Divergent Access to (1,1) and (1,2)-Azidolactones from Alkenes using Hypervalent Iodine Reagents

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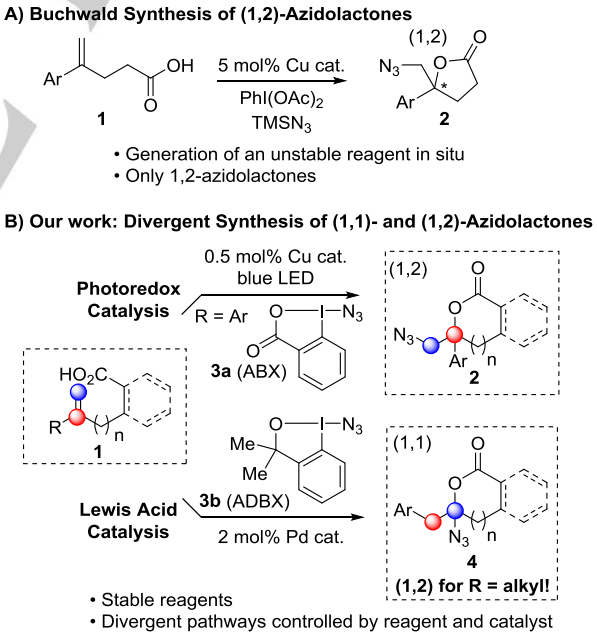
Dedication

Abstract: *A versatile synthesis of azidolactones through azidation and cyclization of carboxylic acids onto alkenes has been developed. Based on either photoredox or palladium catalysis, (1,1) and (1,2) azido lactones can be selectively synthesized. The choice of catalyst and benziodoxol(on)e reagent serving as azide source was essential to initiate either a radical or Lewis Acid mediated process with divergent outcome. These transformations were carried out under mild conditions using a low catalyst loading and gave access to a large scope of azido lactones.*

Amino lactones have found widespread applications in natural product synthesis and in medicinal chemistry.[1] Furthermore, they serve as versatile starting materials for accessing other important building blocks, such as amino alcohols.[2] As non-basic precursors of amines, azides are highly useful synthetic intermediates on the way to nitrogen-rich compounds. They can also be transformed easily into various other nitrogen-containing functional groups.[3] Therefore, azidolactones are versatile and convenient precursors of both amino lactones and alcohols. Nevertheless, the preparation of azidolactones is usually based on multi-step protocols and lacks efficiency. The installation of the azido group commonly proceeds through substitution reactions on pre-functionalized substrates, such as halides.[4] Very recently, a copper catalyzed enantioselective radical azidocarboxylation of alkenes was developed by Buchwald and co-workers using phenyliodine diacetate (PIDA) and $TMSN_3$ as azide source, giving access to (1,2)-azidolactones **2** (Scheme 1, **A**).[5] However, this method is based on the in situ formation of highly reactive and potentially explosive hypervalent iodine reagents for the generation of the needed azide radical. Furthermore, this approach is limited to the synthesis of (1,2)-azidolactones: access to the (1,1) regioisomers, if possible from the same starting materials, would be highly attractive to extend the range of accessible azidolactones. (1,1)-Azidolactones are a largely unexplored class of compounds, which have been reported only rarely in the literature.[6]

In recent years, benziodoxol(on)es, a class of stable cyclic hypervalent iodine reagents, have emerged as privileged reagents for the transfer of functional groups via non-conventional reactivity.[7] AzidoBenziodoXolone (ABX, **3a**) and AzidoDimethyl-BenziodoXole (ADBX, **3b)** (Scheme 1) have been first described by Zhdankin and co-workers[8] and are stable solids decomposing at temperature higher than 100 °C.[9] They have been used as azide transfer reagents in presence of metal catalysts, relying either on radical-based[8,10] or Lewis-acid mediated pathways.[11] In particular, the azidation of styrene-type double bonds has recently attracted much interest and ABX (**3a**) and ADBX (**3b**) have emerged as good sources of azide radicals under reductive conditions.[10a,h,j,l] In 2015, Greaney and co-workers reported the photoredox-catalyzed nucleoazidation of styrenes using the Sauvage/McMillin catalyst $Cu(dap)_2Cl$[12] and ABX reagent **3a**, resulting in particularly mild reaction conditions.[10h] On the other hand, the azidation of ketoesters and silyl enol ethers has been successful in the presence of Lewis acids.[11] Nevertheless, to the best of our knowledge, azidobenziodoxol(on)es have never been used in the synthesis of azidolactones.



Scheme 1. Synthesis of Azidolactones from Alkenes.

Herein, we report the first synthesis of azidolactones based on the use of azidobenziodoxol(on)es (Scheme 1, **B**). The diverging behavior of ABX (**3a**) and ADBX (**3b**) in presence of metal catalysts led to either a radical-based or Lewis Acid mediated pathway, allowing the selective formation of (1,2)- or (1,1)-azidolactones **2** and **4** starting from styrene derivatives. The former was achieved under mild photoredox conditions using visible light irradiation and only 0.5 mol% $Cu(dap)_2Cl$ as catalyst,

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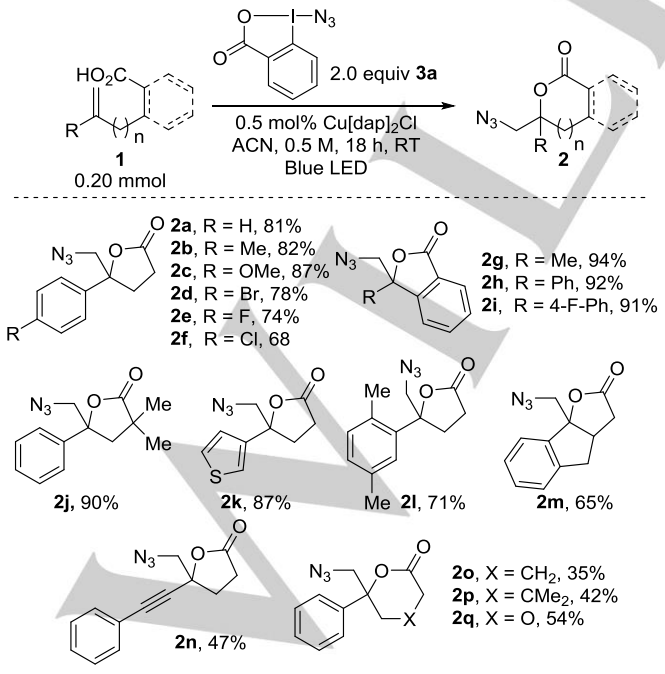
whereas the later was realized by Lewis acid activation of the hypervalent iodine reagent, involving an aryl migration step. Furthermore, the synthesis of (1,2)-azidolactones starting from olefins without arene substituent was possible using Lewis acid activation.

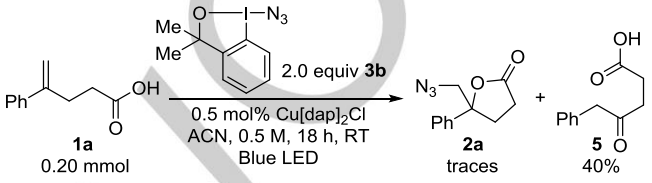
Based on the impressive work of Greaney and co-workers,[10h] we started our investigations with the photoredox catalysis strategy for the formation of (1,2)-azidolactone **2** from unsaturated carboxylic acid **1** (Scheme 2). Only ABX (**3a**) was successful in this transformation. Upon a fine adjustment of the reaction conditions,[13] the desired azidolactone **2a** could be isolated in 81% yield with 0.5 mol% of the photoredox catalyst under blue LED irradiation. Interestingly, while the reaction also worked in the absence of light, conversion to product **2a** dropped to 20%. This indicated that a radical chain process was possible, but less efficient. Using the combination of PIDA and $TMSN_3$ for azide radical formation,[5] only traces of **2a** were detected.

With this simple protocol for azidation in hands, we investigated the scope of the reaction (Scheme 2). A broad series of unsaturated carboxylic acids **1** containing substituted aryl groups was converted into the corresponding azidolactones **2** in good to excellent yields. Electron rich (**2b**, **2c**) as well as halogen-substituted arenes (**2d-f**) were well tolerated. A more rigid benzene backbone led to excellent yields of (1,2)-azido-phthalide derivatives **2g-i**. Dimethyl-substituted lactone **2j** was also obtained in 90% yield. A thiophene heterocycle was compatible with the reaction conditions (**2k**, 87%). An aromatic ring bearing a group in the *ortho* position was also tolerated (**2l**, 71%). Tricyclic (1,2)-azido-γ-butyrolactone **2m** was obtained in 65% yield. When enoic acid **1n** containing a 1,3-enyne motif was used, azidation product **2n** was formed in 47% yield. Importantly, (1,2)-azido-δ-lactones could be also obtained under the same reaction conditions, although lower yields were observed (product **2o-q**). Scale up of the reaction demonstrated that even lower catalyst loadings were possible: 1.0 g of **2e** was isolated in 82% yield using only 0.05 mol% catalyst.



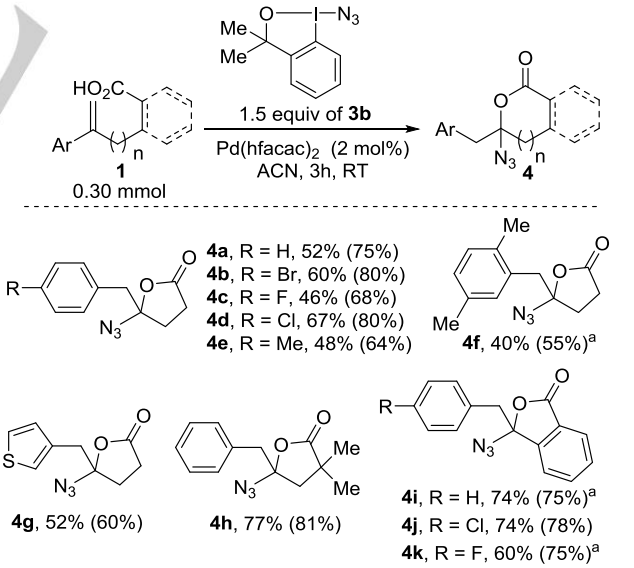
Scheme 2. Scope of the (1,2)-azidolactonization.

In contrast, when ADBX (**3b**) was used instead of ABX (**3a**) under the optimized photoredox conditions, only traces of (1,2)-azido-γ-butyrolactones **2a** were observed. The major product was 4-oxo-5-phenylpentanoic acid (**5**), which was isolated in 40% yield. (Equation 1) We speculated that **5** could originate from the hydrolysis of a (1,1)-azidolactone **4a** formed from reaction of the hypervalent iodine reagent with the double bond followed by 1,2-phenyl migration. In fact, such rearrangements have been observed for oxygenation or fluorination,[14] but are unprecedented for azidation with benziodoxole reagents. In this case, the copper catalyst probably acted as a Lewis acid to activate ADBX (**3b**) and not as a redox active catalyst able to generate the azide radical after a SET event.



Equation 1. Reaction of **1a** with ADBX (**3b**).

In fact, in presence of several Lewis acid catalysts such as $Zn(OTf)_2$, $In(OTf)_3$ and $Sn(OTf)_2$, (1,1)-azidolactone **4a** could be isolated as the major product.[13] $Pd(hfacac)_2$ (2 mol%) was identified as the best catalyst for this transformation leading to **4** in 75% yield by NMR. $Sn(OTf)_2$ provided similar results, but with lower reproducibility. The low catalyst loading is noteworthy, as most reported oxidative rearrangements required stoichiometric amounts of Lewis or Brønsted acids.[14] Although **4a** was sensitive to hydrolysis, it was still possible to purify it by column chromatography (52% pure **4a** isolated).

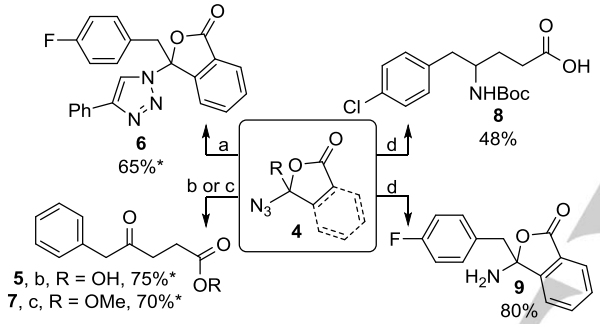


Scheme 3. Scope of (1,1)-azidolactonization of **1**. (isolated yield given, NMR yield in brackets). a) Isolated as a mixture with 2-(2-iodophenyl)propan-2-ol.

The reaction worked efficiently in the presence of halogen and methyl substituents on the aromatic ring, affording products **4b-f** in 55-80% yield. A thiophenyl group was also able to migrate, affording **4g** in 52% isolated yield. A geminal dimethyl substituted substrate **1h** gave the more stable azido lactone **4h** in 77% isolated

yield. Finally, (1,1)-azido-phthalide derivatives **4i**, **4j**, **4k** were also generated in high yields.

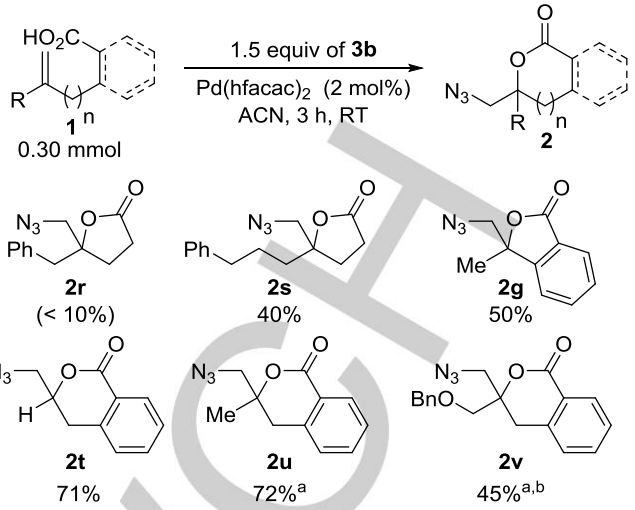
Due to the high sensitivity of the obtained (1,1)-azidolactones, the direct modification of the crude products was then investigated (Scheme 4). Copper catalyzed cycloaddition starting from **4k** and phenylacetylene gave triazole **6** as a stable crystalline solid in 65% yield over two steps starting from the olefin. Hydrogenation of the crude reaction mixture containing **4a** in EtOAc, using 5 mol% of Pd/C, afforded ketone **5** in 75% yield over two steps.[15] The γ-ketoester could be selectively generated through the hydrogenation of the crude material of **4a** in methanol in 70% yield over two steps. When using 10 mol% of Pt black as catalyst with (1,1)-azido-γ-butyrolactone **4d** in the presence of Boc_2O, the N-Boc protected Gamma AminoButyric Acid (GABA) derivative **8** was isolated in 48% yield. The GABA motif is commonly found in many bioactive compounds and is an important target in synthetic chemistry.[16] In the case of (1,1)-azido-phthalide derivative **4k**, only azide reduction was observed under Pt/C catalysis and the (1,1)-amino-phthalide **9** was isolated in 80% yield. These successful transformations demonstrated the potential of (1,1)-azidolactones as useful building blocks.



