Supporting Information for

# Room-Temperature Decarboxylative Cyanation of Carboxylic Acids Using Photoredox Catalysis and Cyanobenziodoxolones: Divergent Mechanism Compared to Alkynylation

Franck Le Vaillant, Matthew D. Wodrich, and Jérôme Waser*

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland

jerome.waser@epfl.ch

**(101 pages)**

## Table of Contents

## 1. Computational Details

The Cartesian coordinates of the structures are given in separate files.

**Table S1.** Electronic energies, free energy corrections, and solvation corrections for relevant species for the TIPS-EBX (**13a**) reaction pathways. PBE0-dDsC/TZ2P electronic energies[1] were obtained from single point computations on M06/def2-SVP geometries. COSMO-RS solvation corrections were obtained at the PBE0-dDsC/TZ2P level in dichloroethane.

| **Compound** | **M06/def2-SVP Electronic Energy (hartree)** | **M06/def2-SVP Free Energy Correction (hartree)** | **PBE0-dDsC/TZ2P Electronic Energy (hartree)** | **COSMO-RS Solvation Energy (kcal/mol)** |
|---|---|---|---|---|
| **Path b** | | | | |
| TIPS-EBX (**13a**) (neutral) | -1437.25862 | 0.32433 | -12.11996 | -19.820 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| $\mathbf{b_0/c_0}$ | -2107.22210 | 0.54583 | -20.24351 | -26.544 |
| $\mathbf{b_{TS1}}$ | -2107.21410 | 0.55072 | -20.23510 | -25.573 |
| **14a** | -1390.52978 | 0.47166 | -16.17122 | -17.103 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **Path c** | | | | |
| TIPS-EBX (**13a**) (neutral) | -1437.25862 | 0.32433 | -12.11996 | -19.820 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| $\mathbf{c_{TS1}}$ | -2107.21080 | 0.54988 | -20.23315 | -26.679 |
| $\mathbf{c_1}$ | -2107.25218 | 0.55426 | -20.27345 | -26.772 |
| $\mathbf{c_{TS2}}$ | -2107.23204 | 0.54933 | -20.25476 | -26.531 |
| **14a** | -1390.52978 | 0.47166 | -16.17122 | -17.103 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **Path d** | | | | |
| TIPS-EBX (**13a**) (neutral) | -1437.25862 | 0.32433 | -12.11996 | -19.820 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| TIPS-EBX (radical anion) | -1437.37429 | 0.31762 | -12.18649 | -58.354 |
| NCp-Cbz (cation) | -669.80125 | 0.19867 | -7.88846 | -52.010 |
| Alkyne-TIPS (anion) | -720.58648 | 0.24398 | -7.99591 | -56.259 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **14a** | -1390.52978 | 0.47166 | -16.17122 | -17.103 |

[1] Note that ADF computes energies relative to atom fragments, which accounts for the magnitude differences between M06 and PBE0-dDsC electronic energies.

**Table S2.** Electronic energies, free energy corrections, and solvation corrections for relevant species for the CBX (**4a**) reaction pathways. PBE0-dDsC/TZ2P electronic energies[1] were obtained from single point computations on M06/def2-SVP geometries. COSMO-RS solvation corrections were obtained at the PBE0-dDsC/TZ2P level in tetrahydrofuran.

| **Compound** | **M06/def2-SVP Electronic Energy (hartree)** | **M06/def2-SVP Free Energy Correction (hartree)** | **PBE0-dDsC/TZ2P Electronic Energy (hartree)** | **COSMO-RS Solvation Energy (kcal/mol)** |
|---|---|---|---|---|
| **Path b** | | | | |
| CBX-Reagant (**4a**) | -809.44026 | 0.06297 | -4.86788 | -13.481 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| $\mathbf{b_0}$ | -1479.40086 | 0.28310 | -12.99159 | -19.417 |
| $\mathbf{b_{TS1}}$ | -1479.39325 | 0.28461 | -12.98212 | -19.748 |
| **7a** | -762.71290 | 0.20919 | -8.92005 | -13.322 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **Path c** | | | | |
| CBX-Reagant (**4a**) | -809.44026 | 0.06297 | -4.86788 | -13.481 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| $\mathbf{c_0}$ | -1479.40317 | 0.28148 | -12.99568 | -18.632 |
| $\mathbf{c_{TS1}}$ | -1479.38777 | 0.28425 | -12.97636 | -21.065 |
| $\mathbf{c_1}$ | -762.68197 | 0.20597 | -8.88777 | -12.962 |
| NCp-Cbz (cation) | -669.80125 | 0.19867 | -7.88846 | -52.010 |
| CN (anion) | -92.79923 | -0.01405 | -0.76633 | -59.158 |
| **7a** | -762.71290 | 0.20919 | -8.92005 | -13.322 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **Path d** | | | | |
| CBX-Reagant (neutral, **4a**) | -809.44026 | 0.06297 | -4.86788 | -13.481 |
| NCp-Cbz (Radical **II**) | -669.94287 | 0.19434 | -8.10368 | -10.068 |
| CBX-Reagant (radical anion) | -809.56268 | 0.05576 | -4.95003 | -48.692 |
| NCp-Cbz (cation) | -669.80125 | 0.19867 | -7.88846 | -52.010 |
| CN (anion) | -92.79923 | -0.01405 | -0.76633 | -59.158 |
| Radical **III** | -716.74487 | 0.05638 | -4.12540 | -10.957 |
| **7a** | -762.71290 | 0.20919 | -8.92005 | -13.322 |

**Determination of computed reduction potentials.** Reported reduction potentials were determined using the Born-Haber cycle given in Scheme S1. Geometries of the different species were determined by optimization at the M06/def2-TZVPP level in implicit THF solvent using the SMD solvation model. Gas phase free energies were obtained from single point energy computations followed by frequency computations, as is standard procedure.[2] The reduction potential is determined as: $\Delta G^{\circ}(soln, redox) = \Delta G^{\circ}(gas, redox) + \Delta G^{\circ}(solv, anion) - \Delta G^{\circ}(solv, radical)$. The standard redox potential ($E^0$) is then obtained as: $E^{\circ} = -\frac{\Delta G^{\circ}(soln,redox)}{ZF}$, where Z is the number of electrons transferred (one in this case) and F is Faraday's constant (23.061 kcal per volt gram equivalent). The reference value of the SCE was taken as 4.522 V.[3]

**Scheme S1**. Born-Haber cycle to calculate the reduction potential of radical species.

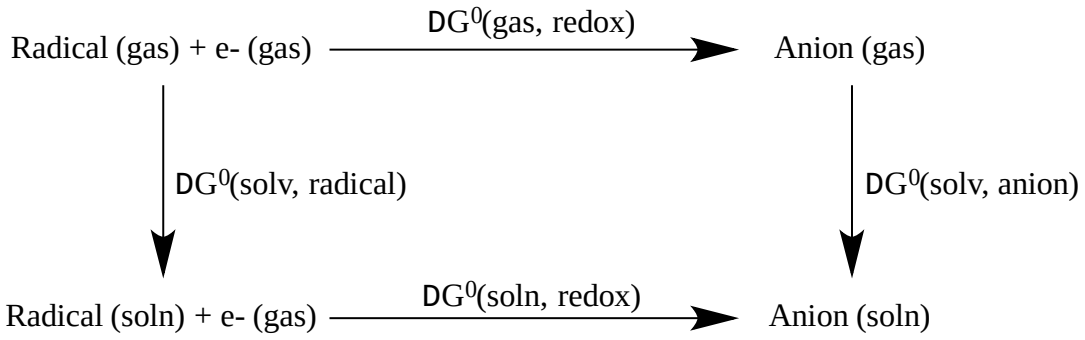



**Table S3.** Computed free energies (at the M06/def2-TZVPP level) used to determine reduction potentials.

| **Species** | **Gas Phase** | **Solution Phase** |
|---|---|---|
| Radical **III** | -717.149821 | -717.168794 |
| Anion **III** | -717.269068 | -717.344168 |
| Benzoyl Radical | -419.962563 | -419.975128 |
| Benzoyl Anion | -420.086894 | -420.165561 |

**Table S4.** Absolute and relative (to SCE) reduction potentials. SCE value taken as 4.522V.

| **Species** | **Absolute Reduction Potential ($E^0$)** | **Reduction Potential Relative to SCE** |
|---|---|---|
| Radical **III** | 4.772 | 0.250 |
| Benzoyl Radical | 5.182 | 0.660 |

[2] Demissie, T. B. ; Ruud, K. ; Hansen, J. H. *Organometallics* **2015**, *34*, 4218-4228.
[3] Isse, A. A. ; Gennaro, A. *J. Phys. Chem. B* **2010**, *114*, 7894-7899.

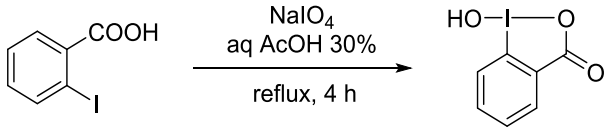
## 2. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, $Et_2O$, $CH_3CN$, toluene, hexane and $CH_2Cl_2$ were dried by passage over activated alumina under nitrogen atmosphere ($H_2O$ content < 10 ppm, *Karl-Fischer* titration). $NEt_3$ and pyridine were distilled under nitrogen from KOH. The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. All carboxylic acid starting materials were commercially available and used as received unless otherwise noted. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure.TLC was performed on Merck silica gel 60 $F_{254}$ TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. $^1$H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-$d_6$ or $CD_3OD$, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).$^{13}$C-NMR spectra were recorded with $^1$H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-$d_6$ or $CD_3OD$, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as $cm^{-1}$ (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. Reactions were performed in test tubes (1.0 to 10 mL) which were hold using a rack for test tubes placed at the center of a crystallization flask, the latter was filled by water, in order to keep the temperature as constant as possible. On this flask were attached the blue LEDs (RUBAN LED 5MÈTRES - 60LED/M - 3528 BLEU - IP65 with Transformateur pour Ruban LED 24W/2A/12V, bought directly on RubanLED.com). The distance between the LEDs and the test tubes was approximatively 3-5 cm. Temperature ranged between 25 and 30°C, and long irradiation resulted in temperature increasing up to 34°C during overnight reactions.

## 3. Preparation of Reagents and catalyst

The synthesis of reagents **4a-b** and **13a-b** had already been described before by our group. The procedures are taken from the indicated publications to facilitate reproduction of the results by having all data in the same file. Catalyst **6** is commercially available and was used as received; it was also synthesized as indicated below, affording comparable yields in the catalytic reactions.

**1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (25)**

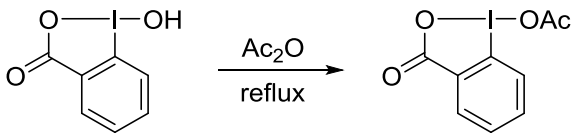



**24** **25**

Following a reported procedure,[4] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**24**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **25** (8.3 g, 31 mmol, 98%) as a colorless solid.

$^1$H NMR (400 MHz, $(CD_3)_2SO$) δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1 H, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1 H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar*H*); $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m); the reported values correspond to the ones in literature.[4]

**1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one** (**26**)




**25** **26**

Following a reported procedure,[5] 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**25**, 10.3 g, 39.1 mmol, 1.00 equiv.) was suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room

[4]a) D. Fernandez Gonzalez, J. P. Brand, J. Waser, *Chem. Eur. J.* **2010**, *16*, 9457. b) L. Kraszkiewicz, L. Skulski, *Arkivoc*. **2003**, *6*, 120.
[5]P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579.

temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* affording **26** (10.8 g, 35.3 mmol, 90%) as a white solid.

$^1$H NMR ($CDCl_3$, 400 MHz): δ 8.24 (dd, 1 H, *J* = 7.6, 1.6 Hz, Ar*H*), 8.00 (dd, 1 H, *J* = 8.3, 1.0 Hz, Ar*H*), 7.92 (ddd, 1 H, *J* = 8.4, 7.2, 1.6 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*), 2.25 (s, 3 H, COC*H*$_3$). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. The values of the NMR spectra are in accordance with reported literature data.[5]

**1-Cyano-1,2-benziodoxol-3-(1*H*)-one** (**4a**)

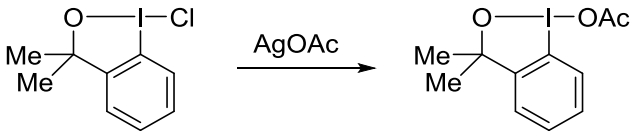

**26** **4a**

Following a reported procedure,[6] 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**26**, 11.8 g, 38.6 mmol, 1.00 eq.) was dissolved under nitrogen in dry dichloromethane (200 mL). To the clear colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 10 mL, 77 mmol, 2.00 eq.) over a five minute time period, then trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 70 µL, 0.386 mmol, 0.01 equiv.). Precipitation occurred within 5 min and the reaction mixture was stirred at room temperature and under nitrogen for 30 min to ensure the completion of the reaction. The resulting thick white suspension was diluted with hexane (5 mL) before being filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **4a** (10.3 g, 37.7 mmol, 98 %) as a white solid.

$^1$H NMR (DMSO-$d_6$, 400 MHz): δ 8.29 (d, *J* = 8.3 Hz, 1 H, Ar*H*), 8.13 (dd, *J* = 7.4, 1.7 Hz, 1 H, Ar*H*), 8.06-7.97 (m, 1 H, Ar*H*), 7.88 (t, *J* = 7.3 Hz, 1 H, Ar*H*). $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 166.7, 136.5, 132.0, 131.9, 130.2, 127.8, 117.5, 87.9. IR ν 3157 (w), 3093 (w), 2160 (w), 1629 (s), 1562 (m), 1439 (m), 1321 (s), 1298 (s), 1148 (m), 839 (m), 747 (s). The characterization data is in accordance with reported literature values.[6]**Error! Bookmark not defined.**

**1-Acetoxy-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole** (**28**)

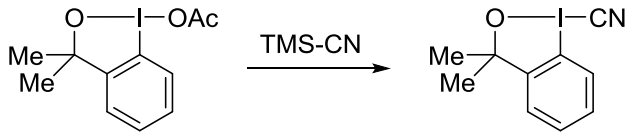
[6] M. Chen, Z. T. Huang, Q. Y. Zheng, *Org. Biomol. Chem*. **2015**, *13*, 8812.




**27** **28**

Following a reported procedure,[7] 1-chloro-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole[8] (**27**, 3.10 g, 10.5 mmol, 1.00 eq.) and silver acetate (1.83 g, 11.0 mmol, 1.05 eq.) were suspended under nitrogen in dry acetonitrile (30 mL). The mixture was stirred in the dark at room temperature for 15 hours. Filtration of the precipitated silver chloride followed by solvent removal *in vacuo* yielded compound **28** (2.98 g, 9.31 mmol, 89%) as a white solid. $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 7.79 (dd, *J* = 8.0, 1.3 Hz, 1 H, Ar*H*), 7.52-7.41 (m, 2 H, Ar*H*), 7.17 (dd, *J* = 7.4, 1.6 Hz, 1 H, Ar*H*), 2.10 (s, 3 H, COC*H*$_3$), 1.52 (s, 6 H, C*H*$_3$). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.4, 149.4, 130.5, 130.0, 129.9, 126.3, 115.8, 84.6, 29.3, 21.6. The characterization data is in accordance with reported literature values.[7]

**1-Cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole** (**4b**)




**28** **4b**

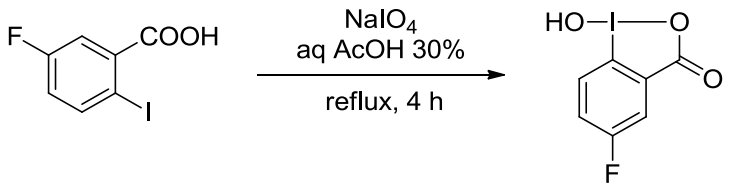
To a solution consisting of 1-acetoxy-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**28**, 2.00 g, 6.25 mmol, 1.00 equiv.) and dry dichloromethane (15 mL) was added dropwise trimethylsilyl cyanide (TMS-CN, 1.71 mL, 12.5 mmol, 2.00 eq.) at room temperature under nitrogen. The clear colorless solution was stirred at room temperature for 20 hours. Solvent removal afforded a white solid, which was suspended in pentane (10 mL), filtered and dried *in vacuo* affording pure compound **4b** (1.73 g, 6.03 mmol, 96%) as a white solid. $R_f$ (pentane:EtOAc 7:3) = 0.54. $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, *J* = 8.3 Hz, 1 H, Ar*H*), 7.62 (t, *J* = 7.3 Hz, 1 H, Ar*H*), 7.58-7.49 (m, 1 H, Ar*H*), 7.33 (d, *J* = 7.5 Hz, 1 H, Ar*H*), 1.48 (s, 6 H, C*H*$_3$). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 148.1, 131.7, 131.0, 128.3, 126.9, 111.6, 98.0, 80.4, 30.3. IR ν 2974 (w), 2925 (w), 2139 (w), 1461 (m), 1436 (m), 1251 (m), 1160 (s), 1003 (w), 954 (s), 869 (m), 761 (s). The characterization data is in accordance with reported literature values.[9]

**5-Fluoro-1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (30)**

[7] P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579.

[8] This commercially available compound can also be synthesized following the practical procedure by V. Matousek, E. Pietrasiak, R. Schwenk, A. Togni, *J. Org. Chem.* **2013**, *78*, 6763.

[9] V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, B. Mismash, J. K. Woodward, A. J. Simonsen, *Tetrahedron Lett.* **1995**, *36*, 7975.

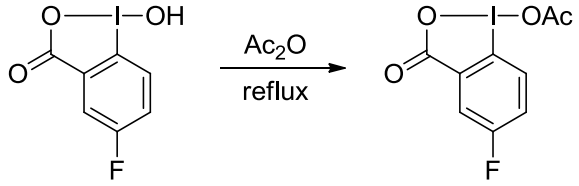



**29** **30**

Following a reported procedure,[10] $NaIO_4$ (760 mg, 3.55 mmol, 1.05 equiv) and 5-fluoro-2-iodobenzoic acid (**29**) (900 mg, 3.38 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (1.8 mL) / $H_2O$ (4.5 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 10 mL) and acetone (3 x 10 mL), and air-dried in the dark to give the pure product **30** (908 mg, 3.22 mmol, 95%) as a colorless solid.

$^1$H NMR (400 MHz, $(CD_3)_2SO$) δ 8.25 (bs, 1 H, O*H*), 7.90 – 7.78 (m, 2 H, Ar*H*), 7.75 (dd, *J* = 8.4, 2.5 Hz, 1 H, Ar*H*). $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 166.7 (d, *J* = 2.6 Hz), 164.0 (d, *J* = 248.3 Hz), 134.2 (d, *J* = 7.5 Hz), 128.5 (d, *J* = 8.7 Hz), 121.98 (d, *J* = 23.9 Hz), 117.4 (d, *J* = 23.6 Hz), 114.4. The reported values correspond to the ones in literature.[10]

**5-Fluoro-1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one** (**38**)




**30** **31**

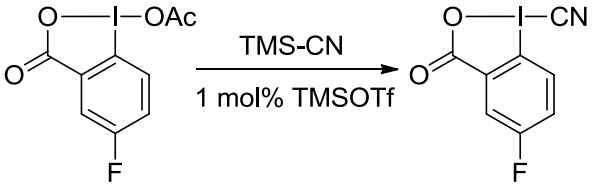
Following a reported procedure,[5] hypervalent iodine precursor **30** (800 mg, 2.84 mmol, 1.00 equiv.) was suspended in acetic anhydride (2.80 mL, 29.7 mmol, 10.5 equiv) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to cool down to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried in vacuo affording the corresponding OAc hypervalent iodine reagent **31** (825 mg, 2.55 mmol, 90%) as a white solid.

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.93 (m, 2H, Ar*H*), 7.64 (ddd, *J* = 9.1, 7.7, 2.9 Hz, 1H, Ar*H*), 2.26 (s, 3H, OC(O)*Me*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 176.4, 166.7 (d, *J* = 2.9 Hz), 165.0 (d, *J* = 254.5 Hz), 131.7 (d, *J* = 8.0 Hz), 131.0 (d, *J* = 8.1 Hz), 123.7 (d, *J* = 24.0 Hz), 120.0 (d, *J* = 24.3 Hz), 111.2 (d, *J* = 2.3 Hz), 20.2.The values of the NMR spectra are in

[10]J. P. Brand, C. Chevalley, R. Scopelliti, Waser, J. *Chem. Eur. J.* **2012**, *18*, 5655.

accordance with reported literature data, with small differences in chemical shifts for several signals.[11]

**5-Fluoro-1-Cyano-1,2-benziodoxol-3-(1*H*)-one** (**4c**)

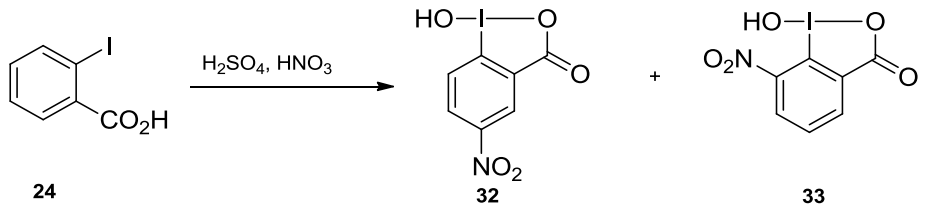



**31** **4c**

Following a reported procedure,[6] 5-Fluoro-1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**31**, 750 g, 2.31 mmol, 1.00 equiv.) was dissolved under nitrogen in dry dichloromethane (15 mL). To the clear colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 0.62 mL, 4.6 mmol, 2.0 equiv.), over a five minute time period, then trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 4.2 µL, 23 µmol, 0.010 equiv.). Precipitation occurred within 5 min and the reaction mixture was stirred at room temperature and under nitrogen for 30 min to ensure the completion of the reaction. The resulting thick white suspension was diluted with hexane (5 mL) before being filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **4c**(610 mg, 2.10 mmol, 91 %) as a white solid.

Mp: 181.1 – 184.1°C (decomp). $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.25 (dd, $J$ = 8.9, 4.2 Hz, 1H, Ar*H*), 7.99 – 7.75 (m, 2H, Ar*H*). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 165.3 (d, $J$ = 2.4 Hz), 164.6 (d, $J$ = 251.5 Hz), 133.1 (d, $J$ = 7.7 Hz), 130.1 (d, $J$ = 8.9 Hz), 123.8 (d, $J$ = 24.5 Hz), 118.4 (d, $J$ = 24.1 Hz), 111.4, 87.4. IR (solid) 3870 (s), 3740 (s), 3686 (s), 3620 (m), 3435 (w), 3335 (w), 3227 (w), 3109 (w), 2988 (w), 2914 (w), 2360 (m), 2162 (w), 2005 (w), 1926 (w), 1865 (w), 1739 (m), 1702 (m), 1647 (m), 1518 (s), 1457 (m), 1419 (m), 1306 (m), 1141 (w), 1025 (s), 823 (w). HRMS (ESI) calcd for $C_8H_4FINO_2^+$ $[M+H]^+$ 291.9265; found 291.9270.

**2-Iodosyl-5-nitrobenzoic acid (30**) **and 2-iodosyl-3-nitrobenzoic acid (33**)




**24** **32** **33**

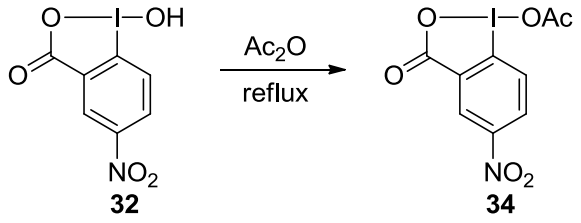
Following a reported procedure,[10] fuming nitric acid (3.3 mL) was added to 2-iodobenzoic acid (**24**) (5.0 g, 20 mmol, 1.0 equiv) in concentrated $H_2SO_4$ (6.7 mL). The reaction was

[11] M. Iinuma, K. Moriyama, H. Togo, *Eur. J. Org. Chem*. **2014**, 772.

equipped with a cooler and a nitrous vapor trap and was heated at 100 °C for 1 h. The reaction mixture was then poured in ice-water and filtered. The resulting solid was refluxed in water (50 mL) and filtered. A second crop of precipitate was filtered from the mother liquors. Both solids were combined, washed with acetone (10 mL) and dried under vacuum to afford **32** (2.19 g, 7.10 mmol, 36 %). The mother liquors were reduced to one third and then kept at 4 °C, the resulting precipitate was filtered, washed with acetone (10 mL) and dried under vacuum to afford **33** (630 mg, 2.04 mmol, 10 %).

**32**: $^1$H NMR (400 MHz, $(CD_3)_2SO$): δ 8.73 (dd, *J* = 8.8, 2.6 Hz, 1H, Ar*H*), 8.58 (d, *J* = 2.4 Hz, 1H, Ar*H*), 8.54 (br s, 1H, O*H*), 8.11 (d, *J* = 8.8 Hz, 1H, Ar*H*). **33**: $^1$H NMR (400 MHz, $(CD_3)_2SO$): δ 7.92 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.79 (m, 1H, Ar*H*), 7.67 (m, 1H, Ar*H*). The reported values correspond to the ones in literature.[10]

**5-Nitro-1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one** (**34**)

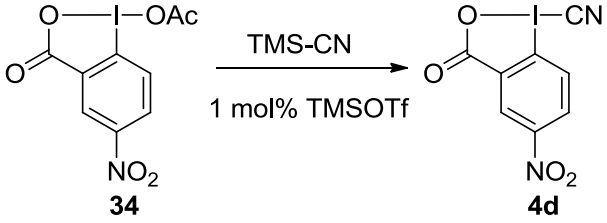



**32** **34**

Following a reported procedure,[5] 5-nitro-1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**32**, 6.55 g, 21.2 mmol, 1.00 eq.) was suspended in acetic anhydride (18 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* affording **34** (5.88 g, 16.7 mmol, 79 %) as a white solid.

$^1$H NMR(400 MHz, Chloroform-d) δ 9.04 (d, *J* = 2.5 Hz, 1H, Ar*H*), 8.71 (dd, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 8.27 (d, *J* = 8.9 Hz, 1H, Ar*H*), 2.30 (s, 3H, OC(O)*Me*).The values of the NMR spectra are in accordance with reported literature data.[5]

**5-Nitro-1-Cyano-1,2-benziodoxol-3-(1*H*)-one** (**4d**)

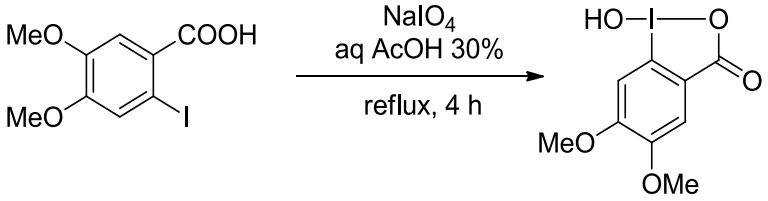



**34** **4d**

Following a reported procedure,[6] 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**34**, 351 mg, 1.00 mmol, 1.00 eq.) was dissolved under nitrogen in dry dichloromethane (7.0 mL). To the clear

colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 0.27 mL, 2.0 mmol, 2.00 eq.) over a five minute time period. then trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 1.8 µL, 10 µmol, 0.01 equiv.). Precipitation occurred within 5 min and the reaction mixture was stirred at room temperature and under nitrogen for 30 min to ensure the completion of the reaction. The resulting thick white suspension was diluted with hexane (5 mL) before being filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **4d** (273 mg, 0.859 mmol, 86 %) as a white solid. $^{1}$H NMR(400 MHz, DMSO-d6) δ 8.77 (dd, *J* = 8.9, 2.7 Hz, 1H, Ar*H*), 8.64 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.54 (d, *J* = 8.9 Hz, 1H, Ar*H*). The characterization data is in accordance with reported literature values.[6]

**4,5-Dimethoxy-1-hydroxy-1,2-benziodoxol-3-(1H)-one (36)**

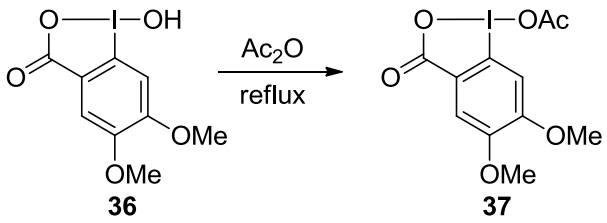



**35** **36**

Following a reported procedure,[6] $NaIO_4$ (840 mg, 3.95 mmol, 1.05 equiv) and 4,5-dimethoxy-2-iodobenzoic acid (**35**) (1.16 g, 3.76 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (1.8 mL in 4.5mL of $H_2O$). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (20 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 10 mL) and acetone (3 x 10 mL), and air-dried in the dark to give the pure product **36** (1.22 g, 3.76 mmol, >99%) as a colorless solid.

$^{1}$H NMR (400 MHz, $(CD_3)_2SO$) δ 7.99 (bs, 1 H, O*H*), 7.44 (s, 1 H, Ar*H*), 7.22 (s, 1 H, Ar*H*), 3.88 (bs, 6 H, OC$H_3$); $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 168.6, 154.1, 150.8, 124.3, 112.5, 110.9, 107.5, 56.2, 56.0. The reported values correspond to the ones in literature.[6]

**4,5-Dimethoxyl-1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one** (**37**)



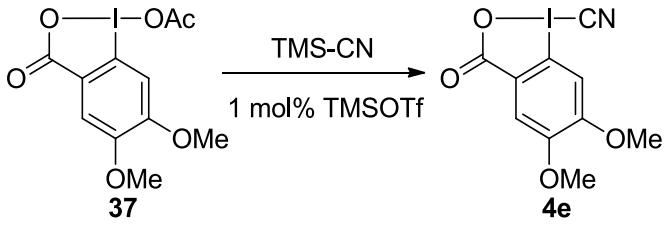

**36** **37**

Following a reported procedure,[7] 4,5-dimethoxyl-1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**36**, 115 mg, 0.355 mmol, 1.00 eq.) was suspended in acetic anhydride (1.0 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up

to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 5 mL) and dried *in vacuo* affording **37** (108 mg, 0.295 mmol, 83 %) as a white solid.

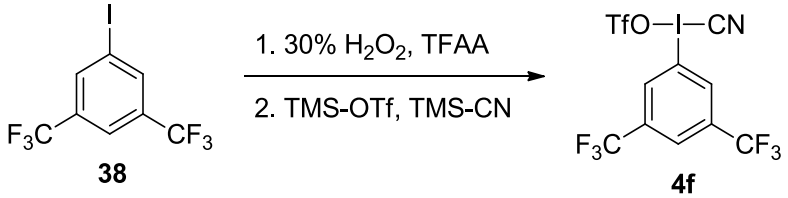
$^{1}$H NMR (400 MHz, $(CD_3)_2SO$) δ 7.47 (s, 1H, Ar*H*), 7.19 (s, 1H, Ar*H*), 3.92 (s, 3H, O*Me*), 3.90 (s, 3H, O*Me*), 2.25 (s, 3H, OC(O)*Me*). $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 174. 5, 167.7, 155.3, 151.2, 122.0, 112.9, 110.6, 109.2, 56.2, 56.1, 20.0. The values of the NMR spectra are in accordance with reported literature data.[6]

**4,5-Dimethoxy-1-Cyano-1,2-benziodoxol-3-(1*H*)-one** (**4e**)



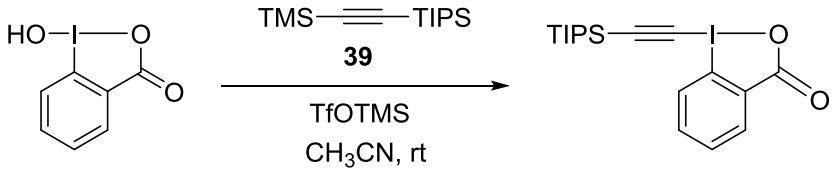

Following a reported procedure,[6] 4,5-dimethoxy-1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**37**, 92 mg, 0.251 mmol, 1.00 equiv.) was dissolved under nitrogen in dry dichloromethane (2 mL). To the clear colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 67 µL, 0.50 mmol, 2.00 equiv.) over a five minute time period, then trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 0.90 µL, 5.03 µmol, 0.02 equiv.). Precipitation occurred within 5 min and the reaction mixture was stirred at room temperature and under nitrogen for 30 min to ensure the completion of the reaction. The resulting thick white suspension was diluted with hexane (5 mL) before being filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **4e** (75 mg, 0.225 mmol, 90 %) as a white solid. $^{1}$H NMR (400 MHz, $(CD_3)_2SO$) δ 7.63 (s, 1H, Ar*H*), 7.53 (s, 1H, Ar*H*), 3.93 (s, 3H, O*C*$H_3$), 3.91 (s, 3H, O*C*$H_3$). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 166.6, 155.2, 151.9, 123.1, 112.7, 109.2, 107.0, 88.7, 56.2, 55.0. The characterization data is in accordance with reported literature values.[6]

**3,5-Di(trifluoromethyl)phenyl(cyano)iodonium triflate** (**4f**)



Following a reported procedure,[12] to a solution consisting of trifluoroacetic anhydride (TFAA, 20 mL) and dichloromethane (25 mL) was added dropwise at -50 °C aq. 30 wt% hydrogen peroxide (4.0 mL). After 10 minutes of stirring at -50 °C, a solution consisting of 1-iodo-3,5-bis(trifluoromethyl)benzene (**38**) (1.02 g, 3.00 mmol, 1.00 eq.) and dichloromethane (5.0 mL) was added dropwise. The reaction mixture was gradually warmed to 15 °C over a 14 hour time period. Next, the mixture was concentrated *in vacuo*, affording the corresponding trifluoroacetate derivative (1.64 g, 2.90 mmol, 97%) as a white solid. The intermediate was dissolved in dry dichloromethane (10 mL) without additional purification and trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 524 µL, 2.90 mmol, 1.00 eq.), followed by trimethylsilyl cyanide (TMS-CN, 388 µL, 2.90 mmol, 1.00 eq.), were added dropwise at room temperature. The resulting white suspension was diluted with dry dichloromethane (5.0 mL) and stirred at room temperature for 60 minutes, after which it was filtered. The white solid was washed with dichloromethane (2 x 10 mL), pentane (2 x 10 mL) and dried *in vacuo* to afford the title compound **4f** (1.46 g, 2.83 mmol, 98%) as a white solid. $^{1}$H NMR ($CD_3CN$, 400 MHz): δ 8.97 (s, 2 H, Ar*H*), 8.45 (s, 1 H, Ar*H*). $^{19}$F NMR ($CD_3CN$, 376 MHz): δ -63.6, -79.3. The values of the NMR spectra are in accordance with reported literature data.[12]

**1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, 13a)**




**25** **13a**

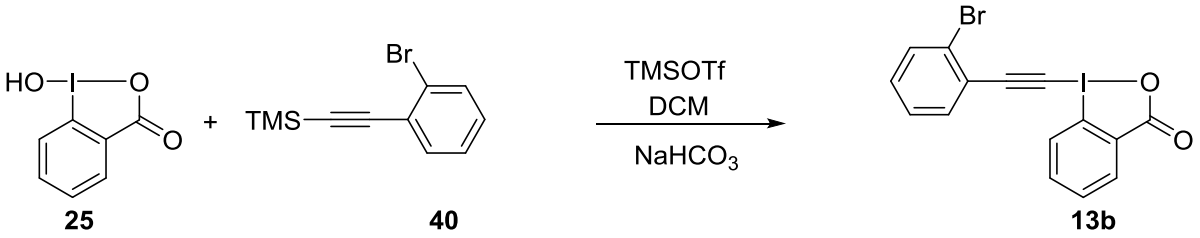
Following a reported procedure,[13] 2-iodosylbenzoic acid (**25**) (21.7 g, 82.0 mmol, 1.0 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added via canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(tri*iso*propylsilyl)acetylene (**39**) (23.0 g, 90.0 mmol, 1.1 equiv) was added via canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added via syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in DCM (200 mL)

[12]V. V. Zhdankin, M. C. Scheuller, P. J. Stang, *Tetrahedron Lett.* **1993**, *34*, 6853.
[13] J. P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.

and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with $CH_2Cl_2$ (200 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL) afforded **13a** (30.1 g, 70.2 mmol, 86%) as colorless crystals.

Mp (Dec.) 170-176 °C. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.44 (m, 1 H, Ar*H*), 8.29 (m, 1 H, Ar*H*), 7.77 (m, 2 H, Ar*H*), 1.16 (m, 21 H, TIPS). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1. IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m); Characterization data of **13a** corresponded to the literature values.[13]

**1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (13b)**



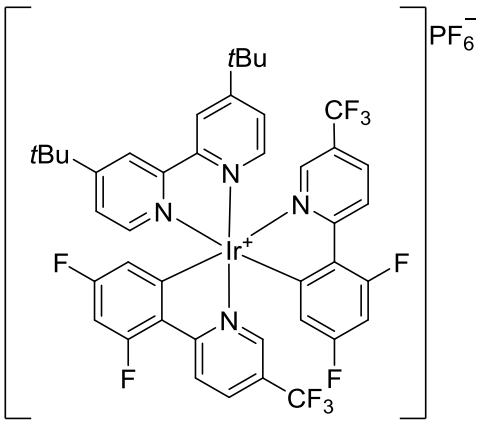

Following a reported procedure,[14**Error! Bookmark not defined.**] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**25**) (1.32 g, 5.00 mmol, 1 equiv) in $CH_2Cl_2$ (15 mL) at RT. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**40**) (1.17 g, 5.50 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in $CH_3CN$ (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **13b** (1.50 g, 3.51 mmol, 70%) as a colorless solid.

Mp 174-177 °C (decomposition). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.44 (td, 2 H, *J* = 7.3, 2.1 Hz, Ar*H*), 7.84 – 7.74 (m, 2 H, Ar*H*), 7.68 (d, 1 H, *J* = 1.1 Hz, Ar*H*), 7.61 (dd, 1 H, *J* = 7.6, 1.7 Hz, Ar*H*), 7.36 (dtd, 2 H, *J* = 22.4, 7.5, 1.5 Hz, Ar*H*).$^{13}$C NMR (101 MHz, $CDCl_3$)[15] δ

[14] J. P Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2012**, *18*, 5655.
[15] One carbon is not resolved.

166.6, 135.2, 134.7, 133.0, 132.7 , 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4. IR ν 2358 (w), 2155 (w), 1638 (s), 1616 (m), 1585 (w), 1466 (w), 1316 (m), 1147 (w). HRMS (ESI) $C_{15}H_9BrIO_2^+$ $[M+H]^+$ calc. = 426.8825; $[M+H]^+$ obs. = 426.8828.

**Iridium catalyst (6)**




Iridium photocatalyst **6** can be purchased from Sigma Aldrich, or it can also be synthetized following a reported procedure in two steps.[16]

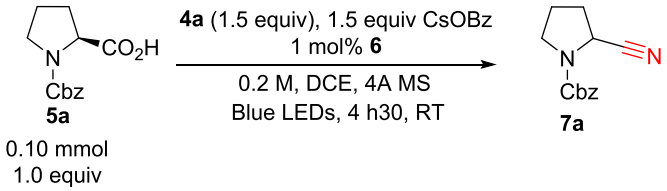
[16]A. Singh, K. Teegardin, M. Kelly, K. S. Prasad, S. Krishnan, J. D. Weaver, *J. Organomet. Chem.* **2015**, *776*, 51.

## 4. Decarboxylative cyanation

### Optimization of the reaction:

Dry degassed THF (0.5 mL) was added in a flame dried 1.5 mL test tube containing a teflon coated stirring bar, Cbz-Pro-OH (**5a**) (25 mg, 0.10 mmol, 1.0 equiv), CBX (**4a**) (41 mg, 0.15 mmol, 1.5 equiv), CsOBz (38 mg, 0.15 mmol, 1.5 equiv), 10 mg of heterogeneous powdered molecular sieves and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (1.1 mg, 0.0010 mmol, 0.01 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 4 h30 at rt.

The reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. Then the crude product was purified by preparative TLC (Heptane/Diethyl Ether 4/6) directly without any further work-up.

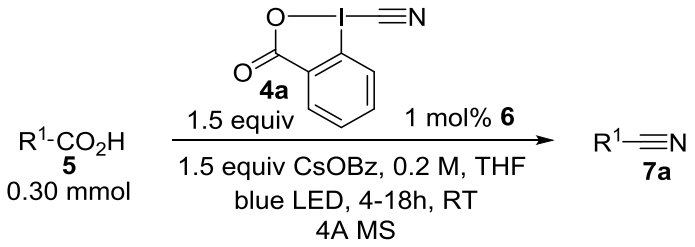



| Entry | Base | Reagent | Solvent | Concentration (M) | Conversion[a] (%) | Yield[b] (%) |
|---|---|---|---|---|---|---|
| 1[c] | 3.0 equiv CsOBz | **4a** | DCE | 0.20 | >95 | 40 |
| 2 | 3.0 equiv CsOBz | **4a** | DCE | 0.20 | >95 | 56 |
| 3 | 1.5 equiv CsOBz | **4a** | DCE | 0.20 | >95 | 78 |
| 4 | 1.2 equiv CsOBz | **4a** | DCE | 0.20 | >95 | 72 |
| 5 | 1.0 equiv CsOBz | **4a** | DCE | 0.20 | 90 | 57 |
| 6 | 0.25 equiv CsOBz | **4a** | DCE | 0.20 | 25 | 25 |
| 7 | 1.5 equiv $Cs_2CO_3$ | **4a** | DCE | 0.20 | >95 | <5 |
| 8 | 1.5 equiv CsOAc | **4a** | DCE | 0.20 | >95 | <5 |
| 9 | 1.5 equiv KOBz | **4a** | THF | 0.20 | >95 | 74 |
| 10 | 1.5 equiv CsOBz | **4a**[d] | DCE | 0.20 | 90 | 70 |
| 11 | 1.5 equiv CsOBz | **4a**[e] | DCE | 0.20 | >95 | 54 |
| 12 | 1.5 equiv CsOBz | **4a** | DCE | 0.05 | 90 | 46 |
| 13 | 1.5 equiv CsOBz | **4a** | DCE | 0.10 | >95 | 72 |
| 14 | 1.5 equiv CsOBz | **4a** | DCE | 0.33 | >95 | 48 |
| 15 | 1.5 equiv CsOBz | **4a** | DCM | 0.20 | >95 | 75 |
| 16 | 1.5 equiv CsOBz | **4a** | MeCN / Toluene | 0.20 | Low | <10 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 17 | 1.5 equiv CsOBz | **4a** | DMF / DMSO | 0.20 | >95 | Decomp. |
| 18 | 1.5 equiv CsOBz | **4a** | THF | 0.20 | >95 | 87 |
| 19 | 1.5 equiv CsOBz | **4a** | 1,4-Dioxane[f] | 0.10 | >95 | 84 |
| 20 | 1.5 equiv CsOBz | **4b** | THF | 0.20 | >95 | <5 |
| 21 | 1.5 equiv CsOBz | **4c** | THF | 0.20 | >95 | 75 |
| 22 | 1.5 equiv CsOBz | **4d** | THF | 0.20 | 75 | 44 |
| 23 | 1.5 equiv CsOBz | **4e** | THF | 0.20 | >95 | 52 |
| 24 | 1.5 equiv CsOBz | **4f** | THF | 0.20 | Low | <5 |
| 25 | 1.5 equiv CsOBz | **TsCN** | THF | 0.20 | Low | <10 |
| 26 | 1.5 equiv CsOBz | **BrCN** | THF | 0.20 | Low | <10 |
| 27 | 1.5 equiv CsOBz | **ICN** | THF | 0.20 | Low | <10 |
| 28 | 1.5 equiv CsOBz | **KCN** | THF | 0.20 | >95 | Decomp. |
| 29[g] | 1.5 equiv CsOBz | **4a** | THF | 0.20 | >95 | <5 |
| 30[h] | 1.5 equiv CsOBz | **4a** | THF | 0.20 | >95 | <5 |
| 31[i] | 1.5 equiv CsOBz | **4a** | THF | 0.20 | Low | <5 |

[a] The conversion of **5a** by NMR is given. [b]Isolated yield after preparative TLC. [c] Same conditions used for the decarboxylative alkynylation (3.0 equiv. CsOBz, no molecular sieves). [d]Using 1.1 equiv of CBX reagent. [e]Using 2.5 equiv of CBX reagent. [f] Solubility issue at 0.20 M. [g]In the dark [h]Without photocatalyst [i]Without base

**General procedure for decarboxylative cyanation.**



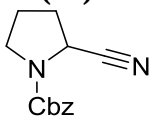

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the carboxylic acid **5** (0.30 mmol, 1.0 equiv), CBX reagent (**4a**) (123 mg, 0.450 mmol, 1.5 equiv), CsOBz (114 mg, 0.450 mmol, 1.5 equiv), 30 mg of heterogeneous powdered molecular sieves (4 ångström) and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (3 mg, 0.003 mmol, 0.01 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 4h30 to 18 h at rt.

After completion of the reaction, the reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. The crude product was then dissolved in DCM, and washed 3 times with saturated aqueous solution of $Na_2CO_3$. The joined organic layers are then washed with brine, dried with $MgSO_4$, filtered and evaporated under reduced

pressure. Final purification was performed by column chromatography (Pentane/Ethyl Acetate) affording the corresponding nitrile.

NB: The mentioned work-up was not applied for N-Fmoc protected amino-acids, which were directly submitted to column chromatography.

**Benzyl 2-cyanopyrrolidine-1-carboxylate (7a)**




Scope scale: Starting from **5a** (75 mg, 0.30 mmol), the crude product was extracted following the previously described work-up prior to being purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7a** as colorless oil (61 mg, 0.27 mmol, 89%).

1 mmol scale: Starting from **5a** (250 mg, 1.00 mmol), **using 1.1 mg of Iridium catalyst 6 (0.1 mol%) and 48 h of irradiation,** the crude product was extracted following the previously described work-up prior to being purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7a** as colorless oil (138 mg, 0.599 mmol, 60%).

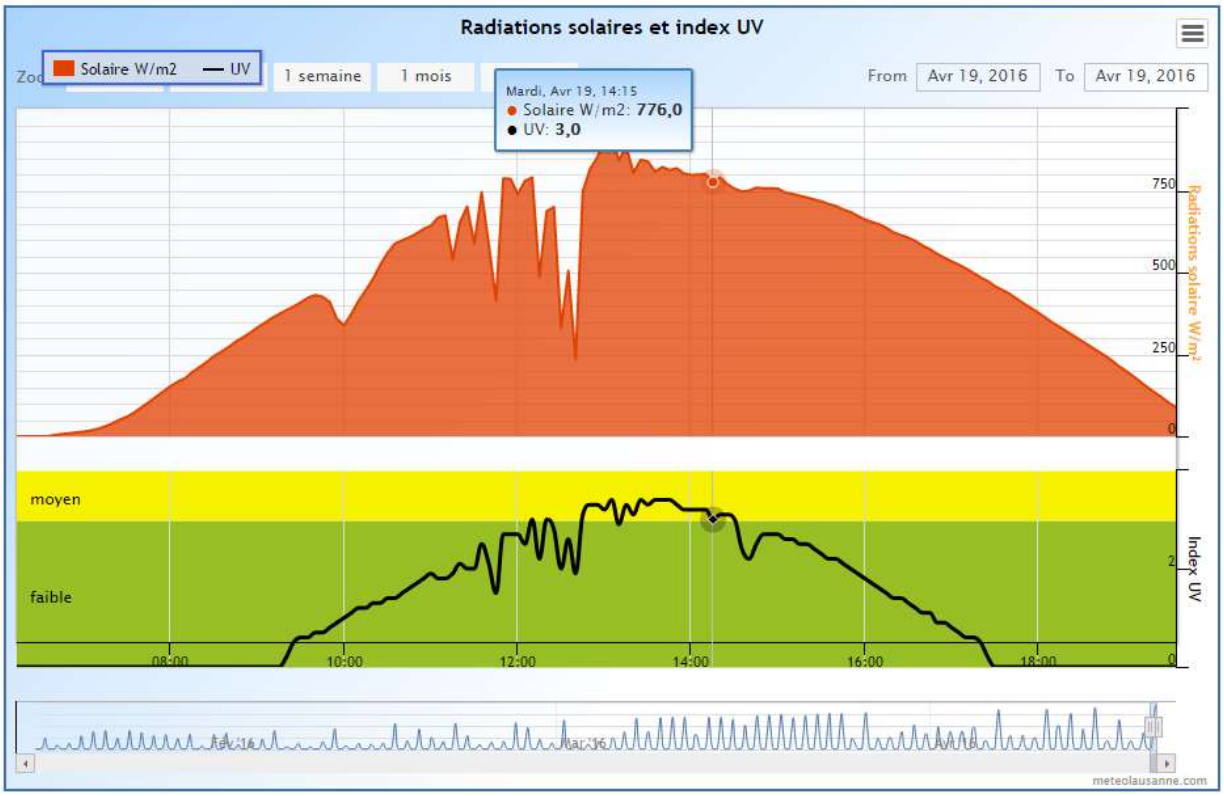
Sunlight experiment: Starting from **5a** (75 mg, 0.30 mmol), the reaction mixture was stirred for 4 h outdoors, under sunlight exposition instead of blue leds. The crude product was extracted following the previously described work-up prior to being purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7a** as colorless oil (62 mg, 0.27 mmol, 90%).

