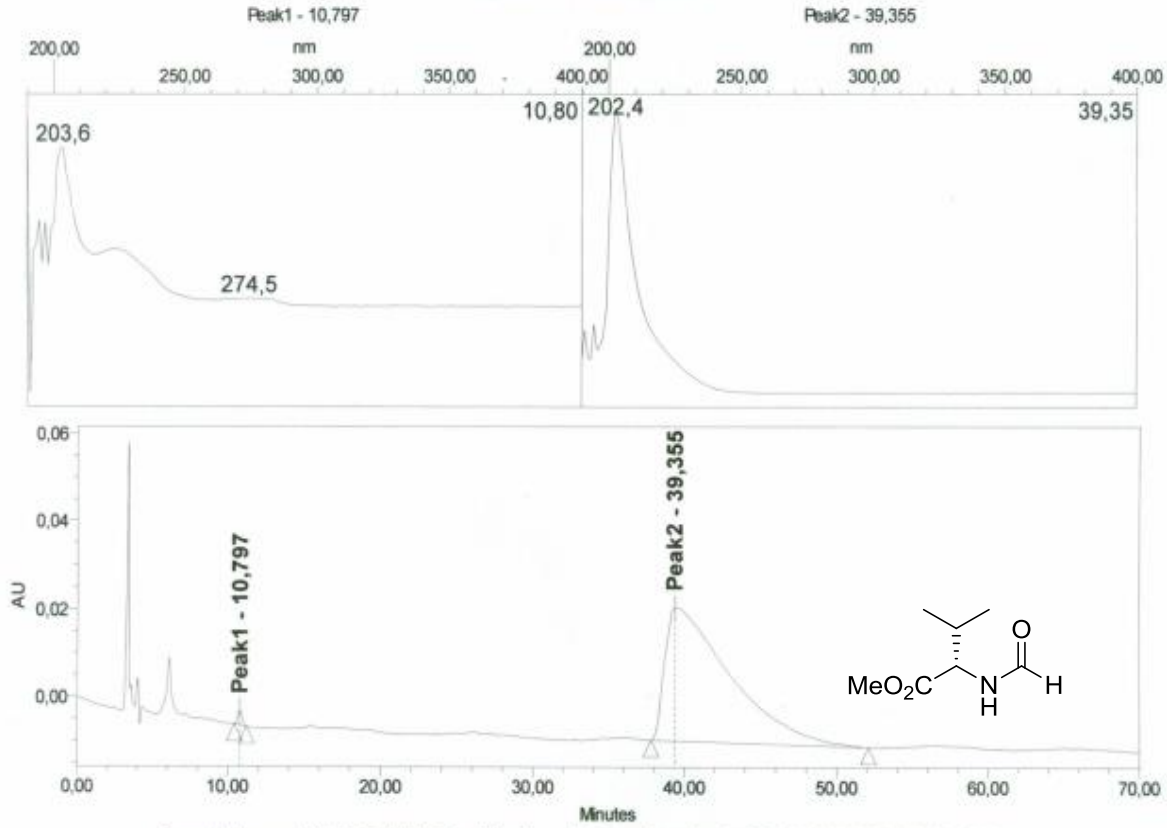
Empower 2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE-132 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | T |
| Vial: | 38 | Acq. Method Set: | PM AMYL2 1ml 9010 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 40,00 ul | Channel Name: | 210,0nm |
| Run Time: | 70,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 06/11/2015 09:53:09 CET | | |
| Date Processed: | 06/11/2015 10:46:47 CET | | |

**Spectrum Index Plot**




SampleName: DE-132; Vial: 38; Injection: 1; Date Acquired: 06/11/2015 09:53:09 CET

**Peak Results**

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 10,797 | 64149 | 0,71 |
| 2 | Peak2 | 39,355 | 9009750 | 99,29 |