Scheme 4. Product modifications. *Isolated yields over two steps from **1**. Reaction conditions: a) CuI (10 mol%), Et_3N (3.0 equiv.), phenylacetylene (2.0 equiv.), THF, 25°C; b) H_2, Pd/C (5 mol%), EtOAc, 25 °C; c) H_2, Pd/C (2.5 mol%), MeOH, 25 °C; d) H_2, Pt black (10 mol%), Boc_2O (2.0 equiv.), THF, 25 °C.

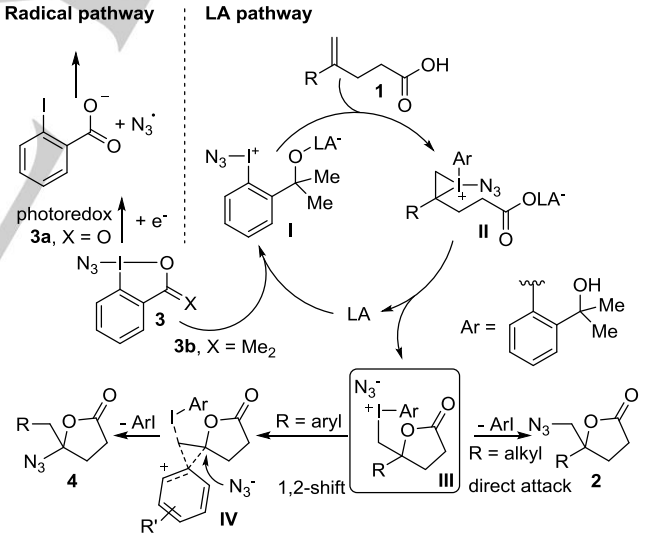
In order to investigate the generality of the 1,2-shift, we then replaced the aryl substituent by a simple alkyl group (Scheme 5). No (1,1)-azidolactone was obtained with a benzyl group: only traces of (1,2)-azidolactonization product **2r** could be observed. 1,2-Azidolactone **2s** could be obtained in 40% with a phenyl group in γ position to the alkene. Interestingly, compounds **2s** is not formed under photoredox conditions, as an aryl group on the alkene is required for oxidation of the carbon centered radical intermediate. Better yields were obtained with more rigid substrates derived from benzoic acid (products **2g** and **2t-v**). γ-lactone **2g** can be synthesized in better yield under photoredox conditions, but δ-lactone **2t-v** can be accessed only with Lewis acid catalysis, showing that the two methods are highly complementary.

Based on the precedence in literature on radical and Lewis acid pathways with hypervalent iodine reagents,[10,14] a speculative mechanism can be proposed for the developed transformations (Scheme 6). The better results obtained with ABX (**3a**) under photoredox conditions could be due to its expected stronger oxidant character when compared to ADBX (**3b**).[17] In contrast, the Lewis acid catalytic cycle would be initiated by the activation of ADBX (**1b**).[18] The resulting more electrophilic complex **I** will react with alkene **1** to give iodocyclopropylium cation **II**.



Scheme 5. Lewis acid catalyzed synthesis of (1,2)-azidolactones. a) 20 h of reaction. b) 10 mol% of $Pd(hfacac)_2$ were used.

A proton transfer can also be expected from the carboxylic acid to the more basic alkoxide, a key step to promote catalyst turnover only possible with **3b**. Ring opening through the attack of the carboxylic acid delivers then the highly electrophilic intermediate **III**. In case of aliphatic substituents, direct substitution with the azide would occur, leading to (1,2)-azidolactones **2**. In case of aryl substituents, 1,2-migration via a phenonium ion or a non-classical carbocation **IV** is faster and gives product **4a**. Further works will be needed to support this speculative mechanism.



Scheme 6. Speculative reaction mechanism.

In conclusion, we have reported a general and versatile synthesis of azidolactones starting from alkene-containing carboxylic acids. A large range of (1,1) and (1,2)-azidolactones were obtained selectively in high yields and with broad functional group tolerance. The fine modulation of the reactivity possible for benziodoxolone reagents was key to enable either a photoredox or a Lewis acid pathway to access (1,1)- and (1,2)-azidolactones respectively. These results further establish the exceptional potential of cyclic hypervalent iodine reagents for group transfer reactions and will allow a broader use of azidolactones as useful building blocks in synthetic and medicinal chemistry.

Acknowledgements

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Keywords: Azides, lactones, hypervalent iodine, photoredox, 1,2 shift.

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[13] See Supporting Information for a complete list of tested reaction conditions.

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[15] In principle, a simple hydrolysis would also lead to the same compound. Nevertheless, better yields were obtained under hydrogenation conditions, probably because prior reduction of the azide facilitates hydrolysis under mild conditions.

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[18] At this stage, a redox catalytic cycle involving different oxidation states of palladium cannot be excluded, but it appears less probable as several Lewis acids were able to catalyze the reactions.

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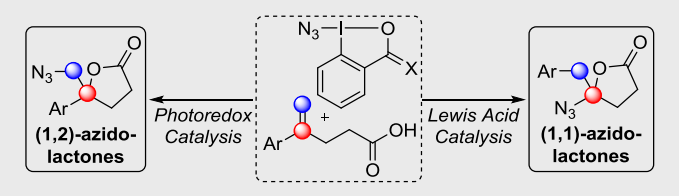
COMMUNICATION



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Supporting Information

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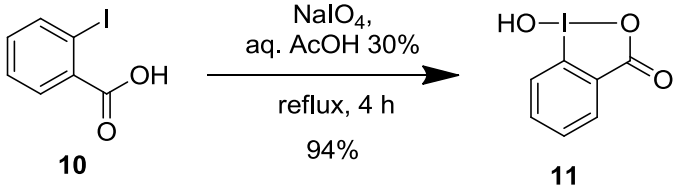
1. General Methods

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. 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 or Seebach stain (Phosphomolybdid acid, $Ce(SO_4)_2$, H_2SO_4, water). 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. 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 continuously flushed with air 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 cm. Temperature ranged between 25 and 30 °C, and long irradiation resulted in temperature increasing up to 34 °C during overnight reactions. $Cu[dap]_2Cl$ complex was purchased from Sigma-Aldrich and used as received.

2. Synthesis of Hypervalent Iodine Reagents

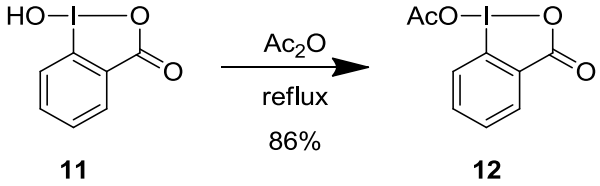
a. Synthesis of 1-azido-1,2-benziodoxole-3-(1H)-one (3a)

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (11)



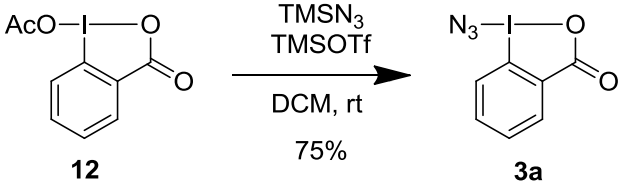
$NaIO_4$ (7.24 g, 33.8 mmol, 1.00 equiv) and 2-iodo benzoic acid (**10)** (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v:v) aq AcOH (48 mL) under air. The mixture was vigorously stirred and refluxed for 4 h. the reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. The mixture is then filtered and further washed with ice water and cold acetone, air dried in the dark overnight to give the pure compound **11** (8.14 g, 30.4 mmol, 94%) as a colorless solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. **IR** 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). NMR data correspond to the reported values. [1]

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (12)



Following a reported procedure,[2] compound **11** (3.00 g, 11.3 mmol, 1.00 equiv) was heated in Ac_2O (10 mL) to reflux until the solution turned clear (without suspension). The mixture was then left to cool down and white crystals started to form. The crystallization was continued at -18 °C. The crystal were then collected and dried overnight under high vacuum to give compound **12** (3.06 g, 10.0 mmol, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 8.00 (dd, *J* = 8.3, 0.5 Hz, 1H, Ar*H*), 7.92 (dt, *J* = 7.0, 1.7 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 0.9 Hz, 1H, Ar*H*), 2.25 (s, 3H, COC*H*$_3$). NMR data correspond to the reported values. [2]

1-Azido-1,2-benziodoxole-3-(1*H*)-one (3a)

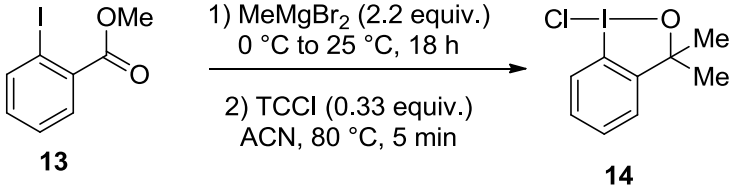


Caution: reaction carried out behind a safety shield! Following a reported procedure,[3] compound **12** (1.00 g, 3.28 mmol, 1.00 equiv) was stirred in dry DCM (3 m) then $TMSN_3$ (0.66

mL, 4.9 mmol, 1.5 equiv) was cautiously added. A catalytic amount of TMSOTf (3 µL, 0.02 mmol, 0.005 equiv) was added last to the mixture which was then stirred for 30 minutes. The reaction mixture was then died in vacuo to give a yellow precipitate, which was washed a few times with hexanes to give compound **3a** (0.70 g, 2.4 mmol, 74%) as a pure pale yellow crystal. **^{1}H NMR** (400 MHz, $CDCl_3$:CH_3CN; 10:1) δ 8.17 (dd, *J* = 7.5, 1.3 Hz, 1H, Ar*H*), 7.93 (m, 2H, Ar*H*), 7.70 (m, 1H, Ar*H*). **^{13}C NMR** (101 MHz, $CDCl_3$:CH_3CN; 10:1) δ 166.2, 134.8, 131.8, 130.4, 125.4, 116.6, 115.4. **IR** 2049 (s), 1639 (s), 1565 (m), 1440 (w), 1347 (w), 1295 (m).The *analysis data* for the characterization of **3a** correspond to the ones reported in the literature.[3] Caution: Although compound **3a** is relatively stable, in our lab laboratory, it detonated in two instances. Diffrential scanning calorimetry analysis confirmed its explosive character.[4]

b. Synthesis of 1-azido-3,3-dimethyl-3-(1H)-1,2-benziodoxole (3b)

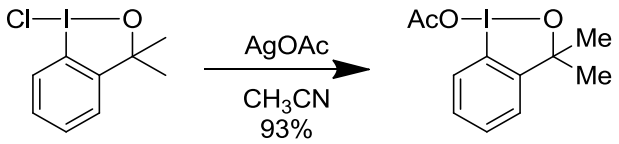
1-Chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (14)



13 **14**

Following a reported procedure,[5] methyl 2-iodobenzoate **13** (12 mL, 76 mmol) was dissolved under N_2 atmosphere in dry diethyl ether (400 mL) and then the solution was cooled down at 0 °C with an ice bath. Methylmagnesium bromide (56.0 mL, 168 mmol, 2.20 equiv) was added dropwise and the reaction was stirred for 30 min at 0 °C. The reaction mixture was then allowed to warm to room temperature and it was further stirred for 16 h. The reaction was quenched with NH_4Cl in an iced bath. The organic layer was separated and extracted with Et_2O (3 x 100 mL), water (2 x 200 mL), brine (1 x 100 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed in vacuum. The crude mixture (9.1 g, 33.0 mmol, 1.0 equiv.) was dissolved in anhydrous ACN (65mL) and the mixture as stirred and heated at 75 °C. In an additional funnel was dissolved the 1,3,5-trichloro-1,3,5-triazinane-2,4,6-trione (2.56 g, 11.0 mmol, 0.33 equiv.) in anhydrous ACN (50 mL). The resulting solution was added to the stirred solution of 2-(2-iodophenyl)propan-2-ol within 5 min. The reaction was refluxed 5 min and filtered on a pad of Celite and the cake was washed with hot ACN (3 x 15 mL). The resulting filtrate was concentrated un vacuum and the solid was washed with pentane (2 x 20 mL) and with a minimum of cold acetone to give the compound **14** (7.11 g, 23.9 mmol, 73 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.1, 1.1 Hz, 1H, Ar*H*), 7.55 (m, 2H, Ar*H*), 7.17 (dd, *J* = 7.3, 1.7 Hz, 1H, Ar*H*), 1.55 (s, 6 H, (CH_3)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.5, 131.0, 130.5, 128.4, 126.1, 114.7, 85.2, 29.2. **IR** 3729 (w), 3626 (w), 2972 (w), 2924 (w), 2362 (w), 2055 (w), 2018 (w), 1742 (w), 1564 (w), 1464 (w), 1439 (w), 1379 (w), 1378 (w), 1366 (w), 1277 (w), 1276 (w), 1256 (w), 1181 (w), 1154 (m), 1112 (w), 1048 (w), 1003 (w), 982 (w), 943 (m), 866 (m), 808 (w), 790 (w), 789 (w), 762 (s), 745 (w), 724 (w), 718 (w). NMR data correspond to the reported values.[5]