$R_f$: 0.35 (Pentane/Ethyl Acetate = 6:4). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.28 (m, 5H, Ar*H*), 5.26 – 5.11 (m, 2H, OC$H_2$Ph), 4.58 (ddd, *J* = 7.3, 2.7 Hz, 1H, NC*H*CN), 3.58 (tdd, *J* =

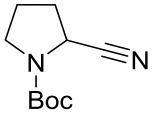
10.7, 7.4, 3.4 Hz, 1H, NC$H_2$CH$_2$), 3.42 (ddd, $J$ = 18.7, 9.7, 5.3 Hz, 1H, NC$H_2$CH$_2$), 2.34 – 1.96 (m, 4H, NCH$_2$C$H_2$C$H_2$CHCN). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.5, 135.9, 135.8, 128.5, 128.2, 128.0, 118.8, 118.6, 67.7, 67.5, 47.4, 46.9, 46.2, 45.8, 31.6, 30.67, 24.5, 23.6. IR 3607 (w), 3524 (w), 3410 (w), 3036 (w), 2960 (w), 2889 (w), 2244 (w), 1965 (w), 1706 (s), 1597 (w), 1540 (w), 1493 (w), 1410 (s), 1353 (s), 1266 (w), 1186 (m), 1120 (m), 1033 (w), 982 (w), 920 (w), 876 (w). HRMS (ESI) calcd for $C_{13}H_{14}N_2NaO_2^+$ $[M+Na]^+$ 253.0947; found 253.0962. The characterization data is in accordance with reported literature values.[17]

NB: Mixture of 2 rotamers with almost 1:1 ratio. They are not completely resolved.

The sunlight experiment took place in Lausanne (46°51' Nm 6°57' E), on April 19th 2016, from 14:00 to 18:00 with a light intensity of 400 to 800 W/m$^2$. Sun spectra during experiment:[18]




**Tert-butyl-2-cyanopyrrolidine-1-carboxylate (7b)**




[17] A. J. A. Cobb, D. M. Shaw, D. A. Longbottom, J. B. Gold, S. V. Ley *Org. Biomol. Chem*. **2005**, *3*, 84 – 96.
[18] Taken from: http://www.meteolausanne.com/soleil-et-uv.html

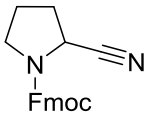
Starting from **5b** (65 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **7b** as colorless oil (50.7 mg, 0.258 mmol, 86%).

$R_f$: 0.40 (Pentane/Ethyl Acetate = 6:4). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.62 – 4.35 (m, 1H, NC*H*CN), 3.59 – 3.41 (m, 1H, NC$H_2$), 3.33 (ddd, *J* = 20.1, 14.3, 8.2 Hz, 1H, NC$H_2$), 2.33 – 1.90 (m, 4H, $NCH_2(CH_2)_2$), 1.47 (s, 9H, $^t$*Bu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 153.6 (m), 152.9 (major), 119.1, 81.4 (major), 80.9 (minor), 47.1 (major), 47.0 (minor), 45.9 (minor), 45.6 (major), 31.6 (major), 30.7 (minor), 28.2, 24.6 (minor), 23.7 (major). IR 2979 (w), 2889 (w), 2244 (w), 1703 (s), 1454 (w), 1391 (s), 1258 (w), 1167 (s), 1125 (m), 1036 (w), 982 (w), 921 (w), 872 (w).

The values of the NMR spectra are in accordance with reported literature data.[19]

NB: Mixture of 2 rotamers (major and minor) with a 1.5:1 ratio. They are not completely resolved.

**(9H-fluoren-9-yl)methyl-2-cyanopyrrolidine-1-carboxylate (7c)**



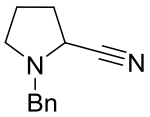

Starting from **5c** (65 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7c** as colorless oil (88 mg, 0.28 mmol, 92%).

$R_f$: 0.35 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.4, 1.1 Hz, 2H, Ar*H*), 7.66 (t, *J* = 6.8 Hz, 1H), 7.59 (t, *J* = 6.9 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.34 (dd, *J* = 7.4, 7.0 Hz, 2H, Ar*H*), 4.66 – 4.55 (m, 1H, NC*H*CN), 4.55 – 4.35 (m, 2H, OC$H_2$CHAr), 4.28 (app dt, *J* = 20.0, 6.8 Hz, 1H, $OCH_2CH$Ar), 3.58 (dddd, *J* = 15.1, 9.7, 7.2, 3.1 Hz, 1H, NC$H_2(CH_2)_2$CHCN), 3.51 – 3.31 (m, 1H, NC$H_2(CH_2)_2$CHCN), 2.40 – 1.98 (m, 4H, $NCH_2(CH_2)_2$CHCN). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.7, 143.8, 143.7, 143.6, 143.5, 141.3, 141.2, 127.8, 127.2, 127.1, 125.0, 124.9, 124.9, 120.0, 118.8, 118.6, 68.1, 67.8, 47.5, 47.1 (probably superposition of 2 signals), 46.9, 46.3, 45.8, 31.8, 30.7, 24.6, 23.6. IR 3062 (w), 2959 (w), 2890 (w), 2249 (w), 1707 (s), 1446 (m), 1414 (s), 1350 (m), 1263 (w), 1188 (m), 1123 (m), 1034 (w), 985 (w), 917 (w), 876 (w). HRMS (ESI) calcd for $C_{20}H_{18}N_2NaO_2^+$ $[M+Na]^+$ 341.1260; found 341.1271.

NB: Mixture of 2 rotamers with almost 1:1 ratio. They are not completely resolved.

**1-benzylpyrrolidine-2-carbonitrile (7d)**

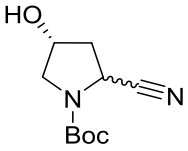
[19] S. Kamijo, T. Hoshikawa, M. Inoue, *Org. Lett.* **2011**, *13*, 5928.




Starting from **5d** (62 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7d** as colorless oil (24 mg, 0.13 mmol, 43%).

$R_f$: 0.32 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 5H, Ar*H*), 3.92 (d, *J* = 12.9 Hz, 1H, NC*H*$_2$Ph), 3.73 – 3.63 (m, 2H, NC*H*CN + NC*H*$_2$Ph), 2.94 (ddd, *J* = 9.5, 8.1, 4.2 Hz, 1H, NC*H*$_2$CH$_2$CH$_2$), 2.59 (td, *J* = 9.0, 7.6 Hz, 1H, NC*H*$_2$CH$_2$CH$_2$), 2.24 – 2.07 (m, 2H, NCH$_2$CH$_2$C*H*$_2$), 1.93 (m, 2H, NCH$_2$C*H*$_2$CH$_2$). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.6, 128.8, 128.5, 127.5, 118.0, 56.5, 53.2, 51.2, 29.5, 21.9. The values of the NMR spectra are in accordance with reported literature data. [20]

**Tert-butyl (4*R*)-2-cyano-4-hydroxypyrrolidine-1-carboxylate (7e)**



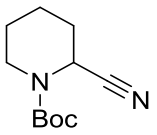

Starting from **5e** (69 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 6:4) to afford **7e** as colorless solid (57 mg, 0.27 mmol, 90%, 2:1 dr).

Major isomer:

MP: 143.5 – 155.5°C. $R_f$: 0.2 (Heptane/Ethyl Acetate = 5:5) $^1$H NMR (400 MHz, $CDCl_3$, *mixture of rotamers not fully resolved, about 2:1 major/minor*) δ 4.65 (d, *J* = 7.2 Hz, 0.4H, NC*H*CN + NCH$_2$C*H*OH), 4.61 – 4.50 (m, 1.6H, NC*H*CN + NCH$_2$C*H*OH), 3.59 (d, *J* = 11.9 Hz, 0.6H, NC*H*$_2$CHOH), 3.55 – 3.45 (m, 1.4H, NC*H*$_2$CHOH), 2.42 – 2.23 (m, 2H, NCH(CN)C*H*$_2$), 2.18 – 1.93 (bs, 1H, O*H*), 1.52 (s, 6H, *tBu*), 1.48 (s, 3H, *tBu*). $^{13}$C NMR (101 MHz, $CDCl_3$, *mixture of rotamers not fully resolved*) δ 153.6 (minor), 153.1 (major), 119.0, 81.9 (major), 81.4 (minor), 70.7 (minor), 69.6 (major), 54.7 (minor), 54.5 (major), 45.5 (major), 45.3 (minor), 39.3 (major), 38.8 (minor), 28.9. IR 3452 (w), 3292 (w), 2979 (w), 2939 (w), 2249 (w), 1697 (s), 1469 (w), 1402 (s), 1340 (w), 1260 (w), 1168 (s), 1126 (m), 1094 (w), 979 (w), 919 (w), 880 (w). HRMS (ESI) calcd for $C_{10}H_{16}N_2NaO_3^+$ $[M+Na]^+$ 235.1053; found 235.1050.

**Tert-butyl 2-Cyanopiperidine-1-carboxylate (7f)**

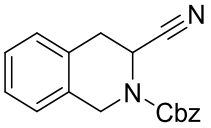
[20] J. Han, B. Xu, G. B. Hammond, *Org. Lett.* **2011**, *13*, 3450.




Starting from **5f** (69 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7f** as colorless solid (45 mg, 0.22 mmol, 72%).

$R_f$: 0.4 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 5.23 (bs, 1H, NC*H*CN), 4.05 (m, 1H, NC$H_2$), 2.93 (m, 1H, NC$H_2$), 1.93 (m, 1H, NCHC$H_2$), 1.86 – 1.76 (m, 1H, NCHC$H_2$), 1.77 – 1.61 (m, 3H, $NCH_2CH_2$ + $NCH_2CH_2CH_2$), 1.47 (s, 10H, *tBu* + $NCH_2CH_2CH_2$). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 154.0, 117.8, 81.4, 44.0, 41.4, 28.5, 28.4, 24.5, 20.3. IR 2945 (w), 2864 (w), 2243 (w), 1704 (s), 1455 (w), 1401 (s), 1327 (w), 1268 (m), 1165 (s), 1088 (w), 1036 (w), 993 (w), 928 (w), 869 (w). HRMS (ESI) calcd for $C_{11}H_{19}N_2O_2^+$ $[M+H]^+$ 211.1441; found 211.1442. The values of the NMR spectra are in accordance with reported literature data. [21]

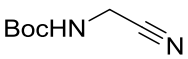
**Benzyl 3-cyano-3,4-dihydroisoquinoline-2(1H)-carboxylate (7g)**




Starting from **5g** (93 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7g** as colorless oil (57 mg, 0.20 mmol, 65 %).

$R_f$: 0.40 (Heptane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 5H, Ar*H*), 7.32 – 7.22 (m, 2H, Ar*H*), 7.22 – 7.09 (m, 2H, Ar*H*), 5.71 – 5.32 (m, 1H, NC*H*CN), 5.24 (s, 2H, C(O)OC$H_2$Ph)), 4.89 (d, *J* = 16.6 Hz, 1H, NC$H_2C_{Ar}$), 4.57 (d, *J* = 16.6 Hz, 1H, NC$H_2C_{Ar}$), 3.26 (dd, *J* = 16.1, 5.8 Hz, 1H, NCHC$H_2C_{Ar}$), 3.16 – 3.01 (m, 1H, NCHC$H_2C_{Ar}$). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 155.0, 135.6, 131.1, 129.6, 129.0, 128.6, 128.5, 128.3, 127.5, 127.3, 126.4, 117.4, 68.4, 43.7, 42.1, 32.3. IR 3064 (w), 3037 (w), 2956 (w), 2854 (w), 2244 (w), 1967 (w), 1708 (s), 1597 (w), 1498 (w), 1454 (w), 1409 (s), 1327 (m), 1226 (m), 1166 (w), 1123 (m), 1093 (w), 999 (m), 910 (w), 822 (w). HRMS (ESI) calcd for $C_{18}H_{17}N_2O_2^+$ $[M+H]^+$ 293.1285; found 293.1283.

**Tert-butyl (cyanomethyl)carbamate (7h)**



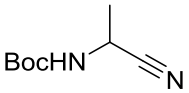

[21] a) T. Hoshikawa, S. Yoshioka, S. Kamijo, M. Inoue, *Synthesis*, **2013**, *45*, 0874. b) F.-Y. Tang, L.-Q. Qu, Y. Xu , R.-J. Ma, Dr. Shu-Hui Chen, G. Li, *Synthetic Communications*, **37**:*21*, 3793.

Starting from **5h** (53 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7h** as colorless oil (31 mg, 0.20 mmol, 66%).

$R_f$: 0.35 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.92 (bs, 1H, *NH*), 4.06 (bd, *J* = 6.1 Hz, 2H, *CH*$_2$), 1.46 (s, 9H, *tBu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.8, 116.5, 81.4, 34.1, 28.1. IR 3587 (w), 3355 (w), 2983 (w), 2939 (w), 2256 (w), 1704 (s), 1517 (s), 1374 (w), 1287 (s), 1255 (s), 1167 (s), 1052 (w), 941 (w), 859 (w). HRMS (ESI) calcd for $C_7H_{13}N_2O_2^+$ $[M+H]^+$ 157.0972; found 157.0970.

The values of the NMR spectra are in accordance with reported literature data.[22]

**Tert-butyl-(1-cyanoethyl)carbamate (7i)**

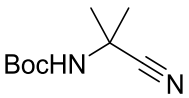



Starting from **5i** (57 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7i** as colorless oil (44 mg, 0.26 mmol, 86%).

$R_f$: 0.29 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.88 (bs, 1H, *NH*), 4.62 (bs, 1H, C*H*), 1.54 (d, *J* = 7.2 Hz, 3H, C*H*$_3$), 1.46 (s, 9H, *t*Bu). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.1, 119.5, 81.2, 37.6, 28.2, 19.6. IR 3668 (w), 3319 (m), 2986 (m), 2947 (m), 2906 (w), 2795 (w), 2249 (w), 1684 (s), 1533 (s), 1451 (w), 1374 (m), 1335 (m), 1302 (m), 1259 (s), 1165 (s), 1074 (m), 1036 (m), 913 (w), 866 (m). HRMS (ESI) calcd for $C_8H_{14}N_2NaO_2^+$ $[M+Na]^+$ 193.0947; found 193.0947.

The values of the NMR spectra are in accordance with reported literature data.[23]

**Tert-butyl (2-cyanopropan-2-yl)carbamate (7j)**



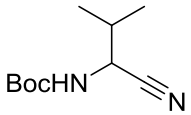

Starting from **5j** (61 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7j** as colorless oil (28 mg, 0.15 mmol, 51%).

$R_f$: 0.25 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.79 (s, 1H, N*H*), 1.66 (s, 6H, NC(*CH*$_3$)$_2$CN), 1.48 (s, 9H, *$^t$Bu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 153.6, 121.2, 81.3, 46.8, 28.2, 27.6. IR 3348 (m), 2982 (m), 2934 (w), 2246 (w), 1695 (s), 1515 (s), 1464 (w),

[22] a) V. V. Sureshbabu , S. A. Naik, G. Nagendra, *Synthetic Communications*, **2009**, *39*, 395-406
b) See also : J. C. Anderson, A. Flaherty, M. E. Swarbrick, *J. Org. Chem*. **2000**, *65*, 9152 - 9156
[23] J.-L. Zhu, F.-Y. Lee, J.-D. Wu, C.-W. Kuo, K.-S. Shia, *Synlett*, **2007**, *8*, 1317.

1373 (m), 1281 (s), 1169 (s), 1088 (m), 960 (w), 861 (w). HRMS (ESI) calcd for $C_9H_{16}N_2NaO_2^+$ $[M+Na]^+$ 207.1104; found 207.1107.

**Tert-butyl-(1-cyano-2-methylpropyl)carbamate (7k)**

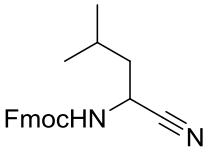



Starting from **5k** (65 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7k** as colorless solid (48 mg, 0.24 mmol, 80%).

$R_f$: 0.35 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.86 (br d, *J* = 9.5 Hz, 1H, *NH*), 4.46 (t, *J* = 7.9 Hz, 1H, BocNH*CH*), 2.11 – 1.91 (m, *J* = 6.7 Hz, 1H, C*H*$Me_2$), 1.46 (s, 9H, *tBu*), 1.09 (d, *J* = 7.0 Hz, 3H, CH*Me*$_2$), 1.07 (d, *J* = 7.0 Hz, 3H, CH*Me*$_2$). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.4, 118.0, 81.1, 48.4, 31.8, 28.2, 18.5, 17.9. IR 3341 (m), 2976 (m), 2934 (w), 2248 (w), 1701 (s), 1519 (s), 1374 (m), 1255 (m), 1168 (s), 1019 (w), 916 (w), 869 (w). HRMS (ESI) calcd for $C_{10}H_{18}N_2NaO_2^+$ $[M+Na]^+$ 221.1260; found 221.1261.

The values of the NMR spectra are in accordance with reported literature data.[24]

**(9H-fluoren-9-yl)methyl-(1-cyano-3-methylbutyl)carbamate (7l)**




Starting from **5l** (106 mg, 0.300 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 10:2) to afford **7l** as white solid (82 mg, 0.24 mmol, 82%).

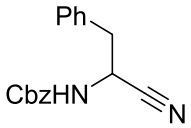
$R_f$: 0.30 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.57 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.41 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.32 (t, *J* = 7.4 Hz, 2H, Ar*H*), 5.16 – 5.05 (m, 1H, N*H*), 4.72 – 4.67 (m, 0.2H, C*H*CN), 4.63 (dd, *J* = 8.0 Hz, 0.80H, C*H*CN), 4.49 (d, *J* = 6.7 Hz, 2H, -OC*H*$_2$CH), 4.21 (t, *J* = 6.7 Hz, 1H, -OCH$_2$C*H*), 1.87 – 1.58 (m, 3H, C*H*$_2$C*H*$Me_2$), 0.97 (d, *J* = 6.4 Hz, 6H, CH$_2$CH*Me*$_2$) $^{13}$C NMR (100 MHz, $CDCl_3$) δ 155.1, 143.4, 141.3, 127.8, 127.1, 124.8, 120.0, 118.7, 67.3, 47.0, 42.0, 41.2, 24.7, 22.1, 21.8. IR 3664 (w), 3326 (m), 3060 (w), 2961 (m), 2877 (w), 2249 (w), 1954 (w), 1918 (w), 1709 (s), 1525 (s), 1456 (m), 1326 (m), 1252 (s), 1168 (w), 1120 (w), 1041 (m), 916 (w), 866 (w). HRMS (ESI) calcd for $C_{21}H_{22}N_2NaO_2^+$ $[M+Na]^+$ 357.1573; found 357.1576

[24] J. E. Mangette, M. R. Johnson, V.-D. Le, R. A. Shenoy, H. Roark, M. Stier, T. Belliotti, T. Capiris, P. R. Guzzo, *Tetrahedron*, **2009**, *65*, 9536.

The values of the NMR spectra are in accordance with reported literature data, with small differences in chemical shifts. [25]

NB: Mixture of rotamers not completely resolved.

**Benzyl-(1-cyano-2-phenylethyl)carbamate (7m)**

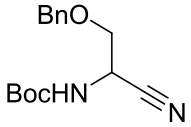



Starting from **5m** (90 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 10:2) to afford **7m** as white solid (66 mg, 0.24 mmol, 78%).

$R_f$: 0.37 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 8H, Ar*H*), 7.29 – 7.23 (m, 2H, Ar*H*), 5.12 (s, 3H, OC$H_2$Ph + N*H*), 4.89 (dd, *J* = 7.3 Hz, 1H, C*H*CN), 3.09 (dd, *J* = 13.8, 6.5 Hz, 2H, NCHC$H_2$Ph). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.9, 135.5, 133.5, 129.4, 129.0, 128.6, 128.5, 128.3, 128.0, 118.0, 67.7, 43.7, 38.9. IR 3322 (m), 3038 (w), 2963 (w), 2783 (w), 2245 (w), 1957 (w), 1887 (w), 1810 (w), 1701 (s), 1531 (s), 1451 (w), 1260 (s), 1151 (w), 1042 (m), 986 (w), 910 (w), 819 (w). HRMS (ESI) calcd for $C_{17}H_{16}N_2NaO_2^+$ $[M+Na]^+$ 303.1104; found 303.1113

The characterization data is in accordance with reported literature values.[26]

***Tert*-butyl (2-(benzyloxy)-1-cyanoethyl)carbamate (7n)**



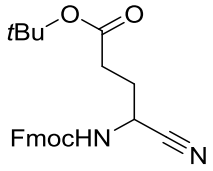

Starting from **5n** (89 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 10:2) to afford **7n** as colorless oil (66 mg, 0.24 mmol, 80%).

$R_f$: 0.45 (Pentane/Ethyl Acetate = 6:4). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 5H, Ar*H*), 5.31 (d, *J* = 9.0 Hz, 1H, N*H*), 4.81 – 4.68 (m, 1H, NC*H*CN), 4.62 (s, 2H, OC$H_2$Ph), 3.72 (dd, *J* = 9.8, 3.6 Hz, 1H, NCHC$H_2$O), 3.64 (dd, *J* = 9.7, 4.2 Hz, 1H, NCHC$H_2$O), 1.46 (s, 9H, $^t$*Bu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.3, 136.7, 128.6, 128.2, 127.8, 117.6, 81.3, 73.6, 69.0, 42.5, 28.2. IR 3659 (w), 3337 (w), 2979 (m), 2935 (w), 2875 (w), 2252 (w), 1711 (s), 1506 (s), 1464 (w), 1366 (m), 1289 (m), 1253 (m), 1165 (s), 1114 (m), 1022 (w), 913 (w), 871 (w). HRMS (ESI) calcd for $C_{15}H_{20}N_2NaO_3^+$ $[M+Na]^+$ 299.1366; found 299.1372

The characterization data is in accordance with reported literature values.[20]

[25] C. Madhu, N. R. Panguluri, N. N., Panduranga V. V. V. Sureshbabu, *Tetrahedron Lett.* **2014**, *55*, 6831.
[26] C. T. Hoang, V. Alezra, R. Guillot, C. Kouklovsky, *Org. Lett.* **2007**, *9*, 2521.

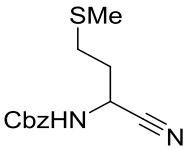
***Tert*-butyl 4-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-cyanobutanoate (7o)**




Starting from **5o** (128 mg, 0.300 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7o** as white solid (80 mg, 0.20 mmol, 66%).

Mp: 74-76°C. $R_f$: 0.25 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.77 (dt, *J* = 7.6, 0.9 Hz, 2H, Ar*H*), 7.57 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.45 – 7.36 (m, 2H, Ar*H*), 7.36 – 7.28 (m, 2H, Ar*H*), 5.66 (d, *J* = 8.4 Hz, 1H, N*H*), 4.68 (app q, *J* = 7.5 Hz, 1H, NC*H*CN), 4.47 (m, 2H, OC$H_2$CHAr), 4.21 (t, *J* = 7.0 Hz, 1H, OCH$_2$C*H*Ar), 2.45 (m, 2H, BocC$H_2$CH$_2$), 2.12 (app q, *J* = 6.9 Hz, 2H, BocCH$_2$C$H_2$), 1.46 (s, 9H, $^t$*Bu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 171.5, 155.6, 143.4, 141.3, 127.8, 127.1, 124.9, 120.0, 118.0, 81.7, 67.4, 47.0, 42.3, 31.1, 28.0, 27.9. IR 3331 (w), 2978 (w), 2253 (w), 1721 (s), 1524 (m), 1452 (m), 1374 (w), 1327 (w), 1250 (s), 1157 (s), 1047 (w), 952 (w), 913 (w), 849 (w). HRMS (ESI) calcd for $C_{24}H_{26}N_2NaO_4^+$ $[M+Na]^+$ 429.1785; found 429.1798.

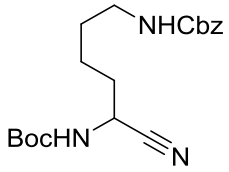
**Benzyl (1-cyano-3-(methylthio)propyl)carbamate (7p)**




Starting from **5p** (85 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7p** as white solid (47 mg, 0.18 mmol, 59%).

Mp: 57-58°C $R_f$: 0.15 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.31 (m, 5H, Ar*H*), 5.37 (s, 1H, N*H*), 5.15 (s, 2H, OC$H_2$Ph), 4.85 (dd, *J* = 8.1, 7.7 Hz, 1H, NC*H*CN), 2.66 (t, *J* = 6.9 Hz, 2H, NCHC$H_2$CH$_2$S), 2.11 (m, 5H, NCHC$H_2$CH$_2$S + S*Me*).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 155.0, 135.5, 128.6, 128.5, 128.3, 118.0, 67.8, 41.9, 32.1, 29.6, 15.5. IR 3321 (m), 3038 (w), 2924 (w), 2349 (w), 2250 (w), 1963 (w), 1712 (s), 1522 (s), 1444 (w), 1331 (w), 1250 (s), 1142 (w), 1053 (m), 974 (w), 914 (w). HRMS (ESI) calcd for $C_{13}H_{17}N_2O_2S^+$ $[M+H]^+$ 265.1005; found 265.1009

**Benzyl *tert*-butyl (1-cyanopentane-1,5-diyl)dicarbamate (7q)**

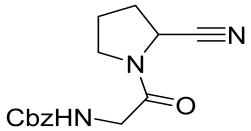



Starting from **5q** (114 mg, 0.300 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 6:2) to afford **7q** as white solid (90 mg, 0.25 mmol, 83%).

$R_f$: 0.3 (Pentane/Ethyl Acetate = 6:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H, Ar*H*), 5.16 (d, *J* = 8.6 Hz, 1H, BocN*H*), 5.09 (s, 2H, OC$H_2$Ar), 4.90 (bs, *J* = 6.2 Hz, 1H, CbzN*H*), 4.50 (app q, *J* = 7.9 Hz, 1H, BocNHC*H*CN), 3.20 (m, 2H, CbzNHC$H_2$), 1.81 (m, 2H, CbzNHCH$_2$(CH$_2$)$_2$C$H_2$), 1.53 (m, 4H, CbzNHCH$_2$(C$H_2$)$_2$), 1.45 (s, 9H, $^t$*Bu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 156.6, 154.4, 136.4, 128.8, 128.5, 128.1, 118.8, 81.1, 66.7, 42.0, 40.1, 32.5, 29.1, 28.2, 22.2. IR 3665 (w), 3327 (w), 2975 (w), 2941 (w), 2876 (w), 2248 (w), 1698 (s), 1523 (s), 1455 (w), 1368 (w), 1252 (s), 1165 (m), 1020 (w), 913 (w), 863 (w). HRMS (ESI) calcd for $C_{19}H_{27}N_3NaO_4^+$ $[M+Na]^+$ 384.1894; found 384.1896

The values of the NMR spectra are in accordance with reported literature data. [27]

**Benzyl (2-(2-cyanopyrrolidin-1-yl)-2-oxoethyl)carbamate (7r)**




Starting from **5r** (92 mg, 0.30 mmol), the crude product was purified by column chromatography (Full DCM to DCM/Acetone = 92:8) to afford **7r** as yellowish oil (49 mg, 0.17 mmol, 56%).

$R_f$: 0.22 (DCM/Acetone = 95:5). $^1$H NMR (400 MHz, $CDCl_3$, mixture of rotamers (major/minor)) δ 7.39 – 7.27 (m, 5H, Ar*H*), 5.80 (s, 0.9H, N*H* (major)), 5.60 (s, 0.1H, N*H* (minor)), 5.14 (s, 0.2H, OC$H_2$Ph (minor)), 5.11 (s, 1.8H, OC$H_2$Ph (major)), 4.80 – 4.69 (m, 0.9H, NC*H*CN (major)), 4.66 (m, 0.1H, NC*H*CN (minor)), 4.18 (m, 0.1H, NC(O)C$H_2$NHCbz (minor)), 4.11 – 3.87 (m, 1.9H, NC(O)C$H_2$NHCbz, (major+minor)), 3.73 – 3.63 (m, 0.1H, NC$H_2$(CH$_2$)$_2$CHCN (minor)), 3.63 – 3.54 (m, 0.9H, NC$H_2$(CH$_2$)$_2$CHCN (major)), 3.49 (m, 0.1H, NC$H_2$(CH$_2$)$_2$CHCN (minor)), 3.41 (m, 0.9H, NC$H_2$(CH$_2$)$_2$CHCN (major)), 2.37 (m, 0.2H, NCH$_2$(C$H_2$)$_2$CHCN (minor)), 2.34 – 2.04 (m, 3.8H, NCH$_2$(C$H_2$)$_2$CHCN (minor+ major)). $^{13}$C NMR (100 MHz, $CDCl_3$, only major rotamer) δ 167.5, 156.3, 136.2, 128.4, 128.1, 127.9, 117.9, 66.9, 46.5, 45.4, 43.4, 29.8, 25.0. IR 3334 (w), 3037 (w), 2956 (w), 2885 (w), 2245 (w), 1722 (s), 1664 (s), 1529 (m), 1442 (s), 1330 (w), 1250 (s), 1168 (w), 1055 (m),

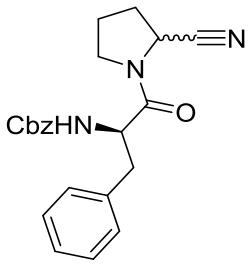
[27] C. Madhu, N. R. Panguluri, N. N., Panduranga V. V. V. Sureshbabu, *Tetrahedron Lett.* **2014**, *55*, 6831.

992 (w), 916 (w), 832 (w). HRMS (ESI) calcd for $C_{15}H_{17}N_3NaO_3^+$ $[M+Na]^+$ 310.1162; found 310.1167.

The values of the NMR spectra are in accordance with reported literature data. [28]

NB: Mixture of rotamers, NMR ratio of 10:1.

**Benzyl ((2*R*)-1-(2-cyanopyrrolidin-1-yl)-1-oxo-3-phenylpropan-2-yl)carbamate (7s)**




Starting from **5s** (119 mg, 0.300 mmol), the crude product was purified by column chromatography (Full DCM to DCM/Acetone = 92:8) to afford **7s** as colorless oil (62 mg, 0.16 mmol, 55%; obtained as a mixture of diastereoisomers (Major:minor = 1.2:1). The major diastereoisomer was generated as a mixture of inseparable rotamers (ratio: 56 : 44). The minor product could be partially isolated in ca. 95% purity).

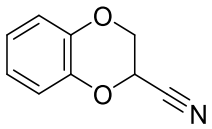
$R_f$: 0.22 (major) 0.20 (minor) (DCM/Acetone = 95:5). $^1$H NMR (400 MHz, $CDCl_3$.) δ 7.37-7.29 (m, 5 H, (minor+major), ArH), 7.25 (m, 3.5 H, (minor + major), ArH), 7.21-7.14 (m, 1.5 H, (minor + major)), 5.69 (d, *J* = 8.5 Hz, 0.75 H, N*H*, (minor + major)), 5.45 (d, *J* = 7.8 Hz, 0.25 H, N*H*, major (rotamer 1)), 5.32 (d, *J* = 6.8 Hz, 0.25 H, major (rotamer 2)), 5.11 (m, 1.5 H, (minor + major)), 5.04-4.94 (m, 0.25 H, major), 4.68-4.62 (m, 1 H, (minor + major)), 4.58 (m, 0.25 H, (minor)), 4.50 (dd, *J* = 7.8, 2.1 Hz, 0.75 H, major), 3.60-3.50 (m, 0.75 H, major), 3.35 (m, 0.25 H, minor), 3.24 (dd, *J* = 14.0, 5.1 Hz, 0.25 H, major), 3.10-3.05 (m, 1 H, (minor + major)), 2.96 (m, 0.75 H, major), 2.58 (m, 0.25 H, minor), 2.50 (m, 0.75 H, major), 2.38-2.22 (m, 0.25 H, major), 2.18-2.07 (m, 1.25 H, (minor + major)), 2.00 (m, 1 H, (minor + major)), 1.94-1.87 (m, 0.25 H, minor), 1.82-1.68 (m, 1.25 H (minor + major) (overlap with impurity)). $^{13}$C NMR (101 MHz, Chloroform-*d*, signals are not fully resolved) δ 171.1, 170.6, 170.4, 156.2, 155.6, 155.5, 136.1, 135.8, 135.4, 129.5, 129.4, 129.3, 128.8, 128.7, 128.5, 128.1, 128.0, 127.8, 127.3, 127.2, 127.1, 118.6, 117.8, 117.5, 67.1, 67.0, 54.2, 54.1, 47.4, 46.3, 46.1, 46.1, 46.0, 40.0, 38.0, 32.2, 29.8, 29.7, 24.9, 24.6, 23.0. IR 3516 (w), 3307 (m), 3060 (w), 3033 (w), 2956 (w), 2887 (w), 2249 (w), 1961 (w), 1713 (s), 1651 (s), 1522 (m), 1439 (s), 1335 (m), 1249 (s), 1151 (w), 1053 (m), 914 (m). HRMS (ESI) calcd for $C_{22}H_{23}N_3NaO_3^+$ $[M+Na]^+$ 400.1632; found 400.1632.

[28] J. Lawandi, S. Toumieux, V. Seyer, P. Campbell, S. Thielges, L. Juillerat-Jeanneret, N. Moitessier, *J. Med. Chem.* **2009**, *52*, 6672.

Characterization data for the minor diastereoisomer:

$^1$H NMR (400 MHz, Chloroform-*d*) δ 7.34 (m, 7H, Ar*H*), 7.30 – 7.16 (m, 3H, Ar*H*), 5.69 (d, *J* = 8.6 Hz, 1H, N*H*), 5.19 – 5.00 (m, 2H, OC*H*$_2$Ph), 4.67 (dd, *J* = 7.9, 3.0 Hz, 1H, NC*H*CN), 4.58 (m, 1H, NC(O)C*H*NHCbz), 3.36 (td, *J* = 9.2, 6.9 Hz, 1H, NC*H*$_2$(CH$_2$)$_2$CHCN), 3.11 – 2.99 (m, 2H, NHCHC*H*$_2$Ph), 2.59 (m, 1H, NC*H*$_2$(CH$_2$)$_2$CHCN), 2.17 – 1.95 (m, 2H, NCH$_2$CH$_2$C*H*$_2$CHCN), 1.95 – 1.71 (m, 2H, NCH$_2$C*H*$_2$CH$_2$CHCN). $^{13}$C NMR (100 MHz, Chloroform-*d*) δ 170.6, 155.6, 136.1, 135.4, 129.5, 128.8, 128.5, 128.2, 128.0, 127.3, 117.5, 67.0, 54.1, 46.2, 46.0, 40.1, 29.7, 24.9. IR 3534 (w), 3304 (w), 3060 (w), 3034 (w), 2957 (w), 2887 (w), 2249 (w), 1962 (w), 1714 (s), 1651 (s), 1526 (m), 1442 (s), 1335 (m), 1249 (s), 1154 (w), 1050 (m), 914 (w).

**2,3-Dihydrobenzo[b][1,4]dioxine-2-carbonitrile (7v)**




Starting from **5v** (54 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **7v** as colorless solid (34 mg, 0.21 mmol, 70%).

$R_f$: 0.4 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.89 (m, 4H, Ar*H*), 5.12 (dd, *J* = 3.7, 2.5 Hz, 1H, C*H*CN), 4.42 (dd, *J* = 11.8, 3.7 Hz, 1H, OC*H*$_2$CHCN), 4.35 (dd, *J* = 11.8, 2.6 Hz, 1H, OC*H*$_2$CHCN). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.3, 140.4, 123.2, 122.6, 117.8, 117.7, 114.7, 64.6, 61.8. IR 3656 (w), 3053 (w), 2980 (w), 2934 (w), 2885 (w), 2224 (w), 1764 (w), 1600 (w), 1496 (s), 1312 (m), 1260 (s), 1190 (w), 1118 (w), 1083 (s), 1018 (w), 931 (w), 883 (w), 832 (w).

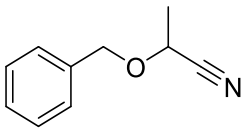
The values of the NMR spectra are in accordance with reported literature data. [29]

Gram scale reaction

Starting from **5v** (1.0 g, 5.6 mmol), the reaction was irradiated for 36h. Then the crude product was extracted following the previously described work-up prior to being purified by column chromatography (twice, Pentane/Ethyl Acetate = 9:1) to afford **7v** as colorless solid (395 mg, 2.45 mmol, 44%).

**2-(Benzyloxy)propanenitrile (7w)**

[29] C. Bolchi, E. Valoti, V. Straniero, P. Ruggeri, M. Pallavicini, *J. Org. Chem.* **2014**, *79*, 6732.

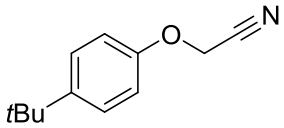


Starting from **5w** (54 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl acetate = 8:2) to afford **7w** as colorless liquid (32 mg, 0.20 mmol, 66%).

$R_f$: 0.45 (Pentane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.29 (m, 5H, Ar*H*), 4.85 (d, *J* = 11.6 Hz, 1H, OC$H_2$Ph), 4.54 (d, *J* = 11.5 Hz, 1H, OC$H_2$Ph), 4.26 (q, *J* = 6.8 Hz, 1H, OC*H*CN), 1.59 (d, *J* = 6.8 Hz, 3H, *Me*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 135.9, 128.6, 128.4, 128.2, 118.8, 72.1, 63.2, 19.8. IR 3068 (w), 3035 (w), 2998 (w), 2938 (w), 2875 (w), 2241 (w), 1967 (w), 1889 (w), 1754 (w), 1599 (w), 1498 (w), 1456 (w), 1386 (w), 1330 (w), 1259 (w), 1212 (w), 1115 (s), 1071 (m), 1017 (m), 911 (w), 876 (w).

The values of the NMR spectra are in accordance with reported literature data. [30]

**2-(4-(Tert-butyl)phenoxy)acetonitrile (7x)**



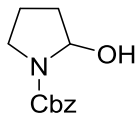
Starting from **5x** (62 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 8:2) to afford **7x** as colorless oil (21 mg, 0.11 mmol, 37%).

$R_f$: 0.25 (Pentane/Ethyl Acetate = 9:1). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.9 Hz, 2H, Ar*H*), 6.92 (d, *J* = 8.9 Hz, 2H, Ar*H*), 4.75 (s, 2H, OC$H_2$CN), 1.31 (s, 9H, *tBu*). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.3, 146.0, 126.7, 115.3, 114.5, 53. 8, 34.2, 31.4.

The values of the NMR spectra are in accordance with reported literature data.[31]

**Side product obtained in presence of water:**

**Benzyl 2-hydroxypyrrolidine-1-carboxylate (8)**

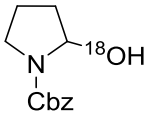


Isolated from the reaction mixture during the optimization (0.10 mmol scale). Reaction without molecular sieves furnished this side product in various amounts depending on the dryness of the reagents and the solvent. Purification by preparative TLC (Heptane/Ethyl Acetate = 6:4) afforded **8** as a colorless oil (10 mg, 90% purity, 0.041 mmol, 41%).

[30] C. Lu, X. Su, P. E. Floreancig, *J. Org. Chem.* **2013**, *78*, 9366.
[31] J. L. Barkin, M. D. Faust Jr., W. C. Trenkle, *Org. Lett.* **2003**, *5*, 3333.

$R_f$: 0.20 (Heptane/Ethyl Acetate = 8:2). $^1$H NMR (400 MHz, Chloroform-*d*, mixture of rotamers partially resolved, 2:1 ratio) δ 7.42 – 7.29 (m, 5H, Ar*H*), 5.52 (m, 1H, NC*H*OH), 5.17 (m, 2H, OC$H_2$Ph), 3.60 (m, 1H, NC$H_2$($CH_2$)$_2$), 3.35 (m, 1H, NC$H_2$($CH_2$)$_2$), 2.23 – 1.73 (m, 4H, NC$H_2$(C$H_2$)$_2$). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 155.8, 155.4, 136.4, 128.5, 128.1, 127.9, 82.2, 81.3, 67.1, 67.0, 46.2, 45.8, 33.6, 32.7, 22.8, 22.0. HRMS (ESI) calcd for $C_{12}H_{15}NO_3Na$: [M+Na] = 244.0950, found 244.0951. The values of the NMR spectra are in accordance with reported literature data.[32]

**Labelling experiment with $^{18}$O-water ($^{18}$O-labelled-8)**




Dry degassed THF (1.0 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the Cbz-Pro-OH **5a** (50 mg, 0.20 mmol, 1.0 equiv), CBX reagent (82 mg, 0.30 mmol, 1.5 equiv), CsOBz (76 mg, 0.30 mmol, 1.5 equiv) and Ir(dF($CF_3$)ppy)$_2$(dtbbpy)$PF_6$ (**6**) (2.2 mg, 0.0020 mmol, 0.01 equiv) under $N_2$ (vaccum / $N_2$ exchange). At this time, 36 µL of $^{18}$O-water (10 equiv, 97% atom $^{18}$O) was added by Hamilton syringe. The reaction mixture was degassed by freeze-pump-thaw cycle (3 times) before being irradiated using blue light LEDs for 10 h at rt.

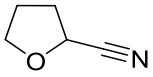
After completion of the reaction, the reaction mixture was filtered using HPLC filter. An HRMS sample was diluted with dry acetonitrile.

Caution: classical filtration using silica gel leads to fast isotopic exchange of the hemiaminal. The labelled product was only observed when the reaction mixture was filtered using dry HPLC filter. NMR analysis showed formation of this side product in a 1:0.08 ratio in favor of nitrile **5a**.

HRMS (ESI): calcd for $C_{12}H_{15}N[^{16}O]_2[^{18}O]Na$: [M+Na] = 246.0992, found 246.0988.

According to the HRMS spectra, the distribution between **8** and **$^{18}$O-labelled-8** is 23:77, meaning incorporation is 77%.

**THF-2-carbonitrile (9)**




[32] A. Piperno, C. Carnovale, S. V. Giofrè, D. Iannazzo, *Tetrahedron Lett.* **2011**, *52*, 6880.

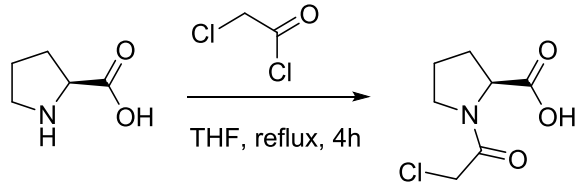
Observed as side product when reaction is performed in THF. For most of the reaction, a 10:1 NMR ratio between the nitrile product **7** and THF-2-carbonitrile (**9**) is observed in the crude mixture at the end of the reaction.

$^1$H NMR (400 MHz, Chloroform-*d*) δ 4.70 (dd, *J* = 6.8, 4.9 Hz, 1H, CHOCN), 4.07 – 3.88 (m, 2H, $CH_2O$), 2.29-2.23 (m, 2H, $CH_2$), 2.08-1.92 (m, 2 H, $CH_2$). The values of the $^1$H NMR spectra are in accordance with reported literature data.[33] The crude reaction spectrum is added in the spectra section.

[33] T. Hoshikawa, S. Yoshioka, S. Kamijo, M. Inoue, *Synthesis* **2013**, *45*, 874.

## 5. Derivatization: Synthesis of a Vildagliptin precursor

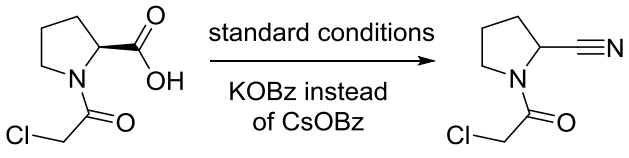
**(2-Chloroacetyl)-L-proline (5z)**




**46** **5z**

Following a reported procedure,[34] In a 250 mL double-neck round bottom flask, the L-Proline (**46**) (10.0 g, 87.0 mmol) was dissolved in THF (100 mL),and chloroacetyl chloride (10.5 mL, 132 mmol) was slowly added for 15 min in ice-bath. After the addition, the reaction mixture was heated to 90 °C stirring for 2.5 h. After full conversion (controlled by TLC (25% MeOH-$CH_2Cl_2$)) the reaction was quenched with water (30 mL) and stirred for additional 20 min. Saturated brine (30 mL) and ethyl acetate (50 mL) were added and the organic layer was collected. The aqueous layer was extracted again with ethyl acetate (3x20 mL). The combined organic extracts were dried over anhydrous $Na_2SO_4$ and concentrated under vacuum. The honey-like residue was recrystallized in diisopropyl ether (30 mL) for 0.5 h at room temperature and the mixture was then cooled to 0 °C for 24 h. The precipitated crystalline white solid was filtered, washed with cold diisopropyl ether and dried at 50 °C under vacuum to obtain compound **5z** (14.1 g, 73.4 mmol, 85 %); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.07 (bs, 1H, COO*H*), 4.58 (dd, *J* = 7.9, 3.6 Hz, 1H, NC*H*COOH), 4.14 – 4.05 (m, 2H, C$H_2$Cl), 3.74 – 3.60 (m, 2H, NC$H_2$), 2.40 – 1.79 (m, 4H, $NCH_2(CH_2)_2CHCOOH$). The values of the NMR spectra are in accordance with reported literature data.[32]

**1-(2-Chloroacetyl)pyrrolidine-2-carbonitrile (7z)**




**5z** **7z**

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the carboxylic acid **5z** (57 mg, 0.30 mmol, 1.0 equiv), CBX reagent (123 mg, 0.450 mmol, 1.5 equiv), KOBz (72 mg, 0.45 mmol, 1.5 equiv), 30 mg of heterogeneous powdered molecular sieves (4 ångström) and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (7 mg, 0.006 mmol, 0.02 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again

[34] W., Haibo, S. Guangjun, L. Xinmiao, K. Yanxiong, *Chin. J. Chem.* **2012**, *30*, 2791 - 2797

degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 6 h at rt.

After completion of the reaction, the reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. Final purification was performed by column chromatography (Pentane/Ethyl Acetate = 1:1) affording the corresponding nitrile **7z** (22 mg, 0.13 mmol, 42%).

$R_f$: 0.20 (Pentane/Ethyl Acetate = 1:1). $^1$H NMR (400 MHz, $CDCl_3$) δ 4.86 (dd, *J* = 7.7, 2.2 Hz, 0.15H, NC*H*CN), 4.81 – 4.71 (m, 0.85H, NC*H*CN), 4.27 – 4.10 (m, 0.3H, C$H_2$Cl), 4.06 (d, *J* = 1.7 Hz, 1.7H, C$H_2$Cl), 3.76 – 3.74 (m, 0.15H, NC$H_2$($CH_2$)$_2$), 3.74 – 3.68 (m, 0.85H, NC$H_2$($CH_2$)$_2$), 3.66 – 3.55 (m, 0.85H, NC$H_2$($CH_2$)$_2$), 3.57 – 3.47 (m, 0.15H, NC$H_2$($CH_2$)$_2$), 2.42 (m, 0.15H, NC$H_2$(C$H_2$)$_2$), 2.37 – 2.26 (m, 1.85H, NC$H_2$(C$H_2$)$_2$), 2.26 – 2.17 (m, 1.85H, NC$H_2$(C$H_2$)$_2$), 2.17 – 2.08 (m, 0.15H, NC$H_2$(C$H_2$)$_2$). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 165.2 (major), 164.8 (minor), 117.8 (not resolved), 47.0 (minor), 46.9 (major), 46.8 (minor), 46.5 (major), 41.5 (not resolved), 32.5 (minor), 30.0 (major), 25.2 (major), 22.8 (minor). IR 3513 (w), 2993 (w), 2959 (w), 2887 (w), 2247 (w), 1668 (s), 1421 (s), 1341 (w), 1274 (w), 1193 (w), 1155 (w), 1104 (w), 1048 (w), 1009 (w), 920 (w), 877 (w), 841 (w). HRMS (ESI) calcd for $C_7H_{10}ClN_2O^+$ $[M+H]^+$: 173.0476; found: 173.0474.

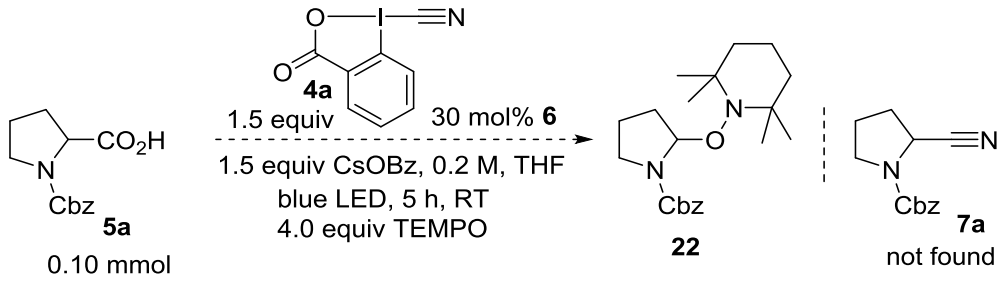
NB: Mixture of rotamers (major/minor ratio 1:0.2), which are not completely resolved.