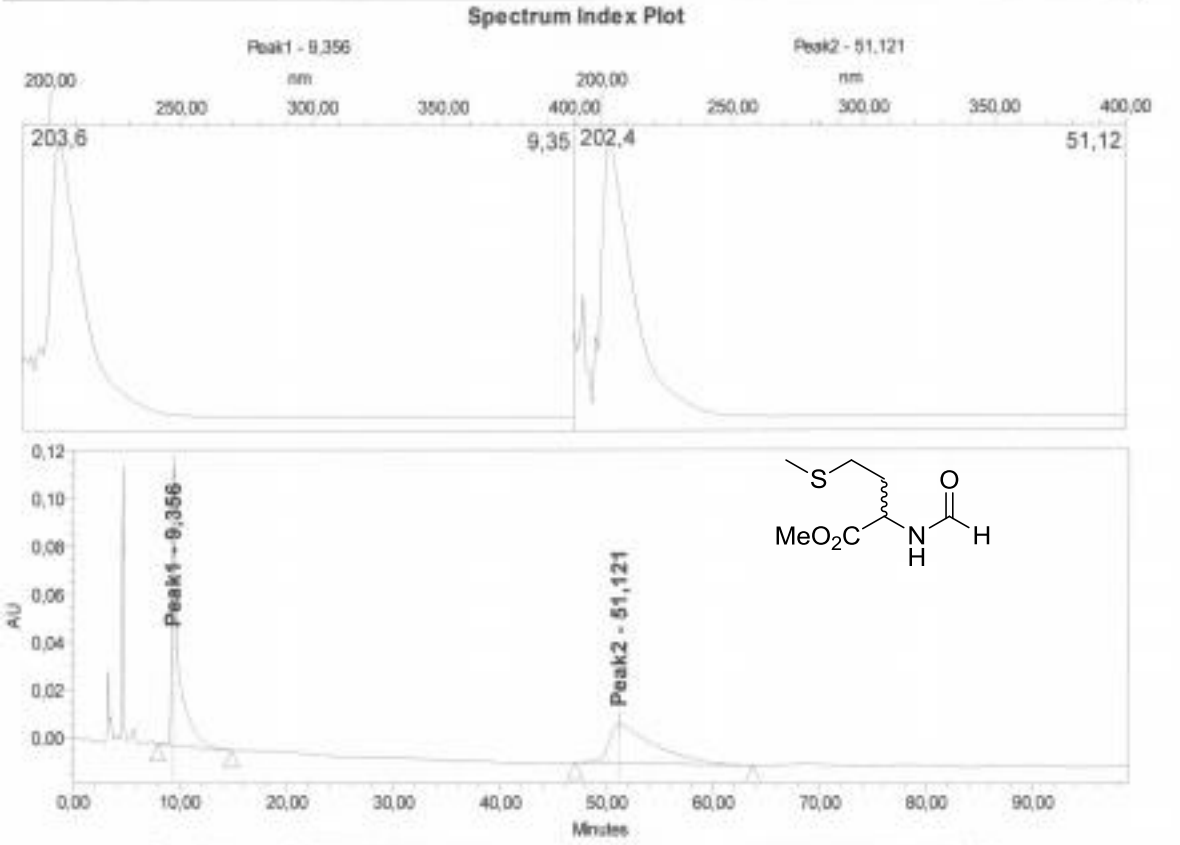
*Rac*-Methyl-*N*-formylmethioninate

Empower 2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE TM 73 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | T |
| Vial: | 37 | Acq. Method Set: | PM AMYL2 1ml 6040 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 10,00 ul | Channel Name: | 210,0nm |
| Run Time: | 230,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 17/11/2015 12:04:10 CET | | |
| Date Processed: | 18/11/2015 10:38:30 CET | | |




SampleName: DE TM 73; Vial: 37; Injection: 1; Date Acquired: 17/11/2015 12:04:10 CET

Peak Results

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 9,356 | 4791117 | 50,25 |
| 2 | Peak2 | 51,121 | 4744062 | 49,75 |