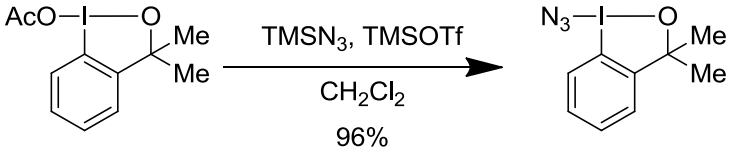
1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (15)



14 **15**

Following a reported procedure[5] 1-Chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole **14** (2.60 g, 8.77 mmol) was dissolved in dry acetonitrile (25 mL) under N_2 atmosphere. The reaction flask was covered with aluminum foils and protected from light. Silver acetate (1.46 g, 8.77 mmol, 1.00 equiv) was then added in one portion. The reaction mixture was stirred in the dark at room temperature for 16 h. Filtration over a Celite plug and evaporation of the solvent yielded compound **15** (2.6 g, 8.8 mmol, 93%) as a light brownish solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.0, 1.3 Hz, 1H, Ar*H*), 7.47 (m, 2H, Ar*H*), 7.18 (dd, *J* = 7.2, 1.7 Hz, 1H, Ar*H*), 2.11 (s, 3H, COC*H*$_3$), 1.52 (s, 6H, (C*H*$_3$)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.4, 149.4, 130.4, 130.0, 129.9, 126.2, 115.7, 84.6, 29.2, 21.5. **IR** 3099 (w), 3057 (w), 2975 (w), 2930 (w), 2930 (w), 2865 (w), 1740 (w), 1640 (s), 1588 (w), 1566 (w), 1462 (w), 1438 (m), 1363 (s), 1294 (s), 1259 (m), 1158 (m), 1114 (w), 1047 (w), 1033 (w), 1009 (w), 949 (m), 926 (w), 866 (w), 761 (s), 723 (w). NMR data correspond to the reported values.[5]

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

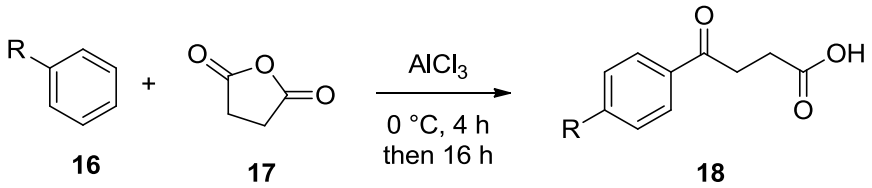


15 **3b**

Caution: This reaction should be carried out behind a safety shield! Following a reported procedure[2] 1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole **15** (2.30 g, 7.18 mmol) was dissolved in dry CH_2Cl_2 (36 mL) under N_2 atmosphere. The reaction was placed in an iced bath and trimethylsilylazide (0.954 mL, 7.18 mmol, 1.00 equiv) was added via syringe, followed by TMSOTf (0.065 mL, 0.36 mmol, 0.050 equiv). The reaction was stirred for 15 min then the ice bath was removed and the stirring was continued for 1 h. The solvent was evaporated and the solid obtained was washed with *n*-hexane (2 x 30 mL, HLPC purity) to afford **3b** as a yellow crystalline solid (2.10 g, 7.18 mmol, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.55 (m, 2H, Ar*H*), 7.23 (d, *J* = 7.2 Hz, 1H, Ar*H*), 1.53 (s, 6H, (C*H*$_3$)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.2, 130.9, 130.4, 127.8, 126.8, 114.0, 83.2, 29.6. **IR** 3254 (w), 3085 (w), 3051 (w), 2976 (w), 2928 (w), 2860 (w), 2486 (w), 2026 (s), 1918 (w), 1764 (w), 1697 (w), 1651 (w), 1589 (w), 1562 (w), 1462 (m), 1428 (m), 1380 (w), 1364 (w), 1312 (w), 1273 (w), 1248 (s), 1182 (w), 1151 (m), 1111 (m), 1031 (w), 1004 (w), 943 (m), 910 (m), 880 (w), 863 (m). NMR data correspond to the reported values. [5]

3. Synthesis of starting materials

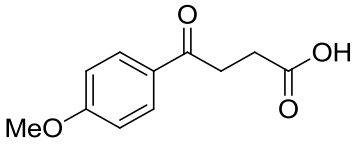
a. General procedure for synthesis of ketone precursors using Friedel-Craft reaction



16 **17** **18**

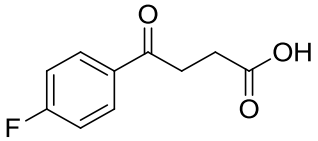
A 100-mL, three-necked, round-bottomed flask is charged with powdered dihydrofuran-2,5-dione **17** (1.0 equiv.) and arene **16** (1.0 equiv.) under dry nitrogen. The resulting white mixture was cooled to 0 °C before anhydrous aluminum trichloride (1.2 equiv.) was added in one portion. The reaction mixture was stirred over a period of 4 h before allowing it to warm to room temperature for 16 h. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice. The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated. Product was engaged in the next step without further purification.

4-(4-Methoxyphenyl)-4-oxobutanoic acid (18a)



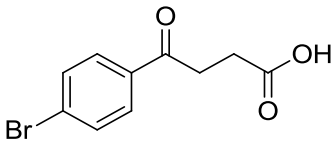
According to the general procedure, starting from dihydrofuran-2,5-dione **17** (2.75 g, 27.5 mmol, 1.0 equiv.), aluminum trichloride (4.41 g, 33.0 mmol, 1.2 equiv.) and anisole **16a** (3.00 mL, 27.5 mmol), the product was obtained as a white solid (4.67 g, 22.4 mmol, 82 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 2H, Ar*H*), 6.94 (d, *J* = 8.8 Hz, 2H, Ar*H*), 3.87 (s, 3H, *Me*), 3.27 (t, *J* = 6.6 Hz, 2H, $CH_2CH_2CO_2H$), 2.80 (t, *J* = 6.6 Hz, 2H, $CH_2CH_2CO_2H$). NMR data correspond to the reported values.[6]

4-(4-Fluorophenyl)-4-oxobutanoic acid (18b)



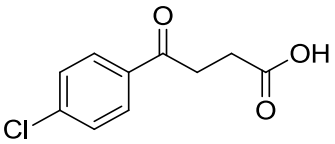
According to the general procedure, starting from dihydrofuran-2,5-dione **17** (2.75 g, 27.5 mmol, 1.0 equiv.), aluminum trichloride (4.41 g, 33.0 mmol, 1.2 equiv.) and fluorobenzene **16b** (3.89 mL, 41.2 mmol 1.0 equiv.), the product was obtained as a white solid (4.12 g, 20.9 mmol, 76 % yield). **^{1}H NM**R (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.6, 5.4 Hz, 2H, Ar*H*), 7.14 (t, *J* = 8.5 Hz, 2H, Ar*H*), 3.28 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.81 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$). NMR data correspond to the reported values.[6]

4-(4-Bromophenyl)-4-oxobutanoic acid (18c)



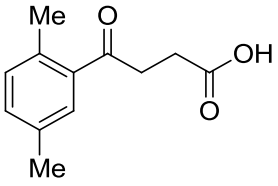
According to the general procedure, starting from dihydrofuran-2,5-dione **17** (2.85 g, 28.5 mmol, 1.0 equiv.), aluminum trichloride (4.56 g, 34.2 mmol, 1.2 equiv.) and bromobenzene **16c** (3.05 mL, 28.5 mmol, 1.0 equiv.), the product was obtained as a white solid (4.80 g, 18.7 mmol, 65 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.61 (d, *J* = 8.6 Hz, 2H, Ar*H*), 3.27 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.81 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$). NMR data correspond to the reported values.[6]

4-(4-Chlorophenyl)-4-oxobutanoic acid (18d)



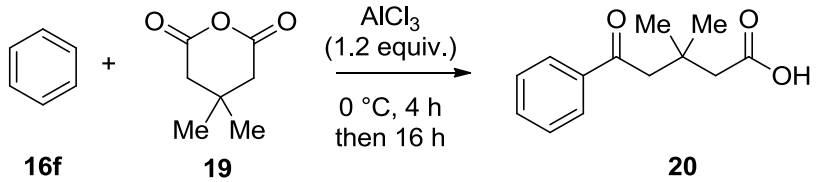
According to the general procedure, starting from dihydrofuran-2,5-dione **17** (2.93 g, 29.3 mmol, 1.0 equiv.), aluminum trichloride (4.69 g, 35.2 mmol, 1.2 equiv.) and chlorobenzene **16d** (3.00 mL, 29.3 mmol, 1.0 equiv.), the product was obtained as a white solid (4.75 g, 22.3 mmol, 76 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.44 (d, *J* = 8.3 Hz, 2H, Ar*H*), 3.28 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.81 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$). NMR data correspond to the reported values. [6]

4-(2,5-Dimethylphenyl)-4-oxobutanoic acid (18e)



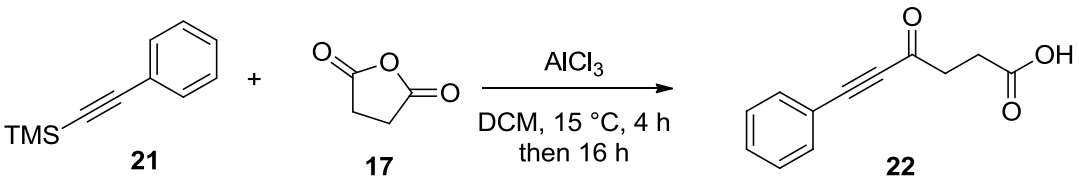
According to the general procedure, starting from dihydrofuran-2,5-dione **17** (2.45 g, 24.5 mmol, 1.0 equiv.), aluminum trichloride (3.92 g, 29.4 mmol, 1.2 equiv.) and p-xylene **16e** (3.00 mL, 24.5 mmol, 1.0 equiv.), the product was obtained as a beige solid (2.7 g, 13 mmol, 53 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.19 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.13 (d, *J* = 7.8 Hz, 1H, Ar*H*), 3.22 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.79 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.45 (s, 3H, *Me*), 2.36 (s, 3H, *Me*). NMR data correspond to the reported values.[6]

3,3-Dimethyl-5-oxo-5-phenylpentanoic acid (20)



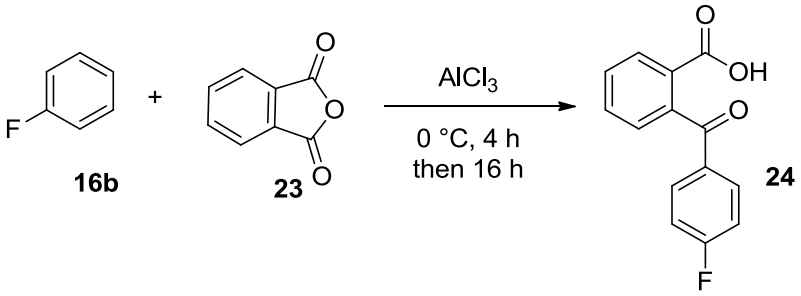
A 100-mL, three-necked, round-bottomed flask was charged with powdered 3,3-Dimethylglutaric anhydride **19** (1.50 g, 10.5 mmol, 1.0 equiv.) and benzene **16f** (3.00 mL, 33.4 mmol, 3.0 equiv.) under dry argon. The resulting white mixture was cooled to 0 °C before anhydrous aluminum trichloride (1.688 g, 12.66 mmol, 1.2 equiv.) is added in one portion. The reaction mixture is stirred over a period of 4 h before allowing it to warm to room temperature for 16 h. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice (2 x 30 mL). The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated to give the expected compound **20** (1.70 g, 7.72 mmol, 73 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.60 – 7.54 (m, 1H, Ar*H*), 7.46 (t, *J* = 7.6 Hz, 2H, Ar*H*), 3.12 (s, 2H, C*H*$_2$CO$_2$H), 2.59 (s, 2H, C=CC*H*$_2$*C*Me$_2$), 1.18 (s, 6H, 2*Me*). NMR data correspond to the reported values.[7]

4-Oxo-6-phenylhex-5-ynoic acid (22)



To a solution of succinic anhydride **17** (1.2 g, 12 mmol, 1.2 equiv.) in DCM (125 mL) in a 250mL round-bottom flask fitted with a thermometer, and solvent addition funnel was added aluminum trichloride (2.3 g, 17 mmol). The reaction mass was cooled under stirring to 15 °C and a solution of trimethyl(phenylethynyl)silane **21** (2.0 mL, 10 mmol) in 10mL of DCM was added dropwise and the reaction mixture was stirred for 16 h at rt. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice (2 x 50 mL). The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated to give the expected compound **22** (1.00 g, 4.95 mmol, 49 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.47 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.39 (t, *J* = 7.5 Hz, 2H. Ar*H*), 3.02 (t, *J* = 6.6 Hz, 2H, CH_2), 2.77 (t, *J* = 6.6 Hz, 2H, CH_2). NMR data correspond to the reported values.[8]

2-(4-Fluorobenzoyl)benzoic acid (24)



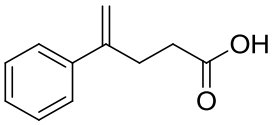
A 100-mL, three-necked, round-bottomed flask is charged with powdered phthalic anhydride **23** (3.26 g, 22.0 mmol, 1.0 equiv.) and fluorobenzene **16b** (6.00 mL, 66.0 mmol, 3.0 equiv.) under dry nitrogen. The resulting white mixture was cooled to 0 °C before anhydrous aluminum trichloride (4.40 g, 33.0 mmol, 1.5 equiv.) was added in one portion. The reaction mixture was stirred over a period of 1 hr before the reaction mixture is allowed to warm to room temperature for 16h. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added

under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice (2 x 30 mL). The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated to give the expected compound **254** (2.35 g, 9.42 mmol, 42 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.74 (dd, *J* = 8.4, 5.5 Hz, 2H, Ar*H*), 7.68 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.58 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.36 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.08 (t, *J* = 8.5 Hz, 2H, Ar*H*). NMR data correspond to the reported values. [9]

b. General procedure for synthesis of enoic acid using Wittig reaction

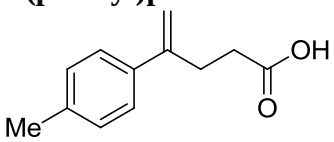
Under nitrogen, to a solution of *t*BuOK (2.6 equiv.) in dry THF (0.5 M) was added bromo(methyl)triphenylphosphorane (1.3 equiv.) in portions at 0 °C. The mixture was stirred at 0 °C for 30 min and a solution of ketone (1.0 equiv.) in dry THF (1 M) was added dropwise and the reaction was stirred at 0 °C for 1 h and at rt overnight. The solvent was removed in vacuo and the residue diluted with DCM and aqueous NaOH (1 M). The aqueous layer was separated, washed with dichloromethane, and acidified to pH 1 with concentrated HCl. DCM was added and the organic compound was extracted twice with DCM. The organic layer was washed with water, dried over $MgSO_4$ and concentrated. The crude product was purified by SiO_2 column chromatography (DCM/MeOH: 100/0 to 95/5 to 9/1) to give pure enoic acid.