The values of the NMR spectra are in accordance with reported literature data.[35]

[35] L. Pellegatti, J. Sedelmeier, *Org. Process Res. Dev.* **2015**, *19*, 551-

## 6. Mechanism investigations.

**Procedure for radical trap experiment in the decarboxylative cyanation**



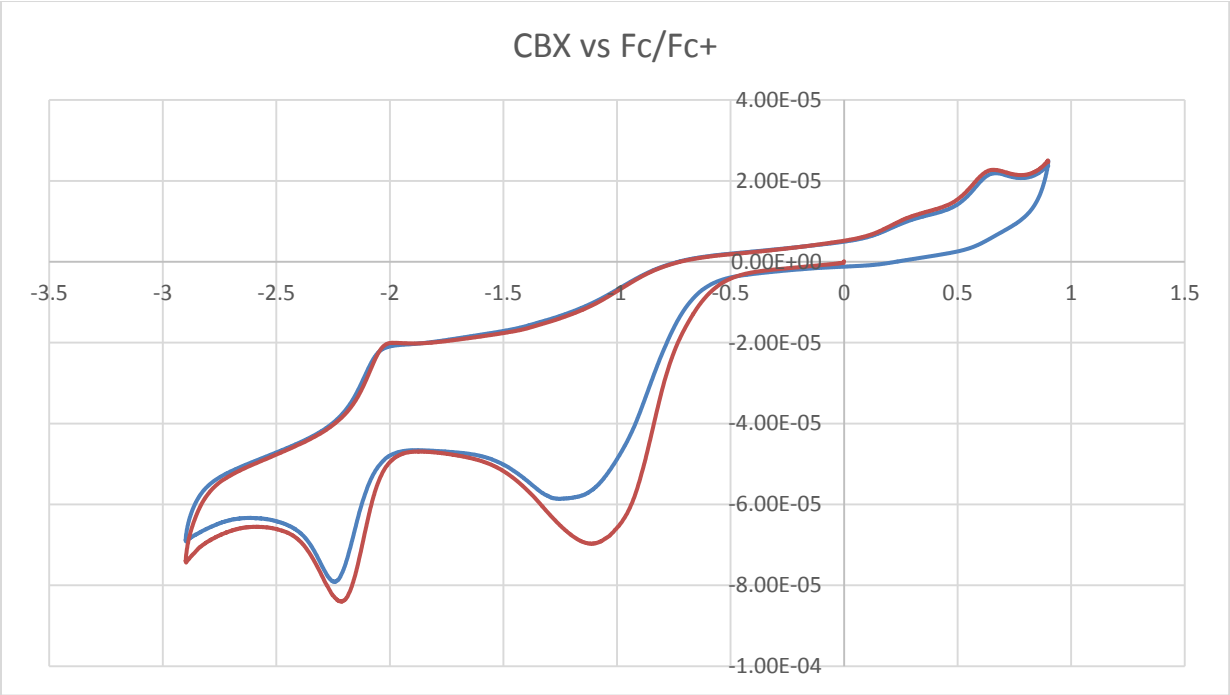

Dry degassed THF (0.5 mL) was added in a flame dried 1.5 mL test tube containing a teflon coated stirring bar, the carboxylic acid **5a** (0.10 mmol, 1.0 equiv), CBX reagent **4a** (0.15 mmol, 1.5 equiv), CsOBz (0.15 mmol, 1.5 equiv), TEMPO (0.60 mmol, 4.0 equiv) and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (0.030 mmol, 0.30equiv) under $N_2$. The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 5 h at rt.

Then a small amount was filtered several time through HPLC filter, before being submitted to MS analysis. Nitrile was not found. TEMPO adduct **22** was found by mass.

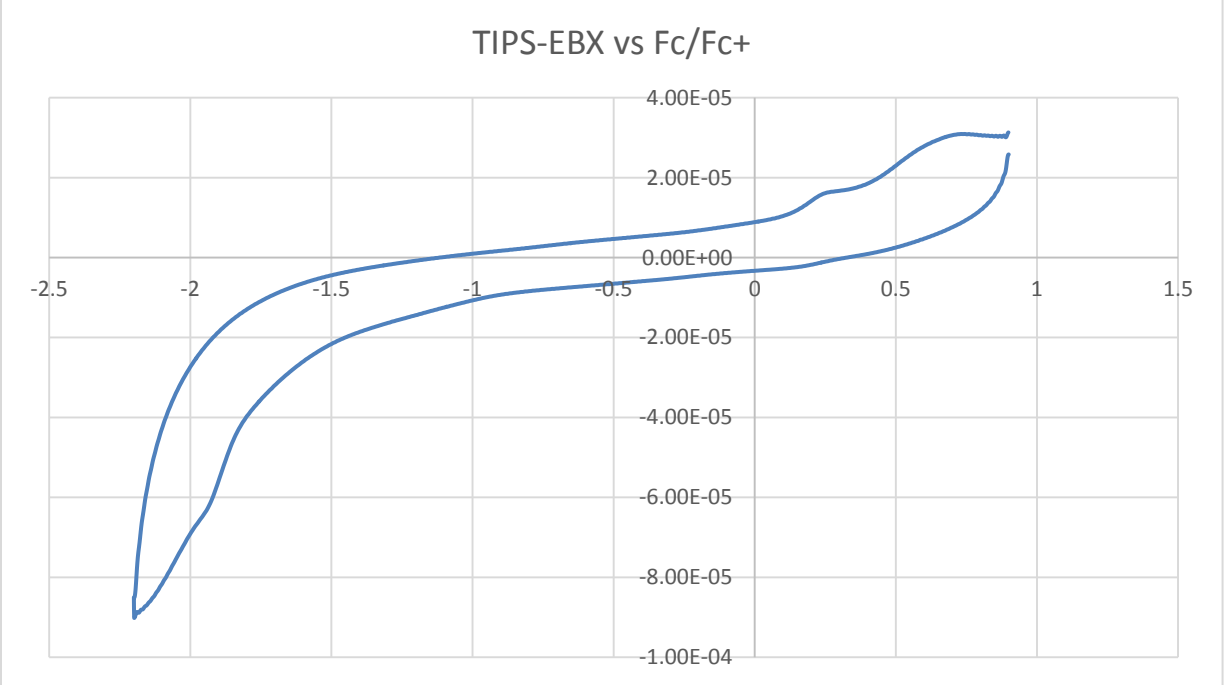
Calculated for: [M+H] = 361.2475, found 361.2445.

**Procedure for cyclic voltammetry**

Cyclic voltammetric measurements were recorded in a glove box by a CHI760E electrochemical workstation that was connected to a glassy carbon working electrode (surface area = 0.07 $cm^2$), a platinum wire auxiliary electrode, and an $Ag/AgNO_3$ (0.01 M) reference electrode filled with acetonitrile and [*n*-$Bu_4$] [$PF_6$] (0.1 M). All potentials were referenced to $Fc/Fc^+$ as internal standard.




Cyclic voltammogram of CBX (**4a**) (4 mM) recorded in $CH_3CN$ solution at scan rate of 100 $mV \cdot s^{-1}$; the potential is referenced to the ferrocene/ferrocenium couple




Cyclic voltammogram of TIPS-EBX (**13a**) (4 mM) recorded in $CH_3CN$ solution at scan rate of 100 $mV \cdot s^{-1}$; the potential is referenced to the ferrocene/ferrocenium couple

**Procedure for $^{13}$C-labelling experiment**

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, Cbz-protected L Proline (**5a**) (0.30 mmol, 1.0 equiv), CBX reagent (**4a**) (123 mg, 0.450 mmol, 1.5 equiv), $K^{13}CN$ (39 mg, 0.60 mmol, 2.0 equiv), CsOBz (114 mg, 0.450 mmol, 1.5 equiv), 30 mg of heterogeneous powdered molecular sieves (4 ångström) and

$Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (3 mg, 0.003 mmol, 0.01 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 4h30 at rt.

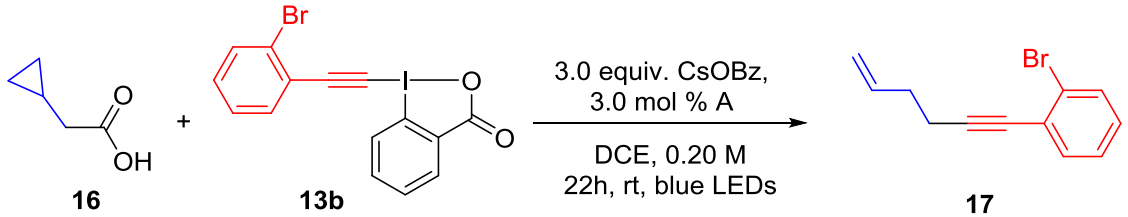
After completion of the reaction, the orange reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. The crude product was then dissolved in DCM, and washed 3 times with saturated aqueous solution of $Na_2CO_3$. The joined organic layers are then washed with brine, dried with $MgSO_4$, filtered and evaporated under reduced pressure. Final purification was performed by column chromatography (Pentane/Ethyl Acetate = 8:2 to 6:4) affording the corresponding $^{13}$C-labelled nitrile **7a** (30 mg, 0.13 mmol, 43%). Incorporation was calculated by $^{13}$C NMR integration (using peak at 135.9 ppm as internal standard), to be 2.2%.

## Control experiment:

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, CBX reagent (**4a**) (123 mg, 0.450 mmol, 1.5 equiv) and $K^{13}CN$ (39 mg, 0.60 mmol, 2.0 equiv), under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being stirred in the dark for 4h30 at rt. Then, filtration led to the isolation of 140 mg of $^{13}$C-labelled reagent (unpure, some decomposition occurred, and still KCN and $^{13}$C-KCN remaining). Incorporation was calculated by $^{13}$C NMR integrations (using peak at 118.5 as internal standard) to be 14.3%.

## Procedure for radical clock experiments

### 1-bromo-2-(hex-5-en-1-yn-1-yl)benzene (17)




**16** **13b** **17**

1:1.5 21%

Dry degassed DCE (1.0 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, cyclopropyl acetic acid **16** (19 µL, 0.20 mmol, 1.0 equiv), EBX reagent **13b** (128 mg, 0.300 mmol, 1.5 equiv), CsOBz (152 mg, 0.600 mmol, 3.0 equiv), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (6.7 mg, 6.0 µmol, 0.03 equiv) under $N_2$ (vaccum / $N_2$

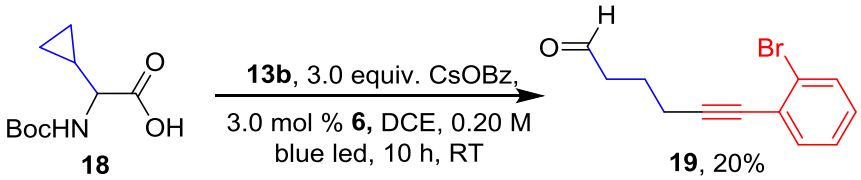
exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 22 h at rt.

The reaction mixture was filtered over silica, eluting with ethyl acetate, and evaporated under reduced pressure (Crude NMR ratio 1:1 product remaining starting material). Then preparative TLC using heptane led to the isolation of 10 mg (about 21% yield, 90% pure) of the open product **17** as a colorless oil and no detection of the product formed after direct alkynylation.

$^1$H NMR (400 MHz, Chloroform-*d*) δ 7.55 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.42 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.22 (td, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.12 (td, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 5.97 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H, $ArCH_2CH_2C\mathit{H}CH_2$), 5.15 (dd, *J* = 17.1, 1.7 Hz, 1H, $ArCH_2CH_2CHC\mathit{H}_2$), 5.07 (dd, *J* = 10.2, 1.6 Hz, 1H, $ArCH_2CH_2CHC\mathit{H}_2$), 2.56 (t, *J* = 7.1 Hz, 2H, $ArC\mathit{H}_2CH_2CHCH_2$), 2.40 (m, 2H, $ArC\mathit{H}_2C\mathit{H}_2CHCH_2$).

The values of the NMR spectra are in accordance with reported literature data.[36]

**6-(2-Bromophenyl)hex-5-ynal (19)**




Dry degassed DCE (1.0 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, cyclopropyl acetic acid **18** (43 mg, 0.20 mmol, 1.0 equiv), EBX reagent **13b** (128 mg, 0.300 mmol, 1.5 equiv), CsOBz (152 mg, 0.600 mmol, 3.0 equiv), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (4.5 mg, 4.0 µmol, 0.02 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 22 h at rt.

The reaction mixture was filtered over silica, eluting with ethyl acetate, and evaporated under reduced pressure. Then preparative TLC using heptane/diethyl ether (6:4) led to the isolation of 10 mg (20% yield) of the open product **19** as a colorless oil and the direct alkynylation product was not detected.

$^1$H NMR (400 MHz, Chloroform-*d*) δ 9.86 (t, *J* = 1.4 Hz, 1H, C*H*O), 7.56 (dd, *J* = 8.1, 1.4 Hz, 1H, Ar*H*), 7.42 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.22 (td, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.13 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 2.73 (td, *J* = 7.3, 1.4 Hz, 2H, $ArCCH_2CH_2C\mathit{H}_2$), 2.56 (t, *J* = 6.8 Hz,

[36] Y. Horino, Y. Nakashima, K. Hashimoto, S. Kuroda, *Synlett* **2010**, *19*, 2879.

2H, ArCC*H*$_2$CH$_2$CH$_2$), 1.97 (p, *J* = 7.0 Hz, 2H, ArCCH$_2$C*H*$_2$CH$_2$). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 201.9, 133.3, 132.3, 128.9, 127.0, 125.6, 125.4, 93.8, 80.4, 42.7, 20.9, 18.9. IR 3677 (w), 3361 (w), 3064 (w), 2930 (w), 2853 (w), 2720 (w), 2239 (w), 1725 (s), 1676 (w), 1587 (w), 1511 (w), 1464 (m), 1432 (w), 1365 (w), 1251 (w), 1169 (w), 1112 (w), 1053 (w), 1028 (w), 916 (w), 866 (w). HRMS (ESI) calcd for $C_{12}H_{12}BrO^+$ $[M+H]^+$ 251.0066; found 251.0068.

**Procedure for competitive experiment between CBX (4a) and TIPS-EBX (13a)**

**Using optimized conditions found for the decarboxylative alkynylation:**

Dry degassed DCE (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, Cbz-protected L Proline (**5a**) (75 mg, 0.30 mmol, 1.0 equiv), TIPS-EBX (**13a**) (96.0 mg, 0.225 mmol, 0.75 equiv), CBX (**4a**) (61.4 mg, 0.225 mmol, 0.75 equiv), CsOBz (0.23 g, 0.90 mmol, 3.0 equiv), and Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ (**6**) (3.4 mg, 3.0 µmol, 0.01 equiv) and under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 4h30 at rt.

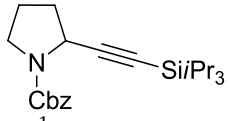
The reaction mixture was filtered over silica, eluting with ethyl acetate, and evaporated under reduced pressure (Crude NMR showed remaining starting material, full conversion was not reached). Then purification by column chromatography starting from 9:1 to 6:4 heptane/ethyl acetate led to the isolation of the alkynylated product **14a** (12 mg, 0.031 mmol, 10 % yield based on Cbz-Pro-OH (**5a**)) and the cyanated product **7a** (17 mg, 0.074 mmol, 25% yield based on Cbz-Pro-OH (**5a**)).

**Using optimized conditions found for the decarboxylative cyanation:**

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, Cbz-protected L Proline (**5a**) (75 mg, 0.30 mmol, 1.0 equiv), TIPS-EBX (**13a**) (96.0 mg, 0.225 mmol, 0.75 equiv), CBX (**4a**) (61.4 mg, 0.225 mmol, 0.75 equiv), CsOBz (0.11 g, 0.45 mmol, 1.5 equiv), and Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ (**6**) (3.4 mg, 3.0 µmol, 0.01 equiv) and 4A molecular sieves (30 mg) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 4h30 at rt.

The reaction mixture was filtered over silica, eluting with ethyl acetate, and evaporated under reduced pressure (Crude NMR showed remaining starting material, full conversion was not reached). Then purification by column chromatography starting from 9:1 to 6:4 heptane/ethyl acetate led to the isolation of the alkynylated product **14a** (16 mg, 0.041 mmol, 14 % yield based on Cbz-Pro-OH (**5a**)) and the cyanated product **7a** (39 mg, 0.17 mmol, 57% yield based on Cbz-Pro-OH (**5a**)).

**Benzyl 2-((triisopropylsilyl)ethynyl)pyrrolidine-1-carboxylate (14a)**




$R_f$: 0.28 (Pentane/Ethyl Acetate = 9:1). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.27 (m, 5H, *Ph*), 5.16 (d, *J* = 3.2 Hz, 2H, C*H*$_2$-O), 4.67 – 4.51 (m, 1H, C*H*-C≡C), 3.64 – 3.49 (m, 1H, C*H*$_2$), 3.47 – 3.30 (m, 1H, C*H*$_2$), 2.21 – 1.98 (m, 3H, C*H*$_2$), 1.99 – 1.87 (m, 1H, C*H*$_2$), 1.11 – 0.93 (m, 21H, *TIPS*). $^{13}$C NMR (101 MHz, $CDCl_3$)[37] δ 154.6, 136.9, 128.4, 127.8, 127.8, 127.6, 107.9, 82.6, 66.9, 66.7, 49.3, 48.8, 46.0, 45.5, 34.3, 33.4, 24.4, 23.6, 18.6, 11.1. IR 2943 (m), 2865 (m), 2170 (w), 1709 (s), 1464 (w), 1410 (s), 1356 (m), 1184 (m), 1119 (m), 1092 (m), 996 (w), 883 (m). HRMS (ESI) calcd for $C_{23}H_{35}NNaO_2Si^+$ $[M+Na]^+$ 408.2329; found 408.2334.

## Actinometry / Quantum yield

For this experiment, our light reactor gave only a very approximate value of the quantum yield because it is circular and therefore more difficult to calculate the amount of incident photons. For this purpose, a Kessil blue LED (40W) was used as light source, furnishing blue light from only one direction. Incident photon flux was measured using a calibrated photodiode from Thorlabs (S120VC), assuming all photons at the peak wavelength of the blue LED (465 nm). The latter was measured with a spectrometer from Ocean Optics (USB2000+XR1-ES).

Dry degassed THF (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, Cbz-Pro-OH **5a** (75 mg, 0.30 mmol, 1.0 equiv), CBX reagent (123 mg, 0.450 mmol, 1.5 equiv), CsOBz (114 mg, 0.450 mmol, 1.5 equiv), 30 mg of heterogeneous powdered molecular sieves and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (3.3 mg, 3.0 µmol, 0.01 equiv)

[37] Mixture of two rotamers, which are not completely resolved.

under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light Kessil LED (40W) for 40 min at rt. Air flow was used to keep the flask at room temperature during the irradiation. The reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. Then purification of the crude material leads to the isolation of 38 mg of the pure nitrile **7a** (0.17 mmol, 55% yield).

Dry degassed DCE (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, Cbz-Pro-OH **5a** (75 mg, 0.30 mmol, 1.0 equiv), EBX reagent **13a** (193 mg, 0.450 mmol, 1.5 equiv), CsOBz (229 mg, 0.900 mmol, 3.0 equiv), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**6**) (3.3 mg, 3.0 μmol, 0.01 equiv) under $N_2$ (vaccum / $N_2$ exchange). The reaction mixture was again degassed by bubbling $N_2$ inside the test tube via syringe for 5 min before being irradiated using blue light Kessil LED (40W) for 40 min at rt. Air flow was used to keep the flask at room temperature during the irradiation. The reaction mixture was filtered over silica, eluting with DCM, and evaporated under reduced pressure. Then purification of the crude material leads to the isolation of 57 mg of the pure alkyne **14a** (0.15 mmol, 49% yield).

*Using Planck-Einstein relation:*
Photon energy at wavelength $\lambda = 465$ nm : $E = h * c / \lambda$

$= 6.626 * 10^{-34} * 2.998 * 10^{8} / (465 * 10^{-9})$

$= 4.27 * 10^{-19}$ [J]

*Where h is Planck constant, c is the speed of light and λ is the wavelength of the LED.*

Power density = light intensity measured / photodiode area

$= 0.0065 / (pi * (0.95/2)^2) = 0.00917$ [J s-1 cm-2]

Photon density = Power density / Photon energy at wavelength λ=465 nm

$=0.00917 / 4.27 * 10^{-19}$

$= 2.14758 * 10^{16}$ [photons s-1 cm-2]

Error margin +/- 4 %

*Finally quantum yield is calculated according to the following equation:*

$\Phi_{cyanation}$ = (mol products) / (mol incident photons)

= (mol products) / (photon density * t * f * area / $N_A$)

= 0.166 * $10^{-3}$ / (2.14758 * $10^{16}$ * 2400 * 0.9999 * 2.2 / 6.022 * $10^{23}$)

= 0.88

$\Phi_{alkynylation}$ = (mol products) / (photon density * t * f * area / 6.022 * $10^{23}$)

= 0.148 * $10^{-3}$ / (2.14758 * $10^{16}$ * 2400 * 0.9999 * 2.2 / 6.022 * $10^{23}$)

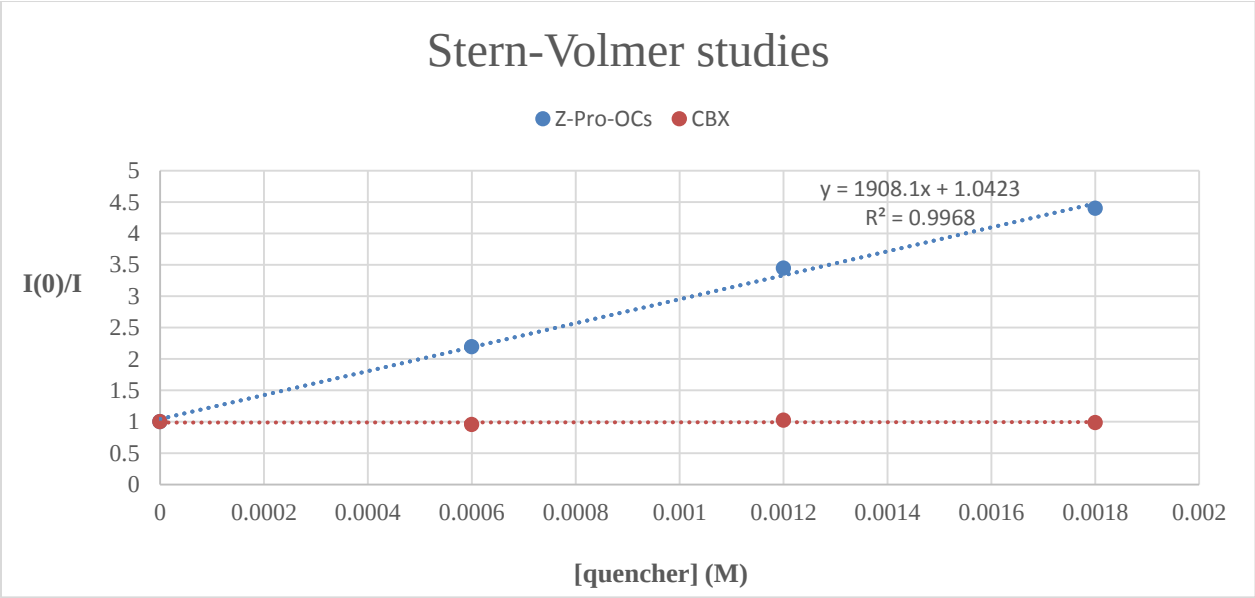
= 0.79

*Where t is time of the irradiation in seconds (40 min = 2400 s); f = 1-10$^{A}$ where A is absorbance. At 465 nm, absorbance was saturated at 1μM and about 0.31 at 5 nM. Concentration of photocatalyst under reaction conditions is 2.0 mM, meaning all the incident light is assumed to be absorbed by the photocatalyst Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ (f > 0.9999). And the irradiated test tube area can be calculated as a rectangle of 1cm wide and 2.2 cm high. Therefore the area is 2.2 cm$^2$. And $N_A$ is Avogadro number.*

**Luminescence Quenching Experiments (Stern-Volmer Studies)**

Luminescence intensities were recorded using a Cary Eclipse SW fluorescence spectrophotometer from Varian.

All solutions were excited at 380 nm and the emissions were detected at the 476 nm. Dry THF was degassed by three freeze-pump-thaw cycles. Samples were prepared as follow: to a degassed ($N_2$ / Vacuum, 3 cycles) glass cuvette capped with septa, was introduced stock solutions of photocatalyst and quencher (CBX or Z-Pro-OH) using Hamilton syringes, and the corresponding volume of THF to get a total volume of 1.0 mL. The concentration of Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ was 4.96 x $10^{-6}$ M. As shown below, the cesium carboxylate is a good quencher whereas CBX doesn't quench the excited state of the photocatalyst.



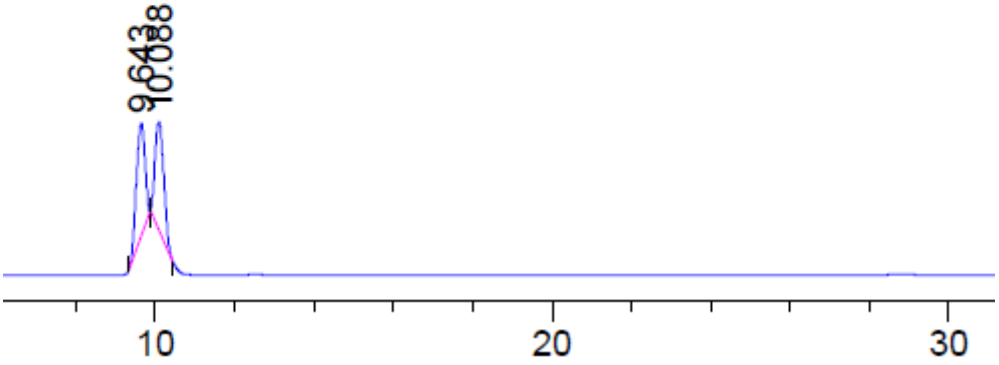

**Determination of the enantiomeric excess of 14a and 7a**

Samples were prepared in a 80/20 hexane/isopropanol mixture, before being submitted in chiral HPLC.

HPLC conditions for the alkyne **14a**: Racemic mixture. Chiralcel IA, 99:1 Hexane/*i*PrOH, 1mL/min, 61min. $t_{R1}$ = 9.6 min. $t_{R2}$ = 10.1 min. λ = 254 nm.

Signal 2: DAD1 B, Sig=210,4 Ref=360,100

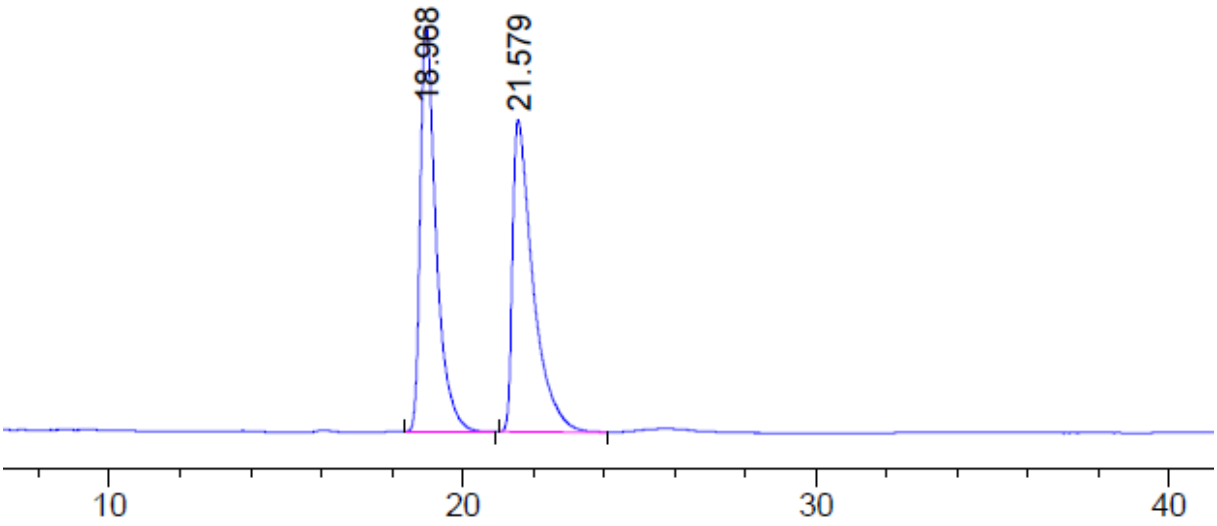
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.643 | BBA | 0.2485 | 2973.02271 | 196.46544 | 50.1923 |
| 2 | 10.088 | BB | 0.2530 | 2950.24585 | 190.15503 | 49.8077 |
| Totals : | | | | 5923.26855 | 386.62047 | |




HPLC conditions for the nitrile **7a**: Racemic mixture. Chiralcel IA, 95:5 Hexane/*i*PrOH, 1mL/min, 61min. $t_{R1}$ = 19.0 min. $t_{R2}$ = 21.6 min. λ = 254 nm.

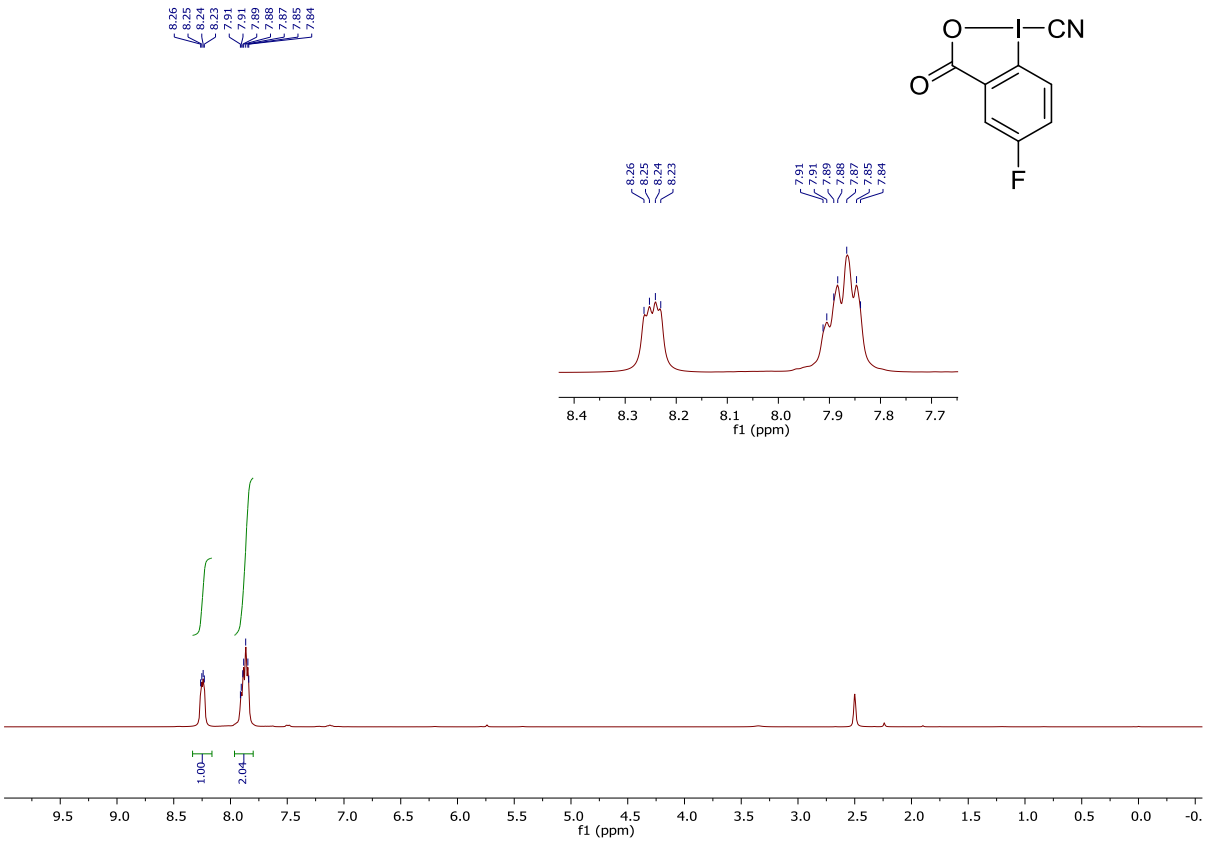
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 18.968 | BB | 0.4622 | 473.51004 | 15.25152 | 50.0575 |
| 2 | 21.579 | BB | 0.5760 | 472.42294 | 11.72652 | 49.9425 |
| Totals : | | | | 945.93298 | 26.97804 | |

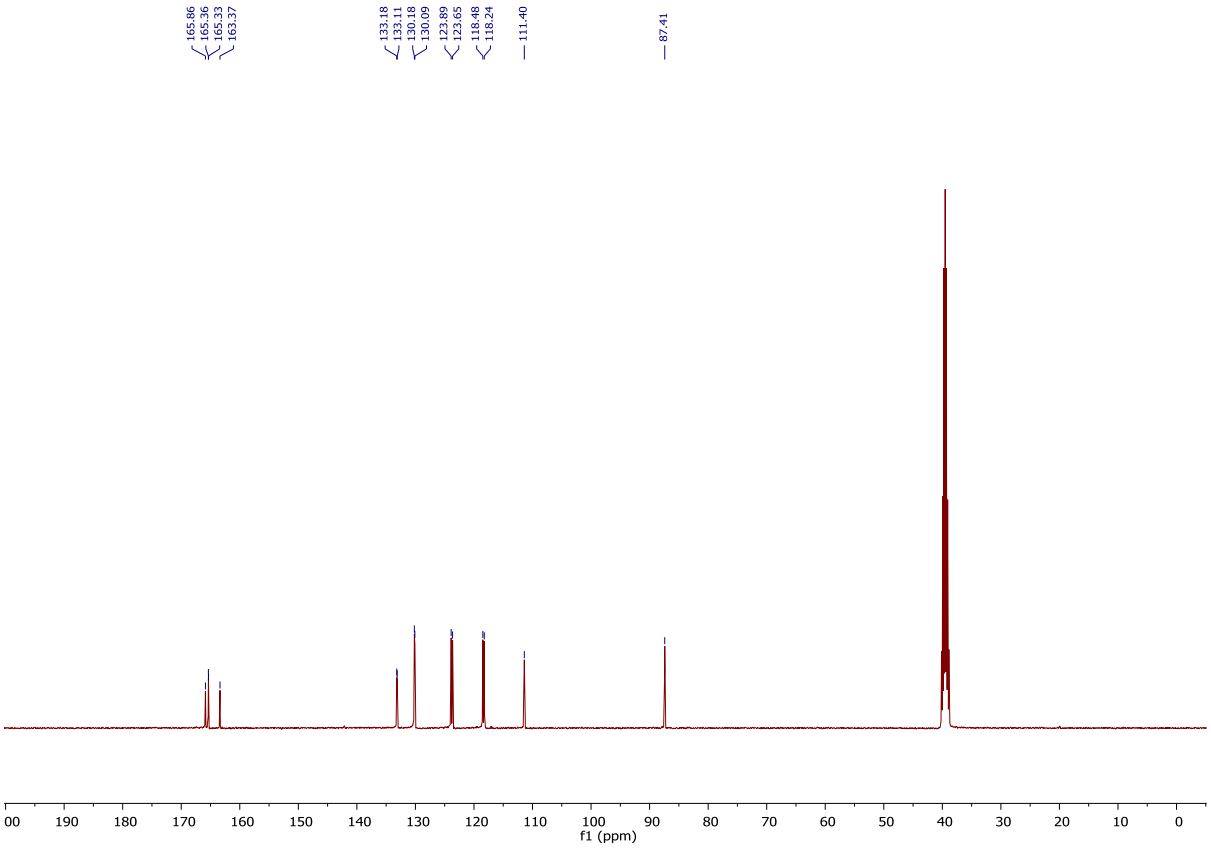


## 7. Spectra of New Compounds

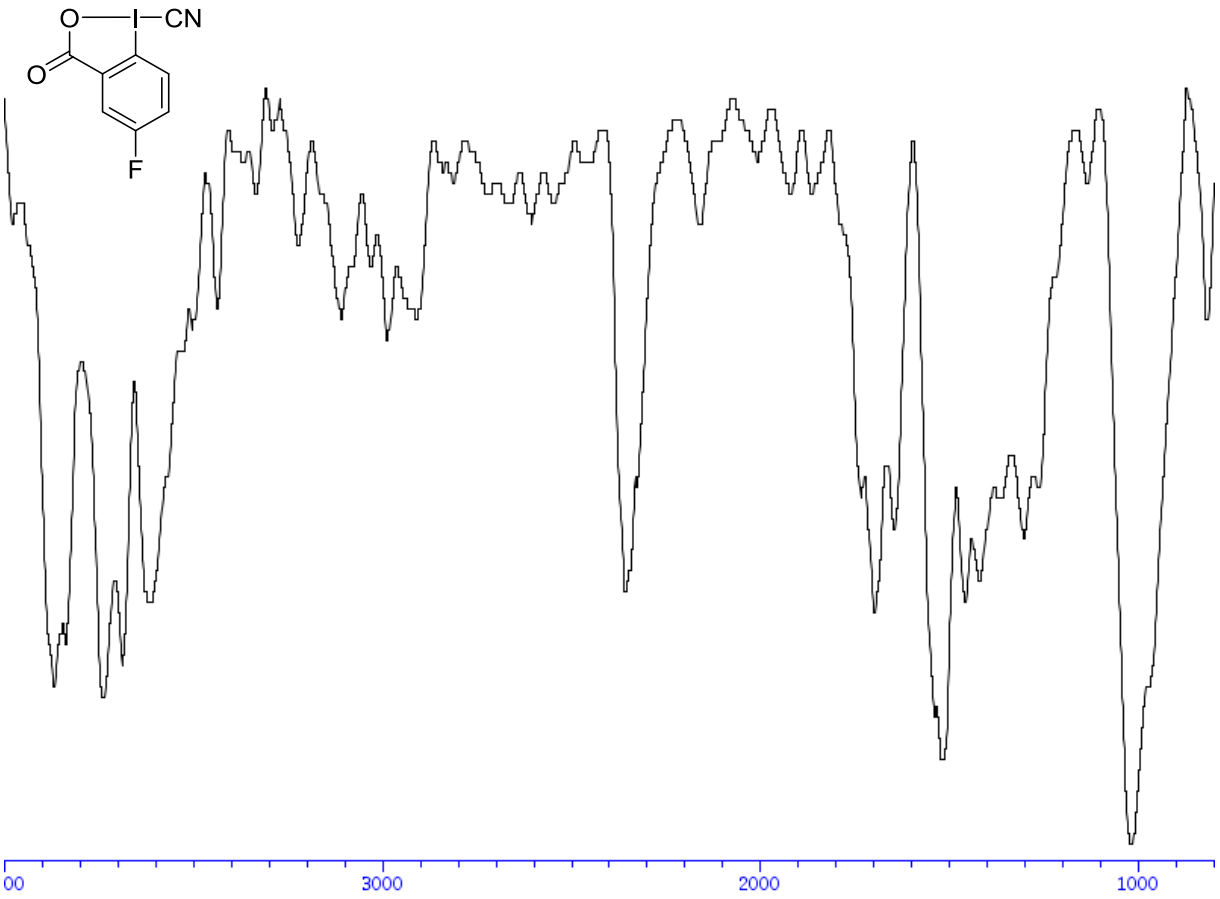
**$^{1}$H-NMR** (400 MHz, DMSO-*d*6) of compound **4c**



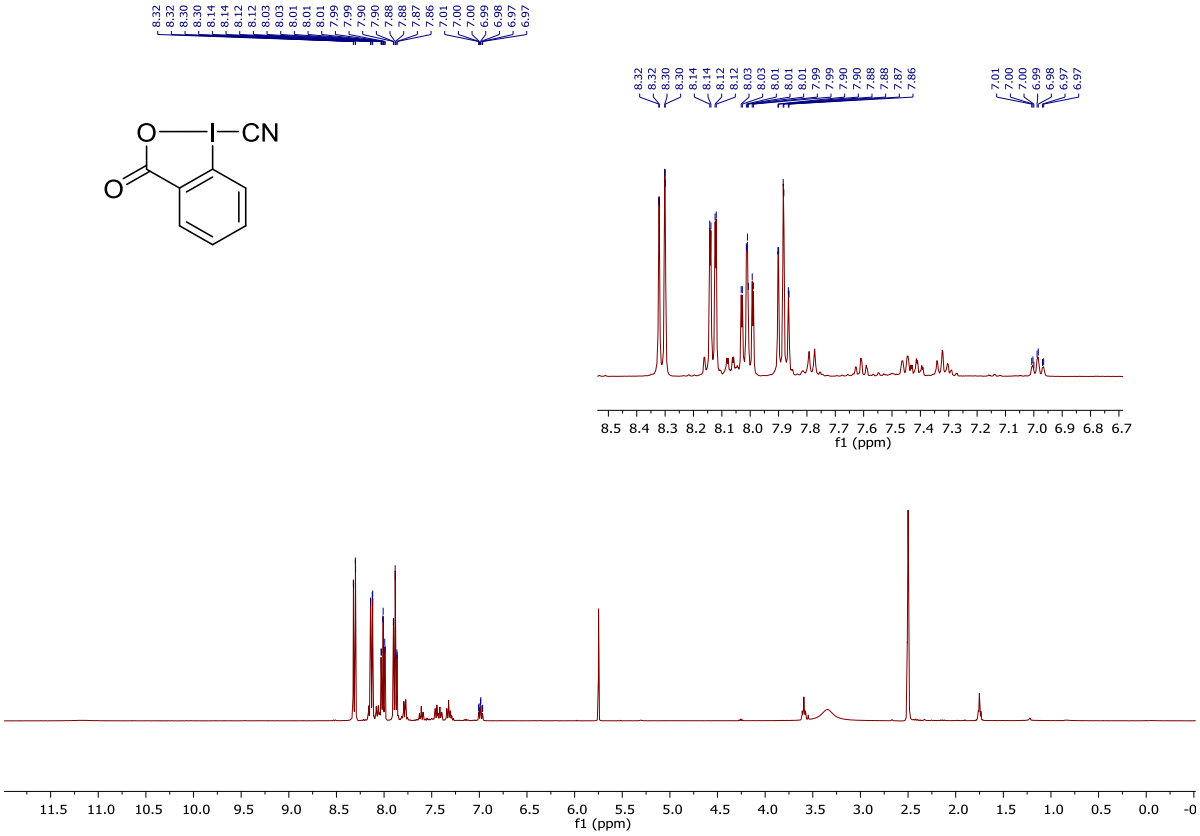

**$^{13}$C-NMR** (100 MHz, DMSO-*d*6) of compound **4c**



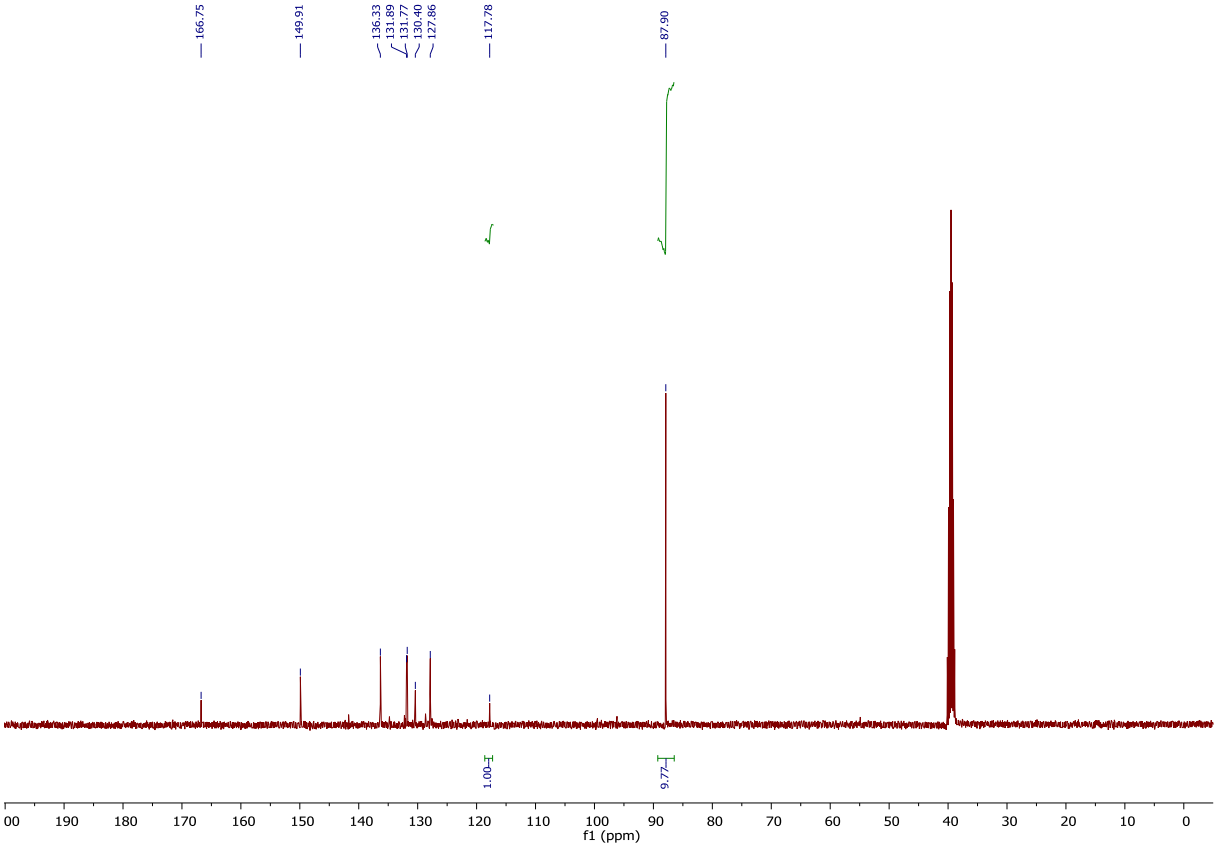
**IR** of compound **4c**



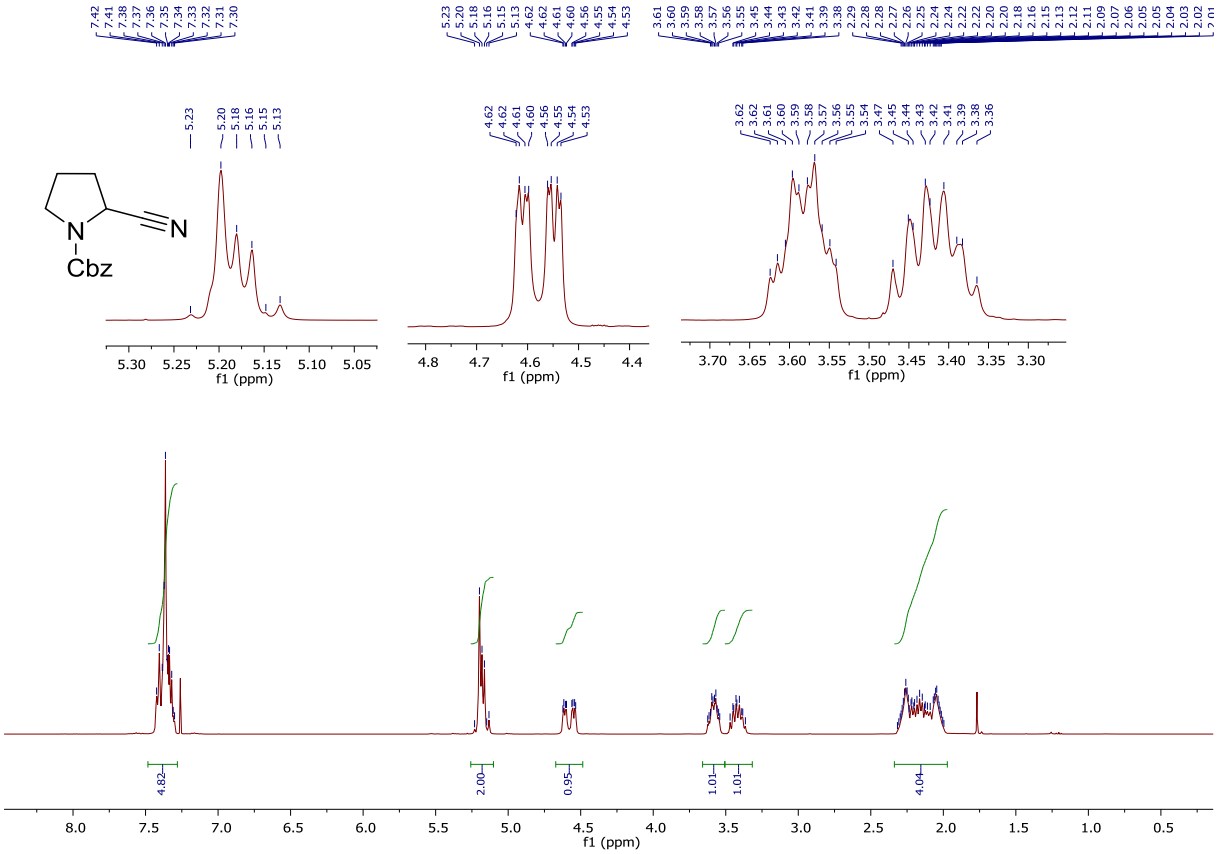
**$^{1}$H-NMR** (400 MHz, DMSO-*d*6) of compound **4a after $^{13}$C incorporation using $^{13}$C-KCN**