(*S*)- Methyl-*N*-formylmethioninate **8f** (Procedure **B**, $HCONH_2$ at 45 °C)

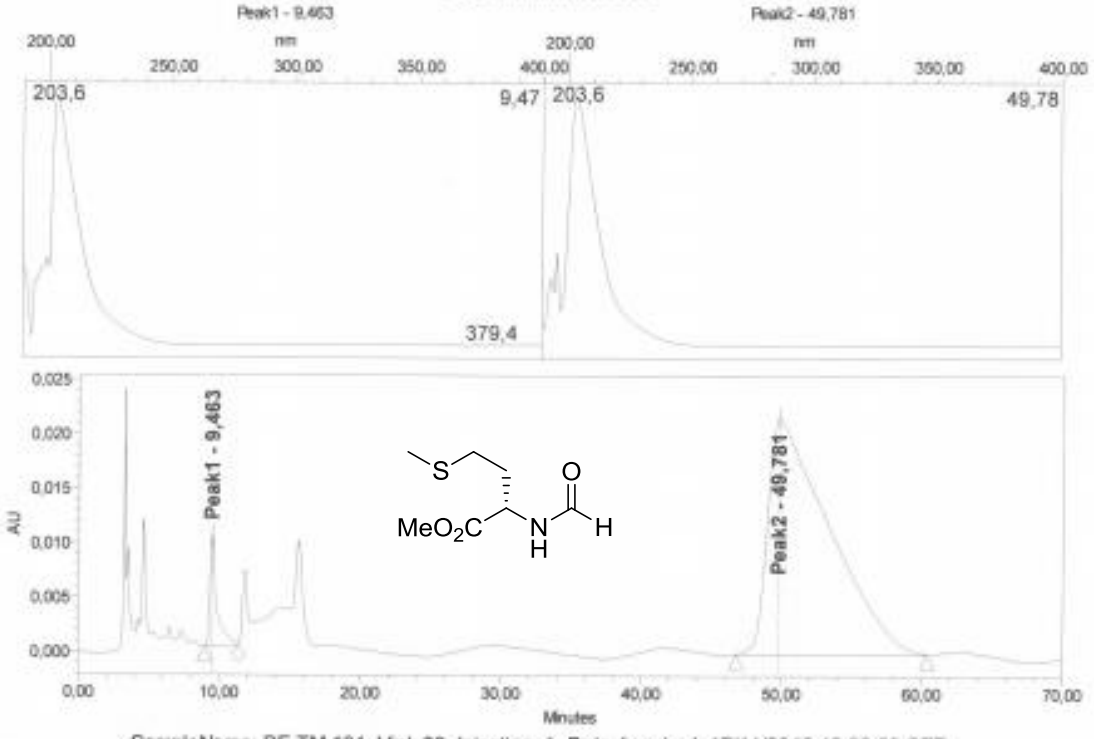
Empower2 software

rapport

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | DE TM 131 | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | T |
| Vial: | 39 | Acq. Method Set: | PM AMYL2 1ml 6040 hept_Prop2 |
| Injection #: | 1 | Processing Method: | 2 |
| Injection Volume: | 10,00 ul | Channel Name: | 210,0nm@4 |
| Run Time: | 70,0 Minutes | Proc. Chnl. Descr.: | PDA 210,0 nm |
| Date Acquired: | 17/11/2015 16:08:55 CET | | |
| Date Processed: | 18/11/2015 10:36:52 CET | | |

Spectrum Index Plot




SampleName: DE TM 131; Vial: 39; Injection: 1; Date Acquired: 17/11/2015 16:08:55 CET

Peak Results

| | Name | RT | Area | % Area |
|---|---|---|---|---|
| 1 | Peak1 | 9,463 | 353507 | 5,10 |
| 2 | Peak2 | 49,781 | 6580905 | 94,90 |