4-Phenylpent-4-enoic acid (1a)



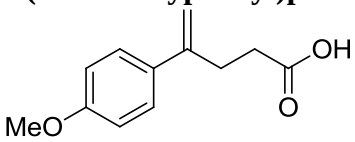
According to the general procedure, starting from 4-oxo-4-phenylbutanoic acid (3.00 g, 16.8 mmol, 1.0 equiv.), tBuOK (4.91 g, 43.8 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (7.82 g, 21.9 mmol, 1.3 equiv.), the product was obtained as a white solid (2.75 g, 15.6 mmol, 93 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.60 (bs, 1H), 7.46 – 7.27 (m, 5H, Ar*H*), 5.35 (s, 2H, C=CH_2), 2.87 (t, *J* = 7.8 Hz, 2H, $CH_2CH_2CO_2H$), 2.56 (dd, *J* = 8.9, 6.7 Hz, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.9, 146.6, 140.5, 128.6, 127.8, 126.2, 113.1, 33.1, 30.2. NMR data correspond to the reported values. [10]

4-(p-Tolyl)pent-4-enoic acid (1b)



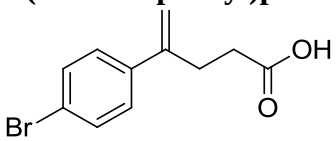
According to the general procedure, starting from 4-oxo-4-(p-tolyl)butanoic acid (2.00 g, 10.2 mmol, 1.0 equiv.), tBuOK (3.00 g, 26.7 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (4.78 g, 13.4 mmol, 1.3 equiv.), the product was obtained as a white solid (1.70 g, 8.94 mmol, 87 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.17 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.33 (d, *J* = 1.0 Hz, 1H, C=CH_2), 5.09 (q, *J* = 1.2 Hz, 1H, C=CH_2), 2.90 – 2.83 (m, 2H, $CH_2CH_2CO_2H$), 2.61 – 2.52 (m, 2H, $CH_2CH_2CO_2H$), 2.38 (s, 3H, *Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.8, 146.4, 137.6, 137.5, 129.2, 126.0, 112.3, 33.2, 30.2, 21.2. NMR data correspond to the reported values. [11]

4-(4-Methoxyphenyl)pent-4-enoic acid (1c)



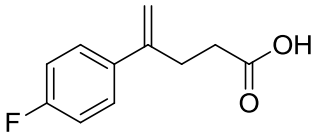
According to the general procedure, starting from 4-(4-methoxyphenyl)-4-oxobutanoic acid **18a** (1.10 g, 5.28 mmol, 1.0 equiv.), tBuOK (1.54 g, 13.7 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (2.45 g, 6.87 mmol, 1.3 equiv.), the product was obtained as a white solid (0.71 g, 3.44 mmol, 65 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 2H, Ar*H*), 6.91 – 6.83 (m, 2H, Ar*H*), 5.25 (d, *J* = 1.0 Hz, 1H, C=CH_2), 5.03 (d, *J* = 1.2 Hz, 1H, C=CH_2), 3.82 (s, 3H, *Me*), 2.88 – 2.75 (m, 2H, $CH_2CH_2CO_2H$), 2.64 – 2.43 (m, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.9, 159.4, 146.0, 133.0, 127.3, 113.9, 111.6, 55.4, 33.1, 30.3. NMR data correspond to the reported values.[11]

4-(4-Bromophenyl)pent-4-enoic acid (1d)



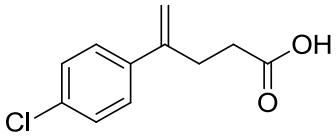
According to the general procedure, starting from 4-(4-bromophenyl)-4-oxobutanoic acid **18c** (2.00 g, 7.78 mmol, 1.0 equiv.), tBuOK (2.27 g, 20.2 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (3.61 g, 10.1 mmol, 1.3 equiv.), the product was obtained as a white solid (1.50 g, 5.88 mmol, 76 % yield**. ^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 12.18 (s, 1H, CO_2H), 7.59 – 7.50 (m, 2H, Ar*H*), 7.45 – 7.38 (m, 2H, Ar*H*), 5.39 (s, 1H, C=CH_2), 5.13 (d, *J* = 1.4 Hz, 1H, C=CH_2), 2.70 (t, *J* = 7.6 Hz, 2H, $CH_2CH_2CO_2H$), 2.36 (dd, *J* = 8.4, 6.7 Hz, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $(CD_3)_2SO$) δ 173.8, 145.4, 139.3, 131.4, 128.0, 120.8, 113.3, 32.5, 29.4. NMR data correspond to the reported values.[12]

4-(4-Fluorophenyl)pent-4-enoic acid (1e)



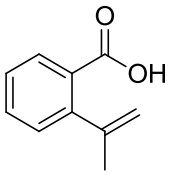
According to the general procedure, starting from 4-(4-fluorophenyl)-4-oxobutanoic acid **18b** (2.00 g, 10.2 mmol), 1.0 equiv.), tBuOK (2.97 g, 26.5 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (4.73 g, 13.2 mmol, 1.3 equiv.), the product was obtained as a white solid (1.70 g, 8.75 mmol, 86 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 2H, Ar*H*), 7.02 (t, *J* = 8.7 Hz, 2H, Ar*H*), 5.27 (s, 1H, C=CH_2), 5.09 (s, 1H, C=CH_2), 2.81 (t, *J* = 7.7 Hz, 2H, $CH_2CH_2CO_2H$), 2.51(t, *J* = 7.9 Hz, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.7, 162.5 (d, *J* = 246.6 Hz), 145.6, 136.6 (d, *J* = 3.3 Hz), 127.8 (d, *J* = 8.0 Hz), 115.4 (d, *J* = 21.3 Hz), 113.1, 33.0, 30.3. NMR data correspond to the reported values.[11]

4-(4-Chlorophenyl)pent-4-enoic acid (1f)



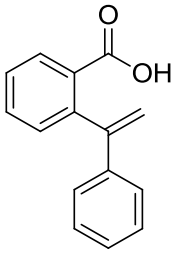
According to the general procedure, starting from 4-(4-chlorophenyl)-4-oxobutanoic acid **18d** (1.65 g, 7.78 mmol, 1.0 equiv.), tBuOK (2.27 g, 20.2 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (3.61 g, 10.1 mmol, 1.3 equiv.), the product was obtained as a white solid (1.0 g, 4.8 mmol, 61 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 4H, Ar*H*), 5.31 (s, 1H, C=CH_2), 5.12 (d, *J* = 1.3 Hz, 1H, C=CH_2), 2.81 (t, *J* = 7.4 Hz, 2H, $CH_2CH_2CO_2H$), 2.52 (m, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 145.6, 139.0, 133.7, 128.7, 127.5, 113.7, 32.9, 30.1. NMR data correspond to the reported values.[11]

2-(Prop-1-en-2-yl)benzoic acid (1g)



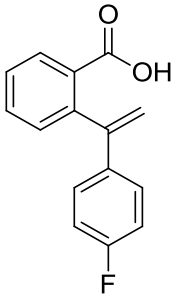
According to the general procedure, starting from 2-acetylbenzoic acid (1.70 g, 10.3 mmol, 1.0 equiv.), tBuOK (3.02 g, 26.9 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (4.81 g, 13.5 mmol, 1.3 equiv.), the product was obtained as a white solid (1.5 g, 9.3 mmol, 89 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.51 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.36 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.27 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.13 (s, 1H, C=CH_2), 4.90 (s, 1H, C=CH_2), 2.13 (s, 3H, *Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.7, 146.8, 146.5, 132.8, 130.9, 129.9, 128.2, 127.2, 114.1, 24.5. NMR data correspond to the reported values. [10]

2-(1-Phenylvinyl)benzoic acid (1h)



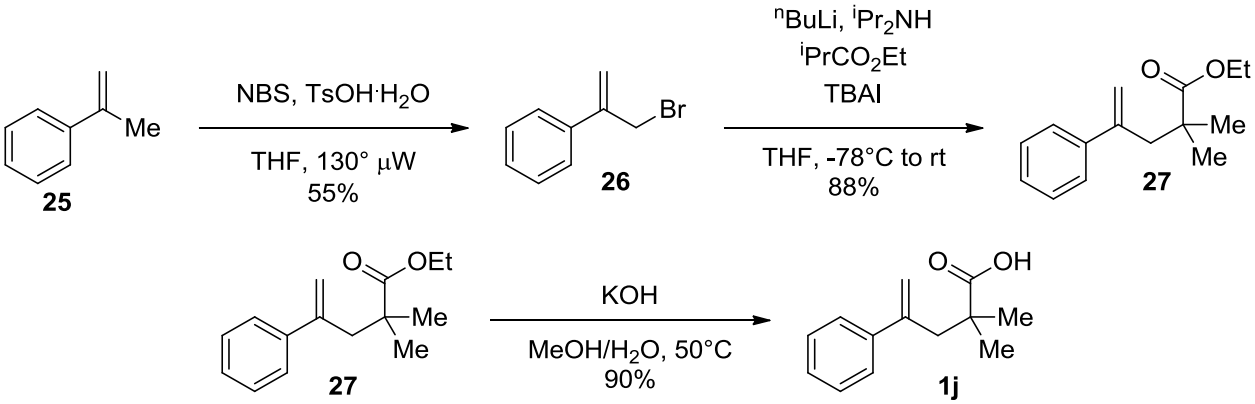
According to the general procedure, starting from 2-benzoylbenzoic acid (1.50 g, 6.63 mmol, 1.0 equiv.), tBuOK (1.93 g, 17.2 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (3.08 g, 8.62 mmol, 1.3 equiv.), the product was obtained as a white solid (0.60 g, 2.7 mmol, 40 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar*H*), 7.57 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.43 (td, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 7.38 (dd, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.28 – 7.18 (m, 5H, Ar*H*), 5.67 (d, *J* = 1.0 Hz, 1H, C=CH_2), 5.23 (d, *J* = 1.0 Hz, 1H, C=CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4, 149.6, 143.7, 141.0, 132.5, 131.7, 130.8, 129.6, 128.20, 127.8, 127.6, 127.0, 114.5. NMR data correspond to the reported values. [10]

2-(1-(4-Fluorophenyl)vinyl)benzoic acid (1i)



According to the general procedure, starting from 2-(4-fluorobenzoyl)benzoic acid **24** (1.50 g, 6.14 mmol, 1.0 equiv.), tBuOK (1.79 g, 15.9 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (2.85 g, 7.98 mmol, 1.3 equiv.), the product was obtained as a white solid (0.25 g, 1.0 mmol, 17 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 7.57 (td, *J* = 7.5, 1.4 Hz, 1H, Ar*H*), 7.44 (td, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 7.36 (dd, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.21 – 7.12 (m, 2H, Ar*H*), 6.97 – 6.85 (m, 2H, Ar*H*), 5.60 (d, *J* = 0.9 Hz, 1H, C=C*H*$_2$), 5.20 (s, 1H, C=C*H*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.7, 162.4 (d, *J* = 246.6 Hz), 148.7, 143.6, 137.3 (d, *J* = 3.3 Hz), 132.7, 131.6, 130.9, 129.5, 128.5 (d, *J* = 8.0 Hz), 128.0 115.0 (d, *J* = 21.5 Hz), 114.3. NMR data correspond to the reported values. [13]

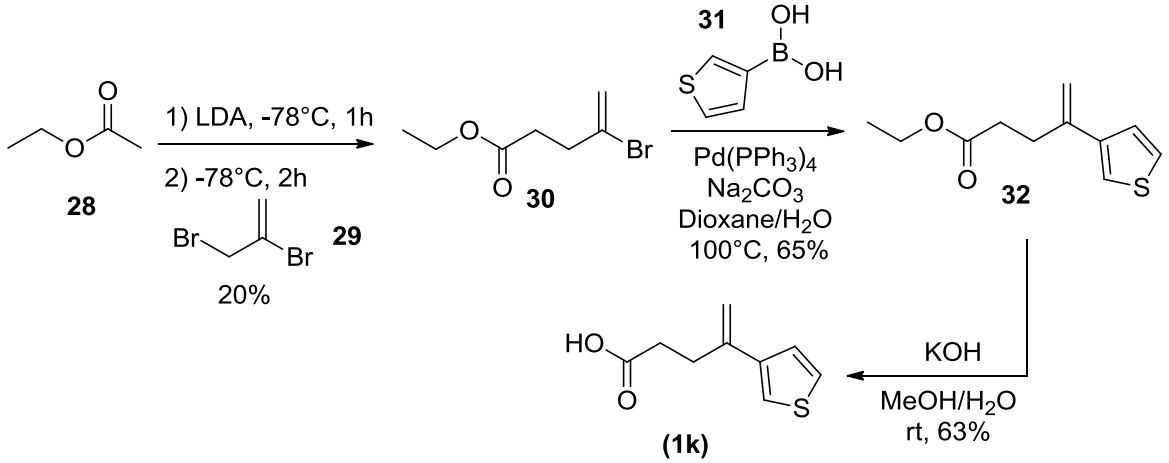
2,2-Dimethyl-4-phenylpent-4-enoic acid (1j)