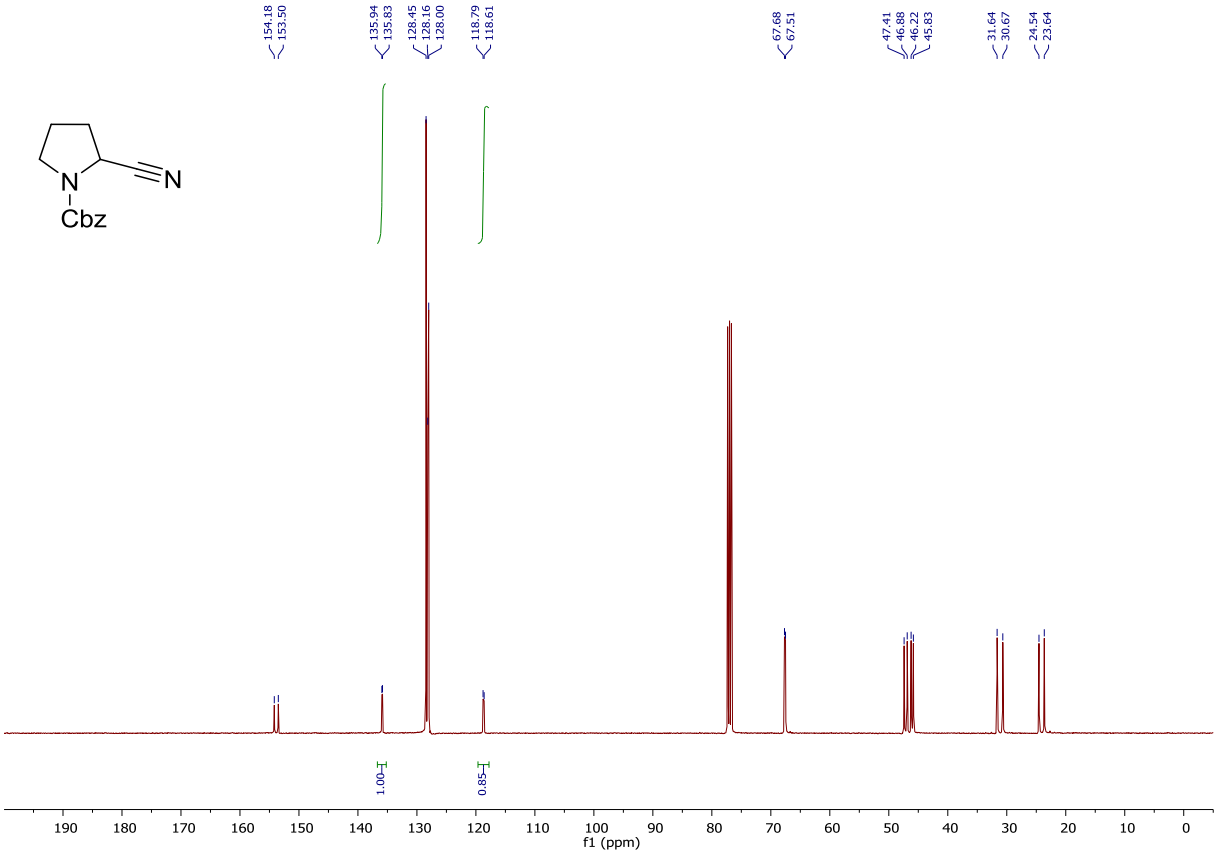
**$^{13}$C-NMR** (100 MHz, DMSO-*d*6) of compound **4d after $^{13}$C incorporation using $^{13}$C-KCN**



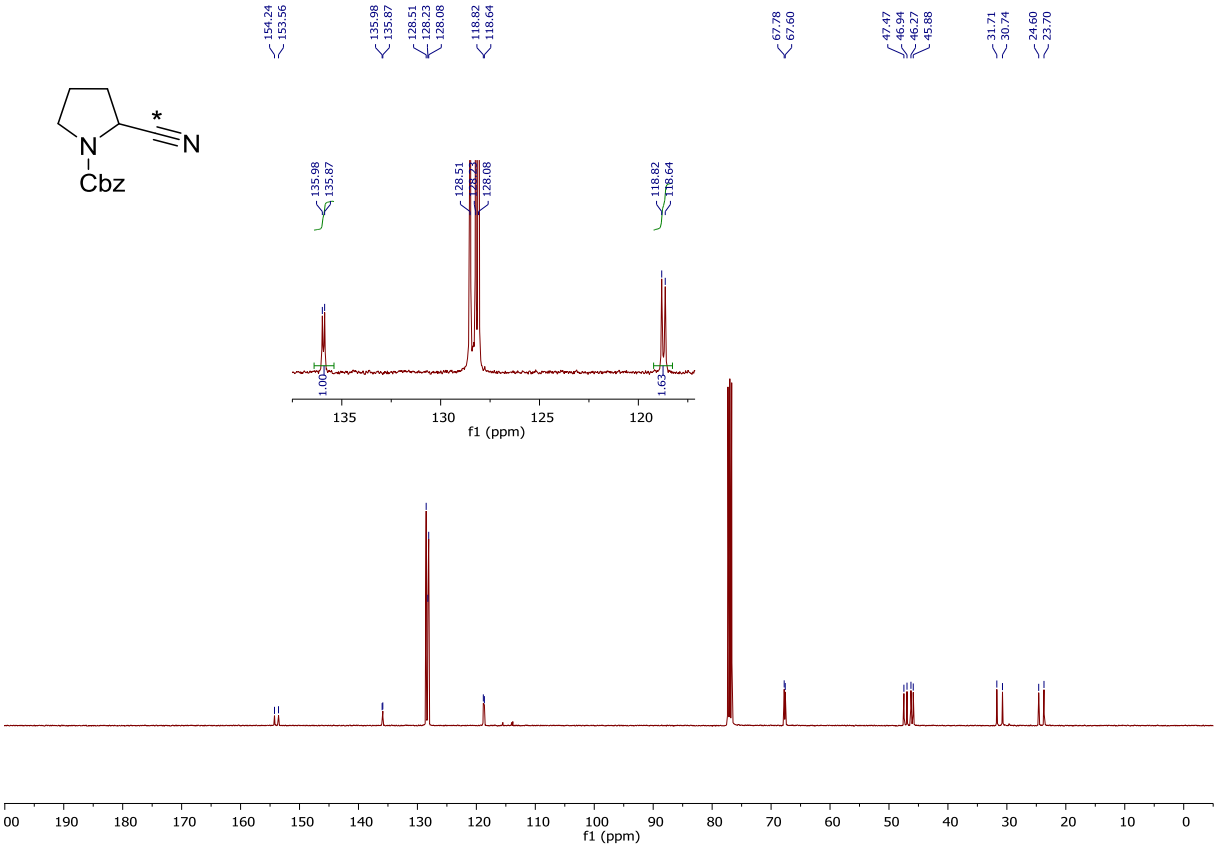
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7a**



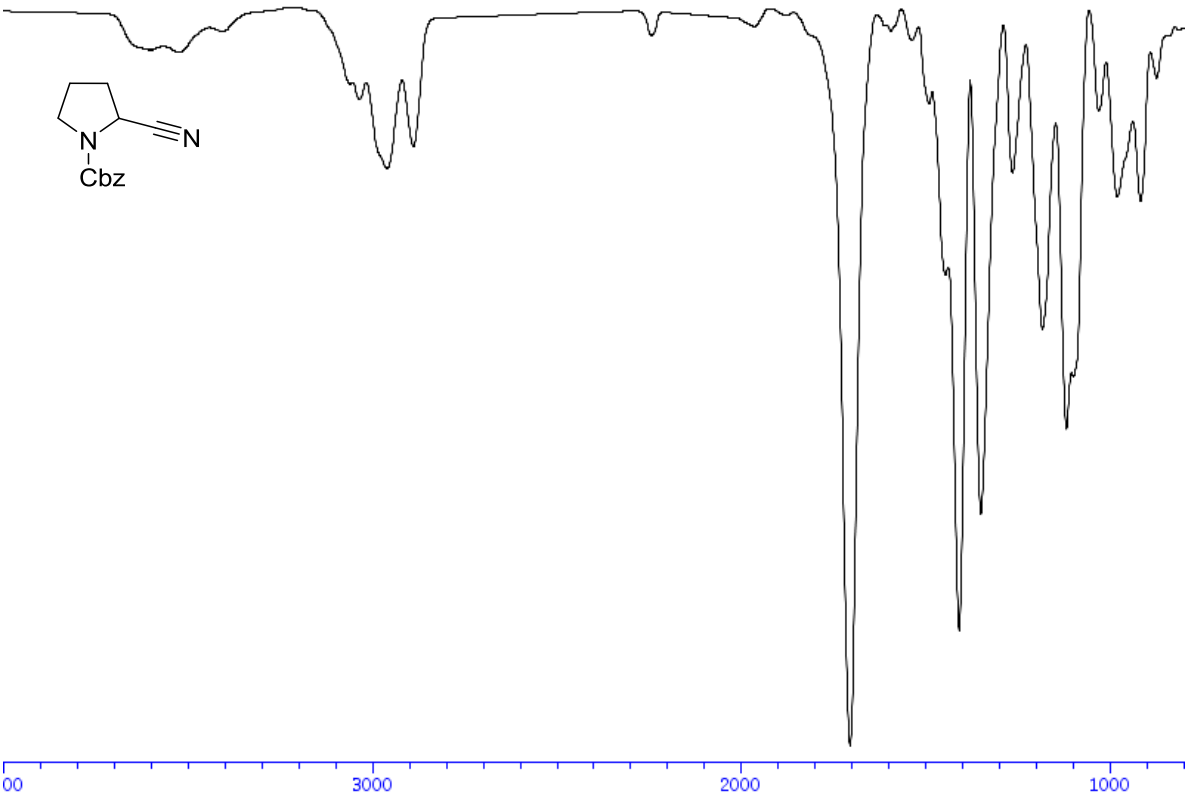

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **7a**



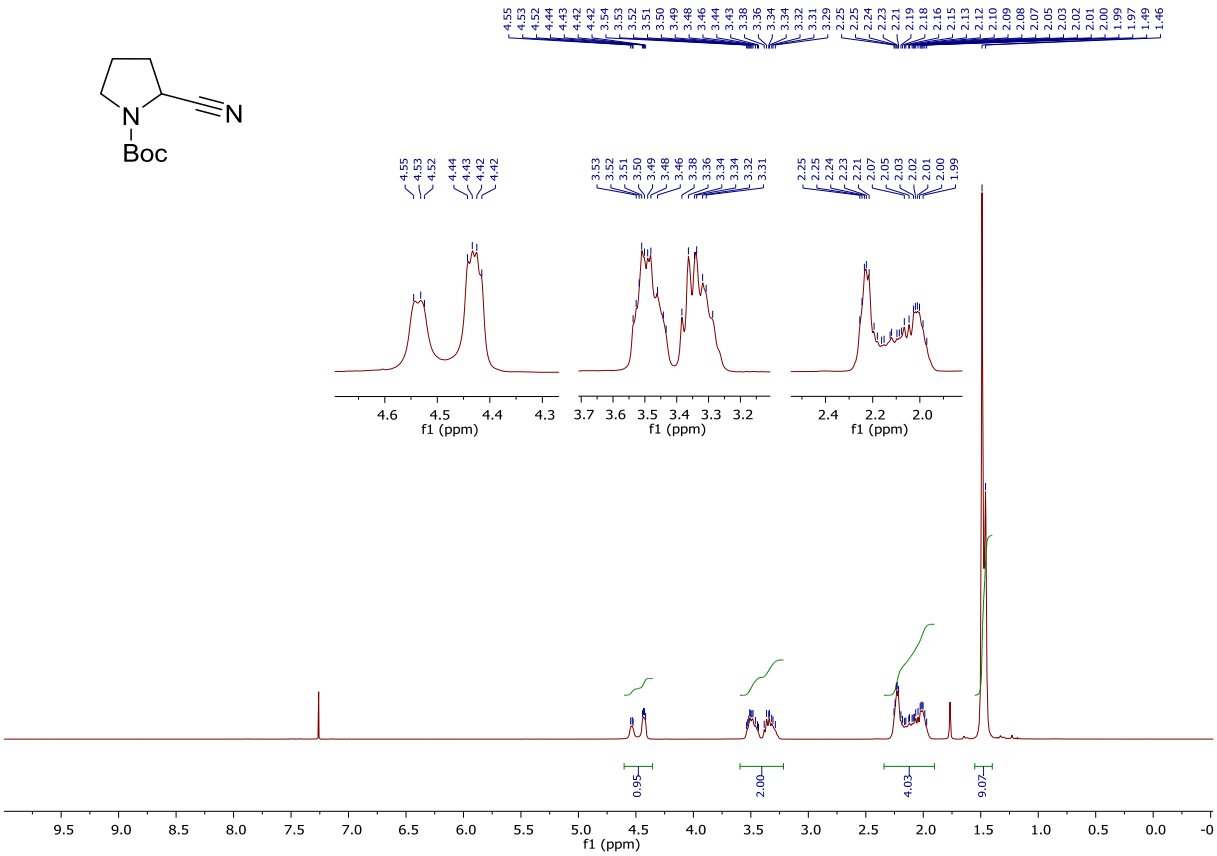
**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7a after $^{13}$C incorporation**



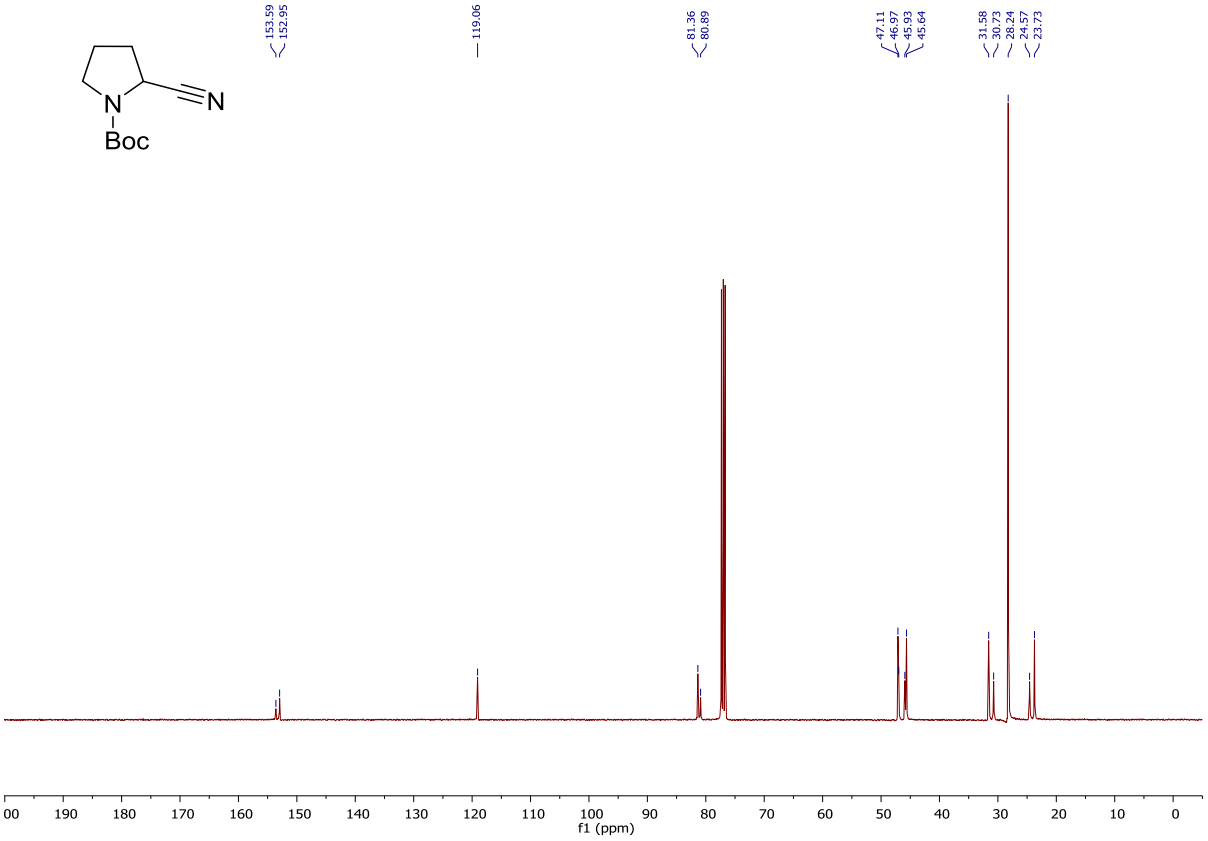

**IR** of compound **7a**



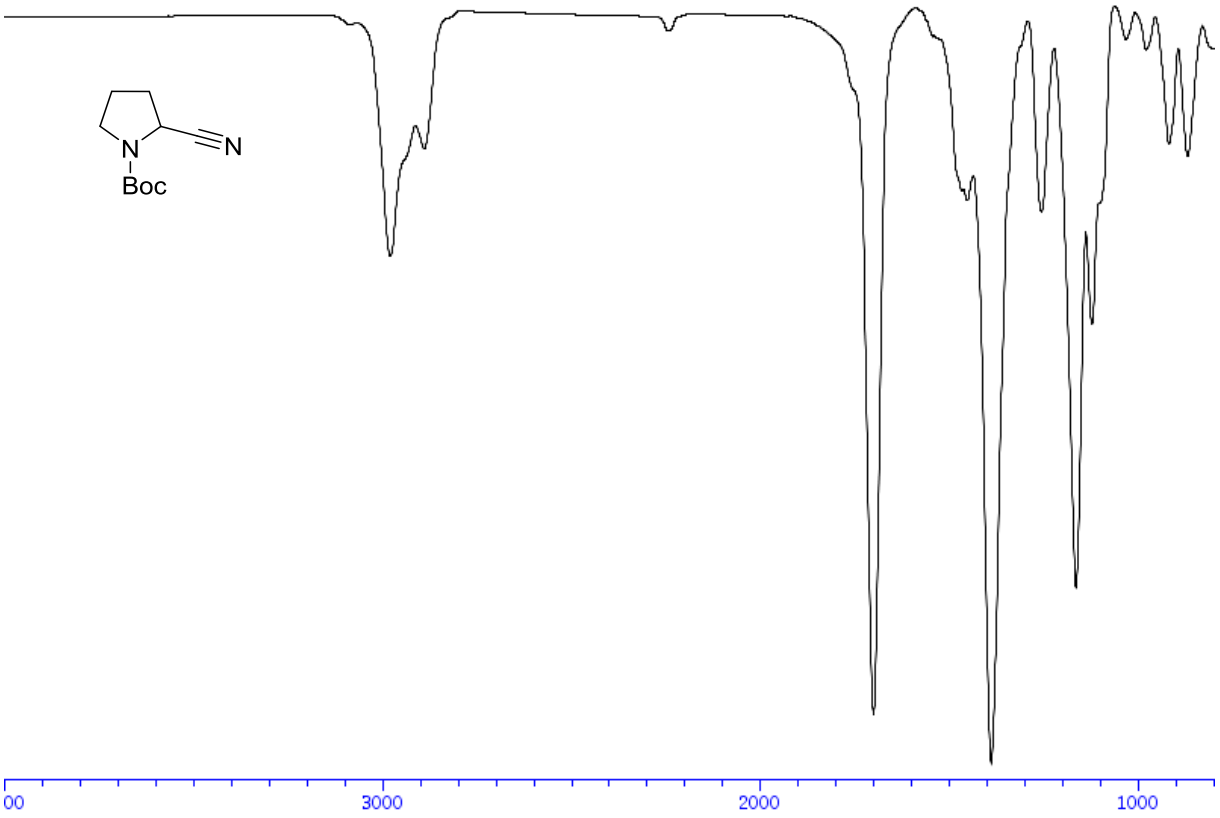
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7b**



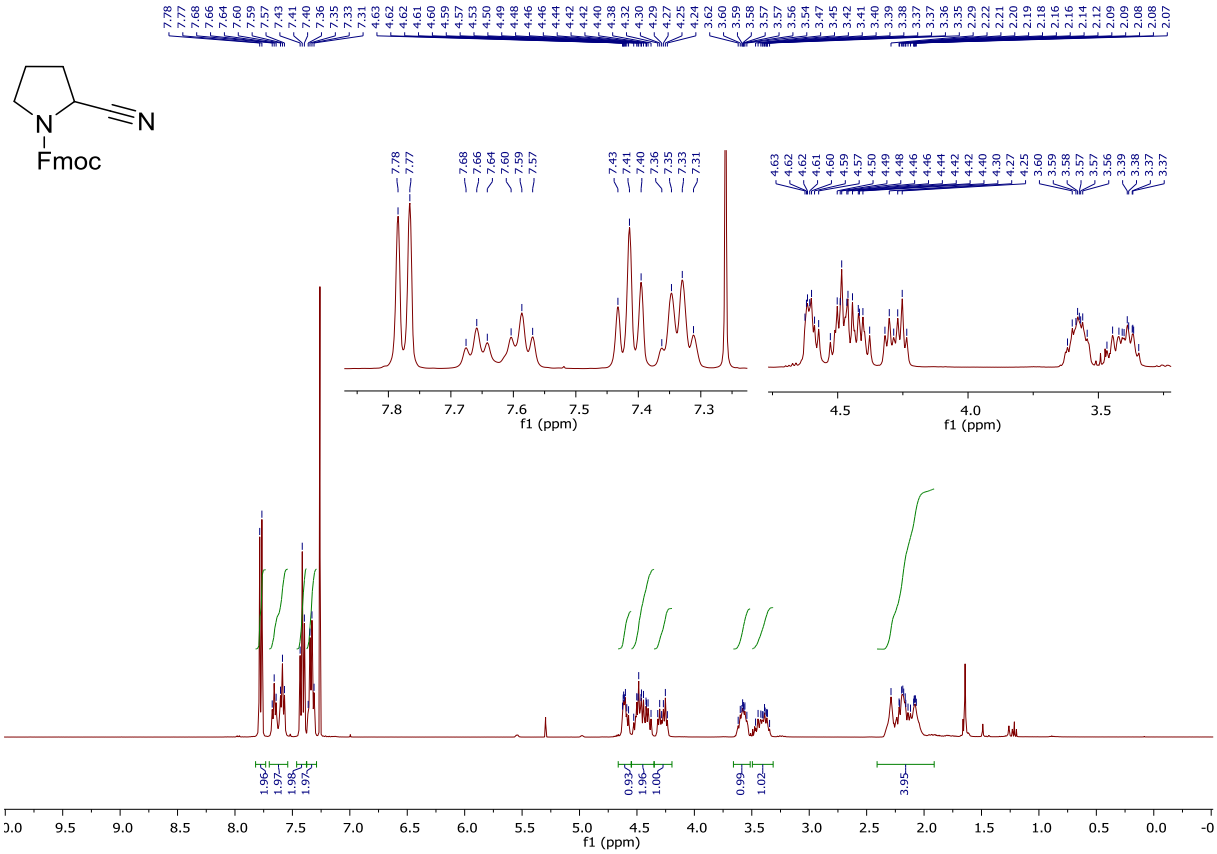

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7b**



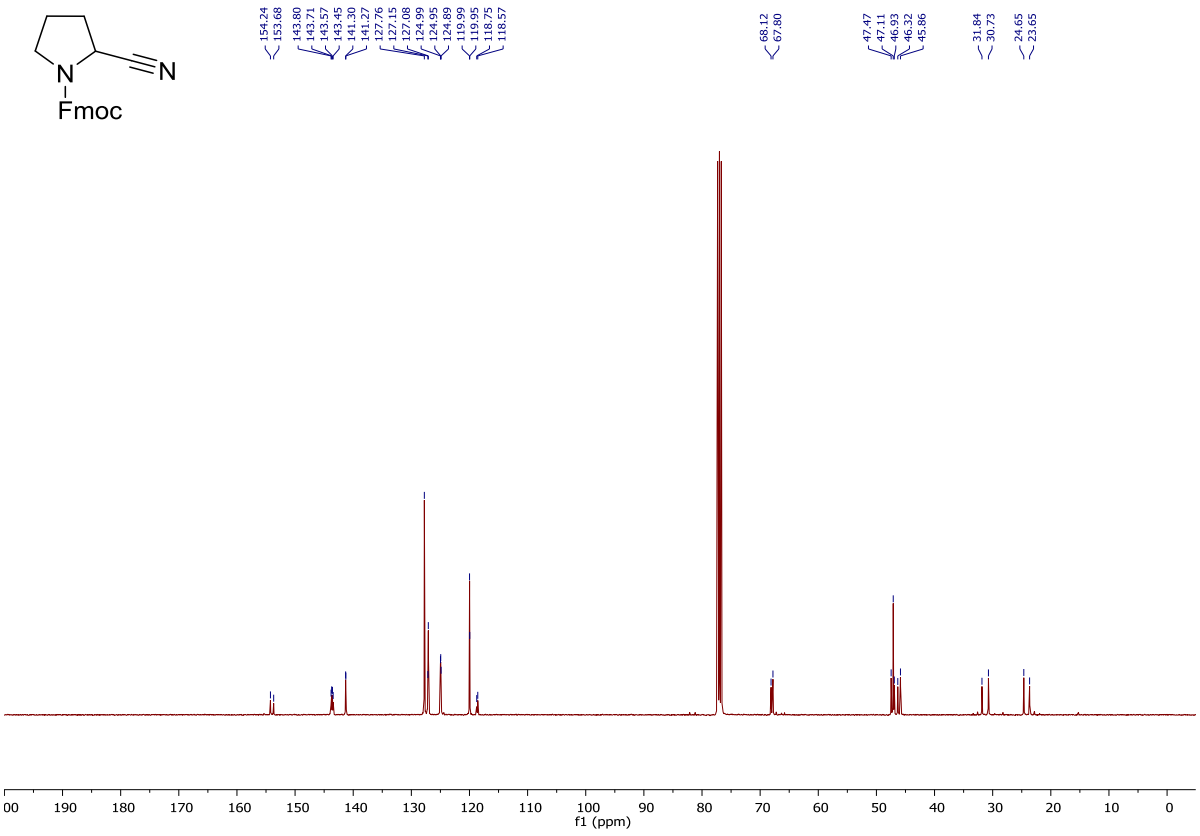
**IR** of compound **7b**



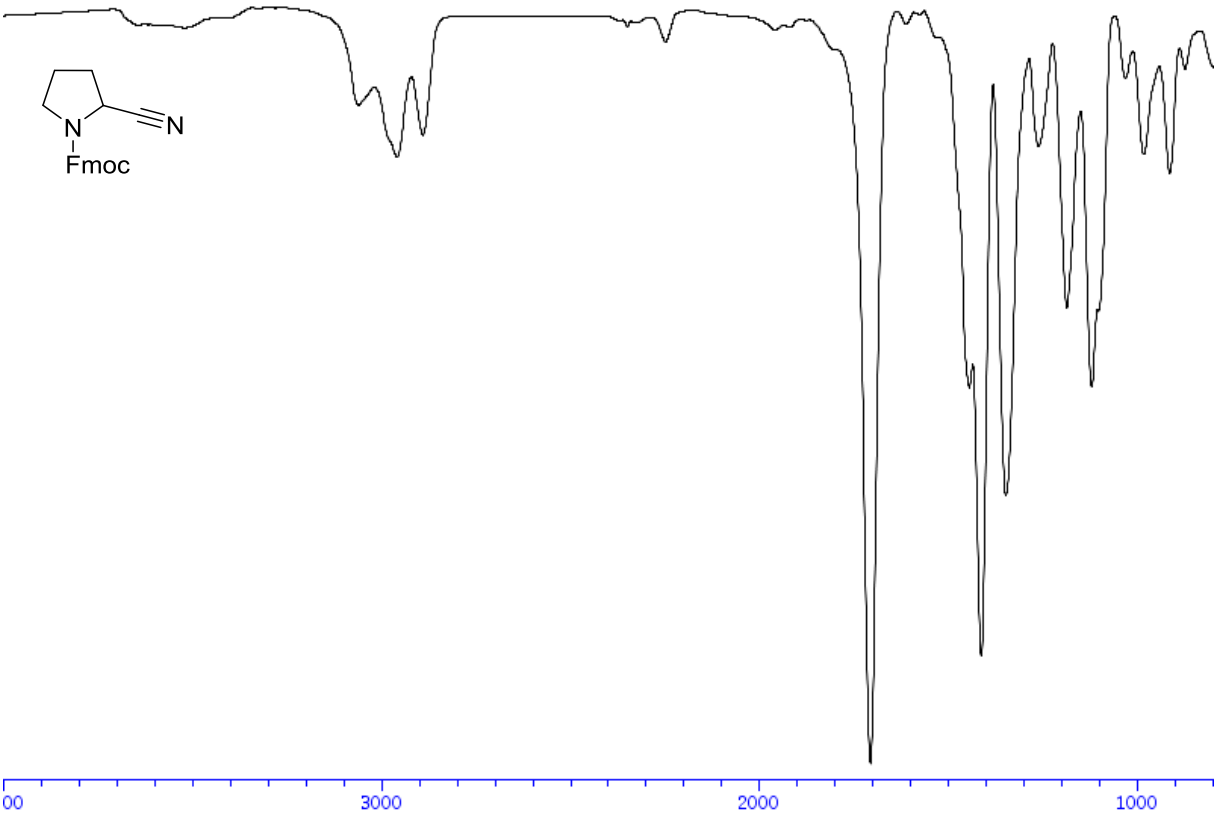
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7c**



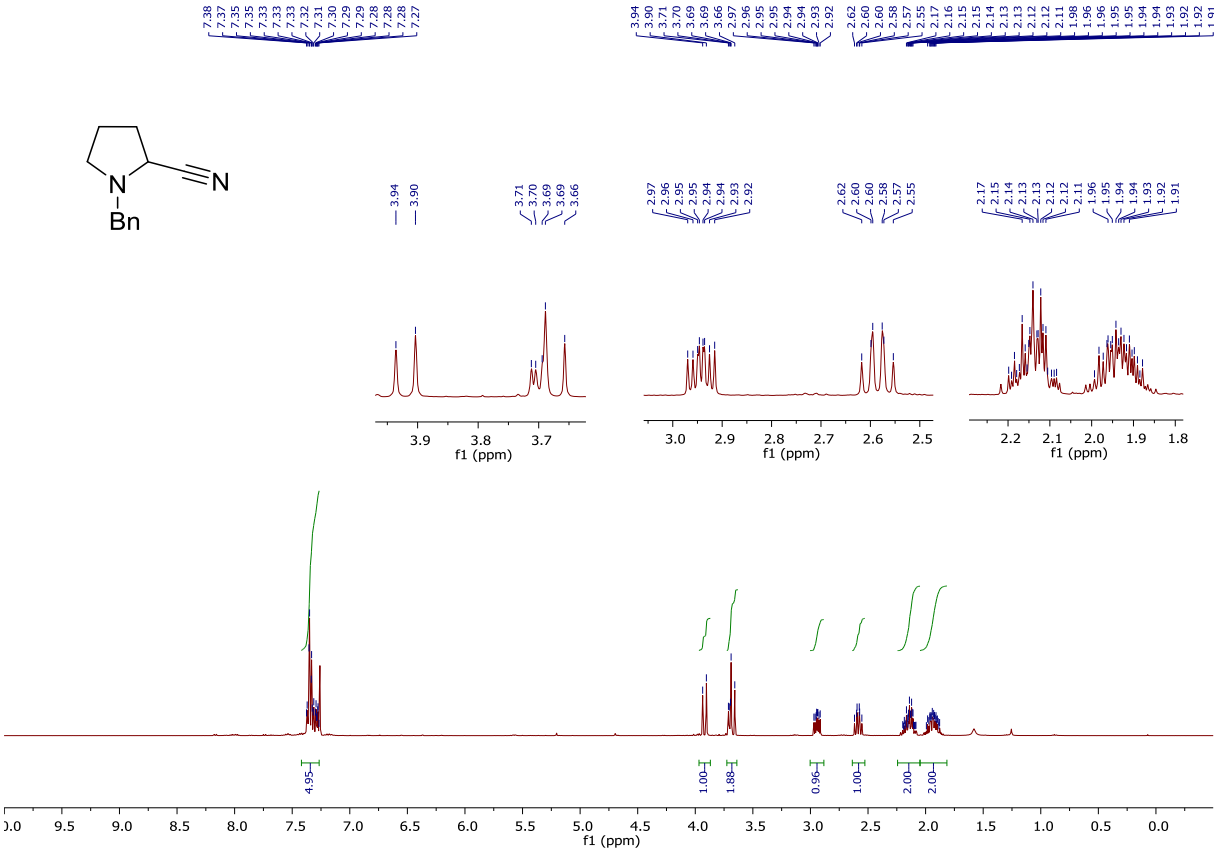

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **7c**



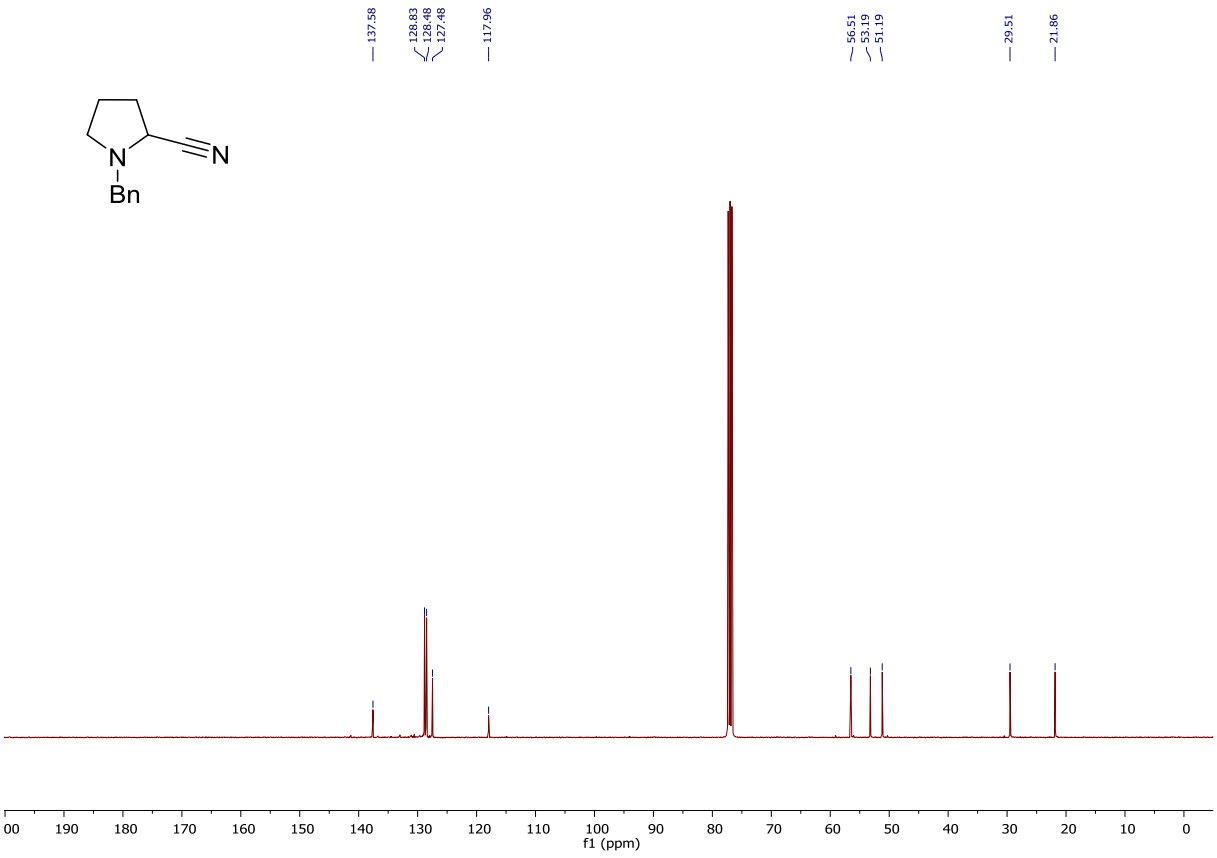
**IR** of compound **7c**



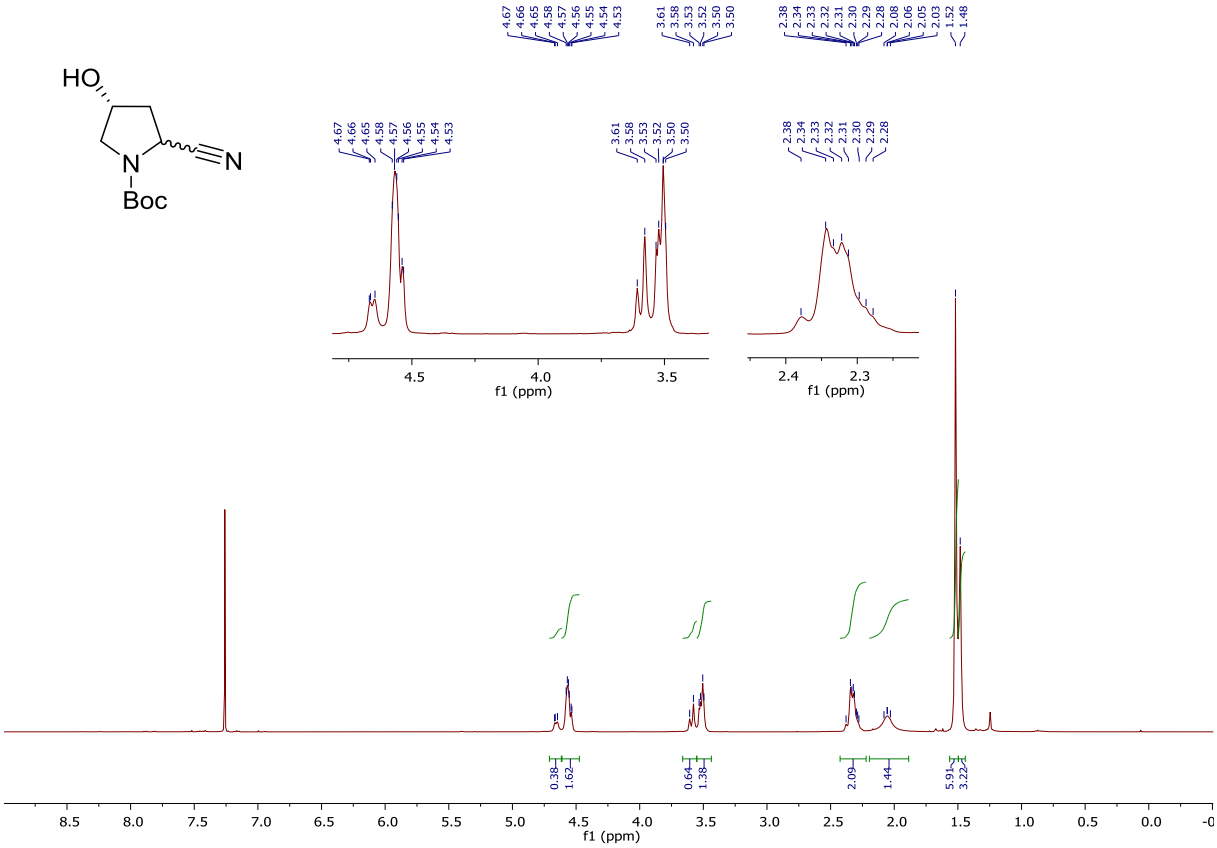
## $^{1}$**H-NMR** (400 MHz, $CDCl_3$) of compound **7d**



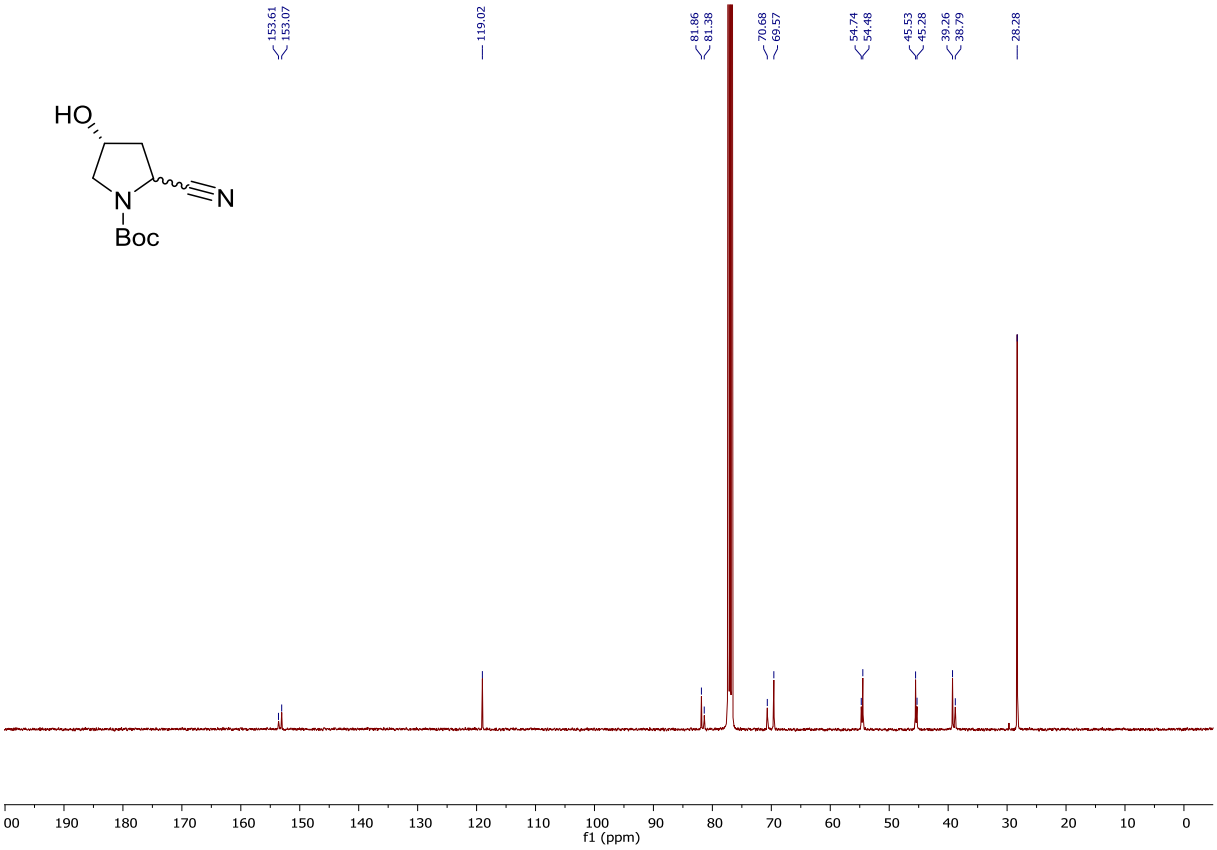

## $^{13}$**C-NMR** (100 MHz, $CDCl_3$) of compound **7d**



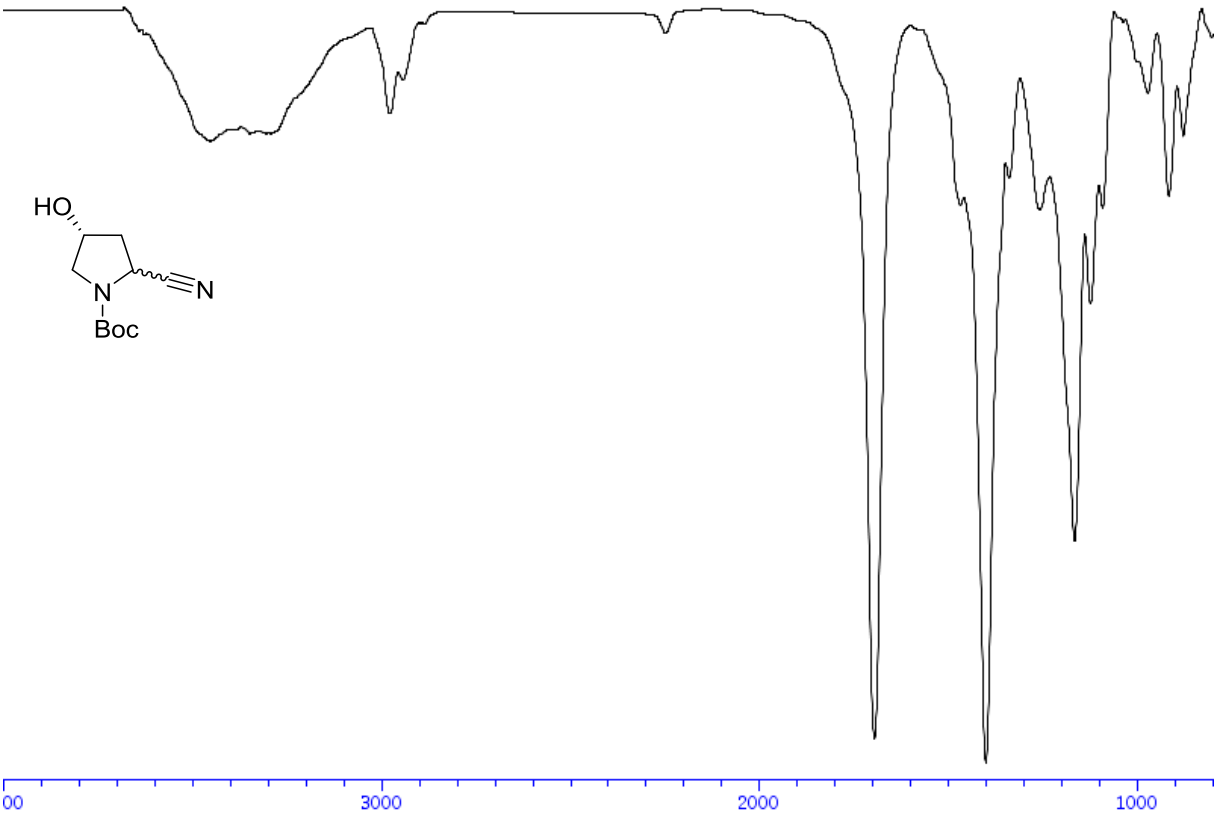
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7e (major isomer)**



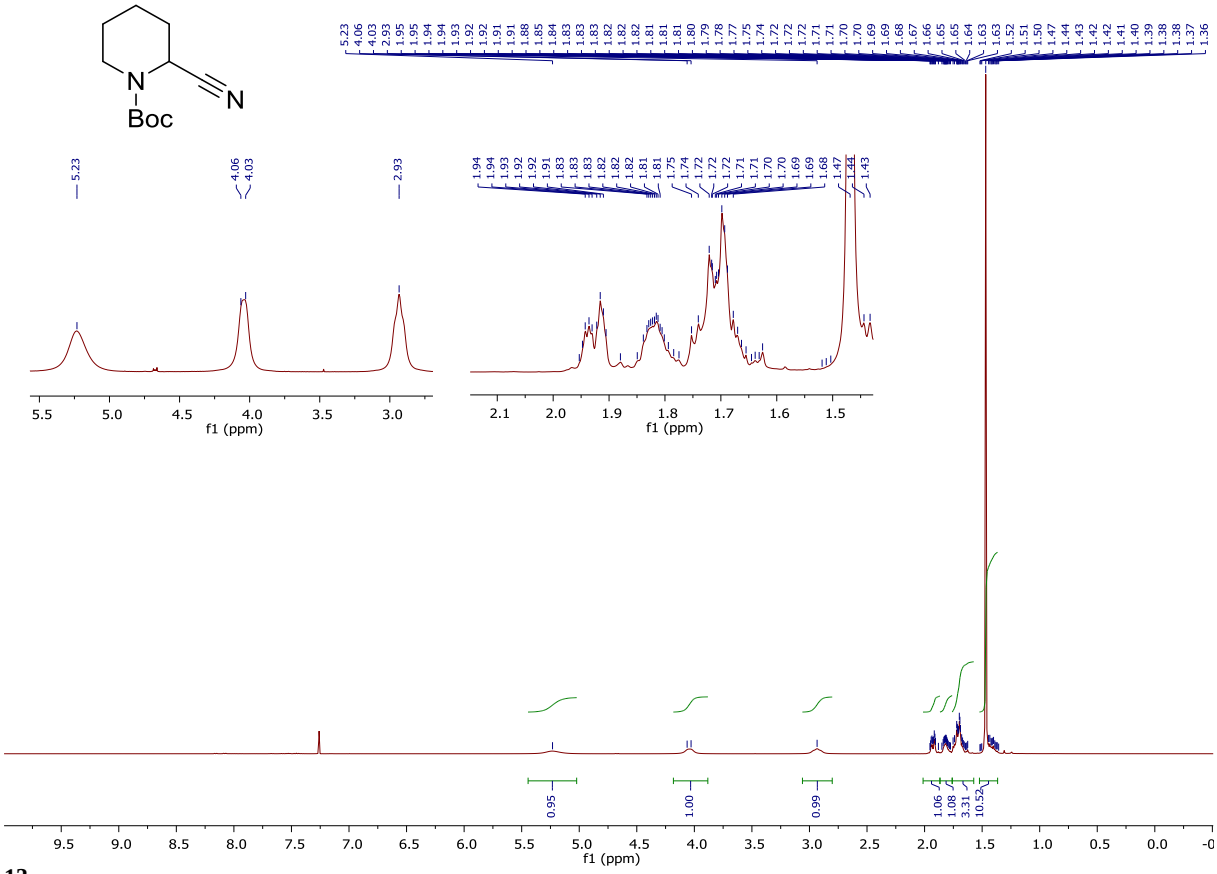

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7e (major isomer)**



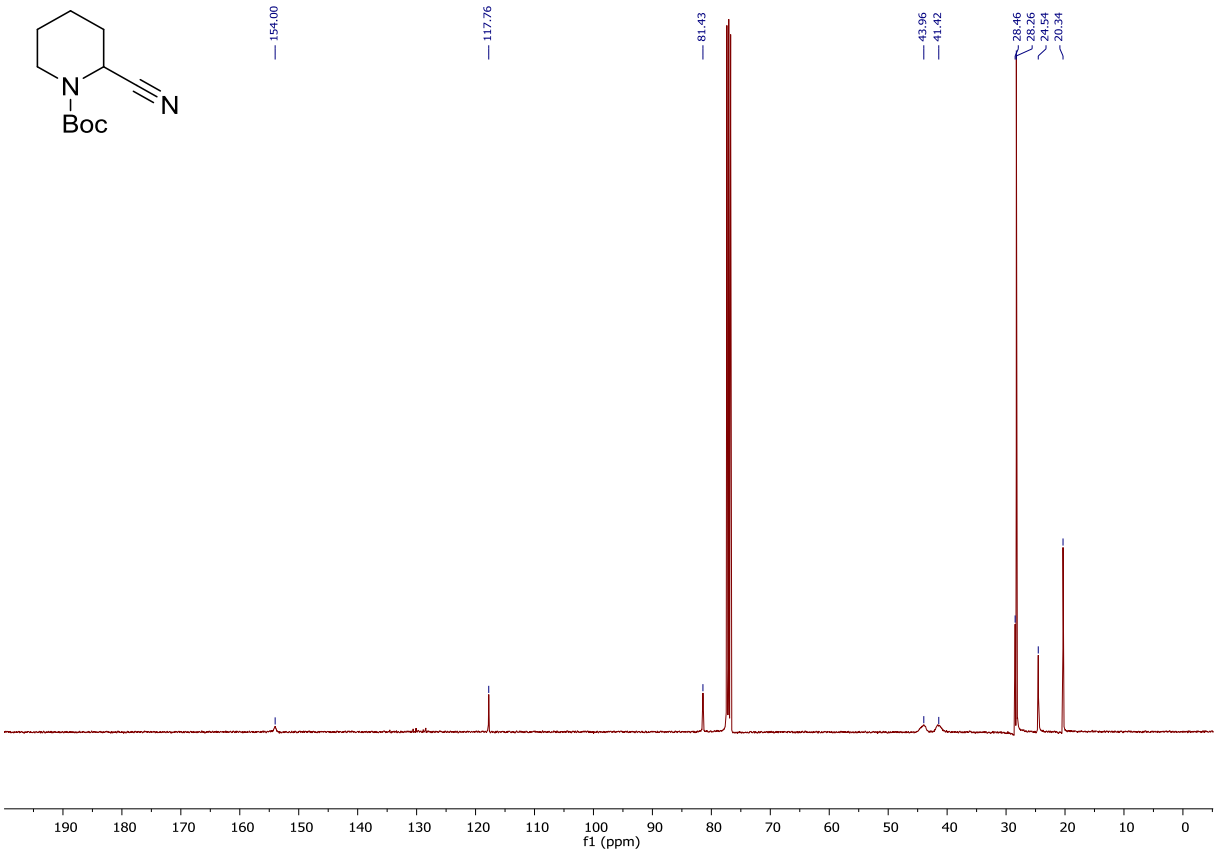
**IR** of compound **7e (major isomer)**