Following a modified version of a reported procedure,[14] N-Bromosuccinimide (2.46 g, 13.8 mmol, 2.0 equiv.) and *p*-toluenesulfonic acid hydrate (0.263 g, 1.38 mmol, 0.2 equiv.) were dissolved in dry THF (20 mL), giving a yellow solution. Alpha methyl styrene **25** (0.90 mL, 6.9 mmol, 1.0 equiv) was added via syringe: the reaction mixture became colorless. The latter was then submitted to irradiation in a microwave reactor at 130 °C for 3 h. The mixture was then allowed to cool down to room temperature and poured into pentane. A solid immediately precipitated. The organic layer was washed with water (4 x 20 mL) and brine (once), finally becoming a clear solution. The latter was dried over $MgSO_4$, filtered and concentrated *in vacuo* to provide a yellow oil. The latter was submitted to column chromatography (SiO_2, pentane, (Rf = 0.95)) to provide pure (3-bromoprop-1-en-2-yl)benzene **26** (0.750 g, 3.81 mmol, 55% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 - 7.48 (m, 2H, Ar*H*), 7.41 - 7.33 (m, 3H, Ar*H*), 5.56 (s, 1H, C=*CH*$_2$), 5.50 (s, 1H, C=*CH*$_2$), 4.39 (s, 2H, *CH*$_2$). NMR data correspond to the reported values.[14] Following a standard procedure, di*iso*propylamine (freshly distilled over CaH_2; 0.50 mL, 3.5 mmol, 1.1 equiv.) was dissolved in dry THF (3.2 mL) and the resulting

solution was cooled to -78 °C (dry ice-acetone bath). *n*BuLi (2.5 M in hexane; 1.3 mL, 3.3 mmol, 1.05 equiv.) was added dropwise at the same temperature. The mixture was then stirred at 0 °C for 40 min, before being cooled back to -78 °C. Ethyl *iso*butyrate (0.44 mL, 3.2 mmol, 1.0 equiv.) was added dropwise to the so-obtained LDA solution and the resulting mixture was stirred at -78 °C for 1 h and then treated with tetrabutylammonium iodide (0.234 g, 0.634 mmol, 0.20 equiv.) and (3-bromoprop-1-en-2-yl)benzene **26** (0.750 g, 3.81 mmol, 1.2 equiv.). After 30 min, the mixture was warmed to room temperature and stirred for another 15 h. After this time, the mixture was diluted with Et_2O and the reaction was quenched by addition of water. The aqueous layer was extracted with Et_2O (3 x 10 mL) and the combined organic extracts were washed with brine (once), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude oil was submitted to column chromatography (SiO_2; pentane/EtOAc 24/1) to provide pure ethyl 2,2-dimethyl-4-phenylpent-4-enoate **27** (0.650 g, 2.80 mmol, 88% yield) (R_f 0.80 Pentane/EtOAc 5/1) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 - 7.20 (m, 5H, Ar*H*), 5.22 (d, *J* = 1.7 Hz, 1H, C=*CH*$_2$), 5.04 (m, 1H, C=*CH*$_2$), 3.73 (q, *J* = 7.1 Hz, 2H, *CH*$_2$$CH_3$), 2.79 (s, 2H, *CH*$_2$), 1.16 - 1.07 (m, 9H, *CH*$_2$$CH_3$ + C*Me*$_2$). NMR data correspond to the reported values.[15] Following a standard procedure, ethyl 2,2-dimethyl-4-phenylpent-4-enoate **27** (0.466 g, 2.01 mmol, 1.0 equiv.) was dissolved in MeOH (4.0 mL). The solution was cooled to 0 °C (ice/water bath) and a solution of KOH (0.56 g, 10 mmol, 5.0 equiv.) in water (0.80 mL) was slowly added. The cooling bath was removed and stirring was continued while heating the mixture at 50 °C for 3 h. During this time, the initial suspension converted into a pale yellow clear solution. The latter was then diluted with water and extracted with ether (2 x 20 mL). It was then acidified with concentrated aq. HCl until acidic pH and extracted with DCM (3 x 20 mL). The combined organic extracts were washed with brine, dried $MgSO_4$, and concentrated *in vacuo* to provide pure 2,2-dimethyl-4-phenylpent-4-enoic acid **1j** (0.370, 1.81 mmol, 90% yield) as an off-white oil, which became a pale pink crystalline solid on standing. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.10 (s, 1H, CO_2*H*), 7.35 (m, 2H, Ar*H*), 7.32 - 7.22 (m, 3H, Ar*H*), 5.27 (d, *J* = 1.4 Hz, 1H, C=*CH*$_2$), 5.10 (s, 1H, C=*CH*$_2$), 2.82 (s, 2H, *CH*$_2$), 1.10 (s, 6H, C*Me*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.5, 145.9, 142.4, 128.2, 127.5, 126.8, 117.3, 45.3, 42.8, 25.2. NMR data correspond to the reported values.[10]

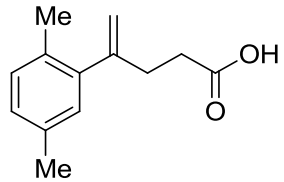
4-(Thiophen-3-yl)pent-4-enoic acid (1k)



Under nitrogen, to a solution of ethyl acetate **28** (1.9 mL, 20 mmol, 1.1 equiv.) in 50 mL of dry THF was added lithium diisopropylamide (2 M solution in THF, 10.0 mL, 20.0 mmol, 1.1 equiv.)

dropwise and the reaction was stirred at -78 °C for 1 h. To the reaction was added 2,3-dibromoprop-1-ene **29** (2.10 mL, 18.2 mmol, 1.0 equiv.) and the reaction was stirred for an additional 2 h at -78 °C. The reaction was warmed at rt and water (20 mL) was added slowly. The crude product was extracted with EtOAc three times (3 x 20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting oil was purified by SiO_2 column chromatography (Pentane/AcOEt : 100/0 to 95/5 to 9/1) to give ethyl 4-bromopent-4-enoate **30** (0.770 g, 3.72 mmol, 20 % yield). **1H NMR** (400 MHz, $CDCl_3$) δ 5.63 (s, 1H, C=CH_2), 5.43 (s, 1H, C=CH_2), 4.13 (t, J = 7.2 Hz, 2H, CH_2CH_3), 2.75 (t, J = 7.5 Hz, 2H, CH_2CO_2Et), 2.57 (t, J = 7.5 Hz, 2H, CH_2), 1.26 (t, J = 7.2 Hz, 3H, CH_2CH_3). NMR data correspond to the reported values.[16] Following a reported procedure,[11] tetrakis palladium (0.127 g, 0.110 mmol, 5 mol %), sodium carbonate (anhydrous; 0.513 g, 4.84 mmol. 2.2 equiv.), and thiophen-3-ylboronic acid **31** (0.338 g, 2.64 mmol, 1.2 equiv.) were suspended in a 7/1 mixture of dioxane (15.4 mL) and water (2.2 mL). Ethyl 4-bromopent-4-enoate **30** (0.456 g, 2.20 mmol, 1.0 equiv.) was then added by syringe and the resulting yellow-brown mixture was stirred under heating at 100 °C overnight. After 16 h, the reaction mixture was allowed to cool down to room temperature. The solvents were removed under reduced pressure and the residue was dissolved in EtOAc (30 mL). The organic solution was washed with water. The aqueous layer was then extracted with EtOAc (3 x 25 mL) and the combined extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo.* The resulting crude product was submitted to column chromatography (SiO_2, pentane/EtOAc 24.6/0.4 to 24/1) to afford ethyl 4-(thiophen-3-yl)pent-4-enoate **32** (90% pure, 0.327g, 1.40 mmol, 65% yield) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31-7.29 (m, 2H, Ar*H*), 7.26 (d, J = 3.9 Hz, 1H, Ar*H*), 5.40 (s, 1H, C=CH_2), 5.06 (s, 1H, C=CH_2), 4.16 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 2.81 (m, 2H, CH_2), 2.58 (m, 2H, CH_2), 1.28 (t, J = 7.1 Hz, 3H, OCH_2CH_3). NMR data correspond to the reported values.[11] Following a standard procedure, ethyl 4-(thiophen-3-yl)pent-4-enoate **32** (0.327 g, 1.55 mmol, 1.0 equiv.) was dissolved in MeOH (3.1 mL). The solution was cooled to 0 °C and a solution of KOH (0.44 g, 7.8 mmol, 5.0 equiv.) in water (0.6 mL) was slowly added. The cooling bath was removed and stirring was continued at room temperature for 2 hours. The latter was then diluted with water and extracted with ether (3 x 20 mL). It was then acidified with concentrated aq. HCl until acidic pH and extracted with DCM (3 x 20 mL). The combined organic extracts were washed with brine, dried $MgSO_4$, and concentrated *in vacuo* to provide a crude solid. The latter was submitted to recrystallization from hexane/chloroform (10/1, 5 mL) to afford 4-(Thiophen-3-yl)pent-4-enoic acid (**1k**) (90% pure, 0.200 g, 0.988 mmol, 63% yield) as an off-white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.00 (br s, 1H, COO*H*), 7.29 (m, 1H, Ar*H*), 7.23 (d, J = 4.1 Hz, 2H, Ar*H*), 5.40 (s, 1H, C=CH_2), 5.06 (s, 1H, C=CH_2), 2.81 (m, 2H, CH_2), 2.62 (m, 2H, CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.9, 141.9, 141.0, 125.9, 125.8, 120.6, 111.6, 33.1, 30.1. NMR data correspond to the reported values.[11]

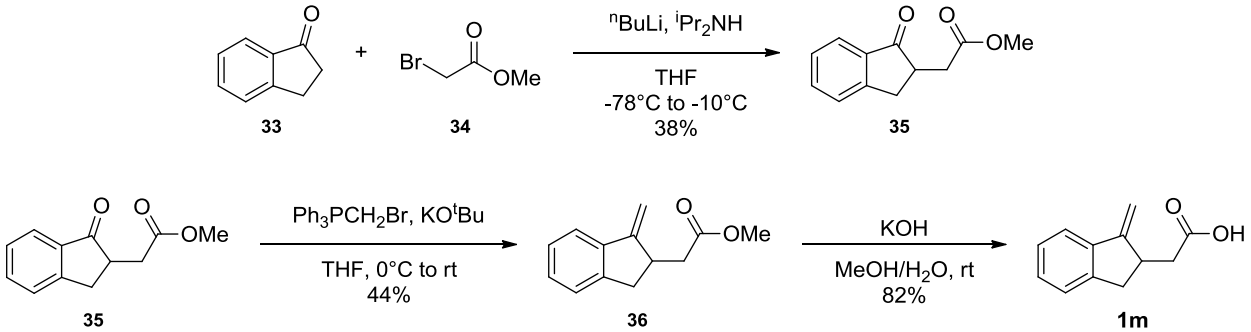
4-(2,5-Dimethylphenyl)pent-4-enoic acid (1l)



According to the general procedure, starting from 4-(2,5-dimethylphenyl)-4-oxobutanoic acid **18e** (1.55 g, 7.54 mmol, 1.0 equiv.), tBuOK (2.20 g, 19.6 mmol, 2.6 equiv.) and

bromo(methyl)triphenylphosphorane (3.50 g, 9.80 mmol, 1.3 equiv.), the product was obtained as a beige solid (1.25 g, 5.87 mmol, 78 % yield). *Two rotamers are observed in NMR analysis. Only the major rotamer is described* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.01 – 6.95 (m, 1H, Ar*H*), 6.89 (d, *J* = 1.8 Hz, 1H, Ar*H*), 5.21 (d, *J* = 1.7 Hz, 1H, C=CH_2), 4.91 (d, *J* = 1.7 Hz, 1H C=CH_2), 2.66 (t, *J* = 7.7 Hz, 2H, $CH_2CH_2CO_2H$), 2.47 (t, *J* = 7.8 Hz, 2H, $CH_2CH_2CO_2H$), 2.30 (s, 3H, CH_3), 2.24 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.8, 148.1, 141.9, 135.0, 131.8, 130.2, 129.1, 127.9, 114.5, 32.6, 32.6, 21.0, 19.4. **IR** 3079 (w), 2979 (w), 2922 (w), 1708 (s), 1639 (w), 1499 (w), 1436 (w), 1295 (w), 1214 (w), 1159 (w), 916 (w). **HRMS (ESI)** calcd for $C_{13}H_{17}O_2^+$ $[M+H]^+$ 205.1223; found 205.1228. **Melting point** : 82 °C.

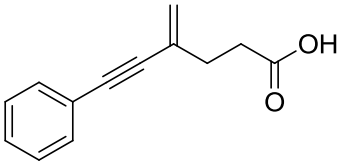
2-(1-Methylene-2,3-dihydro-1*H*-inden-2-yl)acetic acid (1m)



Under nitrogen, di*iso*propylamine (freshly distilled from CaH_2; 1.12 mL, 7.94 mmol, 1.05 equiv.) was dissolved in dry THF (5.0 mL). The solution was cooled down to -70 °C and *n*BuLi (2.5 M in hexanes; 3.0 mL, 7.6 mmol, 1.0 equiv.) was added dropwise at the same temperature. Upon completing the addition, the resulting pale yellow solution was allowed to warm to 0 °C for 15 min. It was then cooled back to -78 °C and added dropwise to a solution of 1-indanone **33** (1.00 g, 7.57 mmol, 1.0 equiv.) in dry THF (24 mL). The mixture was stirred at -78 °C for 40 min. A solution of methyl bromoacetate **34** (0.76 mL, 7.9 mmol, 1.05 equiv.) in dry THF (6.0 mL) was then added dropwise. The resulting pale yellow solution was stirred overnight while allowing it to warm to room temperature. After 20 h, the mixture looked like a yellow clear solution. The reaction was quenched by addition of water, followed by sat. aq. NH_4Cl. The aqueous layer was extracted with ether (3 x 30 mL) and the combined extracts were washed with water and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The obtained crude oil was submitted to column chromatography (SiO_2, pentane/EtOAc 24/1) to afford the pure methyl 2-(1-oxo-2,3-dihydro-1*H*-inden-2-yl)acetate **35** (0.593 g, 2.90 mmol, 38% yield) as a pale yellow oil. R_f 0.85 (Pentane/EtOAc 5/1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.60 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.46 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.38 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.69 (s, 3H, OCH_3), 3.47 (dd, *J* = 17.1, 8.0 Hz, 1H, CH_2), 3.08 - 2.95 (m, 2H, CH_2 and *CH*CO), 2.89 (dd, *J* = 17.1, 4.4 Hz, 1H, CH_2), 2.62 (dd, J = 9.1, 17.1 Hz, 1H, CH_2). NMR data correspond to the reported values.[17] Following a standard procedure, potassium *tert*-butoxide (0.652 g, 5.81 mmol, 2.0 equiv.) was suspended in dry THF (14.5 mL). The suspension was cooled to 0 °C and methyltriphenylphosphonium bromide (2.18 g, 6.10 mmol, 2.1 equiv.) was added, leading to the formation of a bright yellow suspension. The latter was stirred at 0 °C for 30 min. A solution of methyl 2-(1-oxo-2,3-dihydro-1*H*-inden-2-yl)acetate **35** (0.593 g, 2.90 mmol, 1.0 equiv.) in dry THF (1.0 mL) was then added at the same temperature. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by addition of sat. aq. NH_4Cl at 0 °C. The aqueous layer was extracted with Et_2O (3 x 15 mL) and the combined

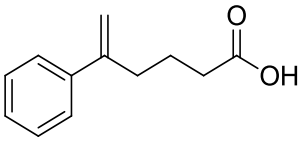
organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellow crude solid. The latter was submitted to column chromatography (SiO_2, pentane/EtOAc 24/1 to 23/2) (Rf = 0.35 Pentane/EtOAc : 9/1) to afford pure compound **36** (0.257 g, 1.27 mmol, 44% yield) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 6.8 Hz, 1H, Ar*H*), 7.23-7.19 (m, 3H, Ar*H*), 5.51 (d, *J* = 1.4 Hz, 1H, C=*CH_2*), 5.00 (s, 1H, C=*CH_2*), 3.71 (s, 3H, O*CH_3*), 3.43 (m, 1H, *CH*), 3.28 (dd, *J* = 8.4, 16.4 Hz, 1H, *CH_2*), 2.73 (m, 1H, *CH_2*), 2.69 (m, 1H, *CH_2*), 2.46 (dd, *J* = 9.6, 15.7 Hz, 1H, *CH_2*). Following a standard procedure, methyl 2-(1-methylene-2,3-dihydro-1*H*-inden-2-yl)acetate **36** (0.257 g, 1.27 mmol, 1.0 equiv.) was dissolved in MeOH (2.6 mL). The solution was cooled to 0 °C and a solution of KOH (0.36 g, 6.3 mmol, 5.0 equiv.) in water (0.5 mL) was slowly added. The cooling bath was removed and stirring was continued at room temperature for 2 hours. During this time, the initial suspension converted into a pale yellow clear solution. The latter was then diluted with water and extracted with ether (3 x 10 mL). It was then acidified with concentrated aq. HCl until acidic pH and extracted with DCM (3 x 10 mL). The combined organic extracts were washed with brine, dried $MgSO_4$, concentrated *in vacuo* to provide pure 2-(1-methylene-2,3-dihydro-1*H*-inden-2-yl)acetic acid (**1m**) (90% pure, 0.195 g, 1.04 mmol, 82% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.88 (br s, 1 H, CO_2*H*), 7.51 (d, *J* = 6.8 Hz, 1H, Ar*H*), 7.35 - 7.17 (m, 3H, Ar*H*), 5.56 (s, 1H, C=*CH_2*), 5.06 (s, 1H, C=*CH_2*), 3.42 (d, *J* = 9.7 Hz, 1H, *CH* or $ArCH_2$), 3.34 (dd, *J* = 16.3, 8.5 Hz, 1H, *CH_2*CO), 2.80 (d, *J* = 5.4 Hz, 1H, *CH* or $ArCH_2$), 2.78 (d, *J* = 6.0 Hz, 1H, *CH* or $ArCH_2$), 2.53 (dd, *J* = 16.1, 9.6 Hz, 1H, *CH_2*CO). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.9, 152.8, 144.3, 140.2, 128.9, 126.9, 125.5, 121.0, 103.4, 40.2, 39.3, 37.4. **IR** 3519 (w), 2923 (s), 2852 (m), 2851 (m), 2360 (w), 2360 (w), 2343 (w), 2342 (w), 1741 (s), 1639 (w), 1439 (m), 1411 (m), 1303 (m), 1280 (m), 1257 (m), 1211 (m), 1210 (m), 957 (w), 875 (m). **HRMS** (ESI) calcd for $C_{12}H_{11}O_2^+$ [M+] 187.0759; found 187.0760.

4-Methylene-6-phenylhex-5-ynoic acid (1n)



According to the general procedure, starting from 4-oxo-6-phenylhex-5-ynoic acid **22** (0.50 g, 2.4 mmol, 1.0 equiv.), tBuOK (0.721 g, 6.43 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (1.15 g, 3.21 mmol, 1.3 equiv.), the product was obtained as a brown solid (0.35 g, 1.8 mmol, 71 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 2H, Ar*H*), 7.35 – 7.29 (m, 3H, Ar*H*), 5.47 (d, *J* = 1.5 Hz, 1H, C=C*H_2*), 5.38 (d, *J* = 1.4 Hz, 1H, C=C*H_2*), 2.68 (ddd, *J* = 8.4, 7.0, 1.7 Hz, 2H, $CH_2CH_2CO_2H$), 2.63 – 2.54 (m, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.2, 131.7, 129.6, 128.4, 128.5, 123.0, 122.3, 90.2, 88.7, 33.0, 32.1. NMR data correspond to the reported values.[18]

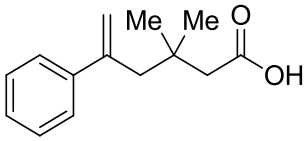
5-Phenylhex-5-enoic acid (1o)



According to the general procedure, starting from 5-oxo-5-phenylpentanoic acid (1.50 g, 7.80 mmol, 1.0 equiv.), tBuOK (2.28 g, 20.3 mmol, 2.6 equiv.) and

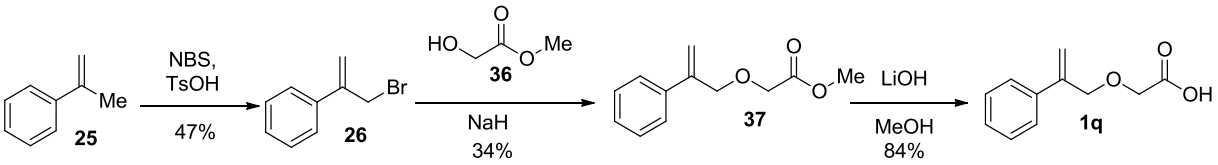
bromo(methyl)triphenylphosphorane (3.62 g, 10.1 mmol, 1.3 equiv.), the product was obtained as a white solid (0.40 g, 2.1 mmol, 27 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 2H, Ar*H*), 7.38 – 7.33 (m, 2H, Ar*H*), 7.32 – 7.27 (m, 1H, Ar*H*), 5.35 (d, *J* = 1.3 Hz, 1H, C=CH_2), 5.12 (d, *J* = 1.4 Hz, 1H, C=CH_2), 2.61 (td, *J* = 7.5, 1.2 Hz, 2H, $CH_2CH_2CH_2CO_2H$), 2.41 (t, *J* = 7.4 Hz, 2H, $CH_2CH_2CH_2CO_2H$), 1.83 (p, *J* = 7.5 Hz, 2H, $CH_2CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.3, 147.4, 140.8, 128.5, 127.6, 126.2, 113.2, 34.5, 33.4, 23.1. NMR data correspond to the reported values.[19]

3,3-Dimethyl-5-phenylhex-5-enoic acid (1p)



According to the general procedure, starting from 3,3-dimethyl-5-oxo-5-phenylpentanoic acid **20** (1.70 g, 7.72 mmol, 1.0 equiv.), tBuOK (2.25 g, 20.1 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (3.58 g, 10.0 mmol, 1.3 equiv.), the product was obtained as a white solid (0.35 g, 1.6 mmol, 21 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H, Ar*H*), 7.30 – 7.26 (m, 2H, Ar*H*), 7.25 – 7.20 (m, 1H, Ar*H*), 5.29 (d, *J* = 2.0 Hz, 1H, C=CH_2), 5.09 (d, *J* = 1.9 Hz, 1H, C=CH_2), 2.65 (s, 2H, CH_2CO_2H), 2.18 (s, 2H, $H_2C=CCH_2$), 0.92 (s, 6H, Me_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.3, 146.6, 143.3, 128.3, 127.3, 126.6, 117.6, 46.9, 45.9, 34.2, 27.8. NMR data correspond to the reported values.[19]

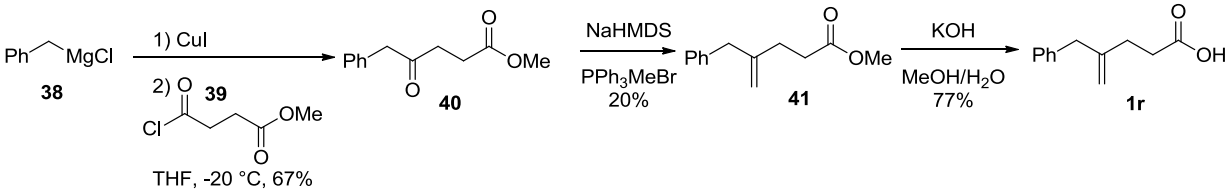
2-((2-Phenylallyl)oxy)acetic acid (1q)



In an oven dried flask, prop-1-en-2-ylbenzene **25** (2.00 mL, 15.4 mmol, 1.0 equiv.) was diluted in dry THF (5 mL) and NBS (2.88 g, 16.2 mmol, 1.05 equiv.) and 4-methylbenzenesulfonic acid (2.65 g, 15.4 mmol, 1.0 equiv.) were added and the solution was refluxed at 100 °C for 4 h. The reaction mixture was cooled to rt and then diluted with Pentane/Et2O (1/1: 20 mL), washed with H_2O. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to obtain a yellow oil. Purification by column chromatography over silica gel using Pentane (Rf = 0.95) as eluent afforded (3-bromoprop-1-en-2-yl)benzene **26** (1.43 g, 7.26 mmol, 47 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 2H, Ar*H*), 7.42 – 7.30 (m, 3H, Ar*H*), 5.56 (s, 1H, C=CH_2), 5.50 (s, 1H, C=CH_2), 4.39 (s, 2H, CH_2). NMR data correspond to the reported values.[14] To the suspension of sodium hydride (104 mg, 2.60 mmol, 1.3 equiv.) in dry THF (4 mL) was added methyl 2-hydroxyacetate **36** (200 µl, 2.60 mmol, 1.3 equiv.) at 0 °C under nitrogen. The resulting mixture was stirred for 30 min at the same temperature. (3-bromoprop-1-en-2-yl)benzene **27** (394 mg, 2.00 mmol, 1.0 equiv.) was then added to the reaction mixture. The mixture was allowed to warm to rt and stirred for 10 h. The reaction was quenched with saturated NH_4Cl aqueous solution. The organic layer was extracted with AcOEt twice (2 x 10mL), washed with brine, dried over with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (Pentane/AcOEt : 2/1) to give methyl 2-((2-phenylallyl)oxy)acetate **37** 0.14 g, 0.68 mmol, 34 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.4 Hz, 2H, Ar*H*), 7.35 (t, *J* = 7.3 Hz, 2H, Ar*H*), 7.32 – 7.28 (m, 1H, Ar*H*), 5.59 (s, 1H, C=CH_2), 5.36 (s, 1H, C=CH_2), 4.52

(s, 2H, *OCH*$_2$CO$_2$Me), 4.13 (s, 2H, *OCH*$_2$), 3.76 (s, 3H, CO$_2$*Me*). NMR data correspond to the reported values.[20] A mixture of methyl 2-((2-phenylallyl)oxy)acetate **37** (140 mg, 0.679 mmol, 1.0 equiv.) and lithium hydroxide (81.0 mg, 3.39 mmol, 5.0 equiv.) in MeOH (7 mL) was stirred for 1 h at 50 °C. The reaction mixture was cooled to rt and acidified with 10% HCl aqueous solution. The product was then extracted with DCM (3 x 10 mL) and dried over with $MgSO_4$ and concentrated in vacuo. The residue was purified by SiO_2 column chromatography (Pentane/AcOEt : 1/1) to give 2-((2-phenylallyl)oxy)acetic acid **1q** (110 mg, 0.572 mmol, 84 % yield) as yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 8.2, 1.8 Hz, 2H, Ar*H*), 7.41 – 7.29 (m, 3H, Ar*H*), 5.60 (s, 1H, C=*CH*$_2$), 5.36 (s, 1H, C=*CH*$_2$), 4.54 (s, 2H, *OCH*$_2$CO$_2$Me), 4.15 (s, 2H, *OCH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.4, 143.1, 138.1, 128.6, 128.2, 126.2, 115.9, 73.5, 66.5. NMR data correspond to the reported values. [20]

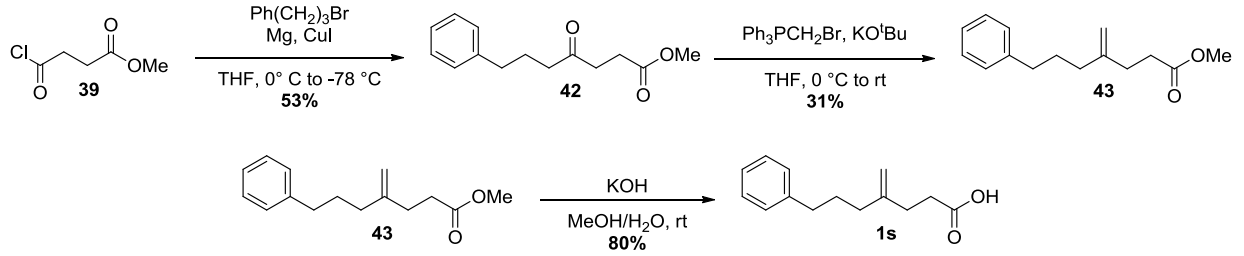
4-Benzylpent-4-enoic acid (1r)