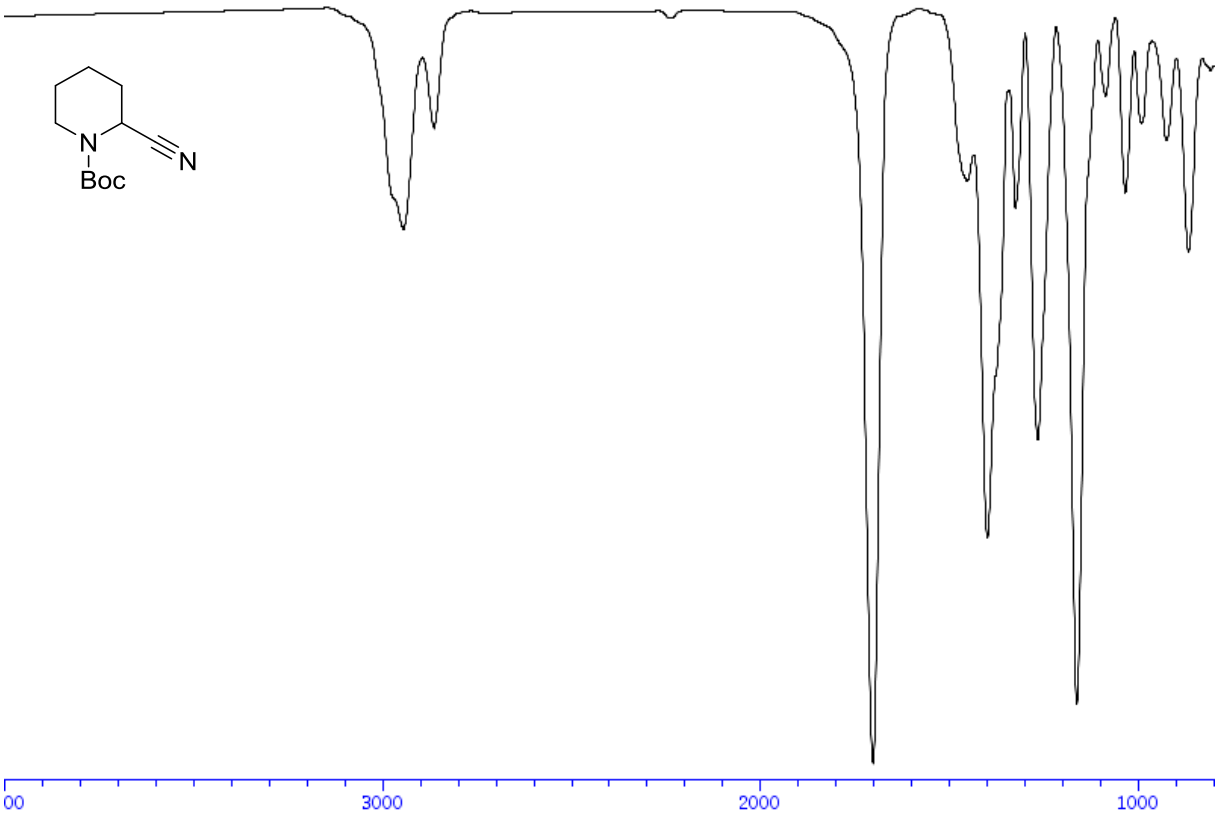
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7f**



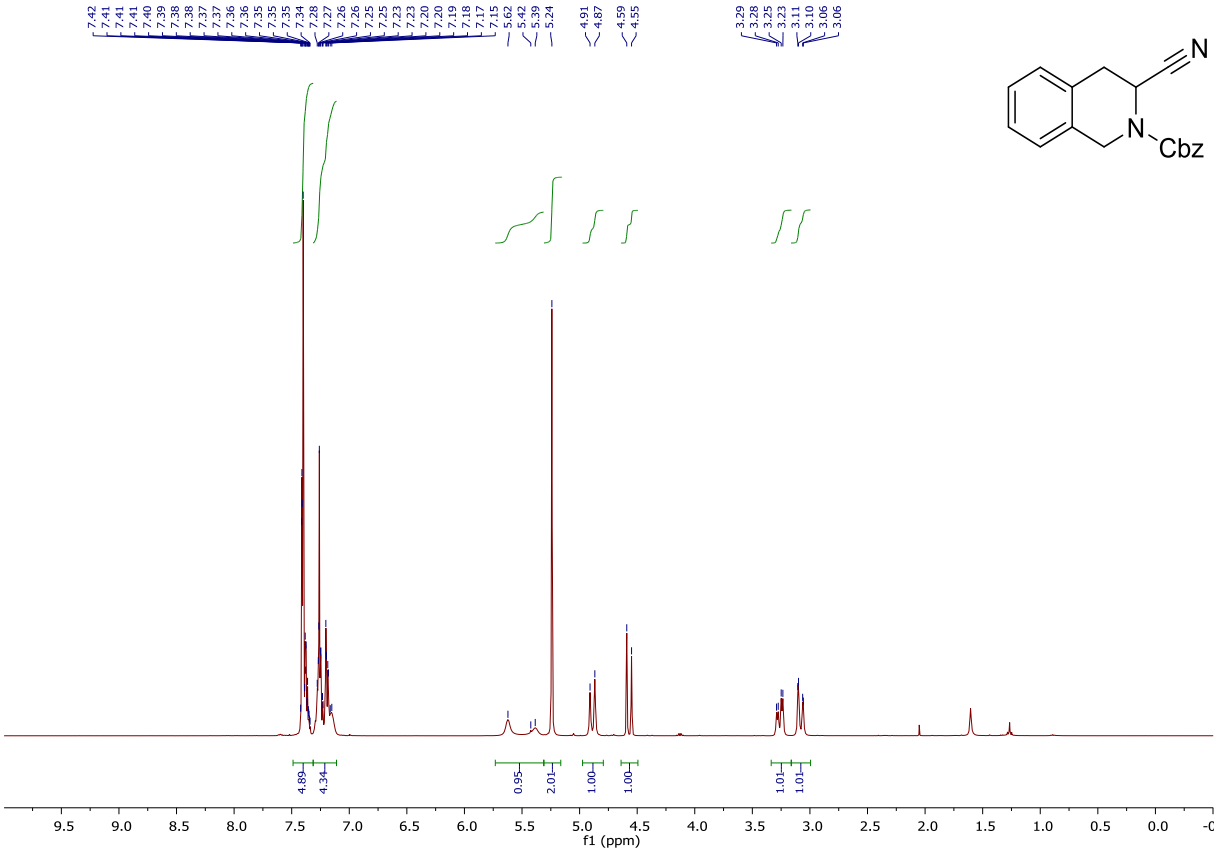

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7f**



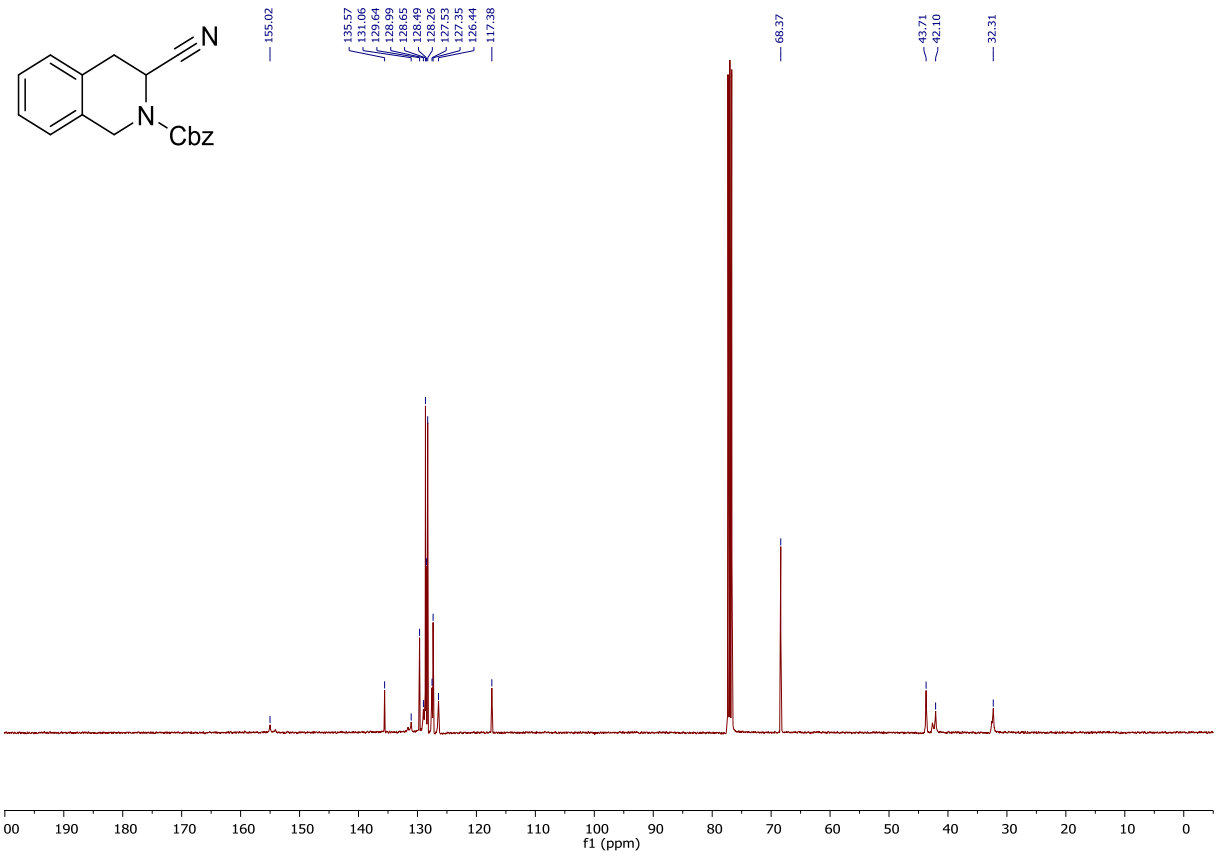
**IR** of compound **7f**



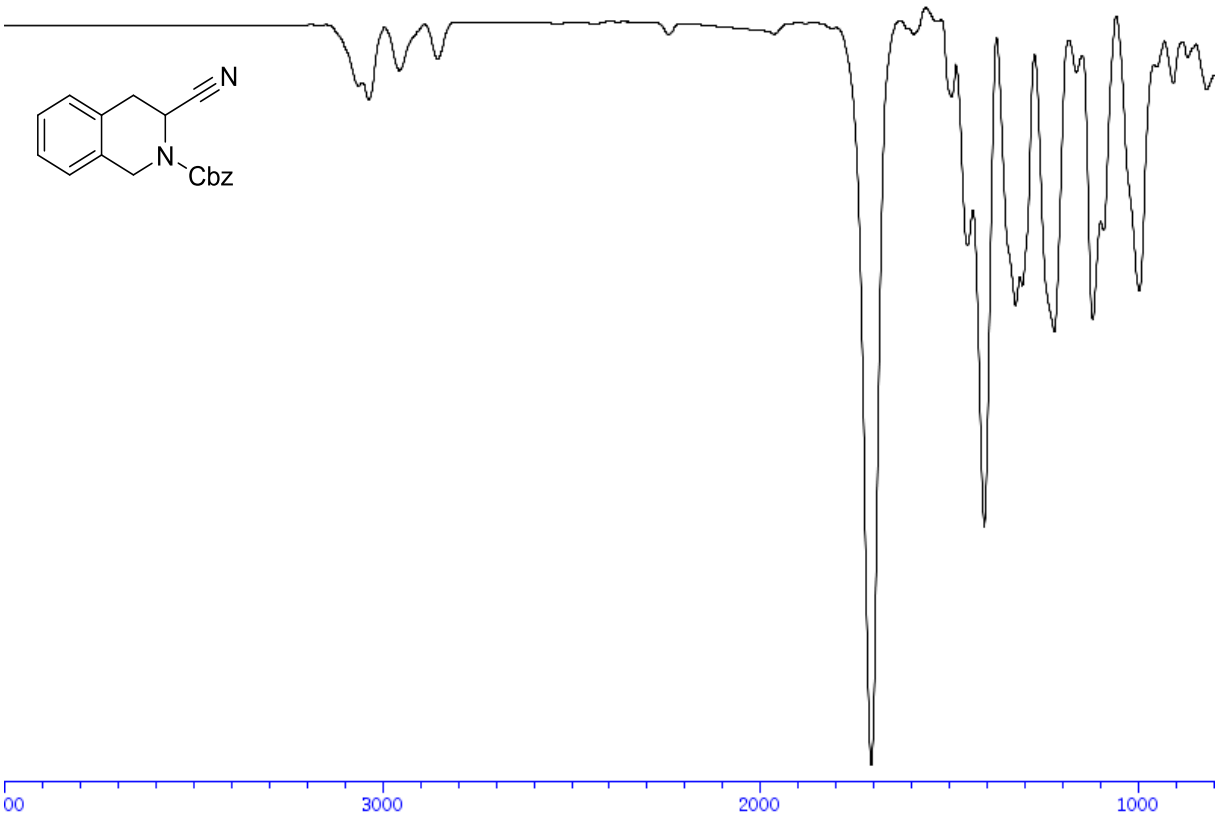
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7g**



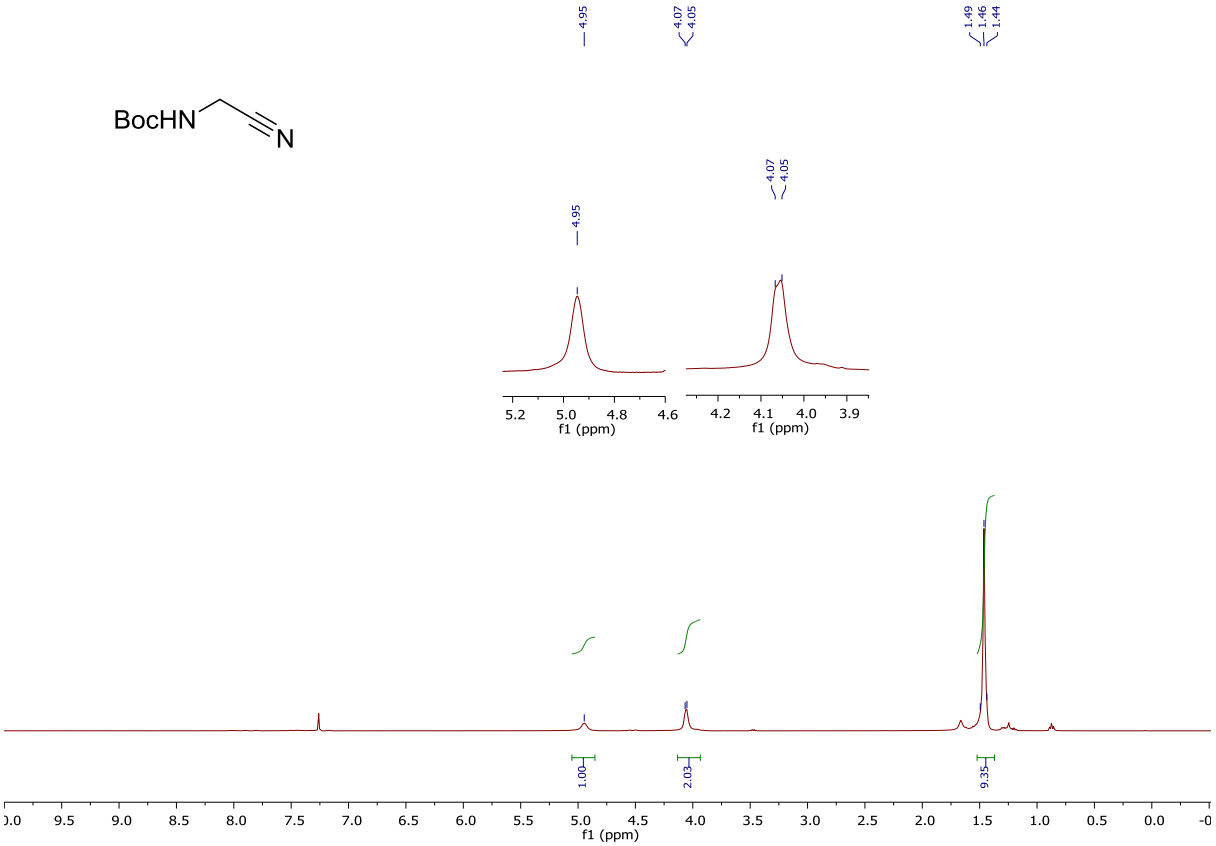

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7g**



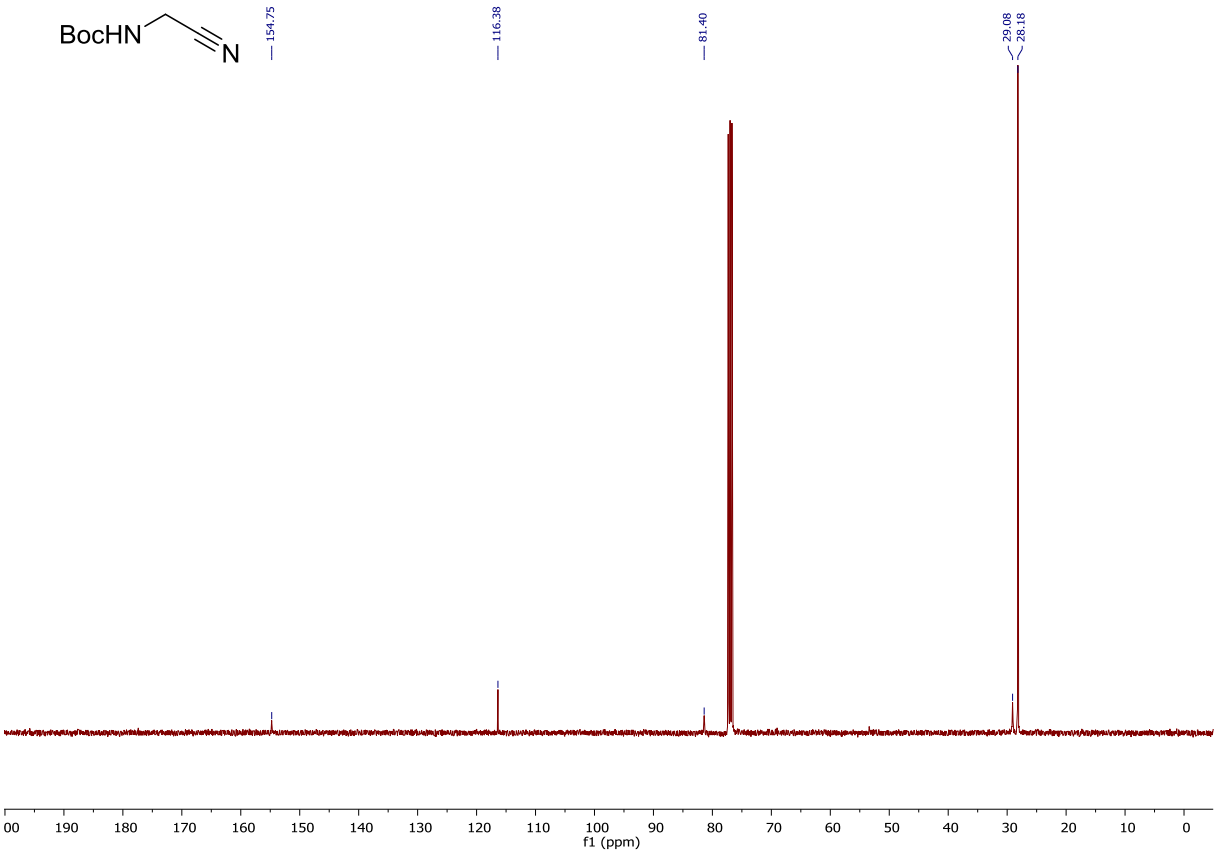
**IR** of compound **7g**



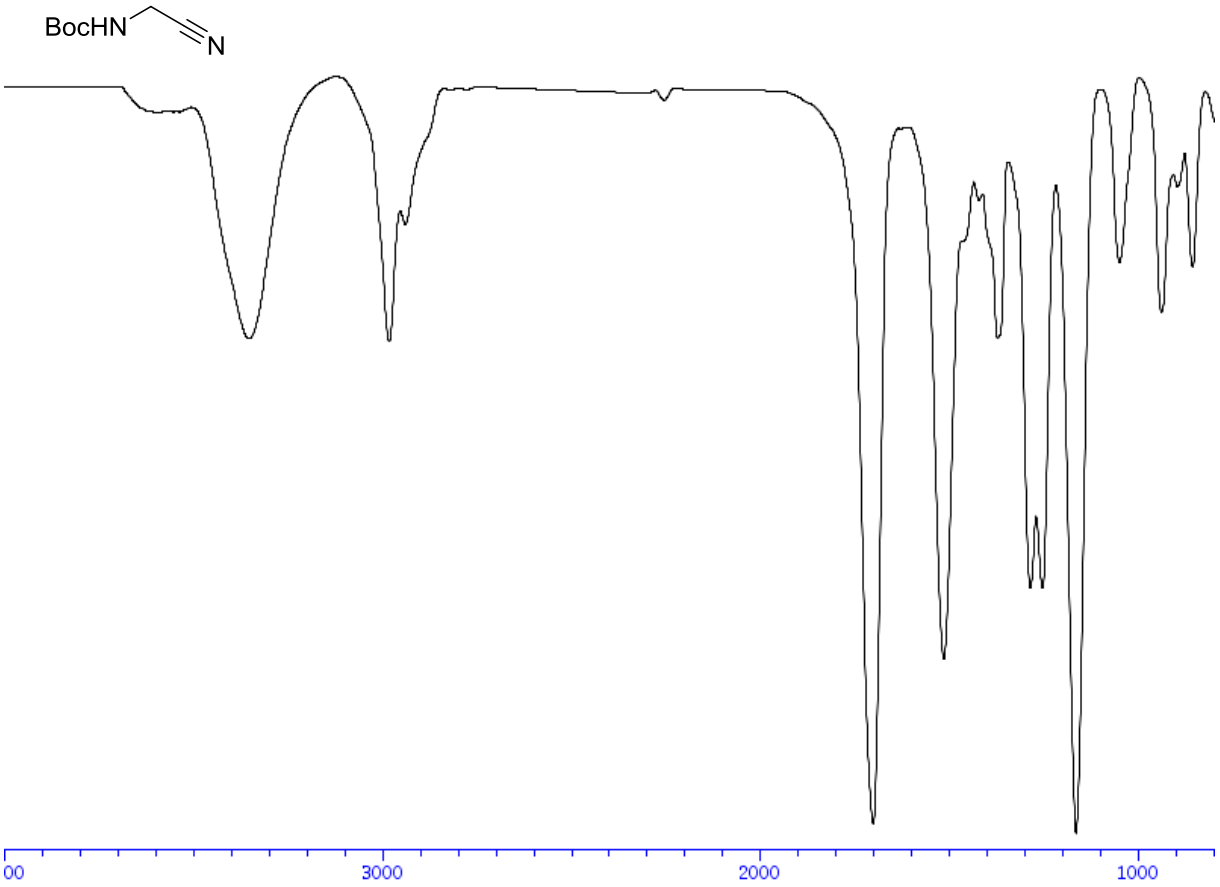
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7h**



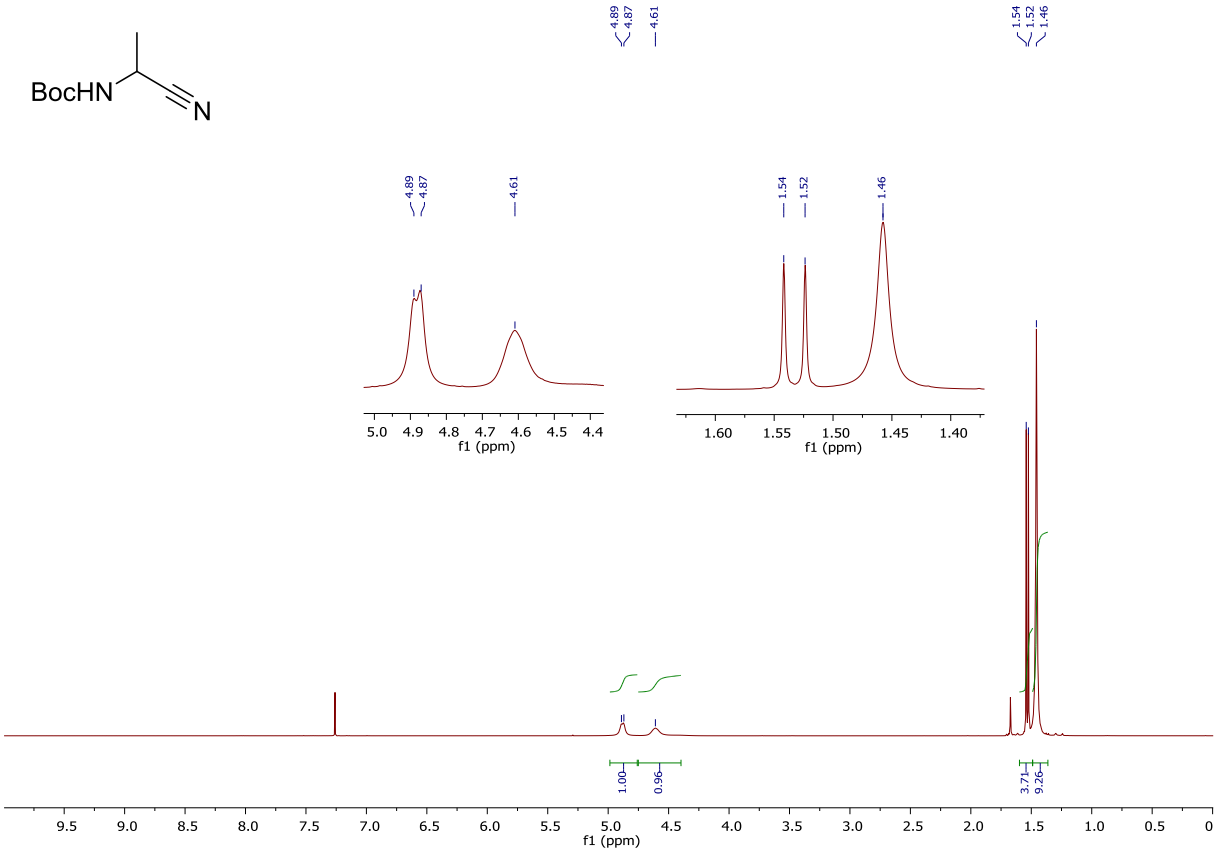

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7h**



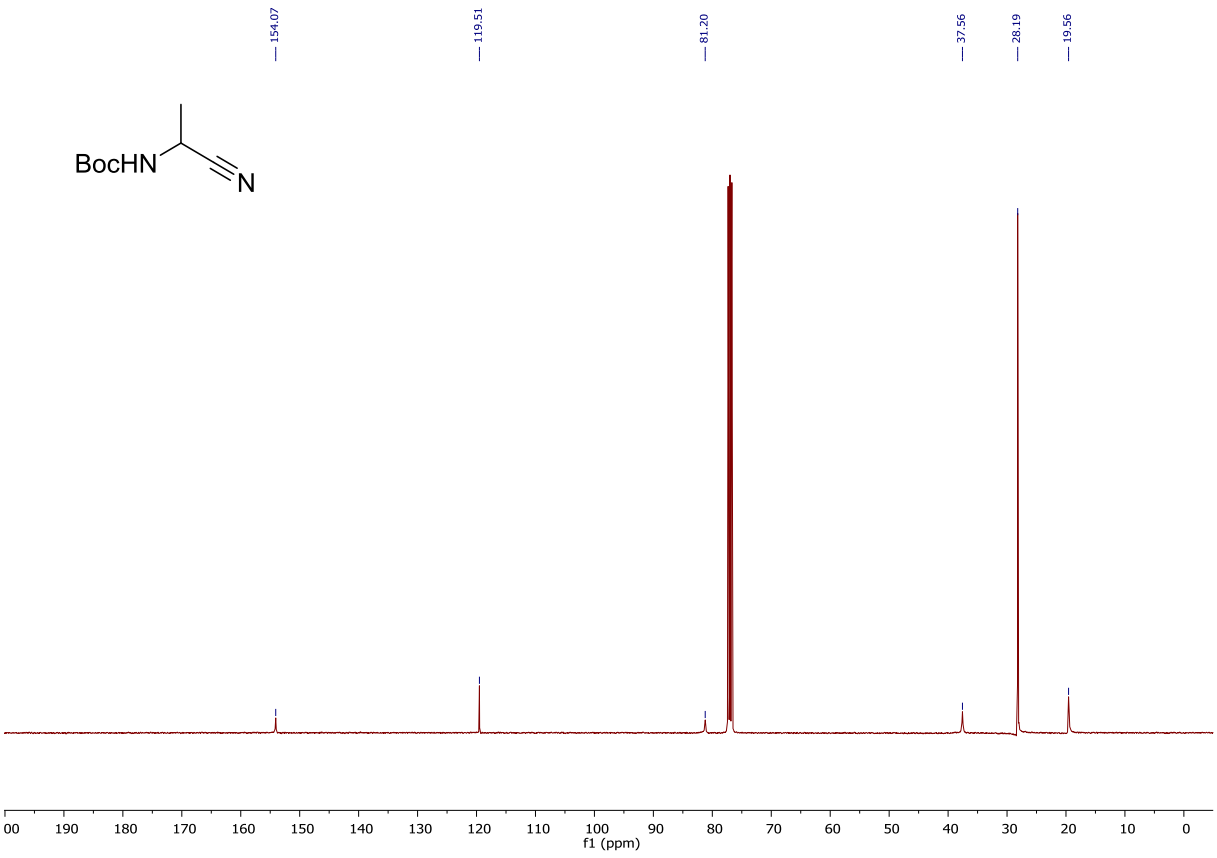
**IR** of compound **7h**



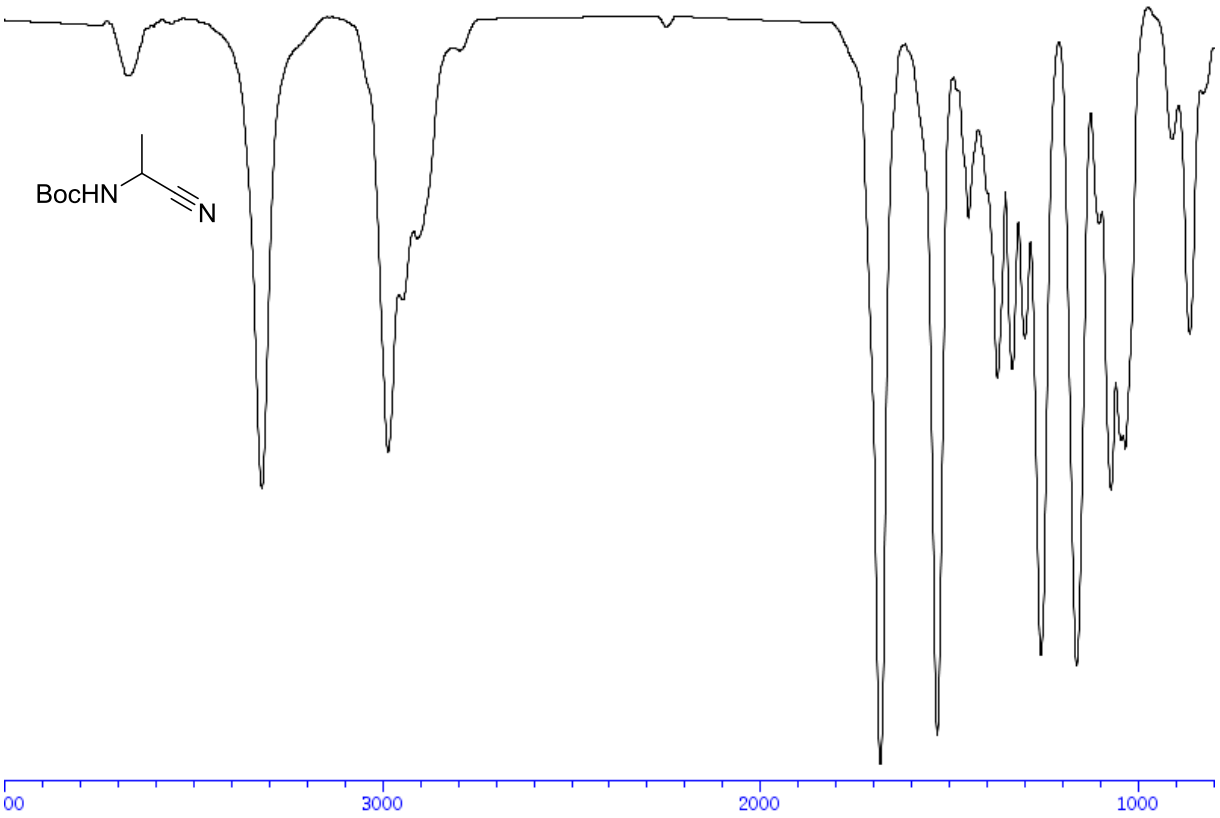
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7i**



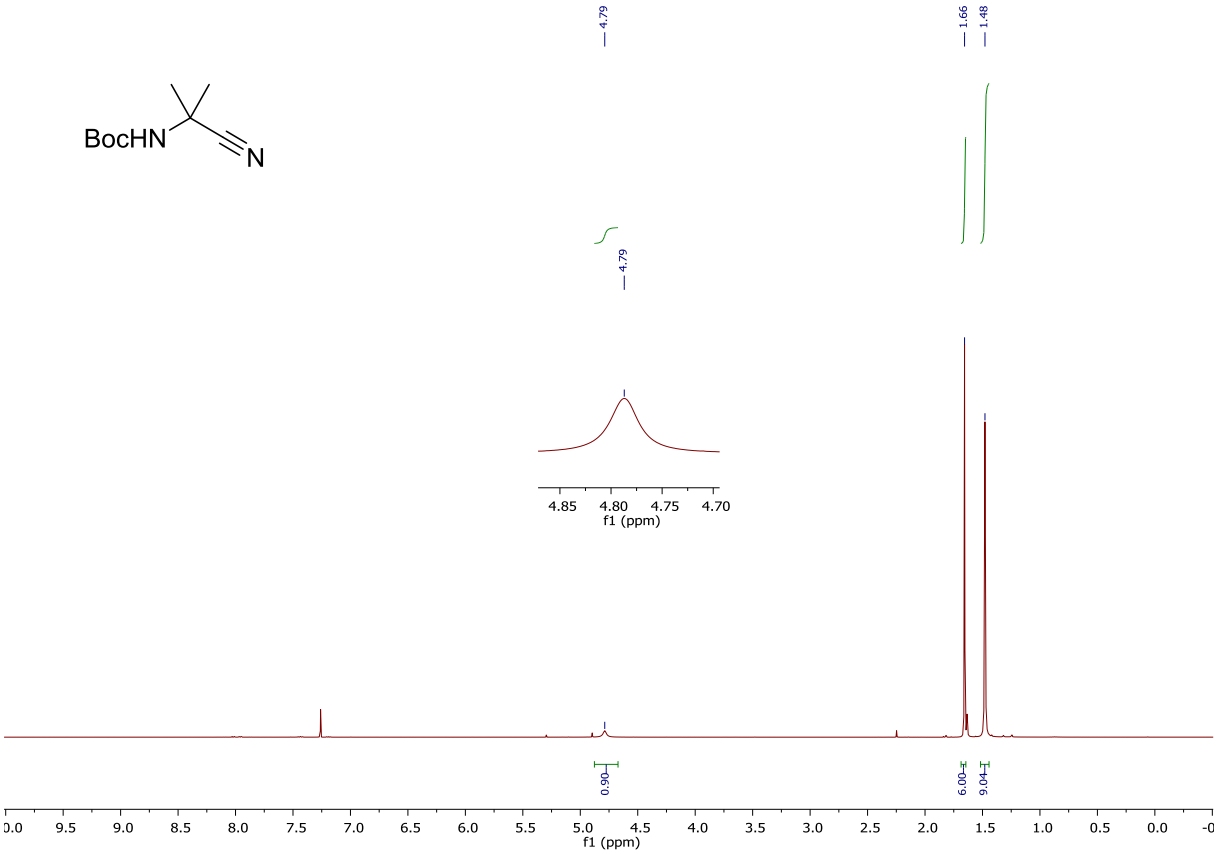

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7i**



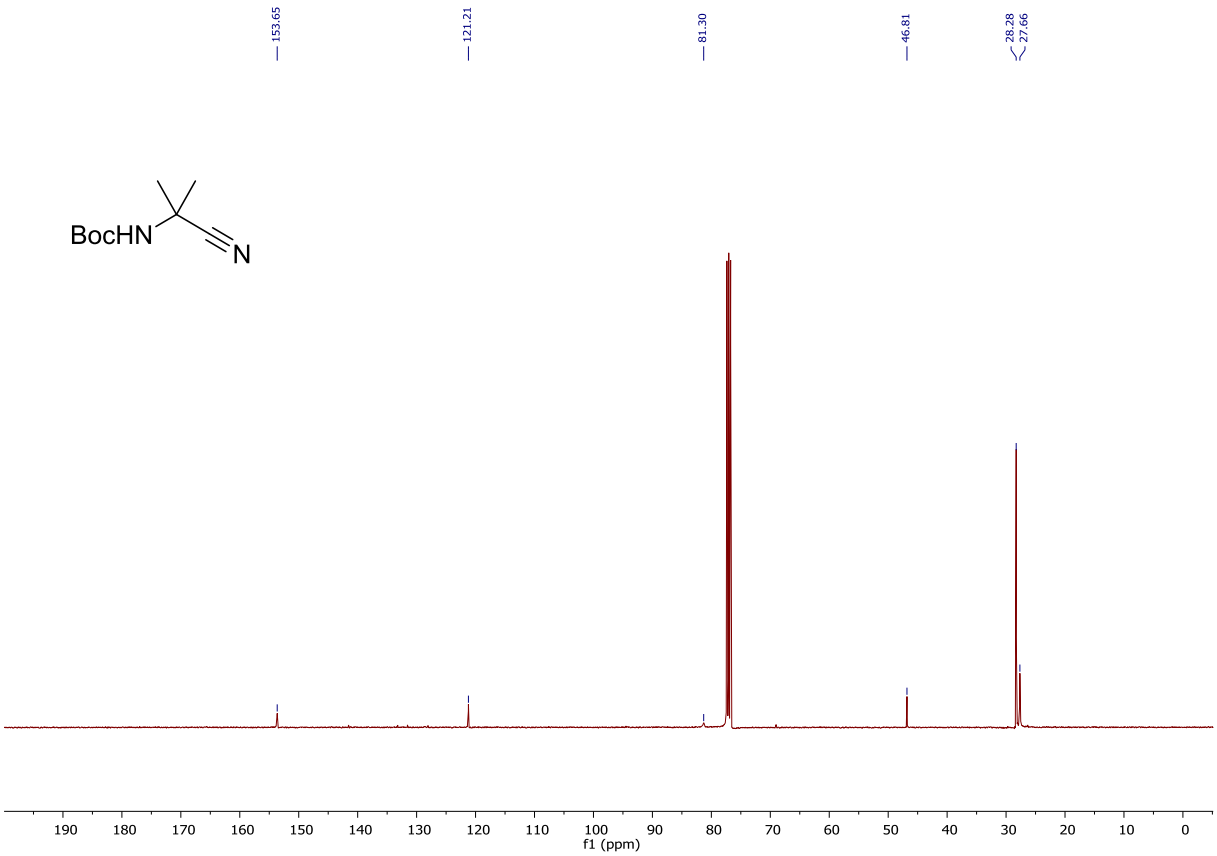
**IR** of compound **7i**



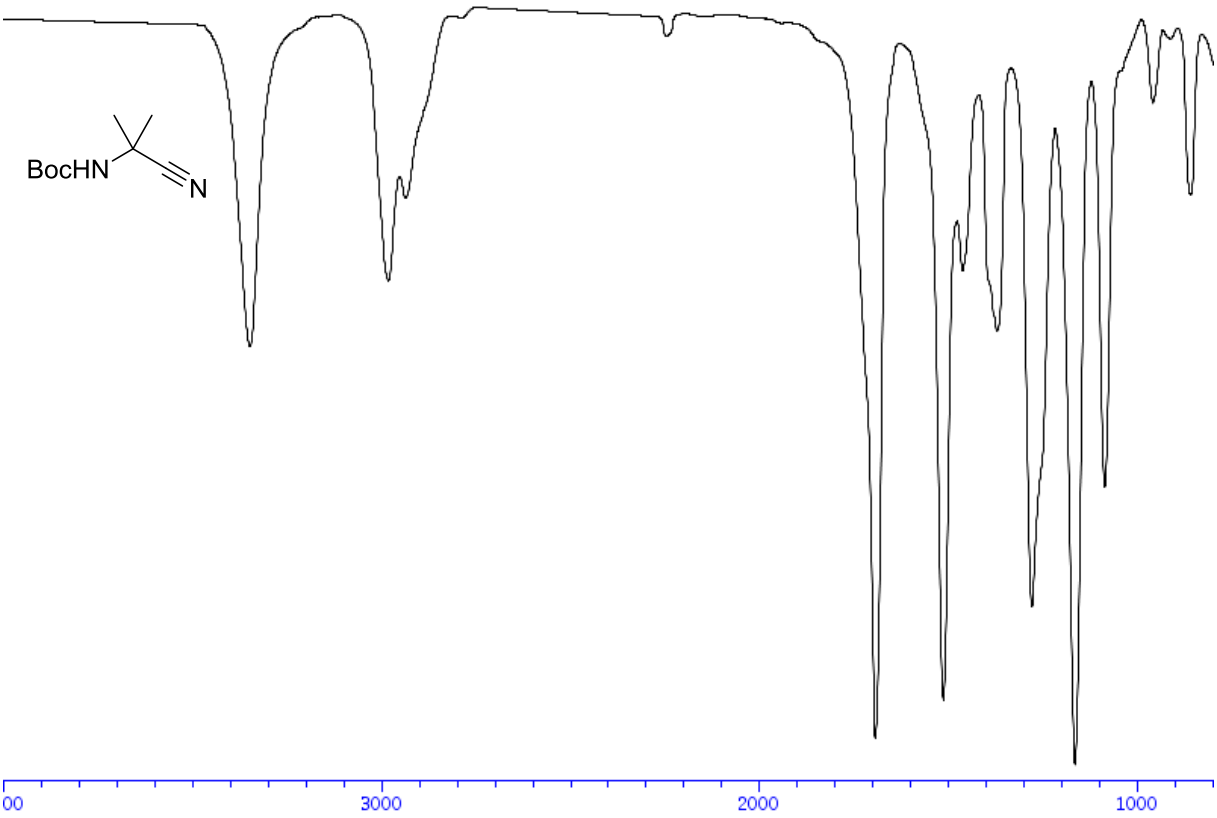
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7j**