To a suspension of copper iodide (2.00 g, 10.5 mmol, 1.2 equiv.) in dry THF (17 mL) was added a solution of benzylmagnesium chloride **38** (2M in THF) (5.25 mL, 10.5 mmol, 1.2 equiv.) was added dropwise between 0 °C and -20 °C. The mixture was stirred between 0 °C and -20 °C for 0.5 h. After cooled at -78 °C, a solution of methyl 4-chloro-4-oxobutanoate **39** (1.00 mL, 8.12 mmol, 1.0 equiv.) in THF (10 mL) was added and the reaction was stirred at -78 °C for 2 h and at room temperature for 30 min. NH_4Cl aq. solution was added to quench the reaction. EtOAc (30 mL) was added and the organic layer was extracted twice with EtOAc (2 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated. The crude product was purified by flash SiO_2 column (Pentane/EtOAc : 95/5 to 9/1) to give methyl 4-oxo-5-phenylpentanoate **40** (1.20 g, 5.82 mmol, 67 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 - 7.30 (m, 2H, Ar*H*), 7.30 - 7.16 (m, 3H, Ar*H*), 3.74 (s, 2H, C*H*$_2$Ar), 3.65 (s, 3H, *Me*), 2.76 (t, J = 6.6 Hz, 2H, C*H*$_2$CH$_2$COOMe), 2.56 (t, J = 6.6 Hz, 2H, CH$_2$C*H*$_2$COOMe).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 173.1, 134.0, 129.4, 128.7, 127.0, 51.7, 50.0, 36.4, 27.7. NMR data correspond to the reported values.[21] Under nitrogen, to a suspension of bromo(methyl)triphenylphosphorane (1.82 g, 5.09 mmol, 1.5 equiv.) in dry THF (8 mL) was added dropwise a solution of sodium bis(trimethylsilyl)amide (2M in THF) (2.04 mL, 4.07 mmol, 1.2 equiv.) at 0 °C. The mixture was stirred at 0 °C for 0.5 h. Than a solution of methyl 4-oxo-5-phenylpentanoate **40** (0.700 g, 3.39 mmol, 1.0 equiv.) in dry THF (8 mL) was added at 0 °C. The reaction was stirred at room temperature overnight. Solvent was removed in vacuo and the residue diluted with dichloromethane. The organic layer was washed with an aqueous 0.5 M NaOH solution, aqueous NH_4Cl solution, brine, dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash SiO_2 column (Pentane/EtOAc : 95/5 to 9/1) to give methyl 4-benzylpent-4-enoate **41** (0.140 g, 0.685 mmol, 20 % yield) as a colorless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H, Ar*H*), 7.24 – 7.15 (m, 3H, Ar*H*), 4.83 (m, 1H, C=C*H*$_2$), 4.81 (m, 1H, C=C*H*$_2$), 3.65 (s, 3H, *Me*), 3.36 (s, 2H, C*H*$_2$Ar), 2.49 – 2.42 (m, 2H, C*H*$_2$CH$_2$COOMe), 2.34 – 2.26 (m, 2H, CH$_2$C*H*$_2$COOMe). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.7, 147.3, 139.4, 129.1, 128.5, 126.3, 111.7, 51.7, 43.4, 32.5, 30.4. **IR** 3085 (w), 3063 (w), 3028 (w), 2987 (w), 2980 (w), 2953 (w), 2911 (w), 2910 (w), 2904 (w), 2903 (w), 2871 (w), 2871 (w), 2870 (w), 2870 (w),

2853 (w), 2844 (w), 2843 (w), 2362 (w), 2342 (w), 2333 (w), 1741 (s), 1649 (w), 1456 (w), 1438 (m), 1199 (w), 1198 (w), 1170 (w), 1042 (w), 912 (s). **HRMS** (ESI) calcd for $C_{13}H_{16}NaO_2$+ $[M+Na]^+$ 227.1042; found 227.1047. To a solution of methyl 4-benzylpent-4-enoate **41** (0.140 g, 0.685 mmol, 1.0 equiv.) in MeOH (1.5 mL) was added a solution of potassium hydroxide (0.173 g, 3.08 mmol, 4.5 equiv.) in water (0.5 mL) at 0 °C. After stirring for 2 h at ambient temperature, the reaction was quenched with concentrated aqueous HCl. The mixture was extracted with AcOEt. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash SiO_2 column (DCM/MeOH : 100 to 95/5) to give 4-benzylpent-4-enoic acid **1r** (0.100 g, 0.526 mmol, 77 % yield) as a white oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 2H, Ar*H*), 7.25 – 7.14 (m, 3H, Ar*H*), 4.85 (d, *J* = 1.6 Hz, 1H, C=C*H*$_2$), 4.83 (q, *J* = 1.2 Hz, 1H, C=C*H*$_2$), 3.37 (s, 2H, ArC*H*$_2$), 2.50 (m, 2H, $CH_2CH_2CO_2H$), 2.30 (t, *J* = 7.7 Hz, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.8, 147.0, 139.3, 129.1, 128.5, 126.4, 111.9, 43.4, 32.5, 30.0. NMR data correspond to the reported values.[22]

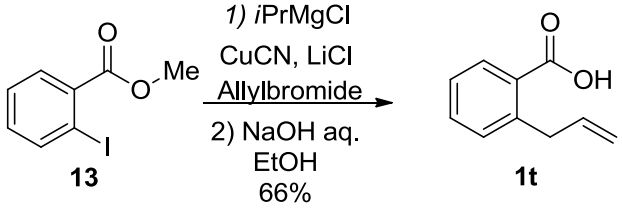
4-Methylene-7-phenylheptanoic acid (1s)



Mg turnings (0.440 g, 18.0 mmol, 2.8 equiv.) and a crystal of iodine were suspended in THF (9.0 mL). (3-Bromopropyl)benzene (1.76 mL, 11.6 mmol, 1.8 equiv.) was then added dropwise leading to the start of the reaction. In a two-necked round-bottomed flask, CuI (2.22 g, 11.7 mmol, 1.8 equiv.) was suspended in THF (18 mL) and the resulting grey mixture was cooled down to 0 °C. The freshly prepared Grignard reagent was then slowly added, which was stirred at 0 °C for 30 min. The mixture was then cooled to -78 °C and a solution of methyl succinyl chloride **39** (2.4 mL, 18 mmol, 1.0 equiv.) in THF (9.0 mL) was added dropwise. After stirring at -78 °C for 5 min, the mixture was warmed back to 0 °C and stirring was continued at this temperature for addition 60 min. The reaction was quenched by addition of water (20 mL), followed by aq. HCl (1.0 M; 20 mL), still at 0 °C. Diethyl ether was added. The aqueous layer was then separated and extracted with diethyl ether (2 x 20 mL). The combined organic layers were washed twice with sat. aq. $NaHCO_3$, once with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellow crude oil. The latter was submitted to column chromatography (SiO_2, Pentane/EtOAc 24/1 to 10/1) to afford pure methyl 4-oxo-7-phenylheptanoate **42** (0.805 g, 3.44 mmol, 53% yield) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 2H, Ar*H*), 7.23-7.14 (m, 3H, Ar*H*), 3.68 (s, 3H, O*CH*$_3$), 2.70 (t, *J* = 6.2 Hz, 2H, CO*CH*$_2$$CH_2CO_2Me$), 2.63 (t, *J* = 7.5 Hz, 2H, CO*CH*$_2$$CH_2CH_2Ph$), 2.58 (t, *J* = 6.2 Hz, 2H, $COCH_2$*CH*$_2$$CO_2Me$), 2.47 (t, *J* = 7.4 Hz, 2H, $COCH_2CH_2$*CH*$_2$Ph), 1.94 (pent, *J* = 7.4 Hz, 2H, $COCH_2$*CH*$_2$$CH_2Ph$). NMR data correspond to the reported values. [23] Following a standard procedure, *t*BuOK (0.771 g, 6.87 mmol, 2.0 equiv.) was suspended in THF (17 mL). The suspension was cooled to 0 °C and methyltriphenylphosphonium bromide (2.58 g, 7.22 mmol, 2.1 equiv.) was added, leading to the formation of a bright yellow suspension. The latter was

stirred at 0 °C for 30 minutes. A solution of methyl 4-oxo-7-phenylheptanoate **42** (0.805 g, 3.44 mmol, 1.0 equiv.) in THF (1 mL) was then added at the same temperature. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by addition of sat. aq. NH_4Cl at 0 °C. The aqueous layer was extracted with ether (3 x 15 mL) and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellow crude solid. The latter was submitted to column chromatography (SiO_2, pentane/EtOAc 24.5/0.5 to 24/1) to afford methyl 4-methylene-7-phenylheptanoate **43** (0.245 g, 1.06 mmol, 31% yield) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 - 7.23 (m, 2H, Ar*H*), 7.22 - 7.14 (m, 3H), 4.78 (s, 1H, C=*CH*$_2$), 4.75 (s, 1H, C=*CH*$_2$), 3.67 (s, 3H, O*CH*$_3$), 2.61 (t, *J* = 7.3 Hz, 2H, aliphatic CH_2), 2.47 (m, 2H, aliphatic CH_2), 2.34 (t, *J* = 7.9 Hz, 2H, aliphatic CH_2), 2.07 (t, *J* = 7.7 Hz, 2H, aliphatic CH_2), 1.77 (p, *J* = 7.7, Hz, 2H, aliphatic CH_2). Following a standard procedure, methyl 4-methylene-6-phenylheptanoate **43** (0.245 g, 0.105 mmol, 1.0 equiv.) was dissolved in MeOH (2.2 mL). The solution was cooled to 0 °C and a solution of KOH (0.30 g, 5.3 mmol, 5.0 equiv.) in water (0.4 mL) was slowly added. The cooling bath was removed and stirring was continued at room temperature for 2 h. During this time, the initial suspension converted into a pale yellow clear solution. The mixture was then diluted with aq. NaOH (1.0 M) and extracted with ether (3 x 10 mL). It was then acidified with concentrated aq. HCl until pH < 3 and extracted with DCM (3 x 10 mL). The combined organic extracts were washed with brine, dried $MgSO_4$, and concentrated in vacuo to provide pure 4-methylene-7-phenylheptanoic acid **1s** (0.185 g, 0.847 mmol, 80% yield) as a colorless viscous oil. **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 10.53 (s, 1H, COO*H*), 7.30 – 7.19 (m, 4H, Ar*H*), 7.19 – 7.13 (m, 1H, Ar*H*), 4.78 (dd, *J* = 2.4, 1.3 Hz, 2H, C=*CH*$_2$), 2.67 – 2.57 (m, 2H, aliphatic CH_2), 2.47 – 2.41 (m, 2H, aliphatic CH_2), 2.38 – 2.29 (m, 2H, aliphatic CH_2), 2.11 (t, *J* = 7.7 Hz, 2H, aliphatic CH_2), 1.83 – 1.70 (m, 2H, aliphatic CH_2). **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 174.3, 149.2, 143.4, 129.3, 129.2, 126.6, 109.9, 36.6, 36.7, 32.8, 31.6, 30.5. **IR** 3074 (m), 3028 (m), 2932 (m), 2864 (m), 2672 (w), 1948 (w), 1708 (s), 1650 (w), 1607 (w), 1493 (w), 1444 (m), 1295 (m), 1217 (w), 1165 (w), 1075 (w), 1026 (w), 936 (w), 896 (m). **HRMS** (ESI) calcd for $C_{14}H_{17}O_2^-$ $[M+H-1]^-$ 217.1234; found 217.1231.

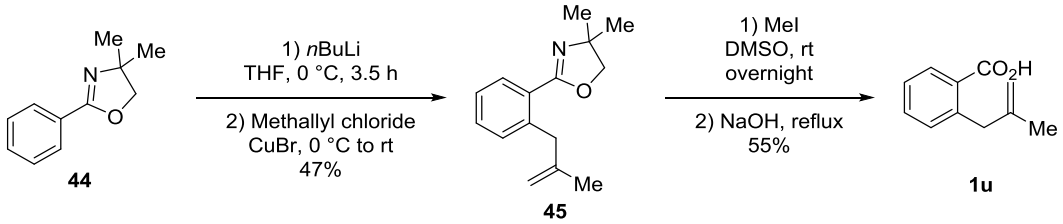
2-Allylbenzoic acid (1t)



Under nitrogen, a solution of isopropylmagnesium chloride (2 M in THF, 5.25 mL, 10.5 mmol, 1.5 equiv.) was added dropwise to a solution of methyl 2-iodobenzoate **13** (1 mL, 7 mmol, 1.0 equiv.) in dry THF (75 mL) at -40 °C. The resulting mixture was stirred at -40 °C for 1.5 h. Then it was added via cannula to a freshly prepared solution of cyanocopper (627 mg, 7.00 mmol, 1.0 equiv.) and lithium chloride (594 mg, 14.0 mmol, 2.0 equiv.) in dry THF (20 mL), followed by dropwise addition of 3-bromoprop-1-ene (2.42 mL, 28.0 mmol, 4.0 equiv.). After being stirred at -40 °C for 4 h, the mixture was allowed to warm to room temperature, diluted with EtOAc (50 mL) and filtered over Celite. The organic solution was washed with a 25% ammonia aqueous

solution. The aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered through a short pad of silica eluting with Pentane/EtOAc = 20/1, and then dissolved in EtOH (50 mL). A 2M NaOH solution (50 mL) was added and the resulting mixture was stirred at room temperature for 4 h. EtOH was then removed under reduced pressure and the aqueous layer was washed with Et_2O (3 x 20 mL). The aqueous solution was acidified to pH 3 with 2 M HCl solution and extracted with Et_2O (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash SiO_2 column (DCM/MeOH : 100 to 95/5) to afford 2-allylbenzoic acid **1t** (750 mg, 4.62 mmol, 66 % yield) (Rf = 0.4 DCM/MeOH : 95/5) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.49 (bs, 1H, CO_2H), 8.09 (dd, *J* = 8.1, 1.5 Hz, 1H, Ar*H*), 7.52 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.39 – 7.29 (m, 2H, Ar*H*), 6.17 – 5.95 (m, 1H, C*H*=*C*H_2), 5.09 (t, *J* = 1.5 Hz, 1H, C=*CH*$_2$), 5.06 (dq, *J* = 7.6, 1.6 Hz, 1H, C=*CH*$_2$), 3.87 (dt, *J* = 6.4, 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 142.9, 137.6, 133.3, 131.7, 131.3, 128.4, 126.5, 115.7, 38.5. NMR data correspond to the reported values.[24]