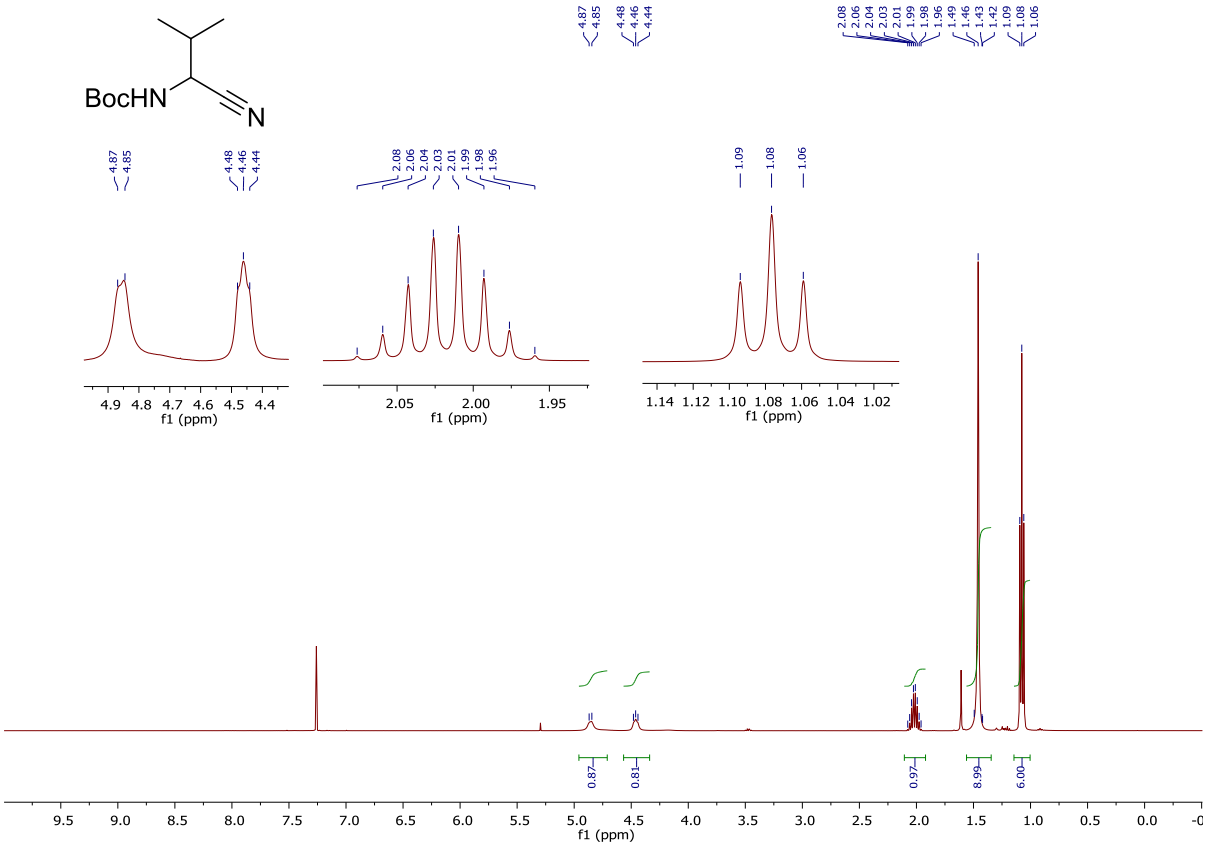

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7j**



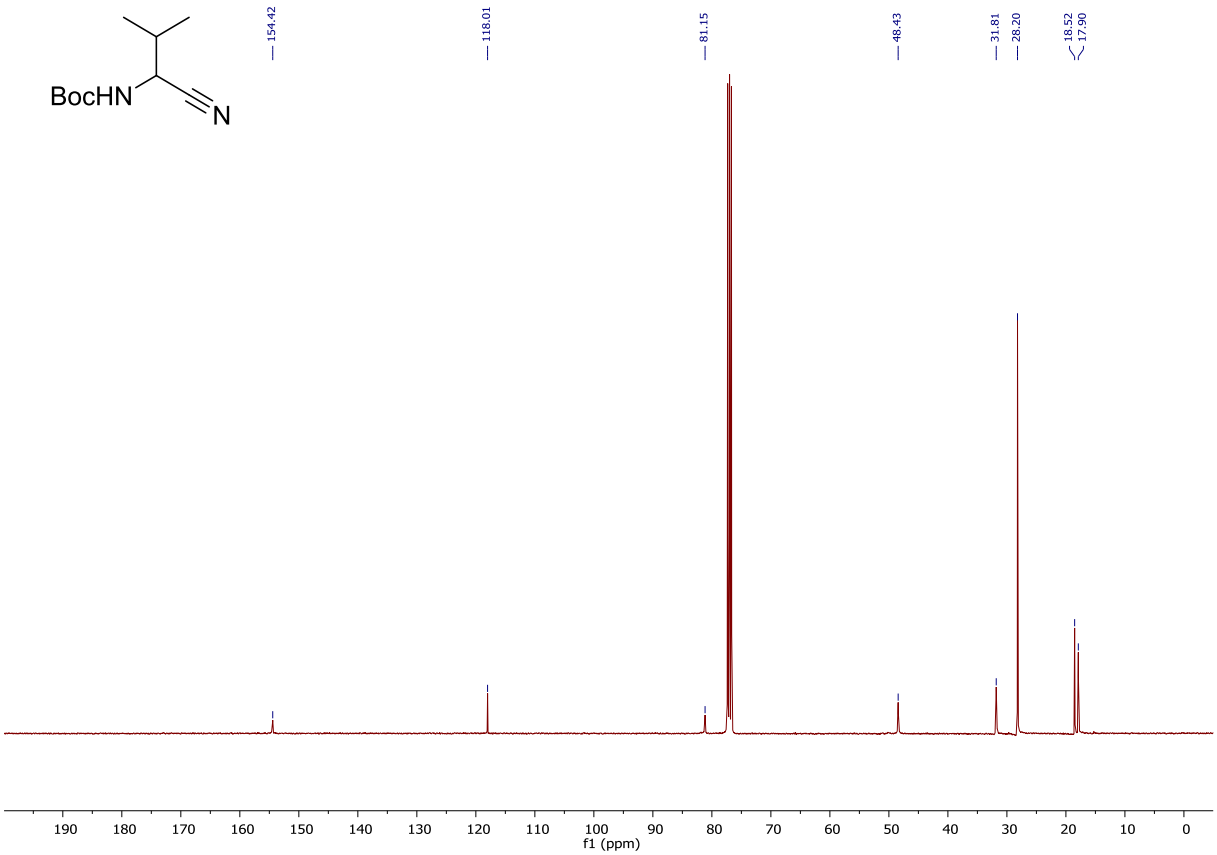
**IR** of compound **7j**



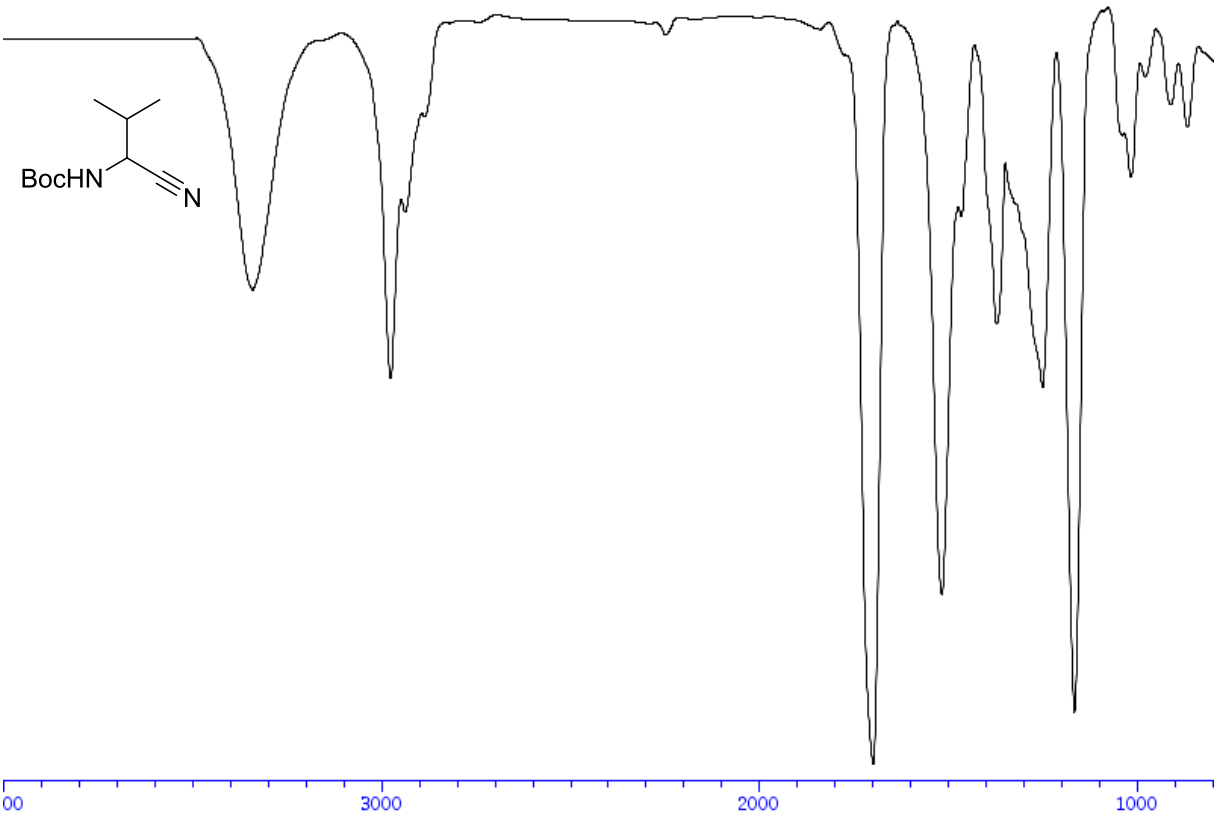
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7k**



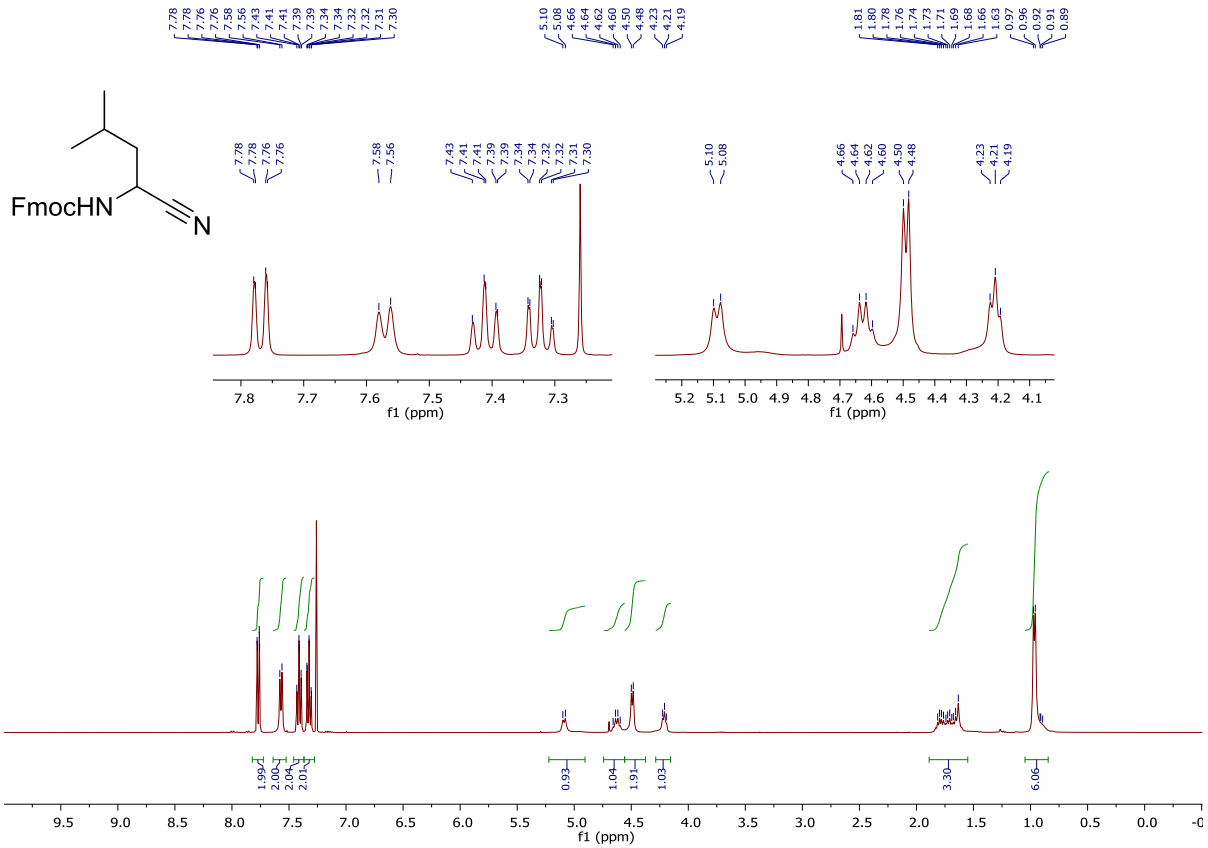

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7k**



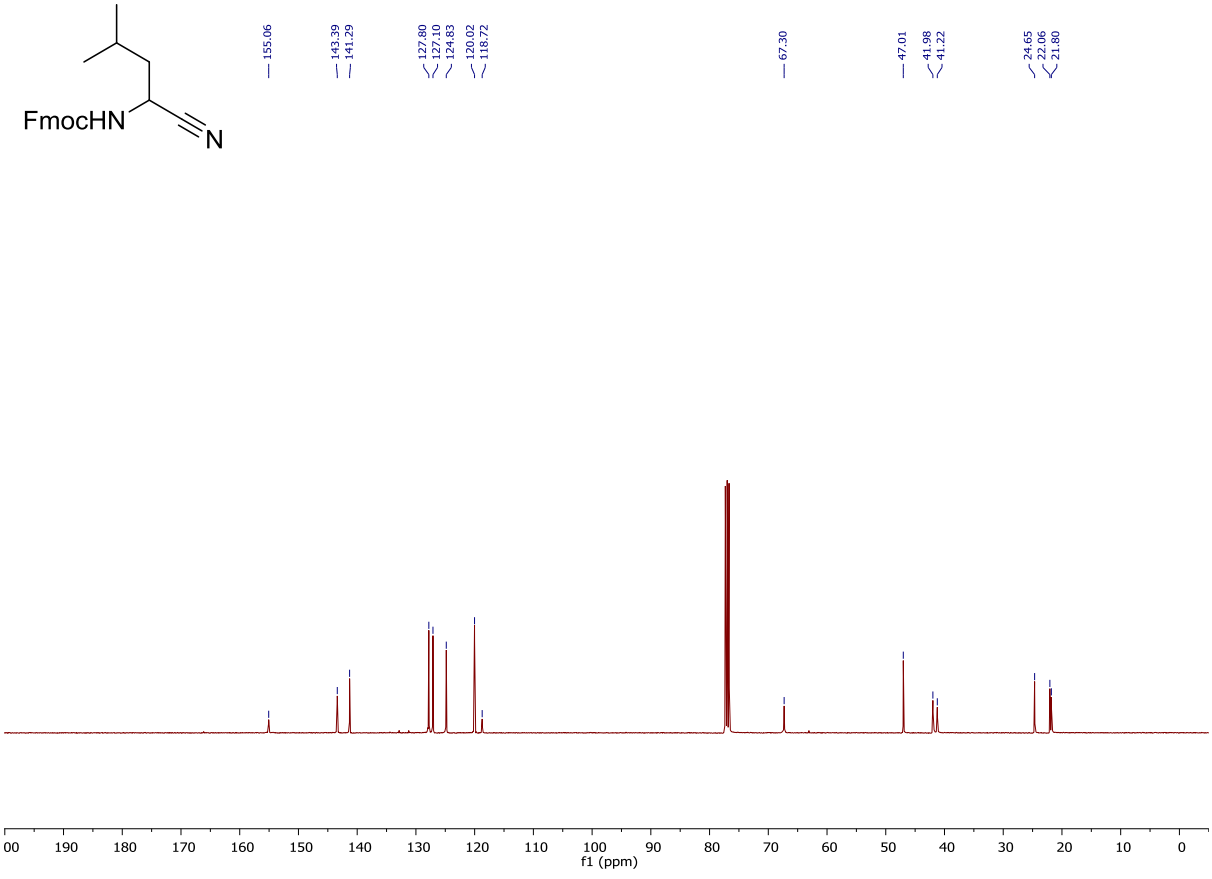
**IR** of compound **7k**



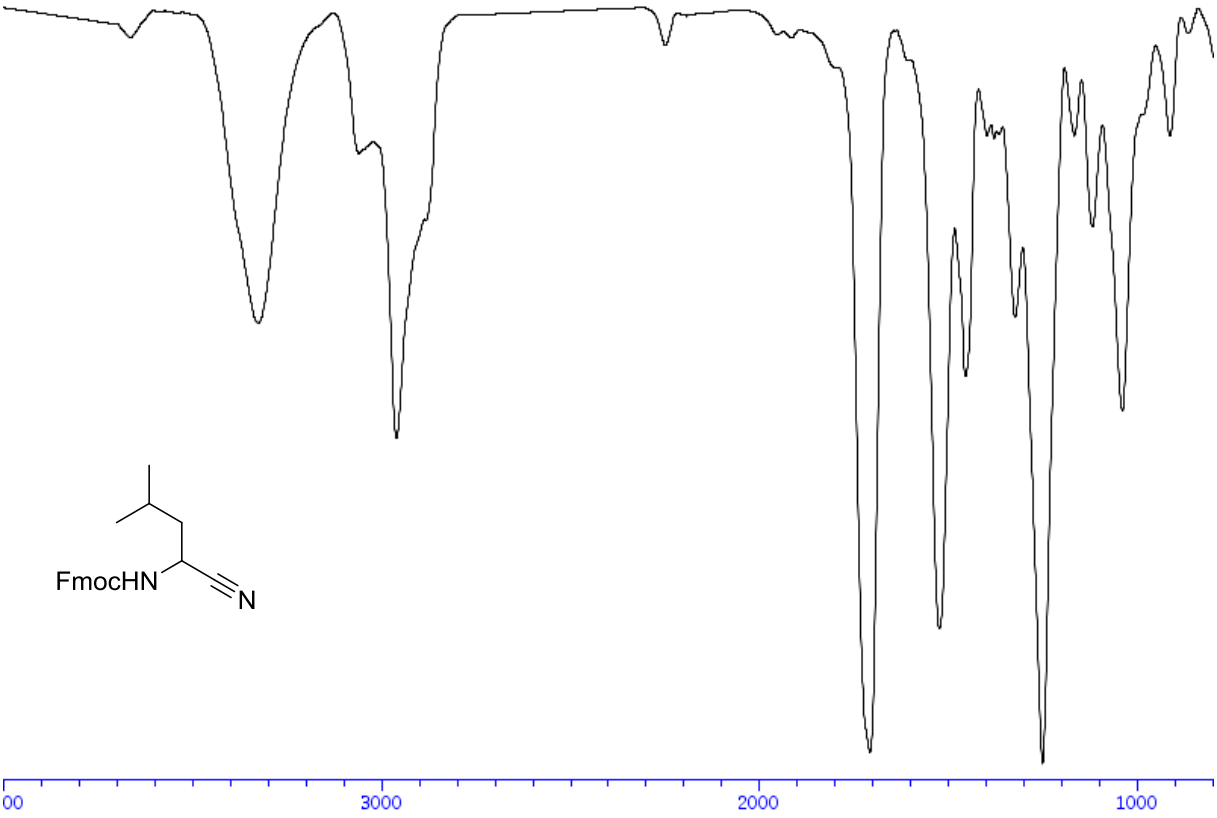
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7l**



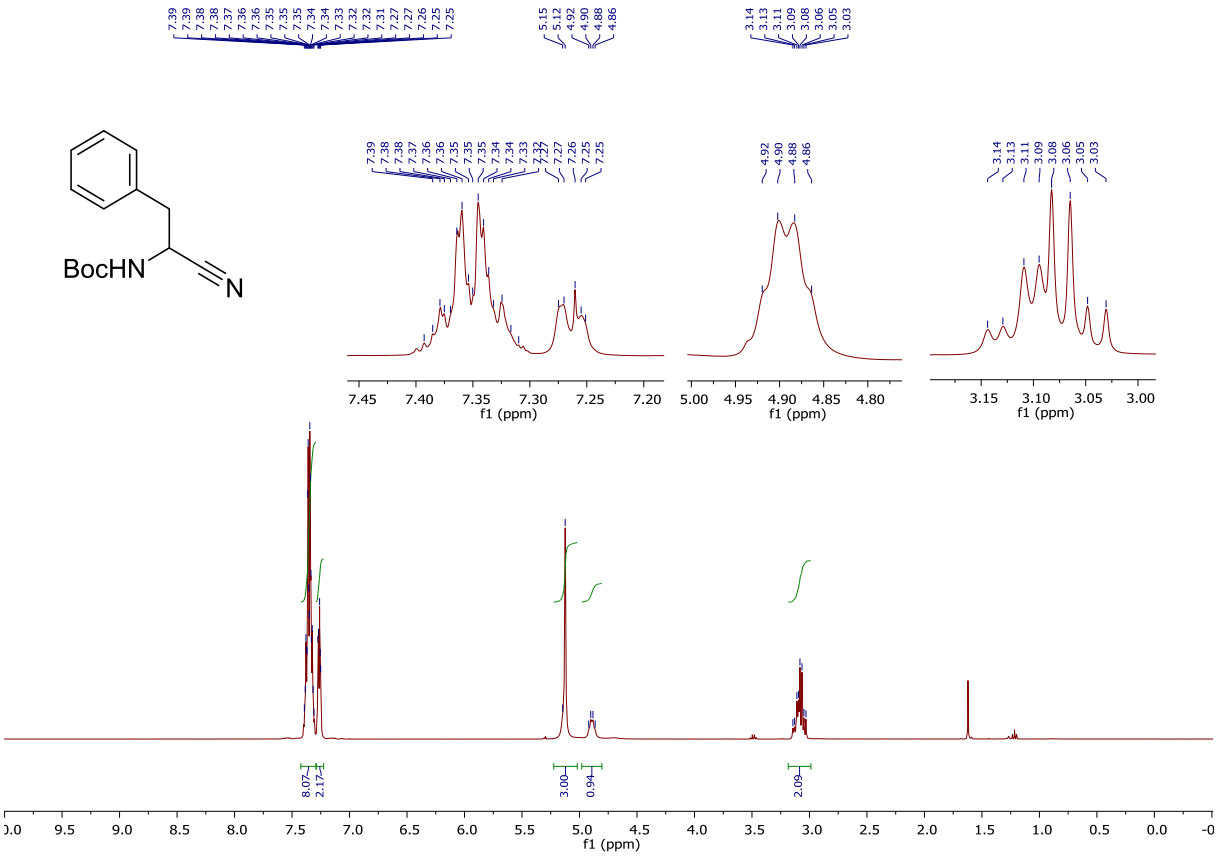

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **XX**



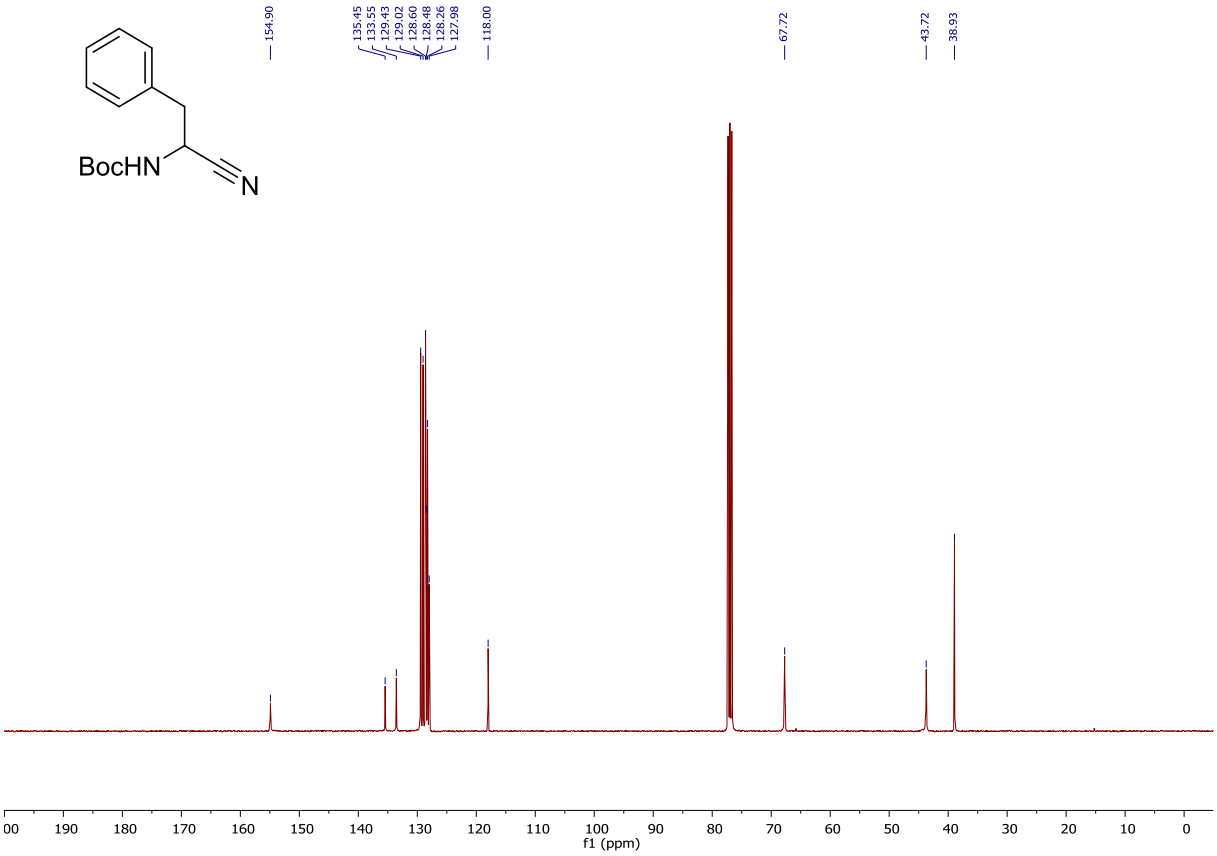
**IR** of compound **7l**



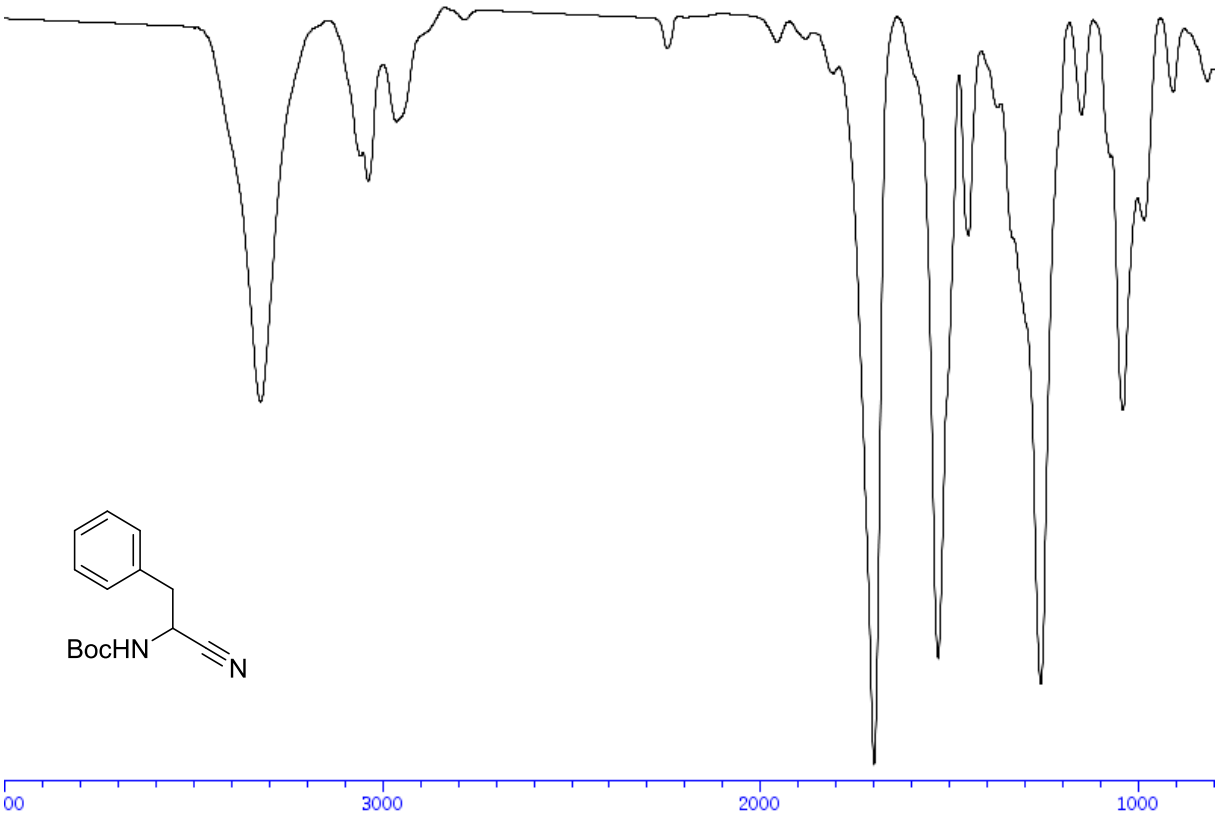
## $^{1}$**H-NMR** (400 MHz, $CDCl_3$) of compound **7m**



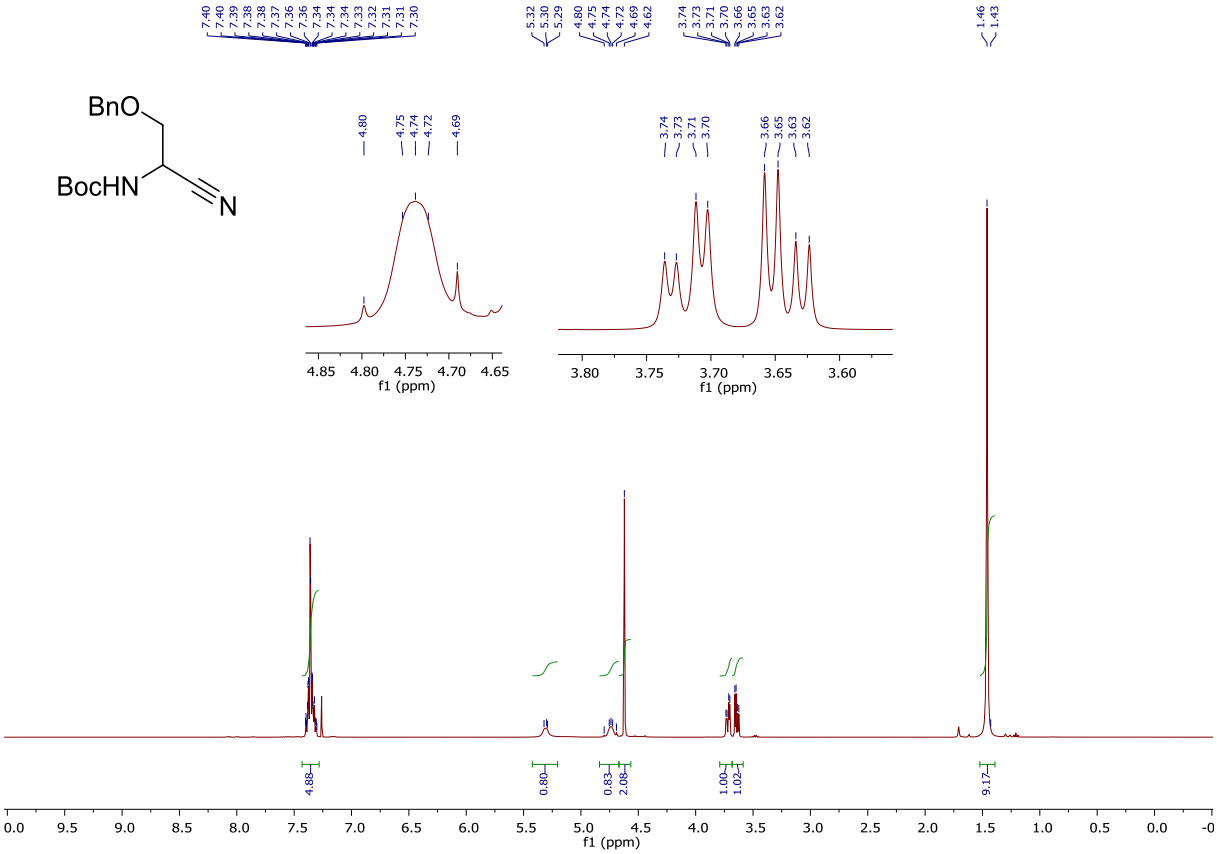

## $^{13}$**C-NMR** (100 MHz, $CDCl_3$) of compound **7m**



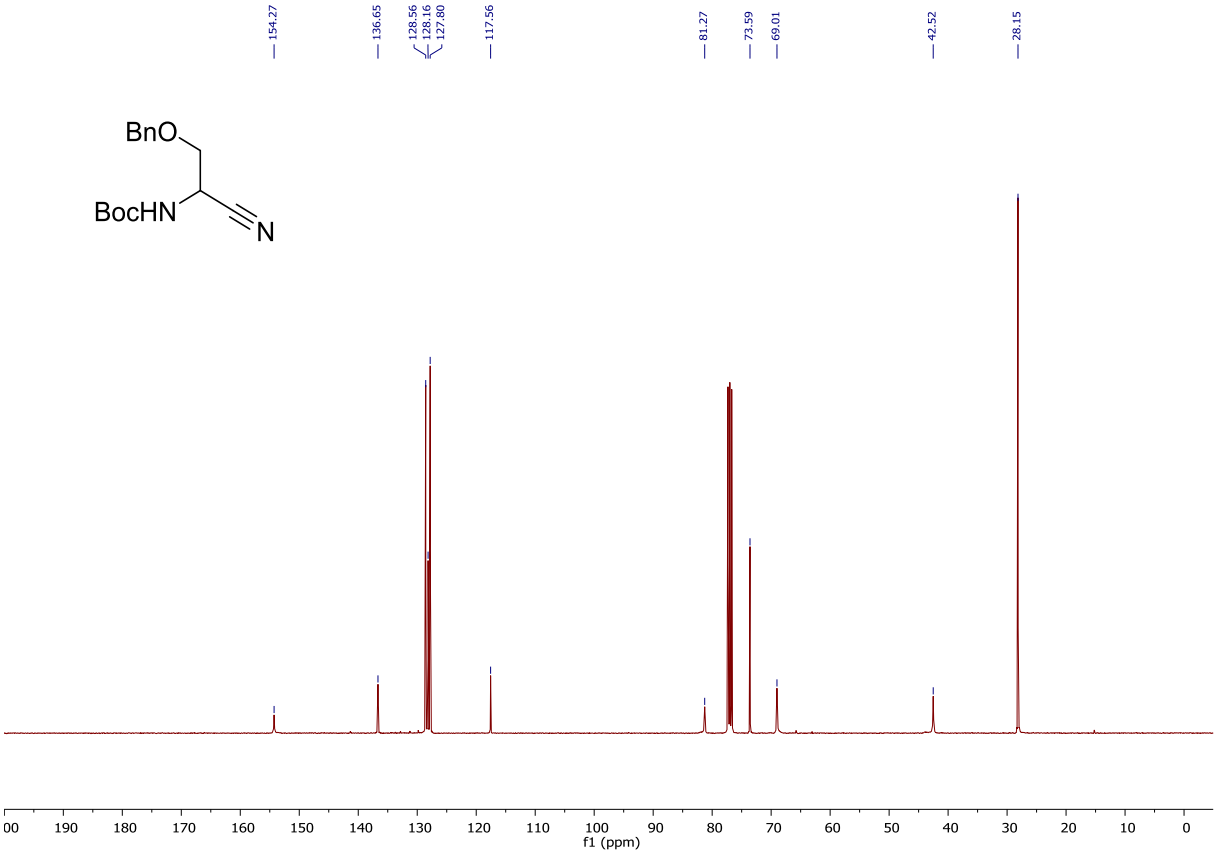
**IR** of compound **7m**



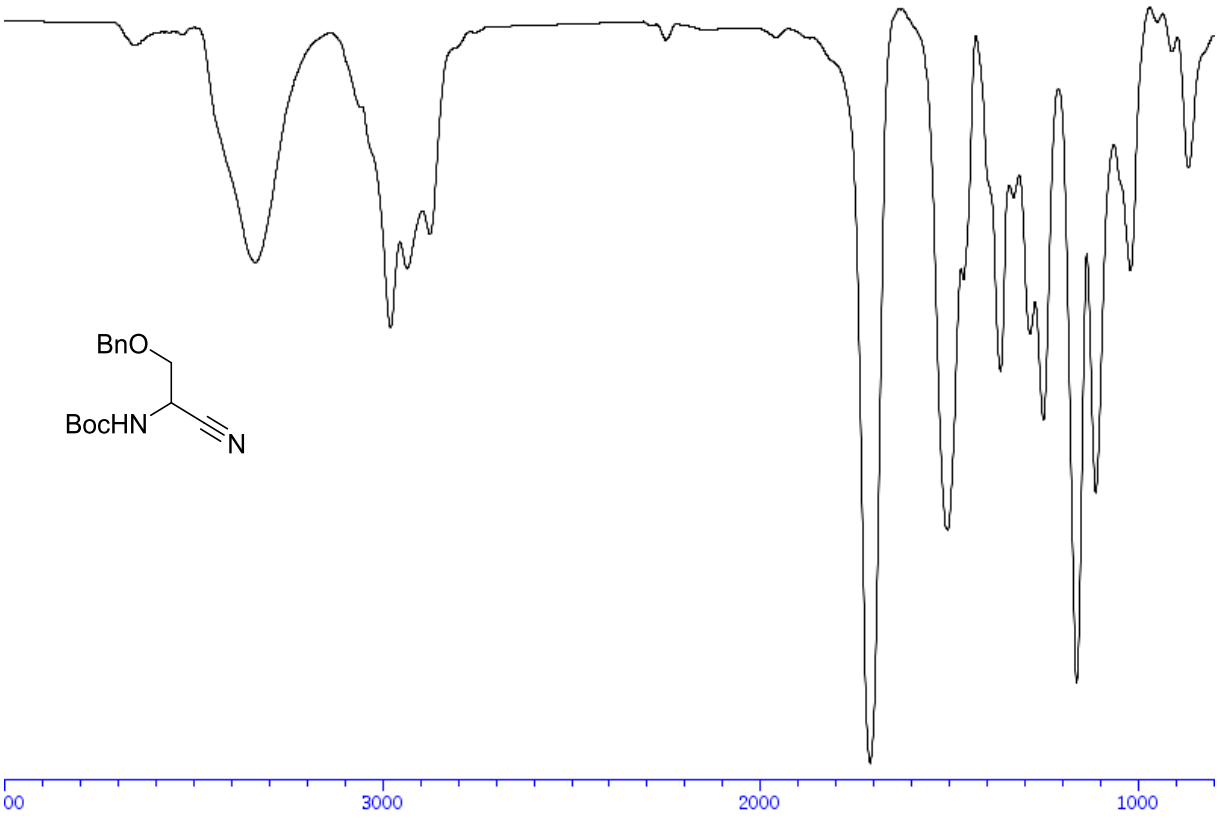
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7n**



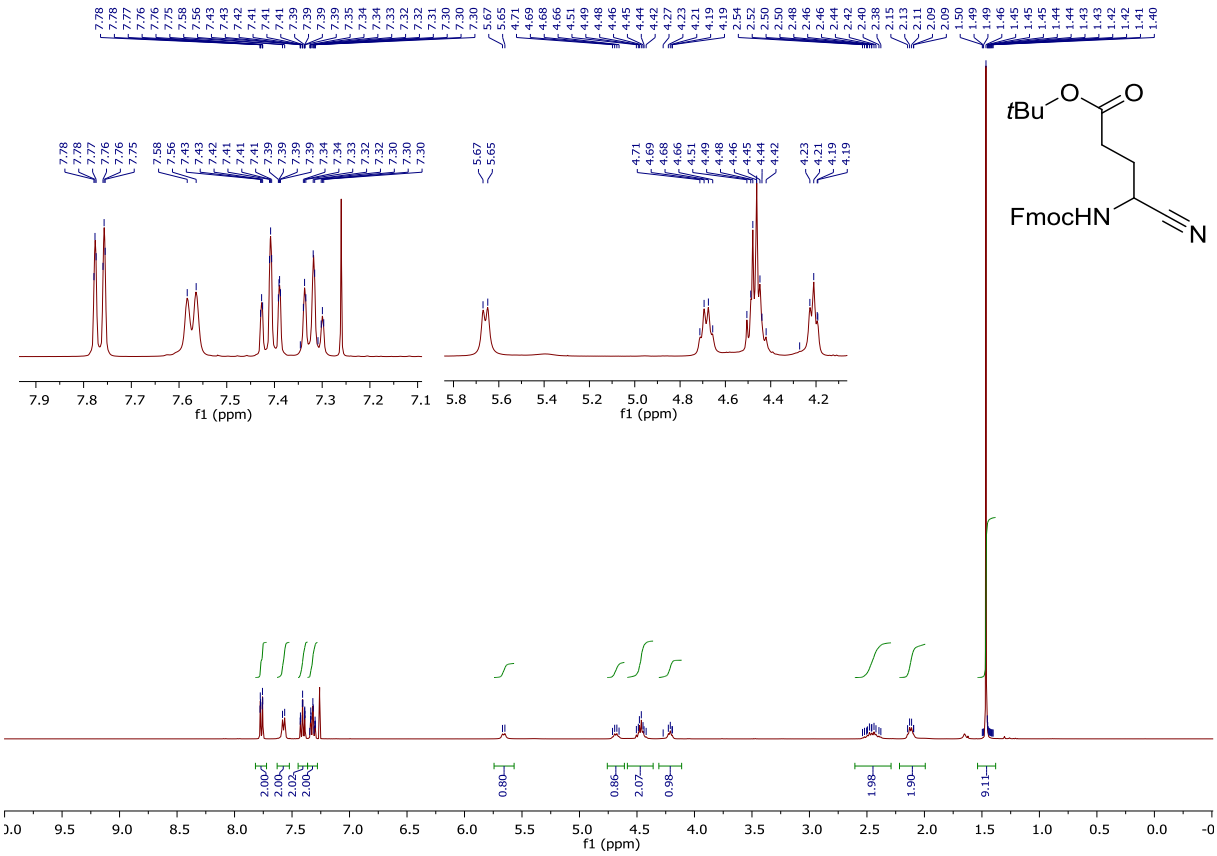

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **7n**



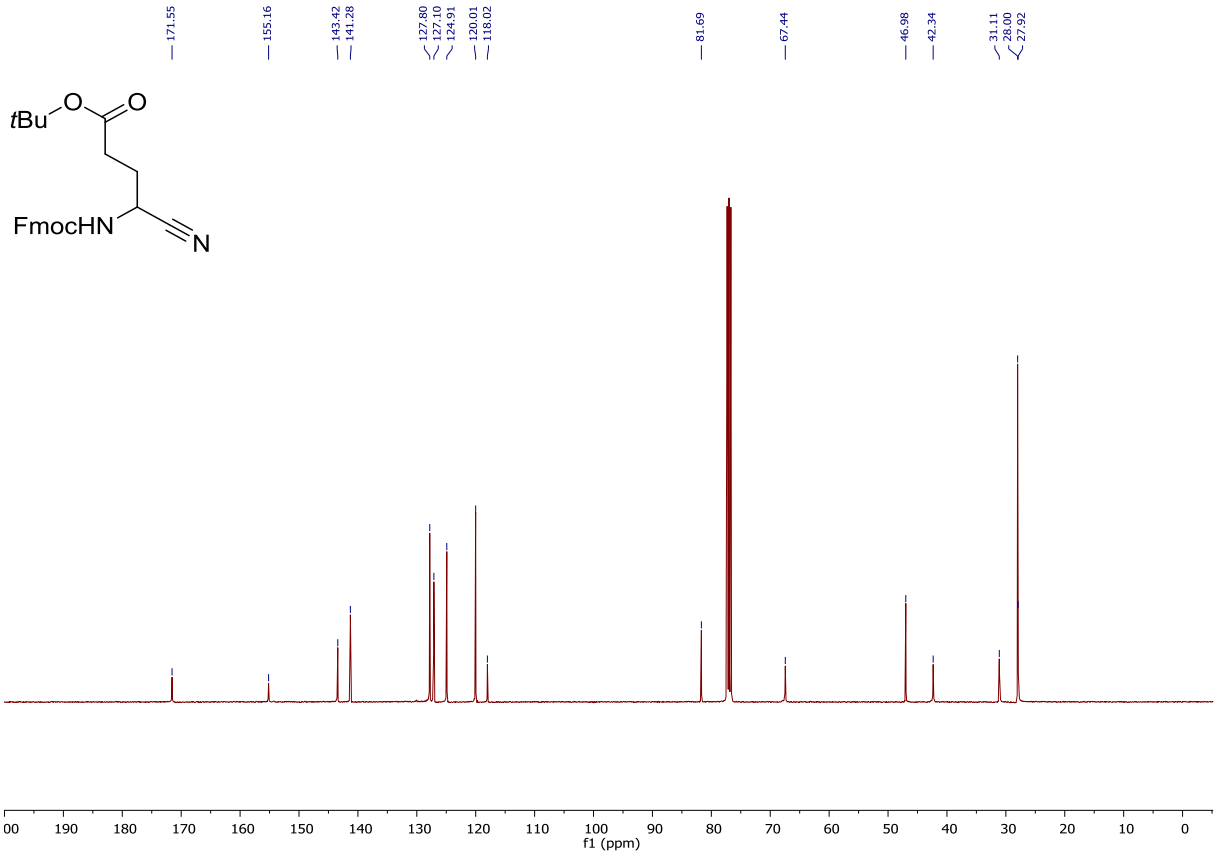
**IR** of compound **7n**



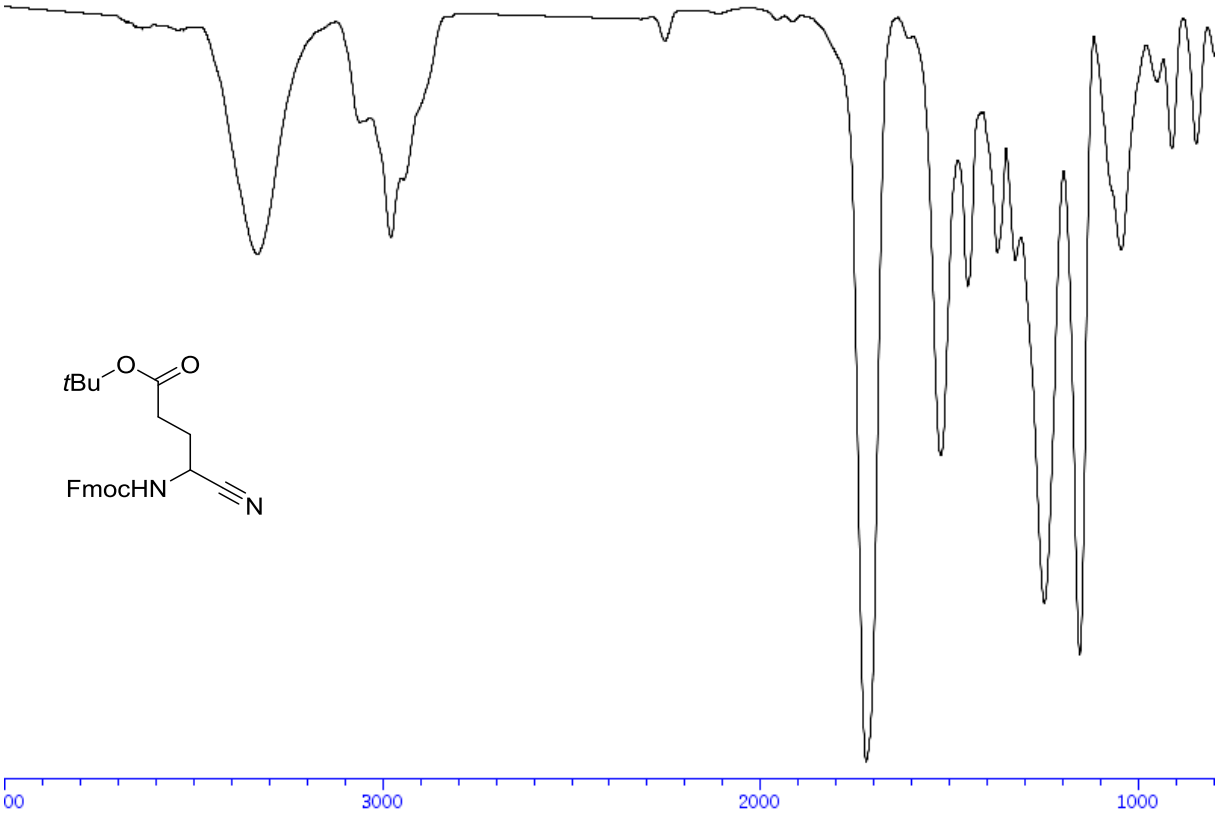
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7o**



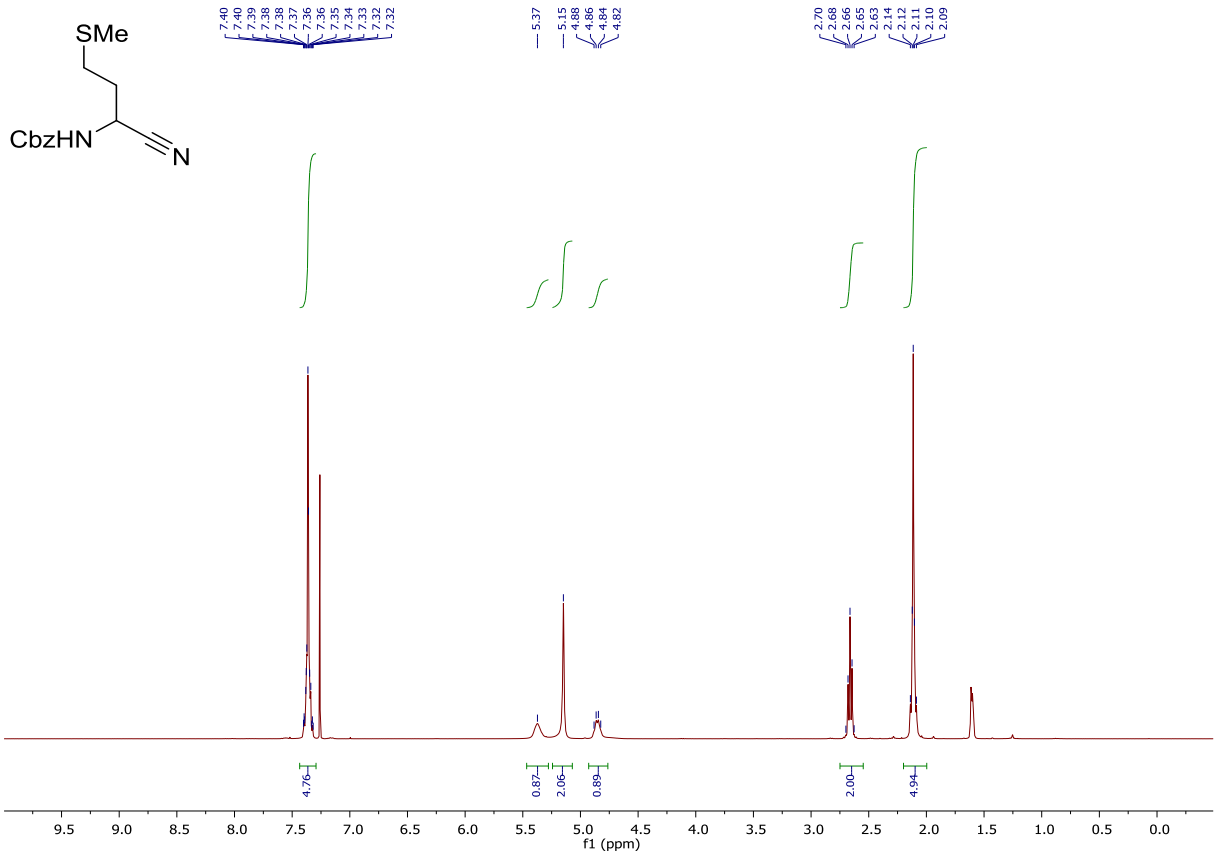

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **7o**



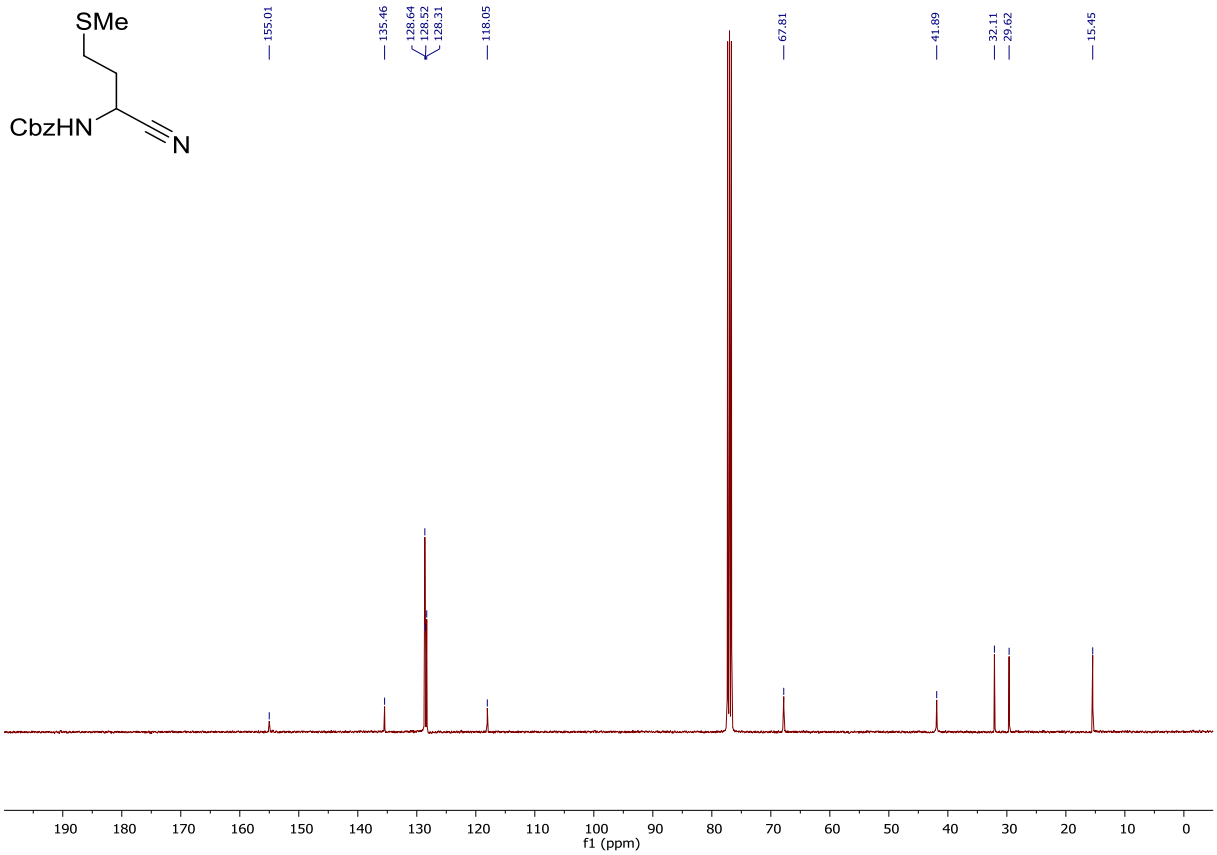
**IR** of compound **7o**



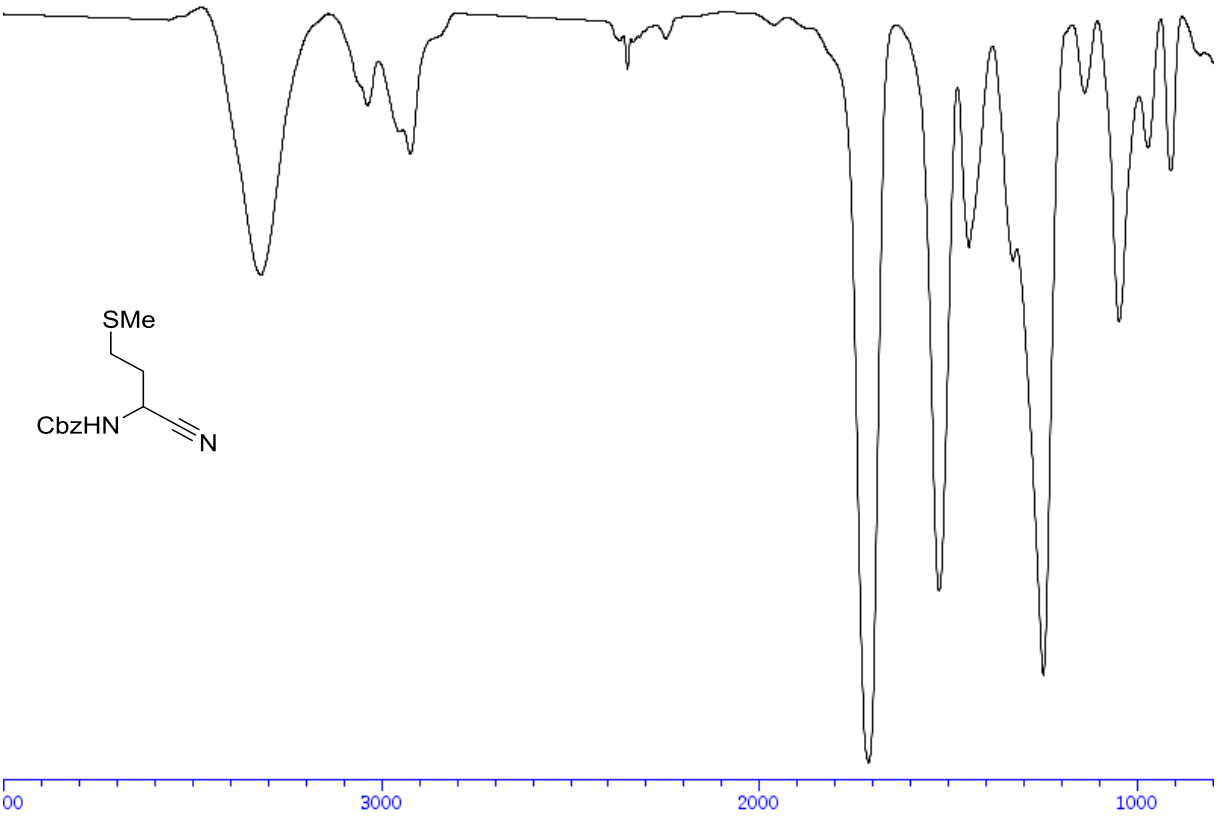
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7p**



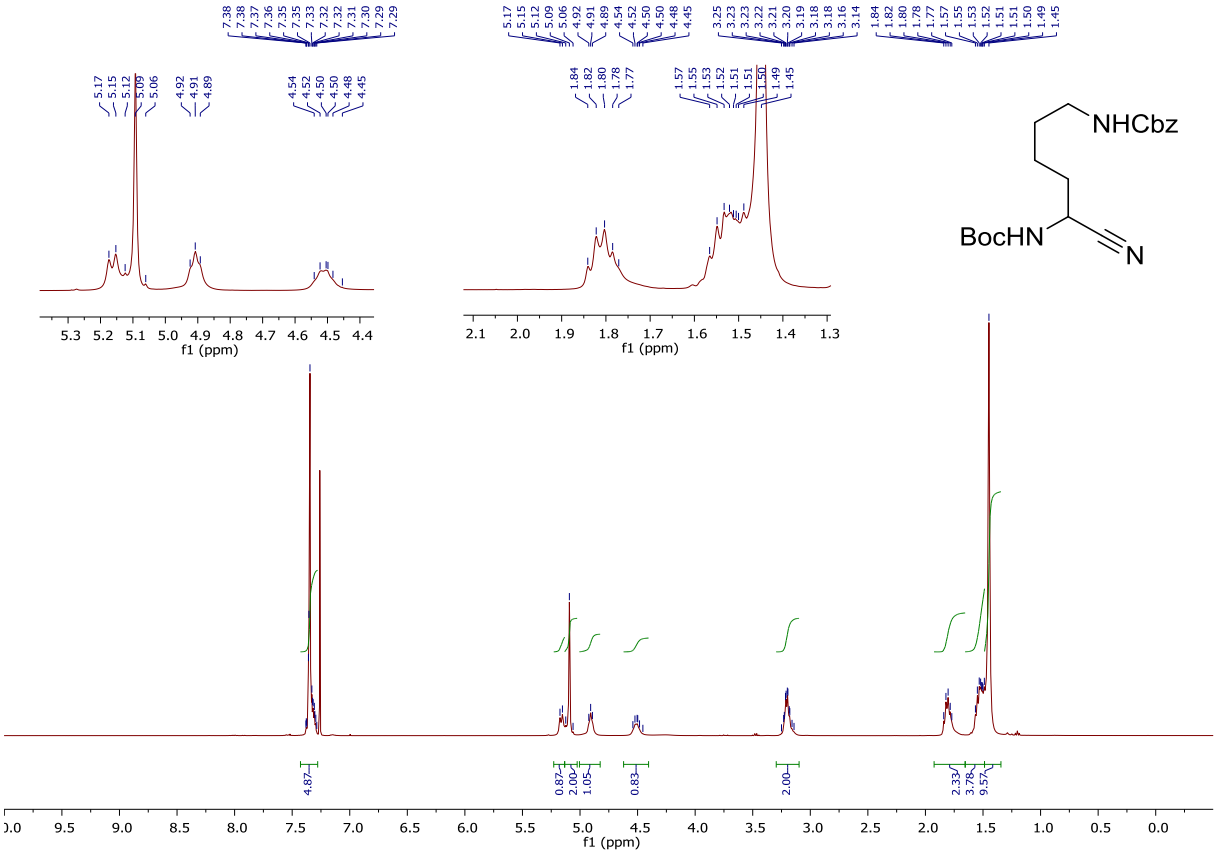

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7p**



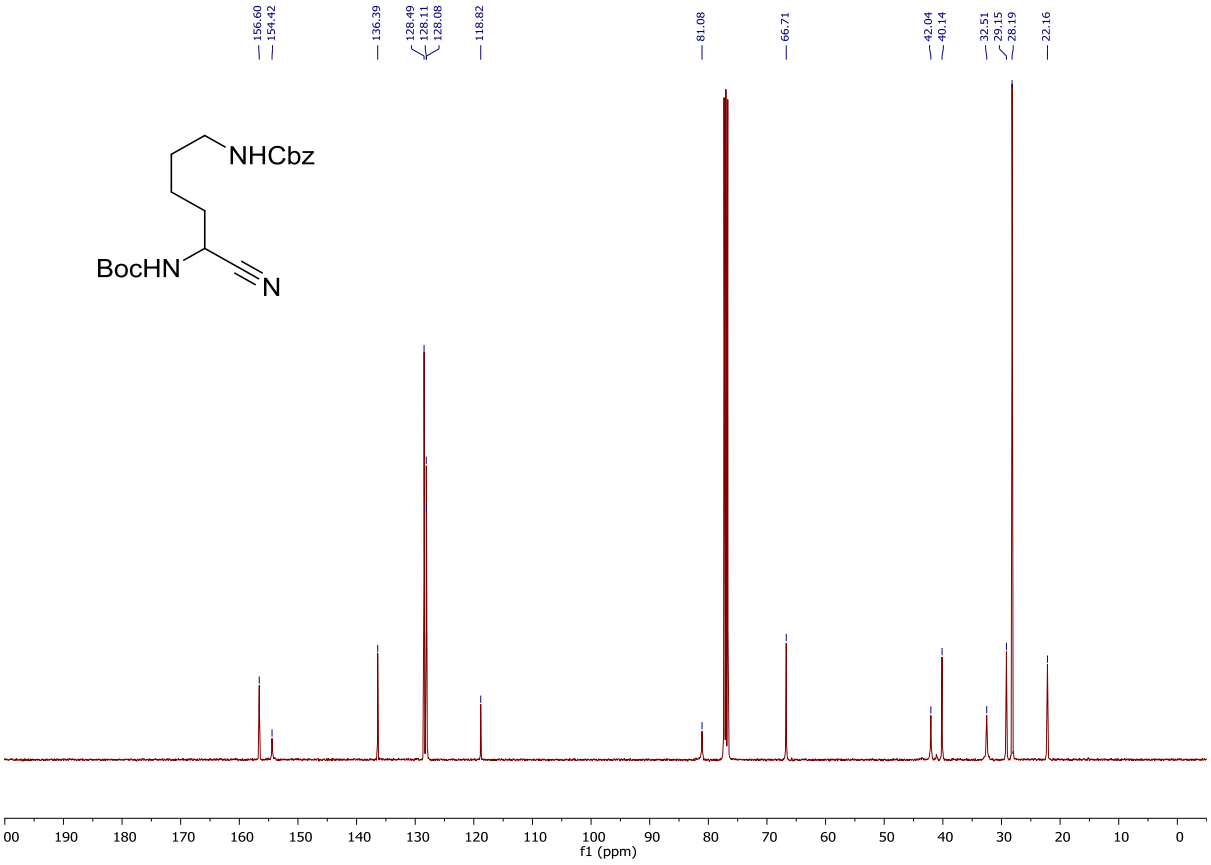
**IR** of compound **7p**



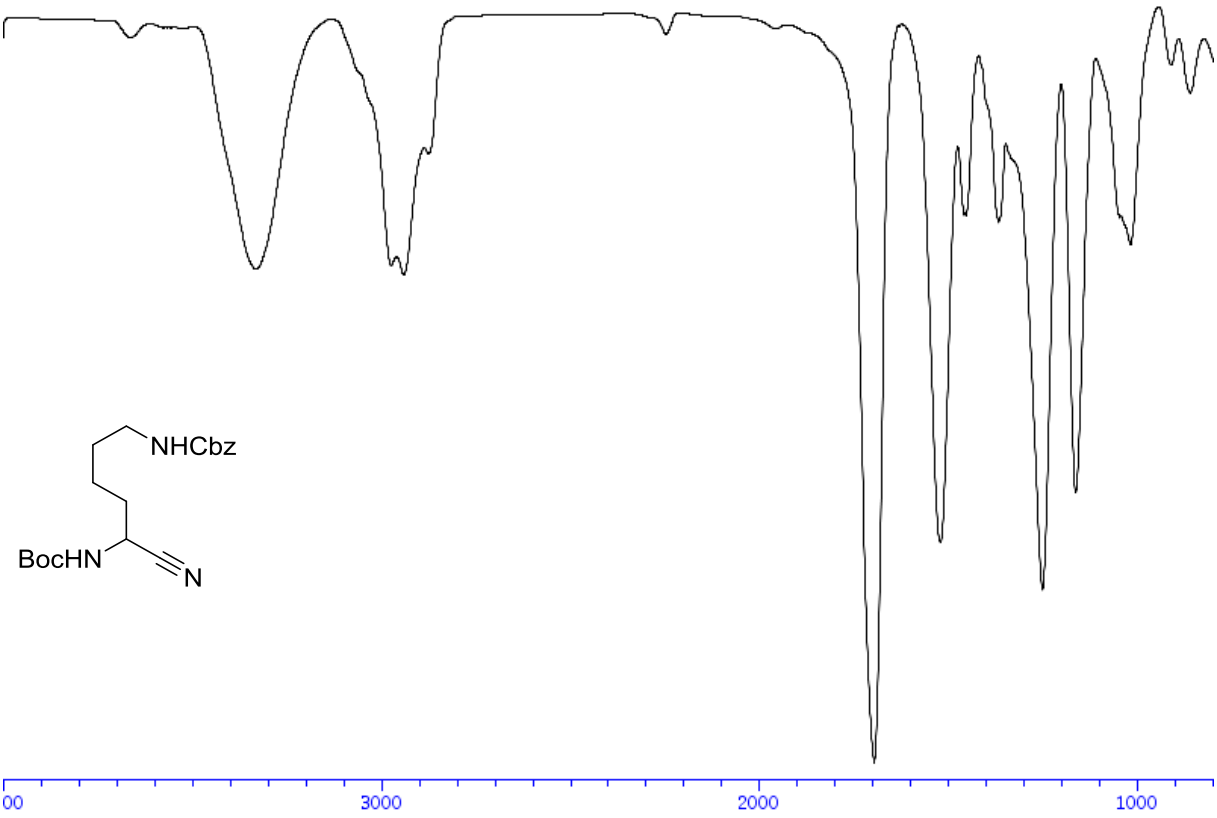
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7q**



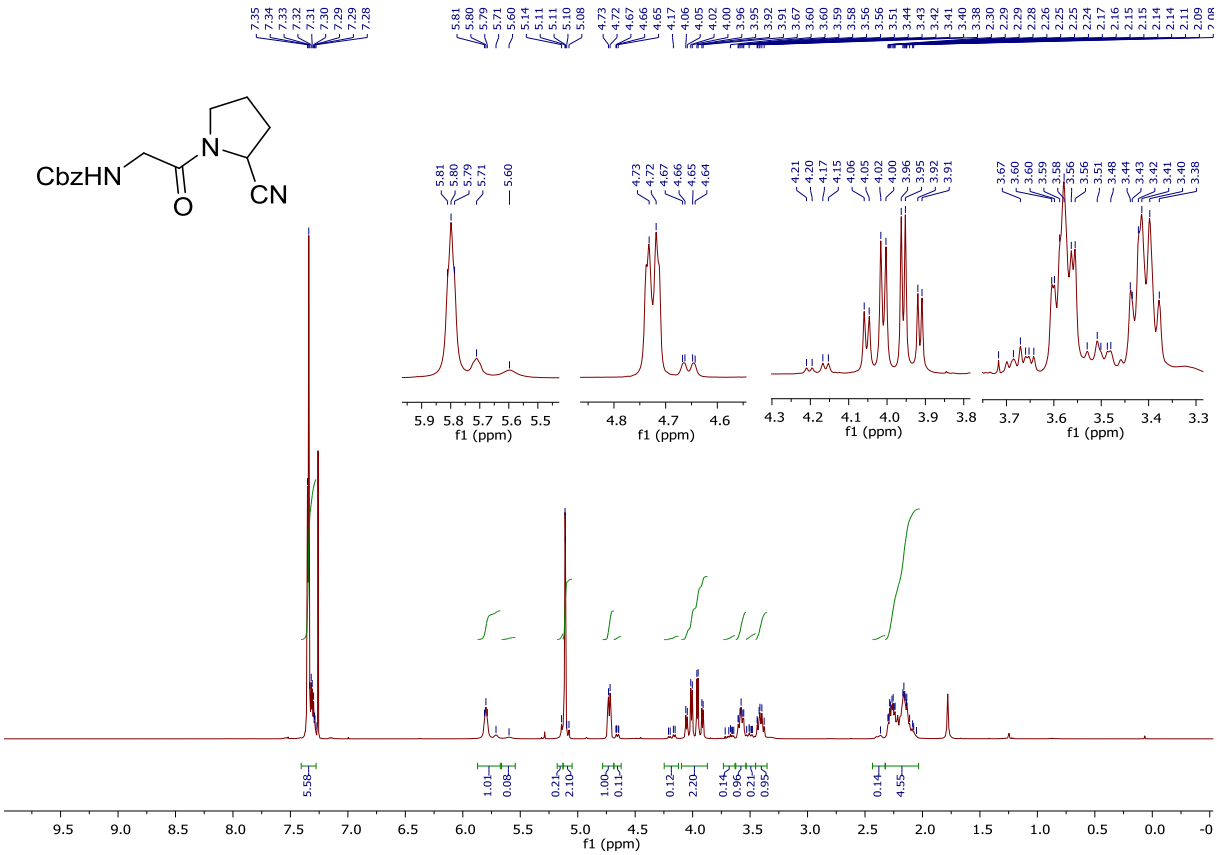

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **XX**



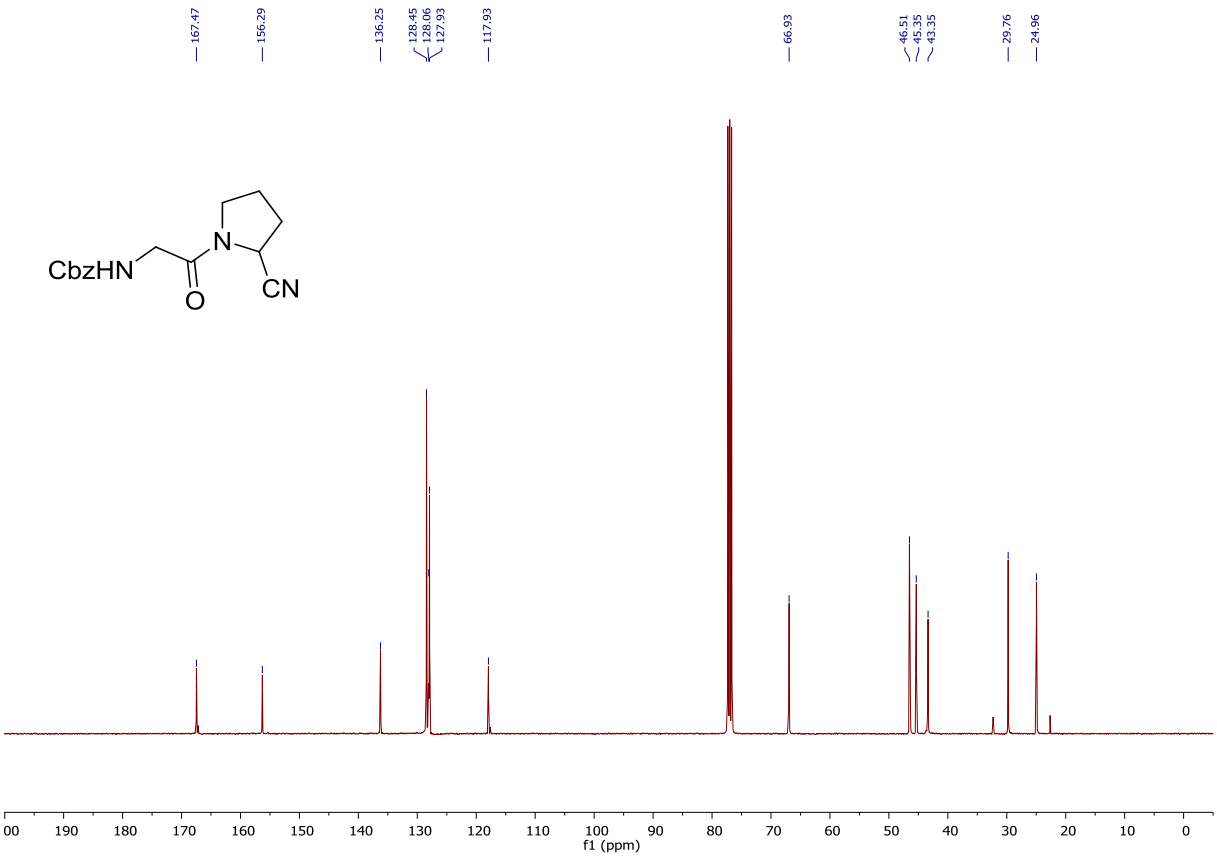
**IR** of compound **7q**



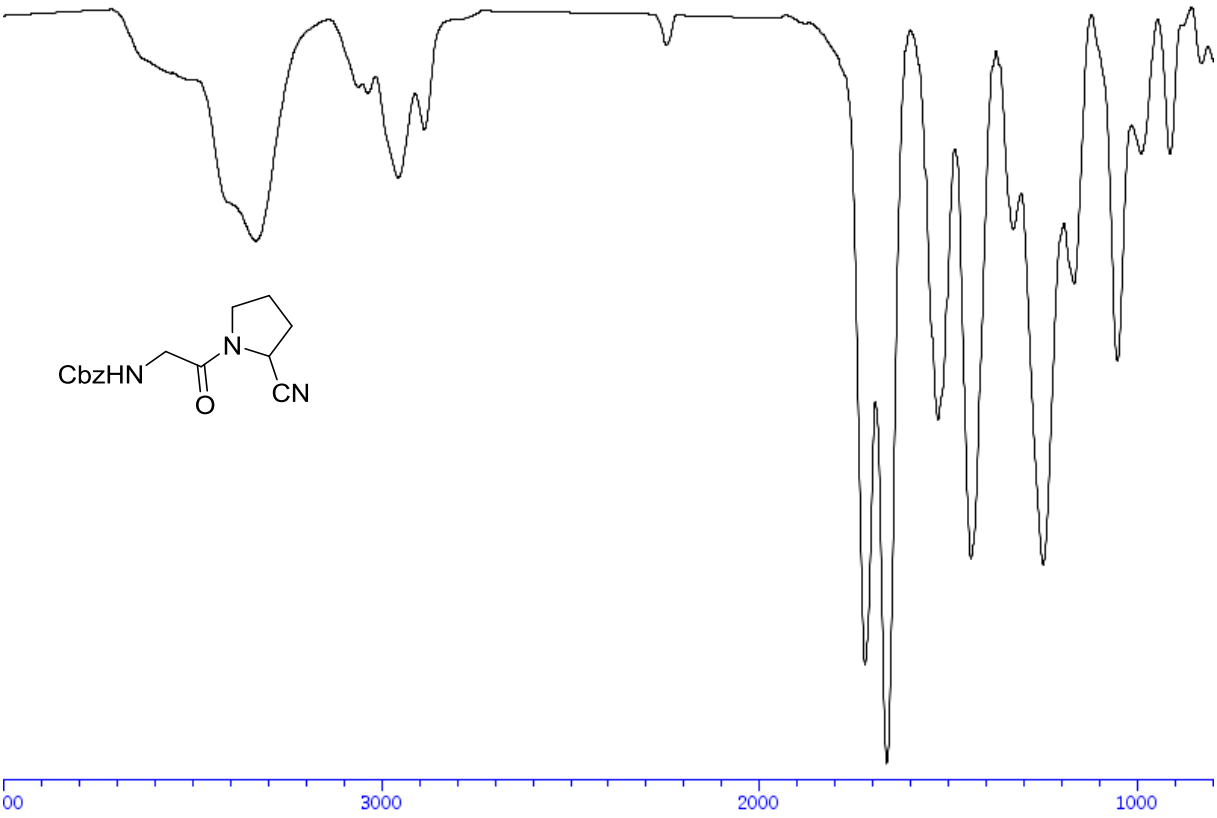
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7r**



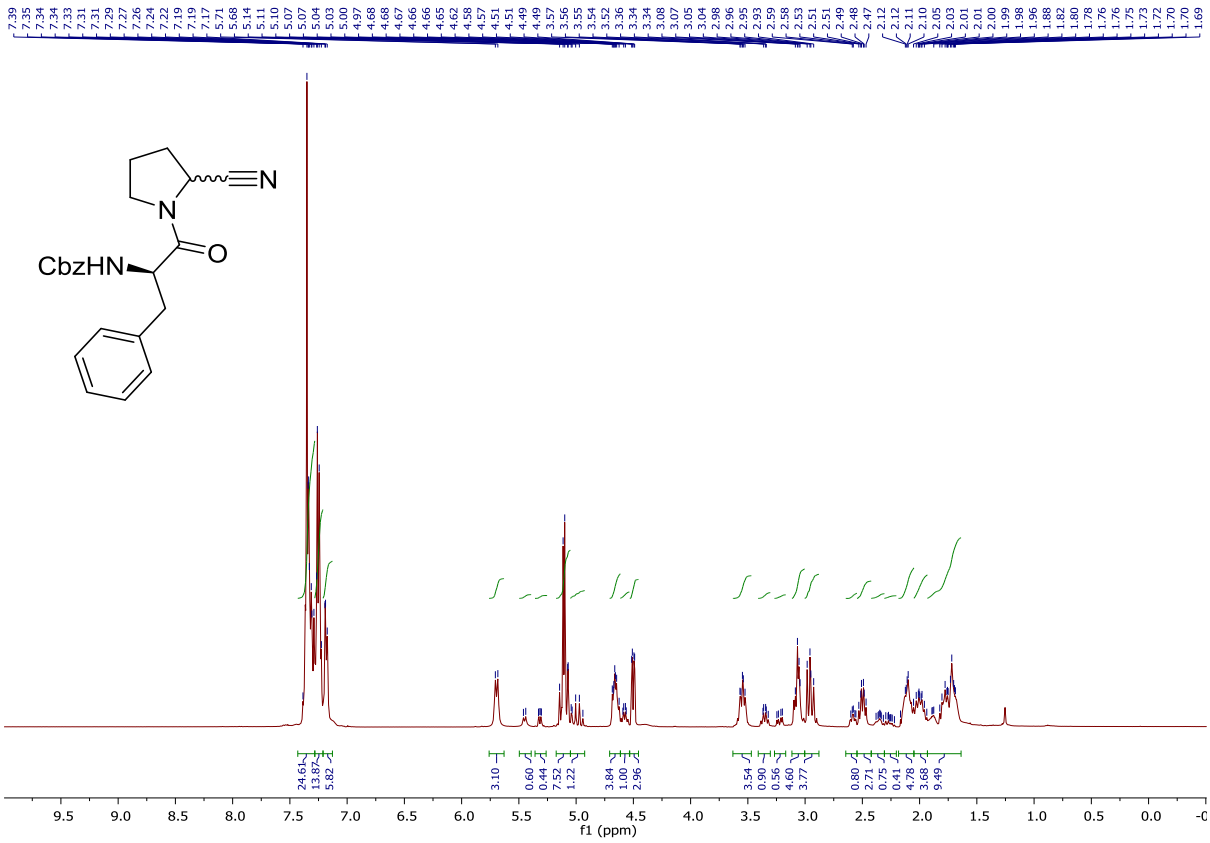

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7r**



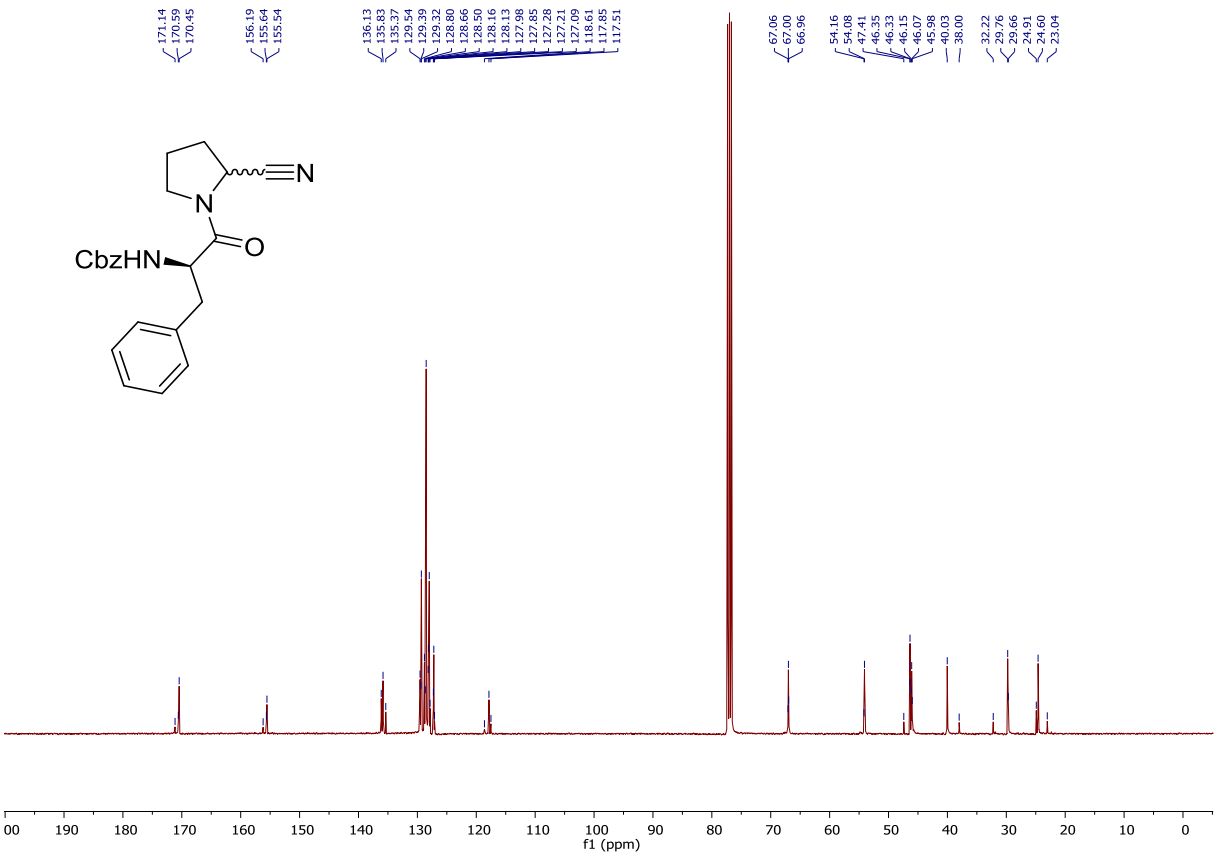
**IR** of compound **7r**



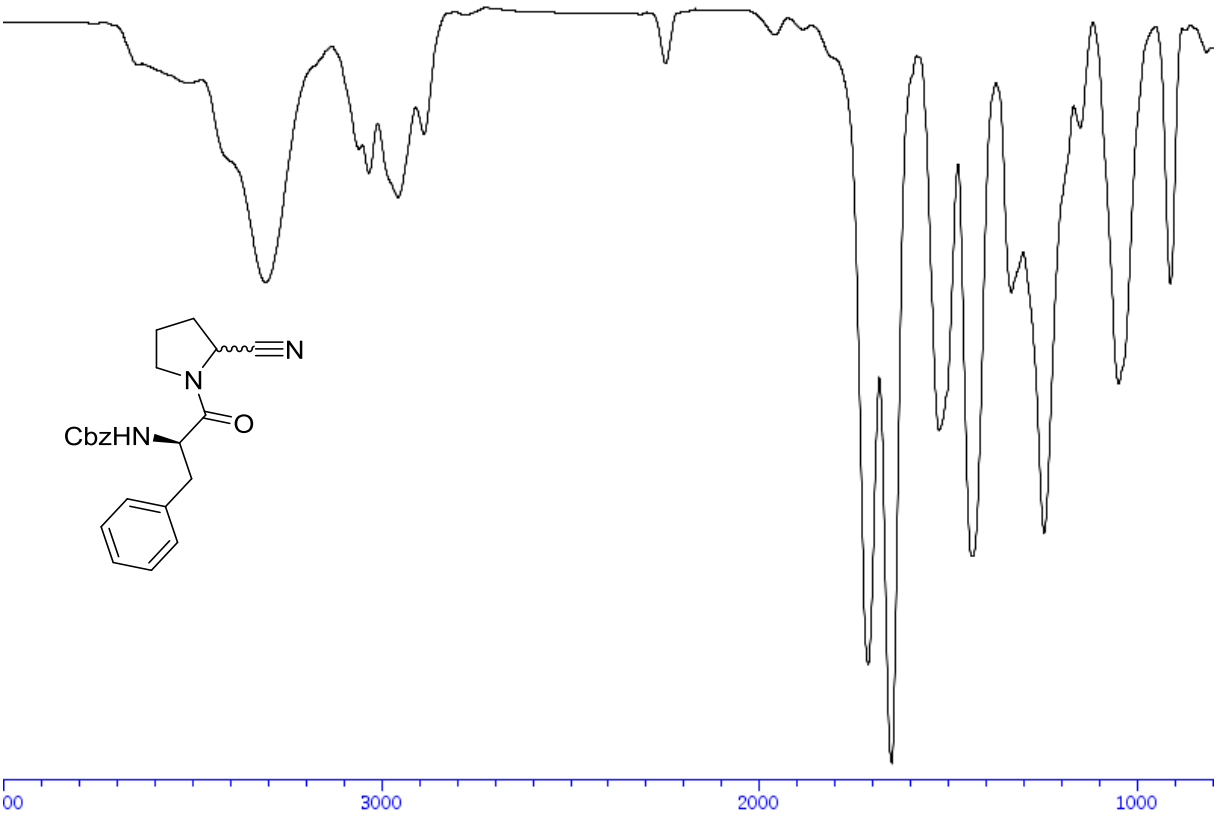
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7s (mixture)**



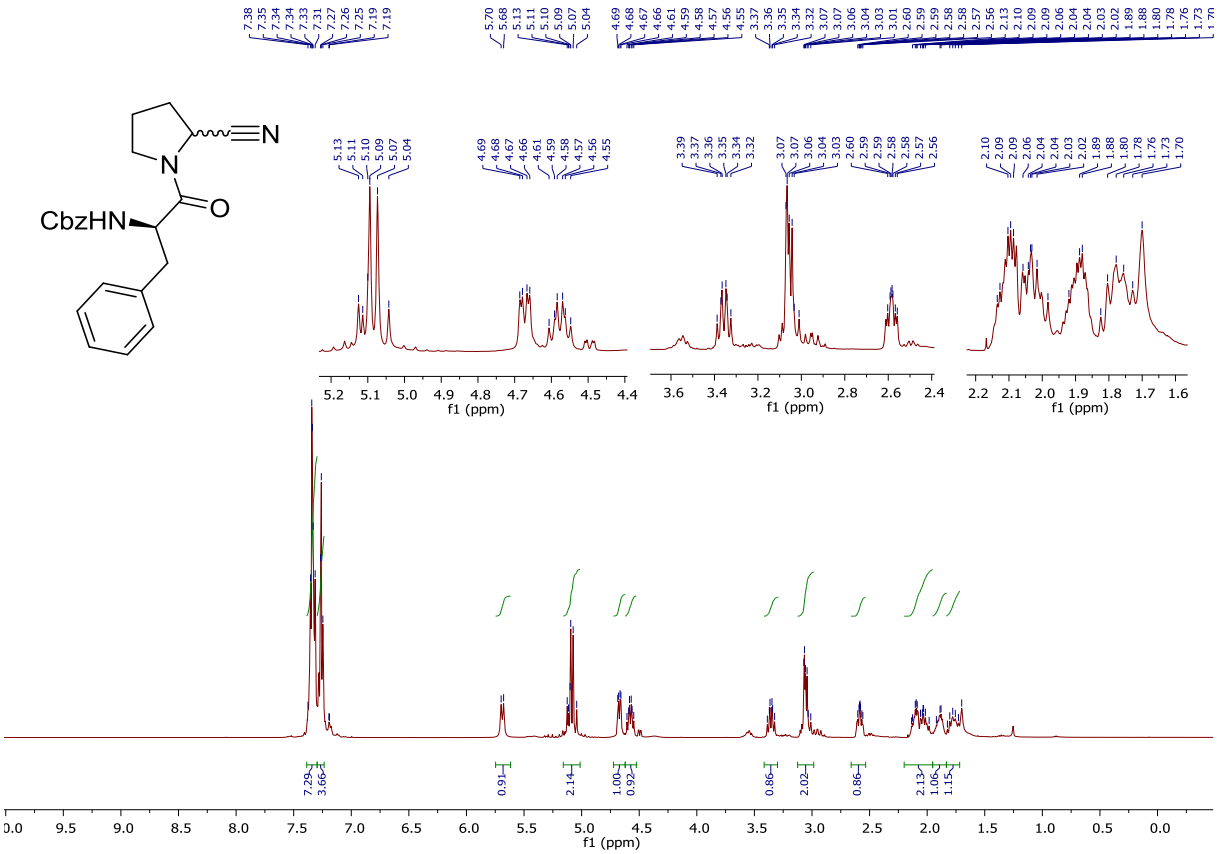

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7s (mixture)**



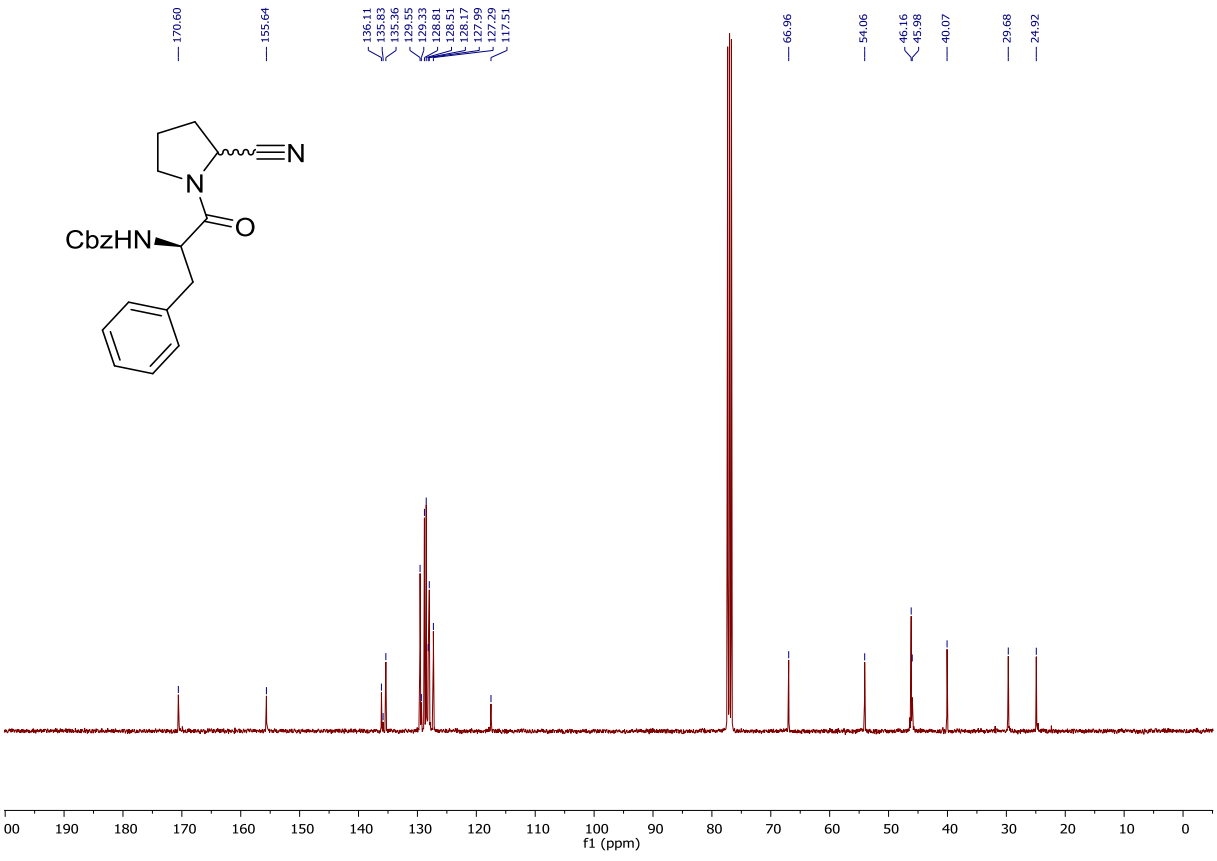
**IR** of compound **7s (mixture)**



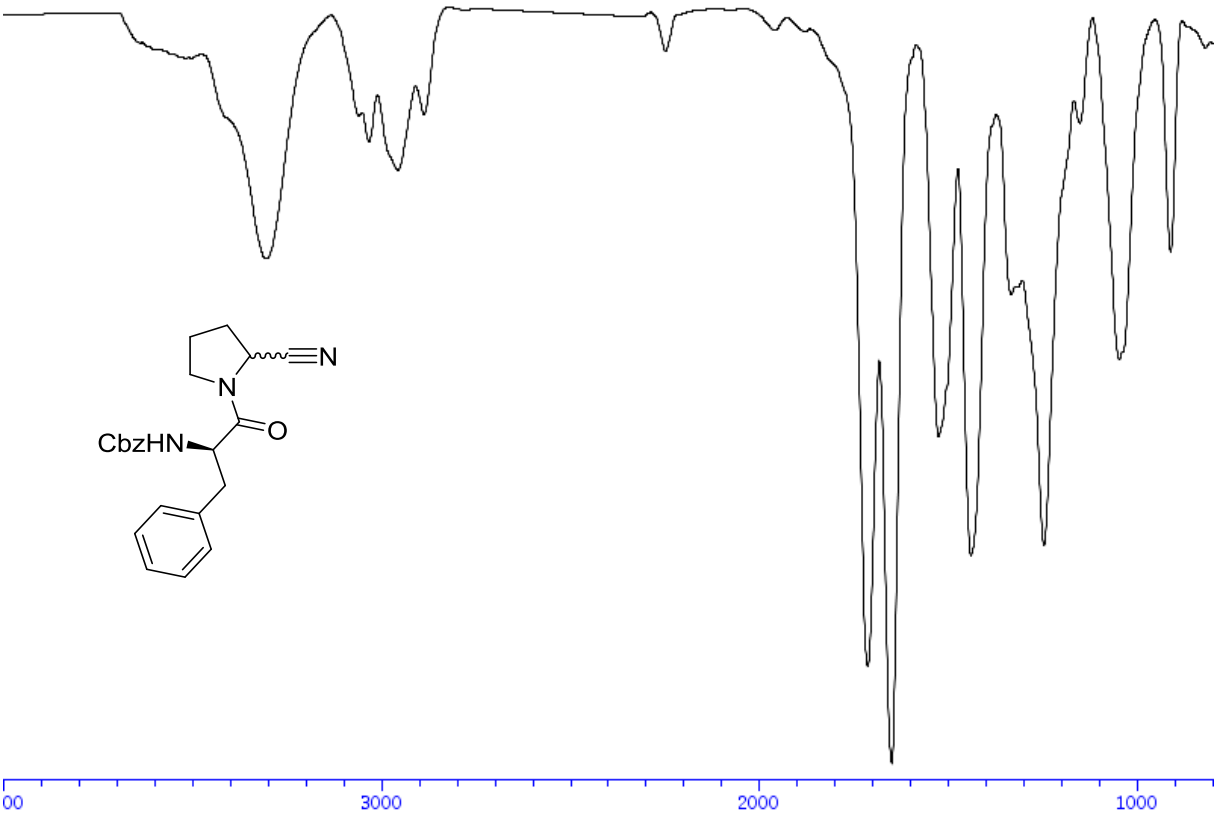
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7s (minor diastereoisomer)**



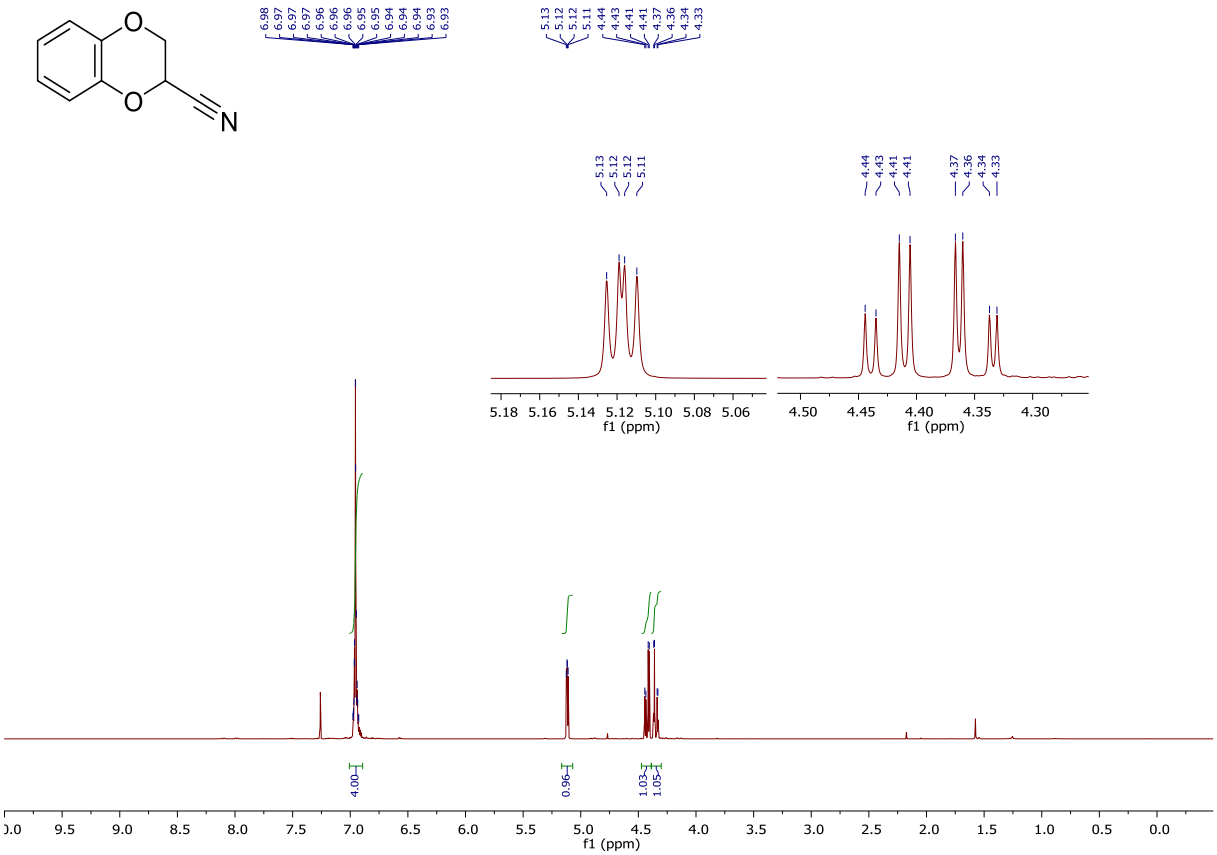

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7s (minor diastereoisomer)**



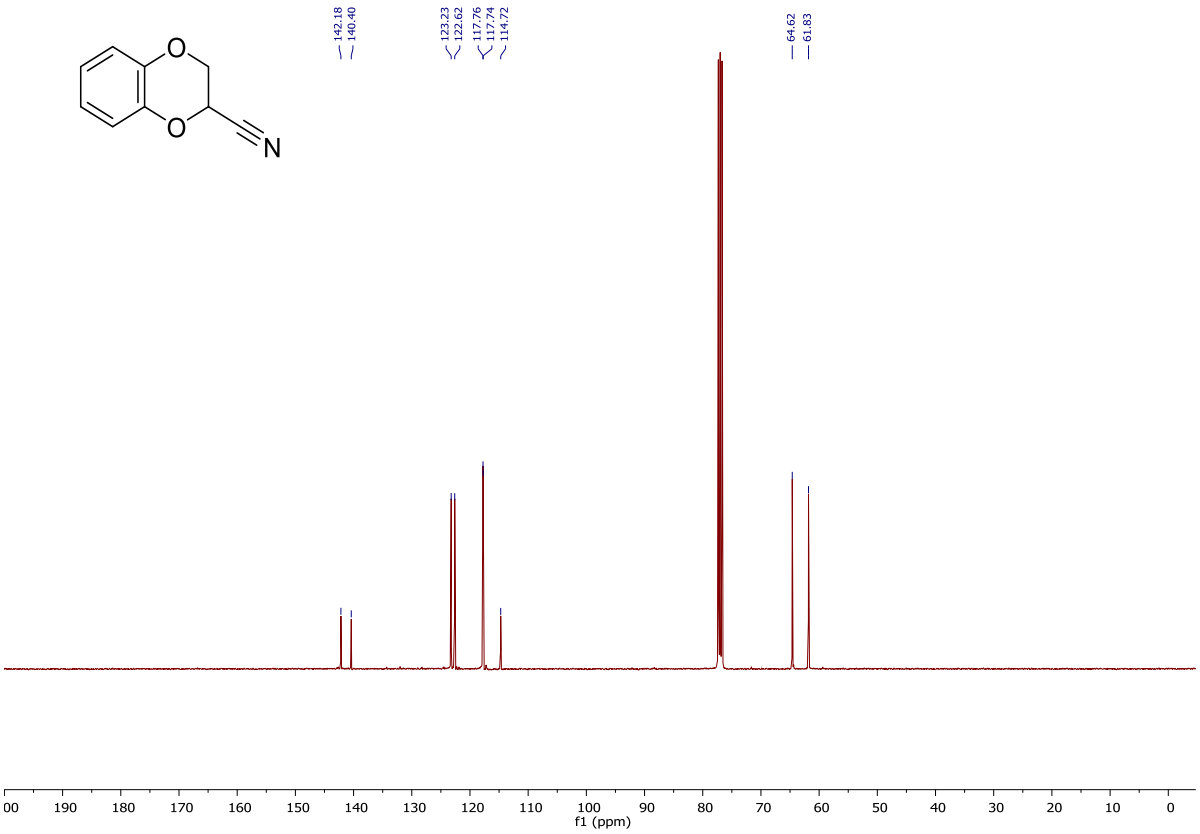
**IR** of compound **7s (minor diastereoisomer)**



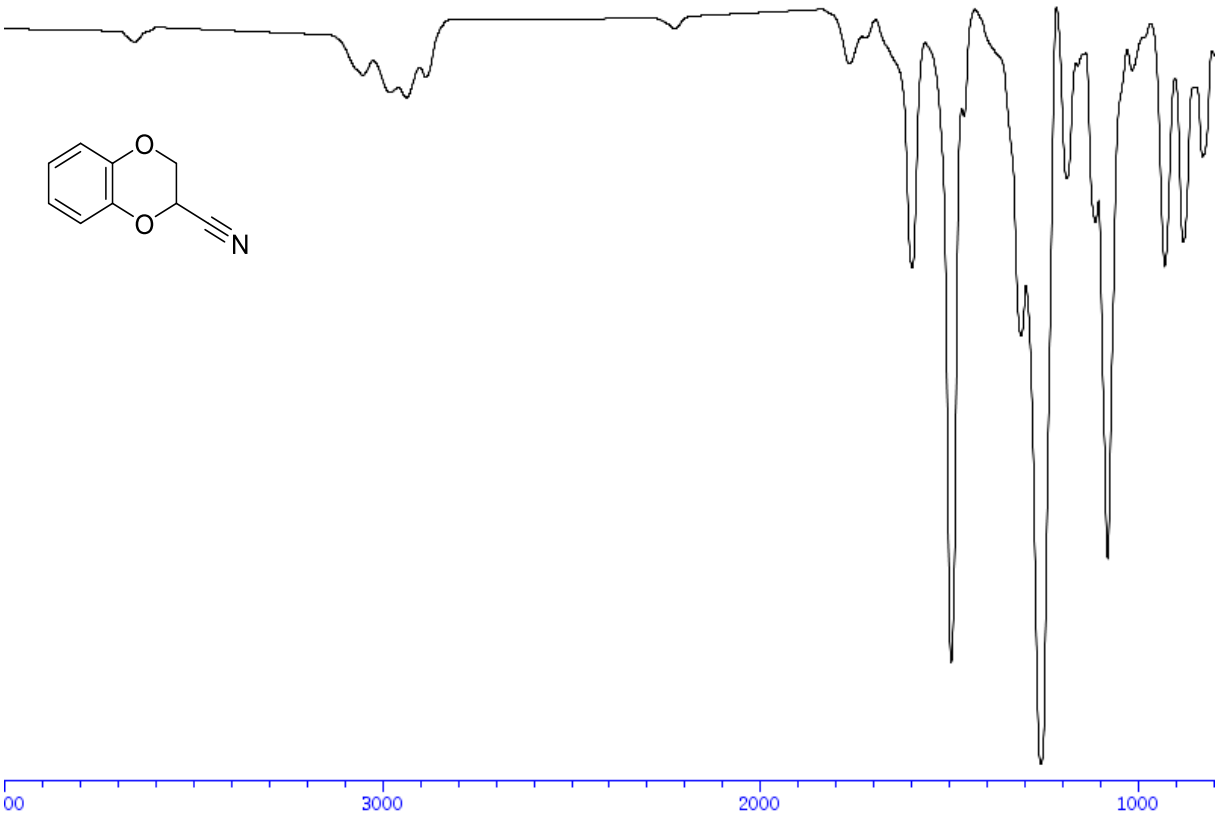
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7v**



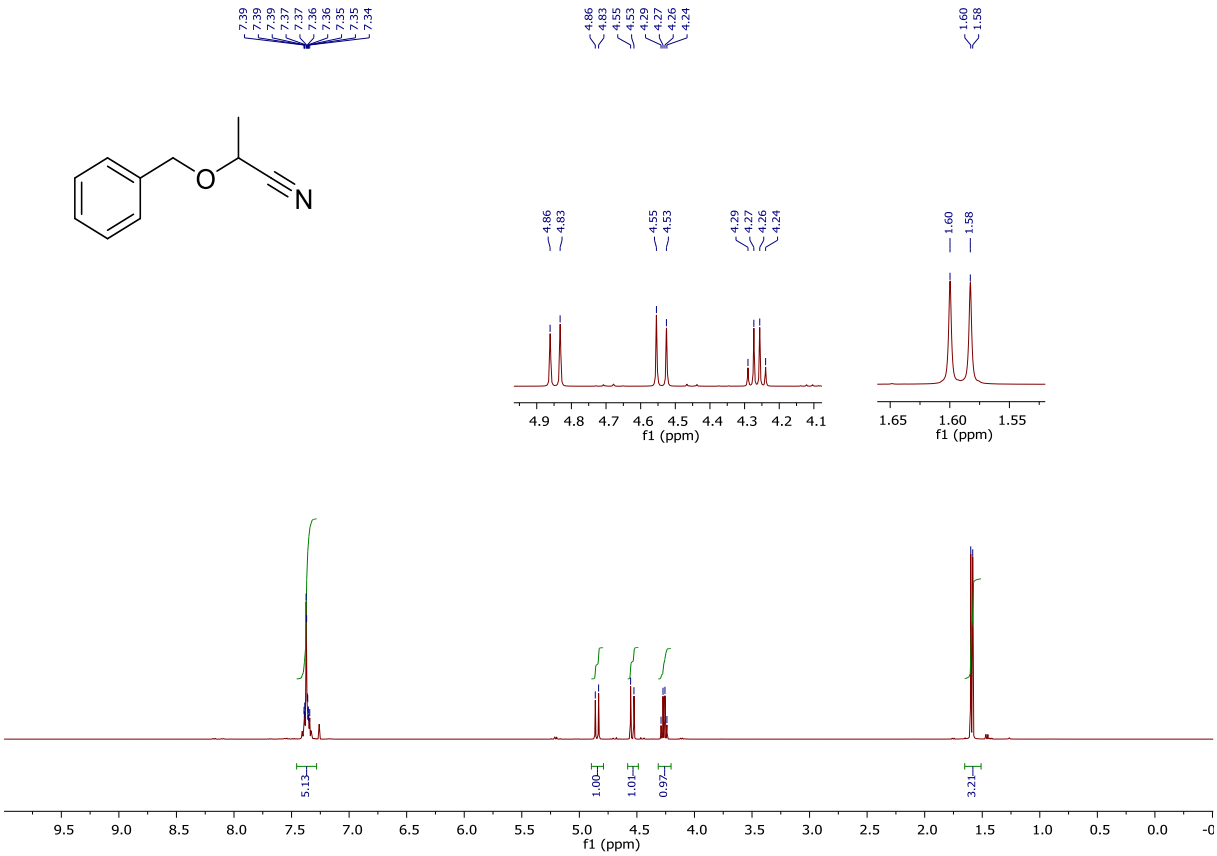

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7v**



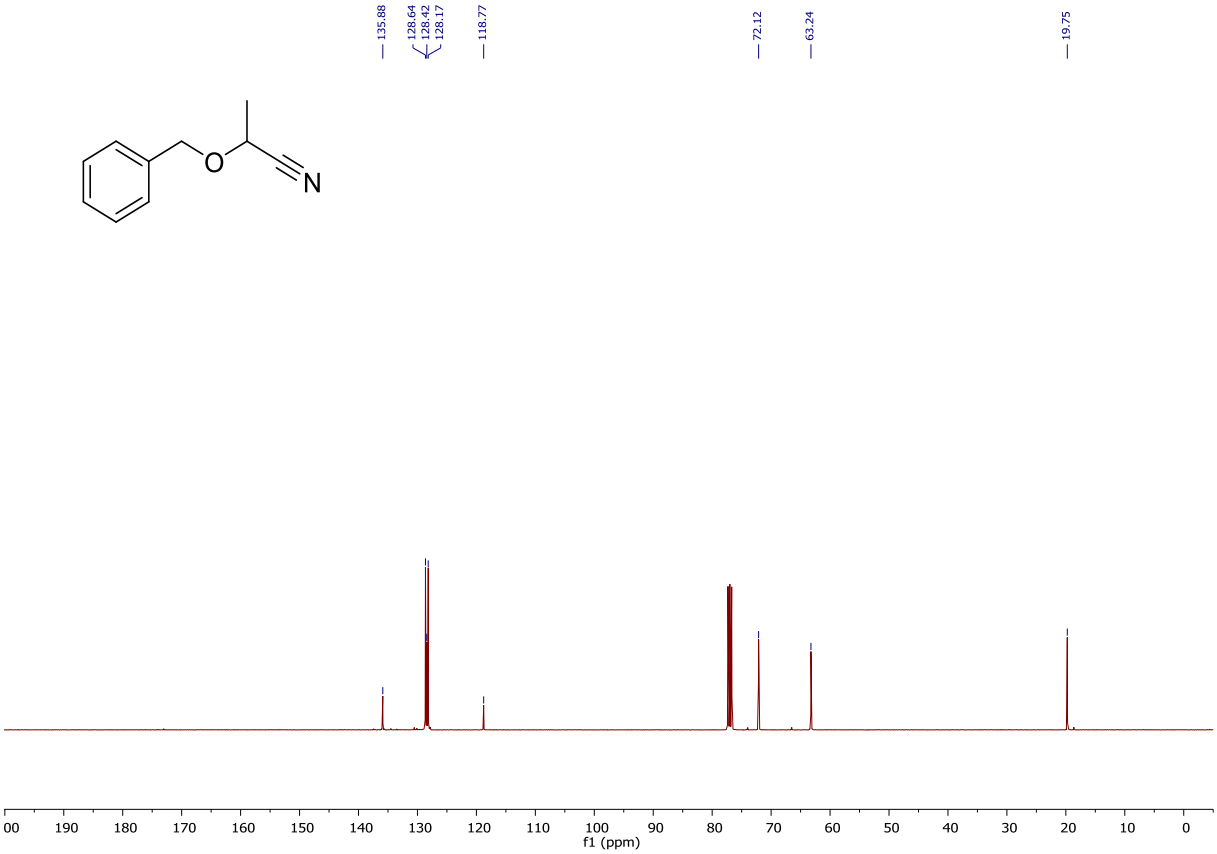
**IR** of compound **7v**



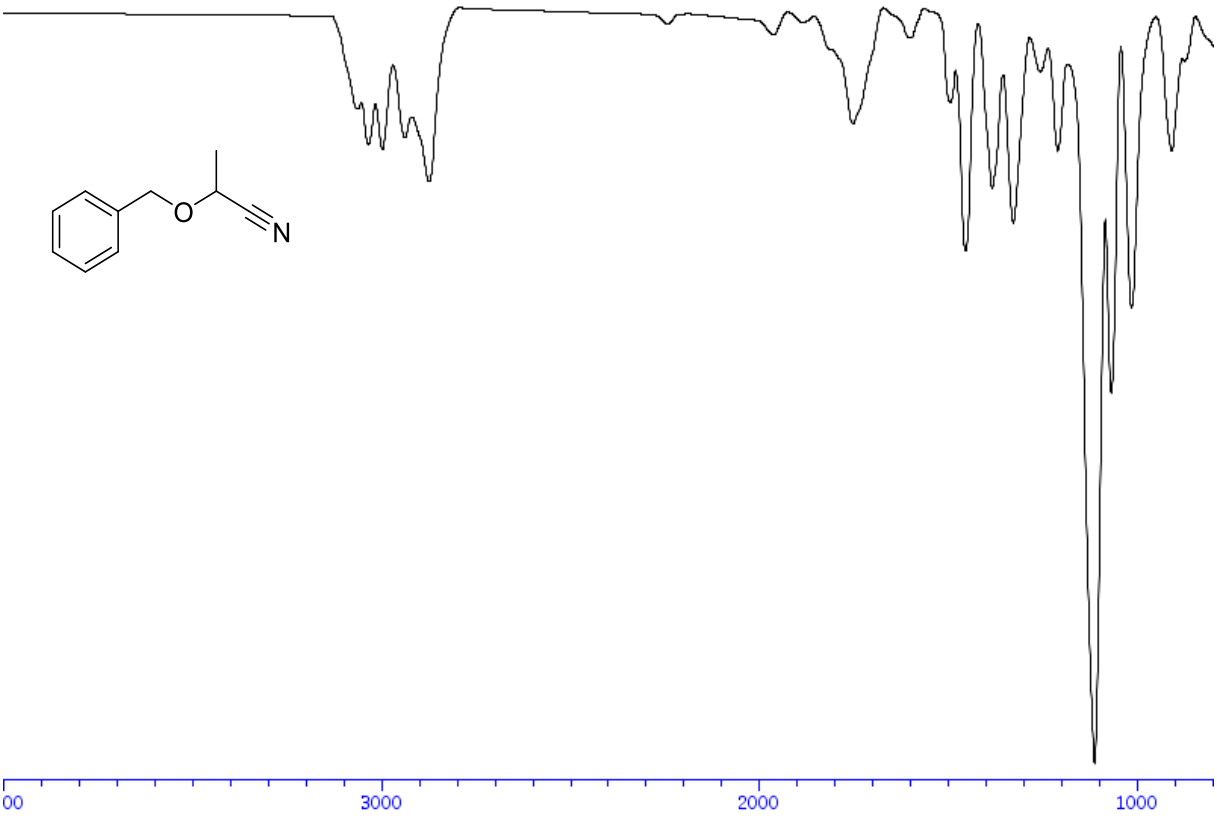
## $^{1}$H-NMR (400 MHz, $CDCl_3$) of compound **7w**



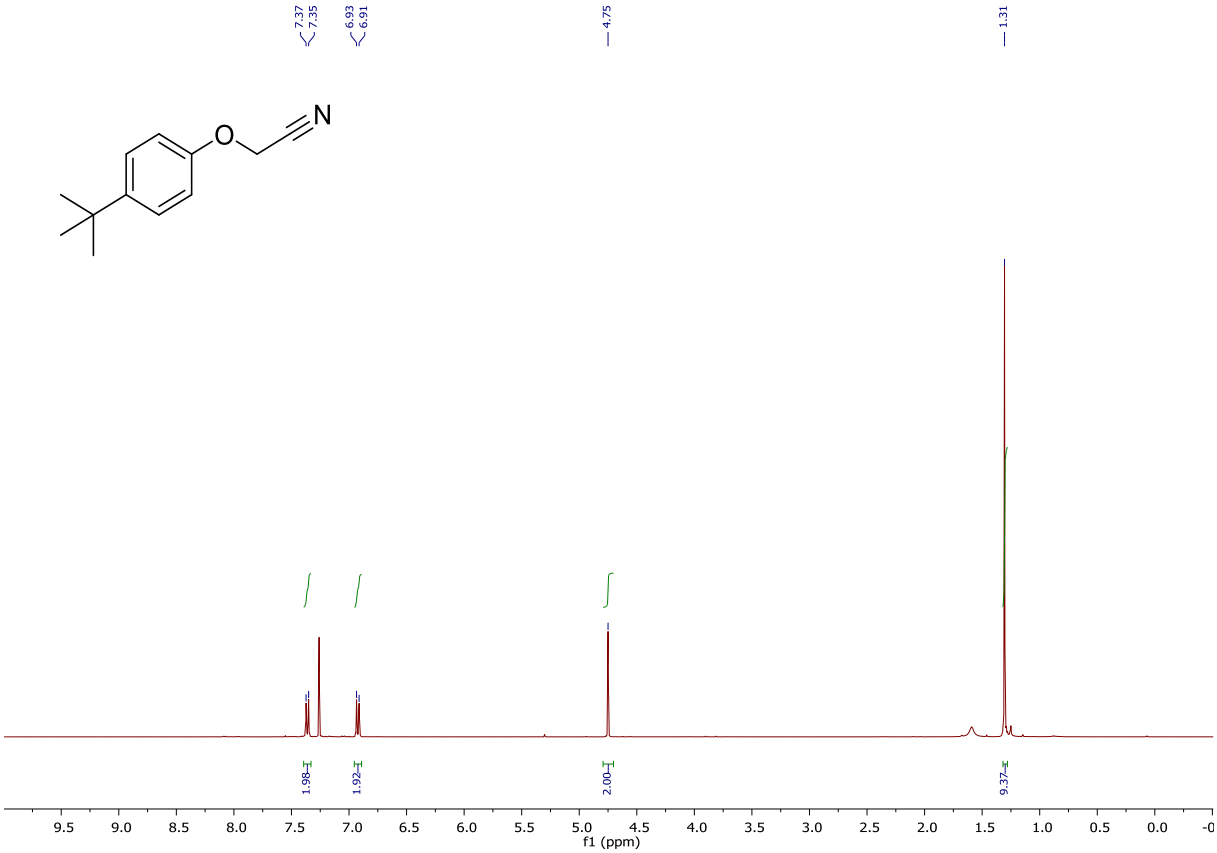

## $^{13}$C-NMR (100 MHz, $CDCl_3$) of compound **7w**



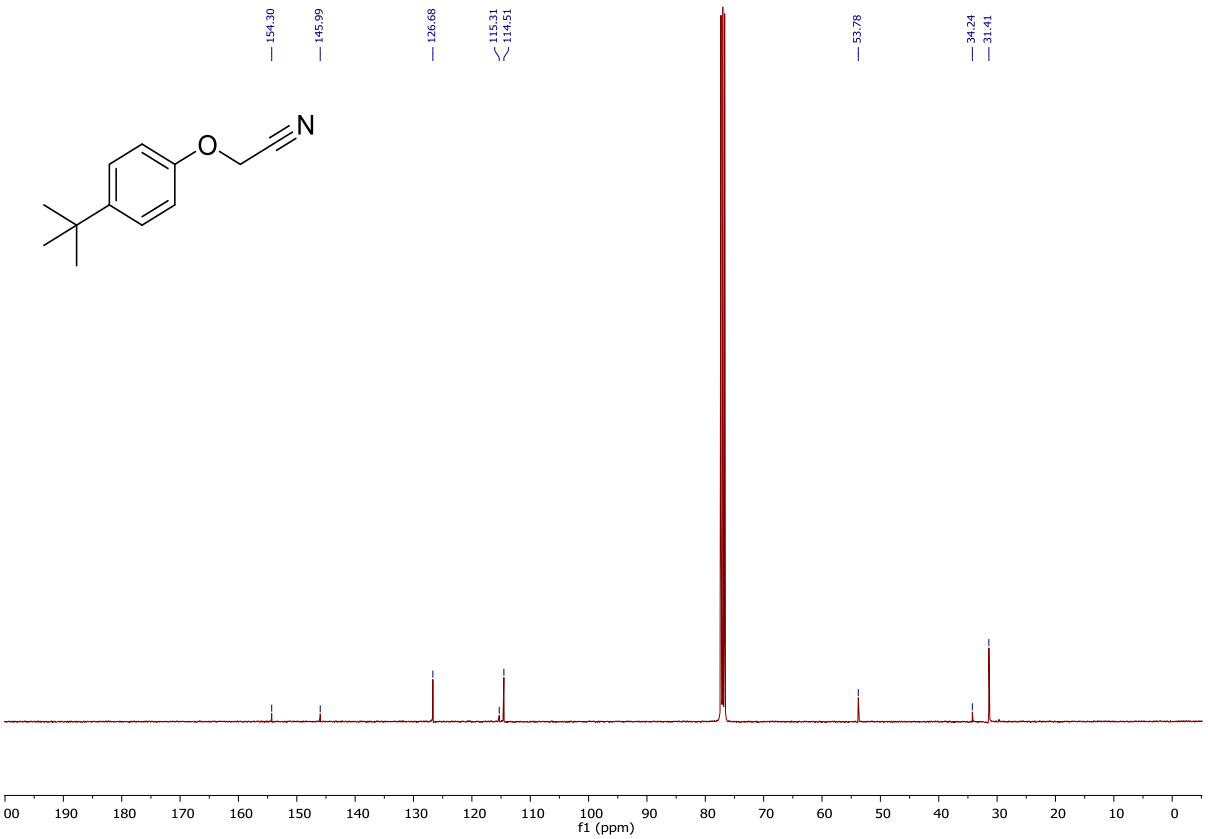
**IR** of compound **7w**



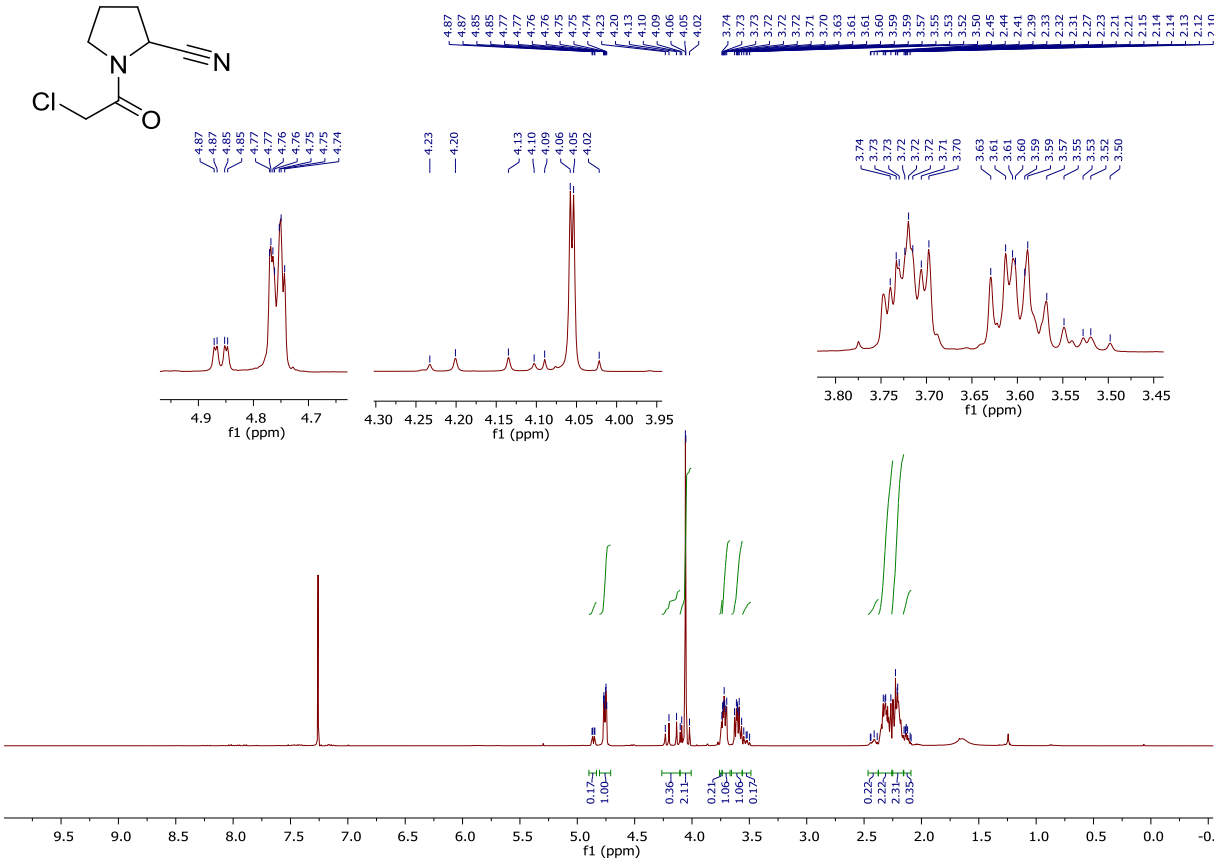
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7x**



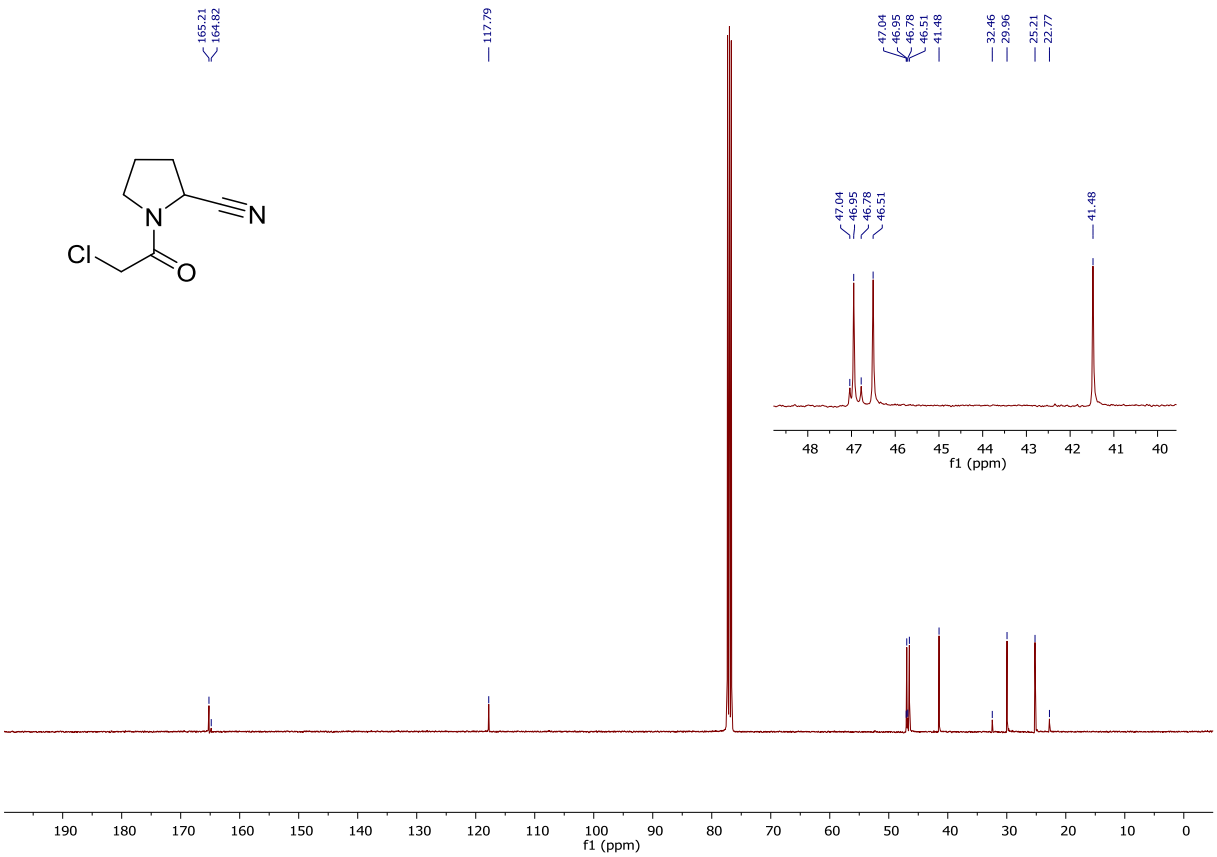

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7x**



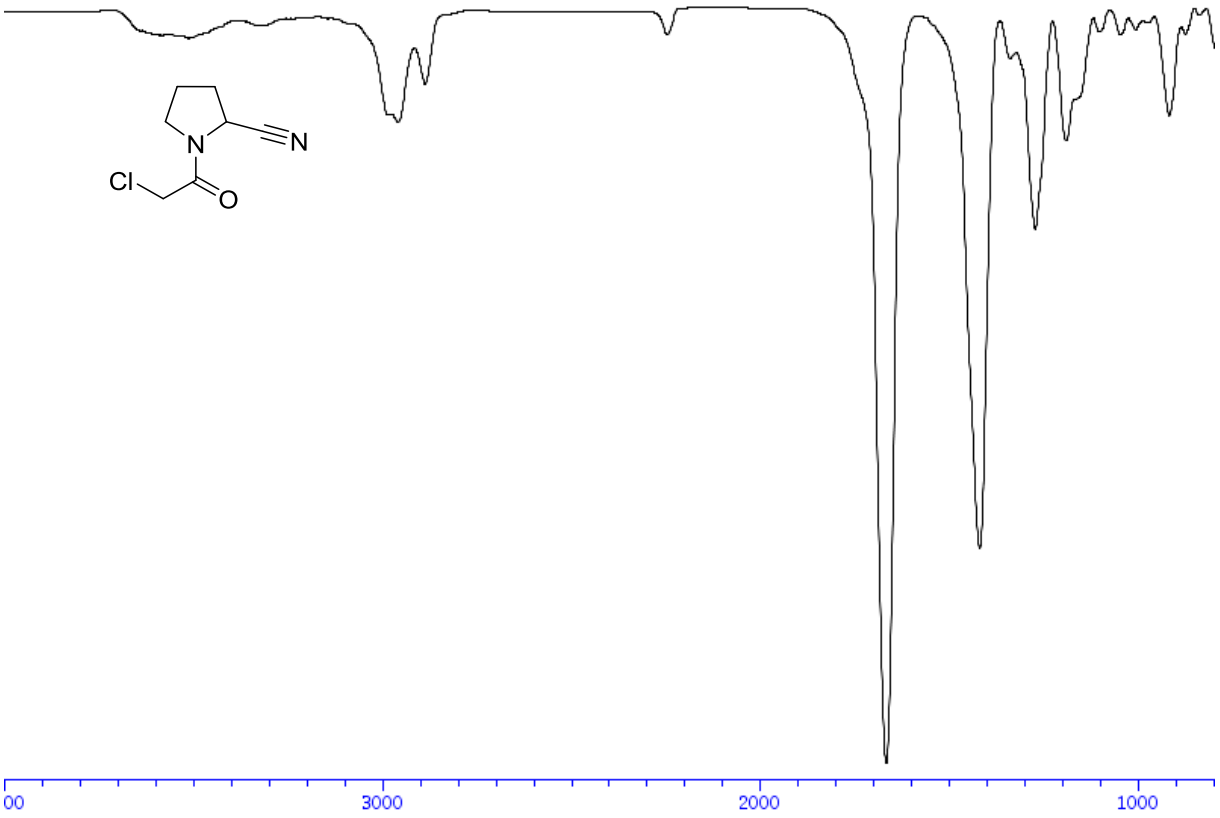
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **7z**



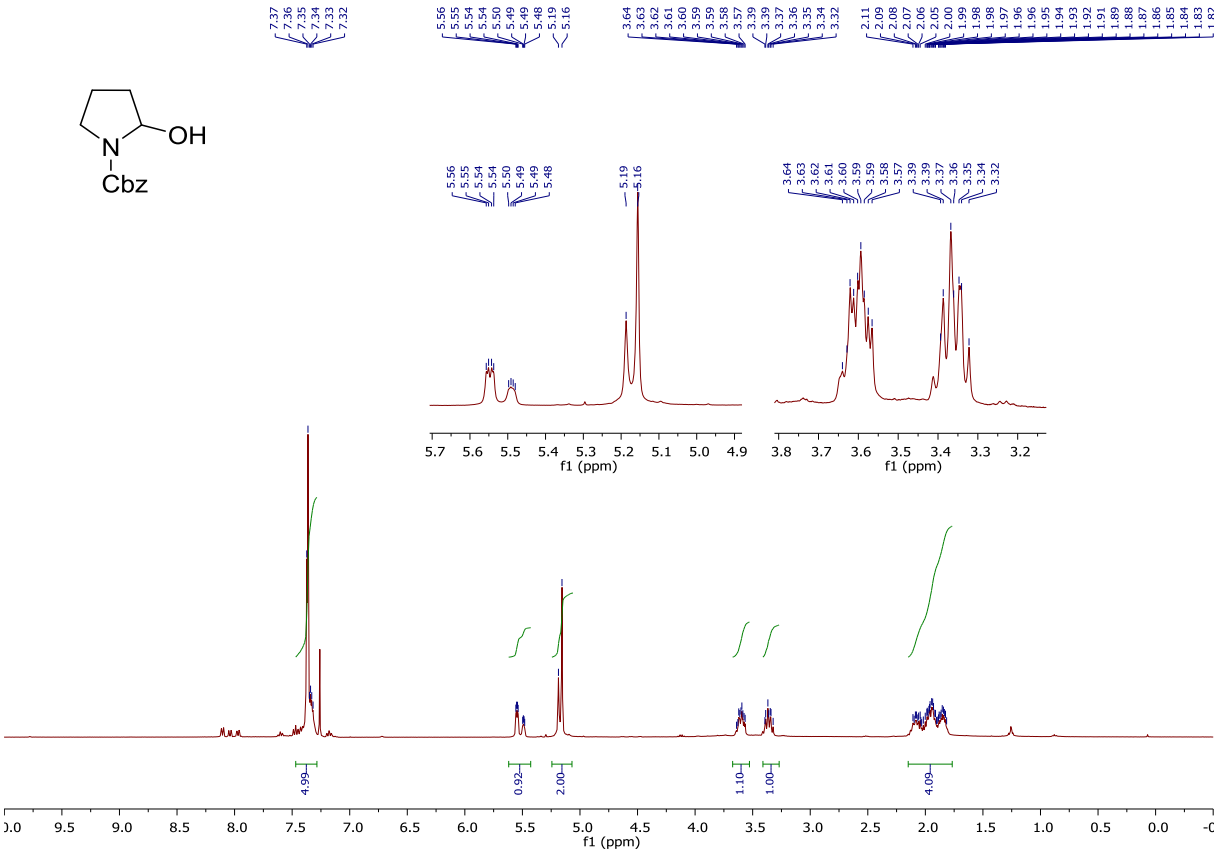

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **7z**



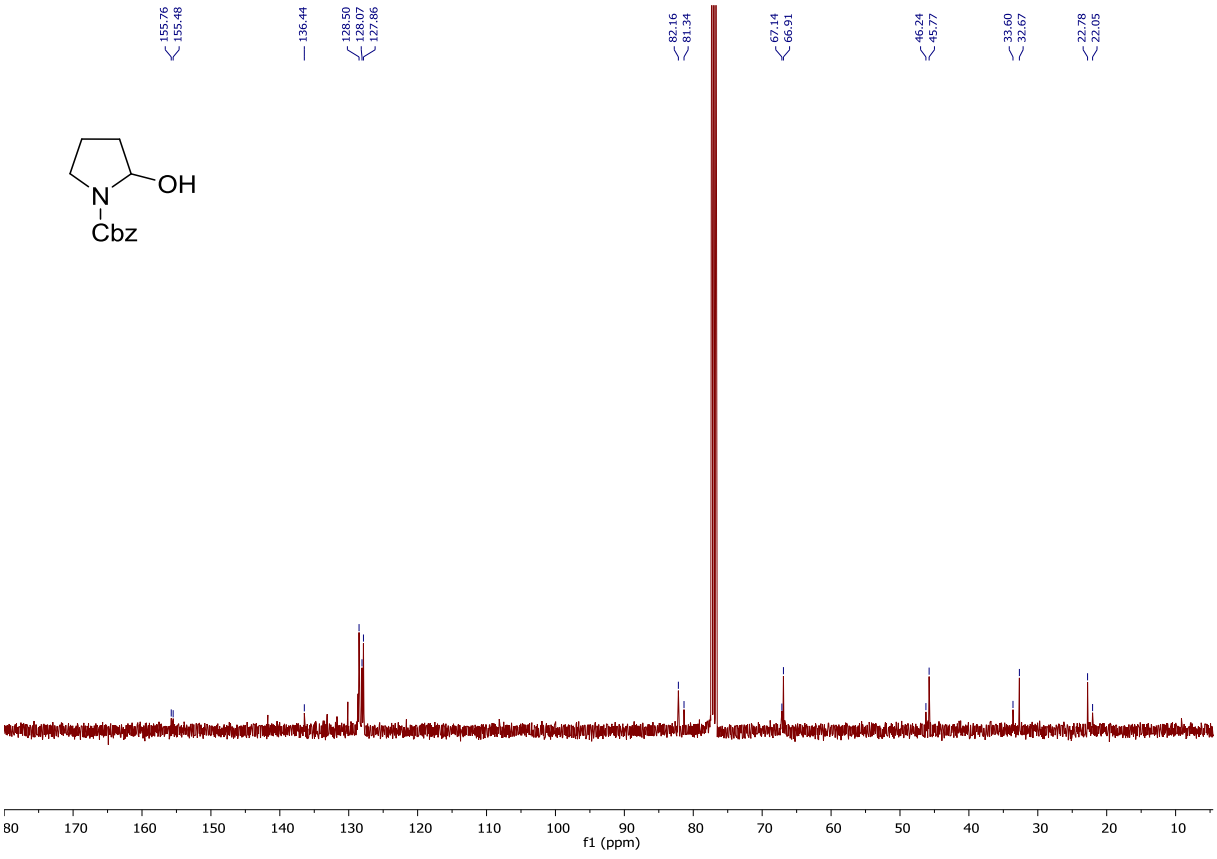
**IR** of compound **7z**



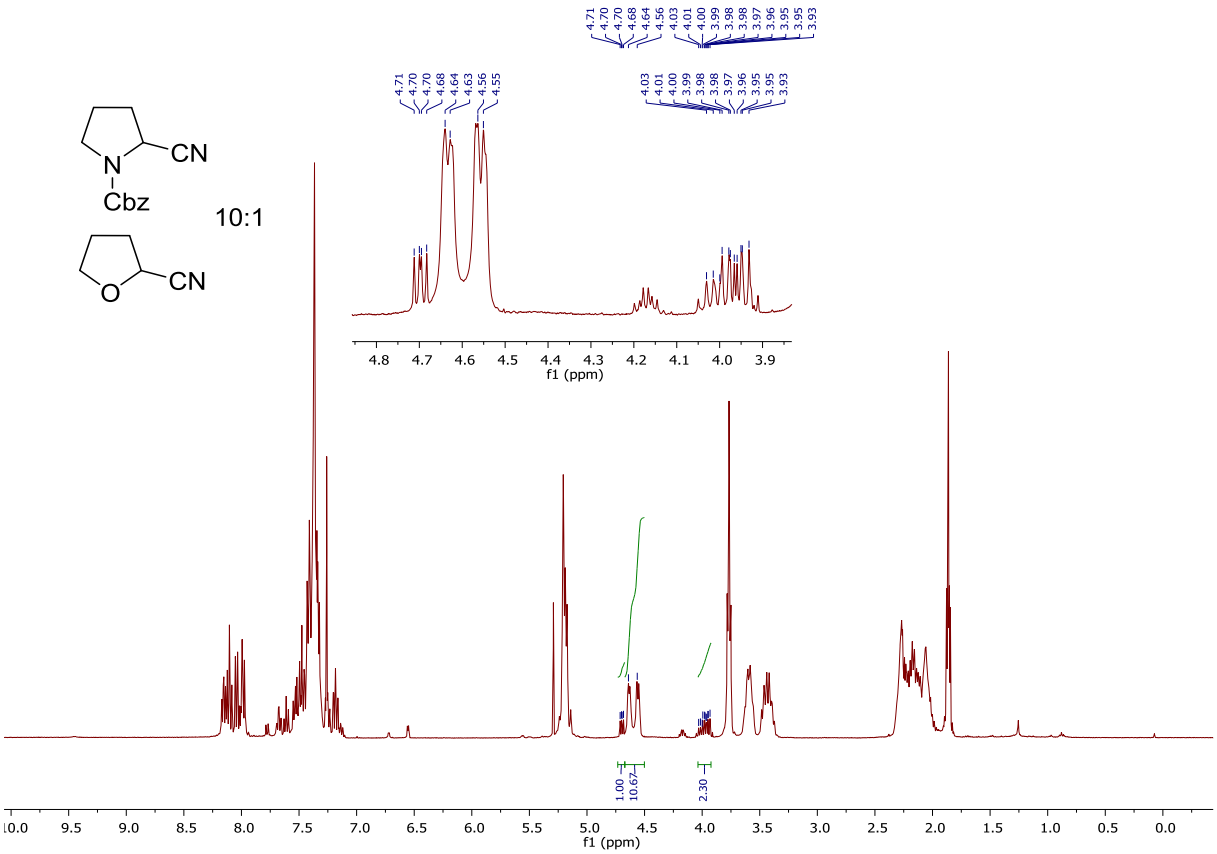
**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **8**



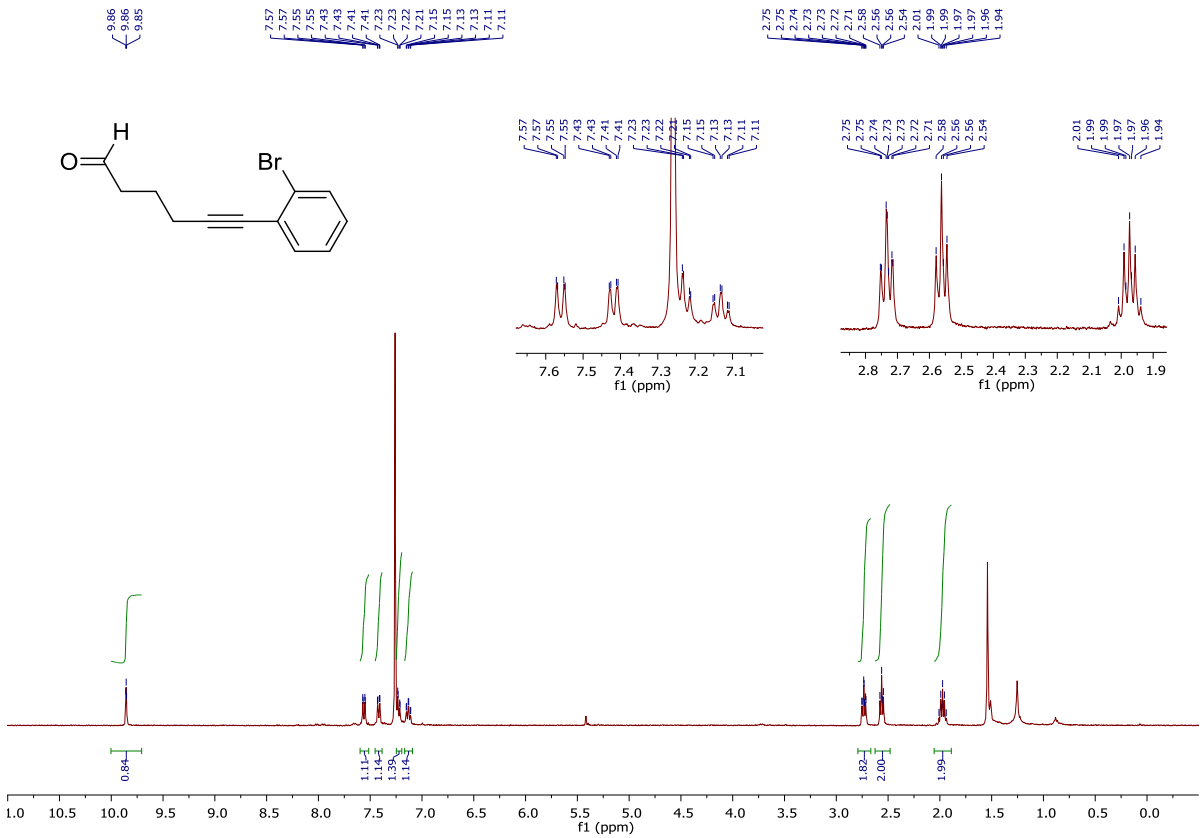

**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **8**



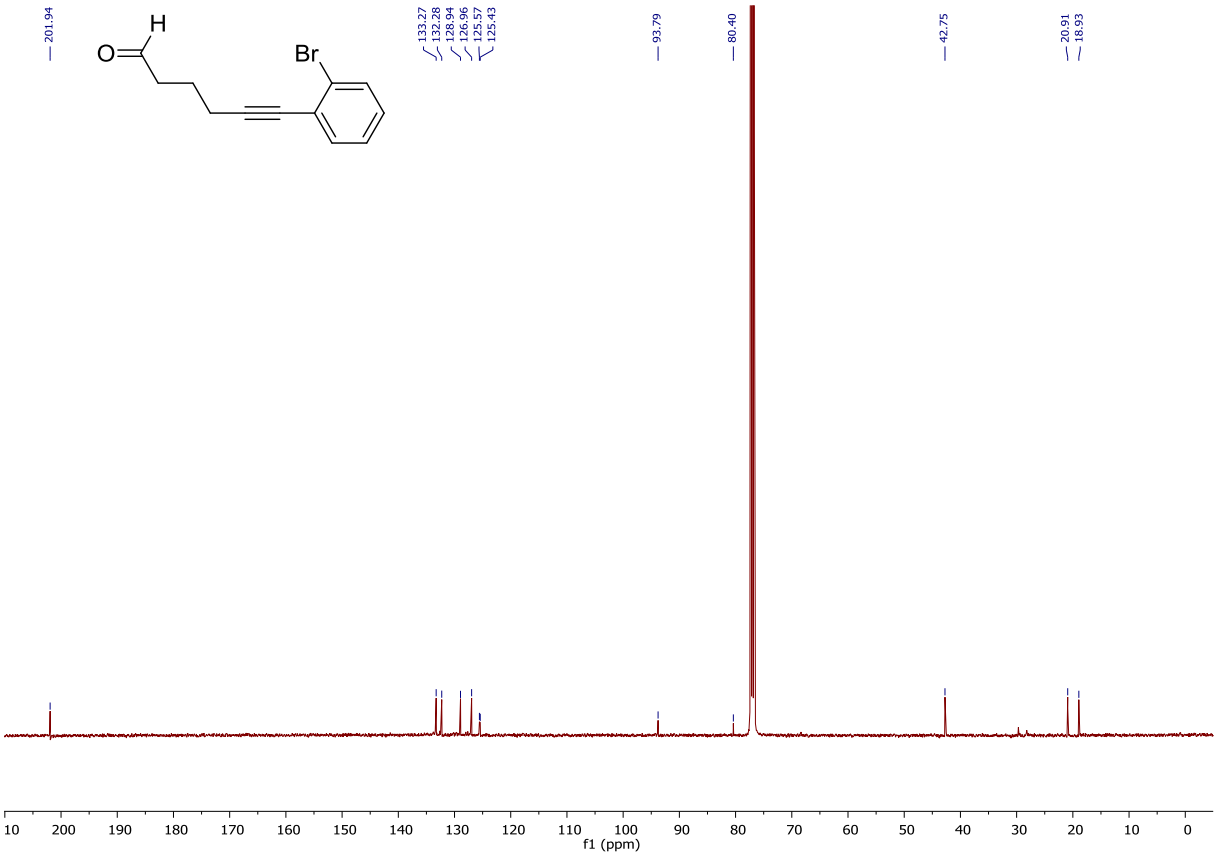
**$^1$H-NMR** (400 MHz, $CDCl_3$) of crude NMR obtained for sunlight irradiation.



**$^{1}$H-NMR** (400 MHz, $CDCl_3$) of compound **19**




**$^{13}$C-NMR** (100 MHz, $CDCl_3$) of compound **19**



**IR** of compound **19**