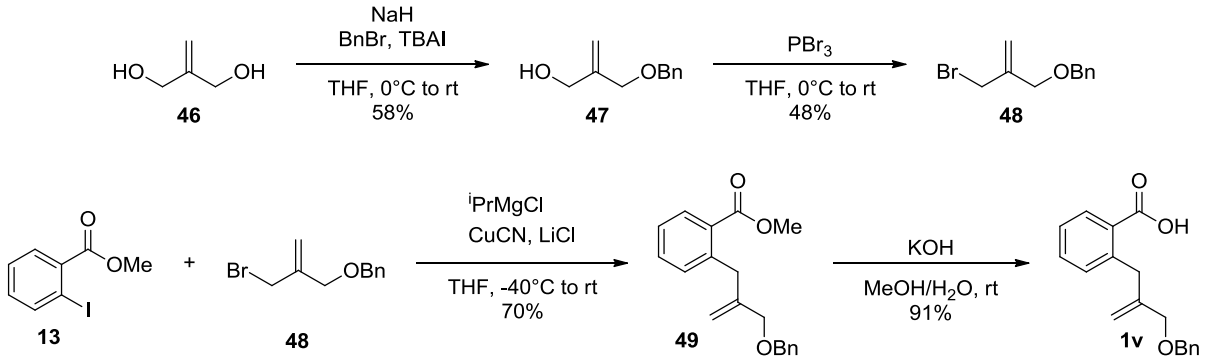
2-(2-Methylallyl)benzoic acid (1u)



Under nitrogen, *n*BuLi (2.5 M in hexanes, 6.1 mL, 15 mmol, 1.3 equiv) was added dropwise to a solution of 4,4-dimethyl-2-phenyl-2-oxazoline **44** (2.0 g, 11 mmol, 1.0 equiv) in dry THF (34 mL, previously flushed with argon) at 0 °C. The mixture was stirred at 0 °C for 3h30 and then it was transferred to a suspension of CuBr (1.61 g, 11.2 mmol, 0.99 equiv) in dry THF (10 mL) via cannula. The resulting green mixture was stirred at 0 °C for 1h30, methallyl chloride (1.0 mL, 10 mmol, 0.9 equiv) was added and the reaction mixture was stirred at rt overnight. The reaction was then quenched by addition of water (10 mL) and aqueous NH_3 (25% v/v. solution, 10 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2, Hexane/EtOAc 10/1) afforded 4,4-dimethyl-2-(2-(2-methylallyl)phenyl)-4,5-oxazoline **45** (1.26 g, 5.49 mmol, 47 % yield) as a dark oil. Oxazoline **45** was converted to the methiodide salt by stirring in excess MeI (2.1 mL, 33 mmol, 6 equiv) and DMSO (1.2 mL) overnight at rt. The solvents were then evaporated *in vacuo* and the crude oxazoline methiodide was treated with aqueous NaOH (2.0 M; 17.3 mL) at reflux for 9 h. The solution was then allowed to cool to rt and washed with CH_2Cl_2 (3 x 20 mL). The aqueous layer was acidified to pH 1 with concentrated HCl and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered on SiO_2 to afford 2-(2-methylallyl)benzoic acid **1u** (0.53 g, 3.1 mmol, 55% yield) as a colorless solid. R_f 0.42 (28:12:1 hexane/Et_2O/HCO_2H); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.2 (bs, 1H, CO_2H), 8.03 (dd, *J* = 7.4, 0.9 Hz, 1H, Ar*H*), 7.49 (td, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 7.36-7.26 (m, 2H, Ar*H*), 4.80 (d, *J* = 0.7 Hz, 1H, C=*CH*$_2$), 4.47 (d, *J* = 0.7 Hz, 1H, C=*CH*$_2$), 3.78 (s, 2H, *CH*$_2$), 1.76 (s, 3H, *CH*$_3$); **^{13}C NMR**

(100 MHz, $CDCl_3$) δ 173.1, 145.4, 142.2, 132.7, 131.6, 131.5, 128.8, 126.3, 111.6, 41.8, 23.0. NMR data correspond to the reported values.[25]

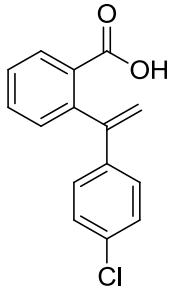
2-(2-((Benzyloxy)methyl)allyl)benzoic acid (1v)



Following a standard procedure, 2-methylenepropane-1,3-diol **46** (0.70 mL, 8.6 mmol, 1.0 equiv.) was dissolved in THF (dry; 26.8 mL) and the resulting solution was cooled to 0 °C. NaH (60% suspension in mineral oil; 0.343 g, 8.58 mmol, 1.0 equiv.) was then added, immediately resulting in vigorous gas release. The pale yellow mixture was stirred at 0 °C for 30 min and then at room temperature for 10 min. TBAI (0.158 g, 0.429 mmol, 5 mol %) was then added, immediately followed by benzyl bromide (0.87 mL, 7.3 mmol, 0.85 equiv.). Stirring was then continued at room temperature for 4 h. The reaction was therefore quenched by cautious addition of water, followed by sat. aq. NH_4Cl. The aqueous layer was then extracted with EtAOc (3 x 25 mL). The combined extracts were washed with water, brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a pale yellow crude oil. The latter was purified through column chromatography (SiO_2; pentane/EtAOc 4/1) to afford 2-((benzyloxy)methyl)prop-2-en-1-ol **47** (1.53 g, 5.02 mmol, 58% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H, Ar*H*), 5.21 (d, *J* = 1.6 Hz, 1H, C=*CH*$_2$), 5.16 (d, *J* = 1.2 Hz, 1H, C=*CH*$_2$), 4.53 (s, 2H, O*CH*$_2$Ph), 4.20 (m, 2H, O*CH*$_2$C=C), 4.10 (d, *J* = 1.1 Hz, 2H, O*CH*$_2$C=C). NMR data correspond to the reported values.[26] Following a reported procedure,[27] 2-((benzyloxy)methyl)prop-2-en-1-ol **47** (0.890 g, 4.99 mmol, 1.0 equiv.) was dissolved in dry Et_2O (25 mL). The resulting solution was cooled down to 0 °C (ice-water bath) and phosphorus tribromide (0.56 mL, 6.0 mmol, 1.2 equiv.) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was quenched through cautious, dropwise addition of water (exothermy!!). The aqueous layer was then extracted with ether (3 x 25 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude oil was submitted to column chromatography (SiO_2; pentane/Et_2O 80/20) to afford (((2-(bromomethyl)allyl)oxy)methyl)benzene **48** (0.574 g, 2.38 mmol, 48% yield) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 4H, Ar*H*), 7.31 (m, 1H, Ar*H*), 5.36 (d, *J* = 0.9 Hz, 1H, C=*CH*$_2$), 5.27 (d, *J* = 1.4 Hz, 1H, C=*CH*$_2$), 4.54 (s, 2H, *CH*$_2$), 4.16 (d, *J* = 1.2 Hz, 2H, *CH*$_2$), 4.05 (d, *J* = 0.8 Hz, 2H, *CH*$_2$). NMR data correspond to the reported values.[28] Following a reported procedure,[10] In a 25 mL two-necked round-bottomed flask, methyl 2-iodobenzoate **13** (0.23 mL, 1.5 mmol, 1.0 equiv.) was dissolved in dry THF (3.0 mL) and the solution was cooled to -40 °C (acetonitrile/dry ice bath). *iso*Propyl magnesium chloride (2.0 M in THF; 1.0 mL, 2.0 mmol, 1.35 equiv.) was added dropwise, resulting in the formation of a bright yellow suspension, which was stirred at the same temperature for 1 h. A freshly prepared solution of CuCN (0.133 g, 1.48 mmol, 1.0 equiv.) and LiCl (0.126 g, 2.97 mmol, 2.0 equiv.) in dry THF

(3.0 m) was then added dropwise and the resulting mixture was stirred at -40 °C for additional 40 min. A solution of (((2-(bromomethyl)allyl)oxy)methyl)benzene **48** (0.555 g, 2.30 mmol, 1.55 equiv.) in dry THF (0.50 mL) was finally added dropwise at -40 °C. The mixture converted at this point into a green-brownish suspension, which was stirred overnight while allowing it to warm to room temperature. The reaction was then quenched by pouring the mixture onto a mixture of ice and sat. aq. NH_4Cl. Upon separation from the organic layer, the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to provide a pale yellow crude oil. The latter was then submitted to column chromatography (SiO_2; pentane/EtOAc 24/1 to 10/1) to afford methyl 2-(2-((benzyloxy)methyl)allyl)benzoate **49** (0.440 g, 1.48 mmol, 70% yield) R_f 0.85 (pentane/EtOAc 5/1) as a colorless oil. The latter (0.245 g, 0.105 mmol, 1.0 equiv.) was dissolved in MeOH (2.2 mL). The solution was cooled to 0 °C and a solution of KOH (0.30 g, 5.3 mmol, 5.0 equiv.) in water (0.4 mL) was slowly added. The cooling bath was removed and stirring was continued at room temperature for 2 h. During this time, the initial suspension converted into a pale yellow clear solution. Most of MeOH was then removed under reduced pressure. The resulting aqueous mixture was diluted with aq. NaOH (1.0 M) and extracted with ether (3 x 10 mL). It was then acidified with concentrated aq. HCl until pH < 3 and extracted with DCM (3 x 10 mL). The combined organic extracts were washed with brine, dried $MgSO_4$, concentrated in vacuo to provide pure 2-(2-((benzyloxy)methyl)allyl)benzoic acid **1v** (0.267 g, 0.946 mmol, 91% yield) as a crystalline solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.03 (br s, 1H, CO_2H), 8.03 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.49 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.41 - 7.26 (m, 7H, Ar*H*), 5.12 (q, *J* = 1.4 Hz, 1H, C=CH_2), 4.68 (d, *J* = 1.7 Hz, 1H, C=CH_2), 4.51 (s, 2H, PhCH_2O), 4.01 (s, 2H, C=CCH_2O), 3.86 (s, 2H, ArCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0, 145.5, 141.4, 138.2, 132.7, 131.9, 131.6, 129.0, 128.3, 127.7, 127.5, 126.4, 113.2, 73.2, 71.9, 37.6. **IR** 3065 (m), 3030 (m), 2911 (w), 2858 (m), 2718 (w), 2717 (w), 2657 (w), 2560 (w), 1774 (w), 1691 (s), 1654 (w), 1602 (w), 1576 (w), 1495 (w), 1455 (w), 1407 (w), 1365 (w), 1351 (w), 1302 (m), 1272 (m), 1167 (w), 1138 (w), 1094 (m), 1075 (m), 1029 (w), 909 (m). **HRMS** (ESI) calcd for $C_{18}H_{17}O_3^-$ $[M+H-1]^-$ 281.1183; found 281.1187. **Melting Point**: 78.5-80.3 °C.

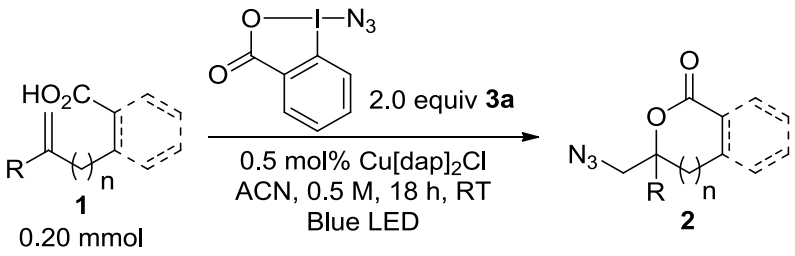
2-(1-(4-Chlororophenyl)vinyl)benzoic acid (1w)



According to the general procedure, starting from 2-(4-chlorobenzoyl)benzoic acid (2.81 g, 10.8 mmol, 1.0 equiv.), tBuOK (3.14 g, 28.0 mmol, 2.6 equiv.) and bromo(methyl)triphenylphosphorane (5.00 g, 14.0 mmol, 1.3 equiv.), the product was obtained as a white solid 2 (1.3 g, 5.03 mmol, 47 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.44 (td, *J* = 7.6, 1.3 Hz, 1H), 7.35 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.16 – 7.11 (m, 2H), 5.65 (d, *J* = 0.9 Hz, 1H, C=CH_2), 5.23 (d, *J* = 0.9 Hz, 1H, C=CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.0, 148.5, 143.2, 139.4, 133.3, 132.7, 131.5, 130.9, 129.1, 128.2, 128.0, 127.9, 114.7. NMR data correspond to the reported values.[13]

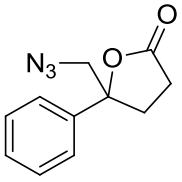
4. Photoredox Catalysis

a. General procedure for the photoredox catalysis.



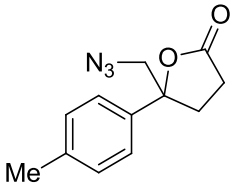
Dry acetonitrile (1.0 mL) degassed by bubbling nitrogen for 5 min, was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1** (0.20 mmol, 1.0 equiv), ABX reagent **3a** (116 mg, 0.400 mmol, 2.0 equiv) and Cu[dap]$_2$Cl (0.8 mg, 0.9 µmol, 0.5 mol%). The resulting solution was irradiated under stirring using blue light LEDs for 18 h at rt. The reaction mixture was filtered, eluting with ethyl acetate, and evaporated under reduced pressure. The residue was purified by flash SiO_2 column (Pentane/EtOAc : 100 to 90/10 to 80/20) to give the corresponding azidolactone product **2**. *(The flash SiO_2 column has to be deactivated by flashing mixture of pentane/Et_3N (95/5) before flashing 100% pentane).*

5-(Azidomethyl)-5-phenyldihydrofuran-2(3H)-one (2a)



Starting from 4-phenylpent-4-enoic acid **1a** (35 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2a** as yellow solid (35 mg, 0.16 mmol, 81 % yield). Rf: 0.45 (Pentane/Ethyl Acetate = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 5H, Ar*H*), 3.68 (d, *J* = 13.2 Hz, 1H, CH_2N_3), 3.53 (d, *J* = 13.2 Hz, 1H, CH_2N_3), 2.81 – 2.64 (m, 2H, CH_2CH_2), 2.57 – 2.38 (m, 2H, CH_2CH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.7, 140.6, 129.0, 128.6, 124.8, 87.7, 60.0, 31.5, 28.8. NMR data correspond to the reported values. [18]

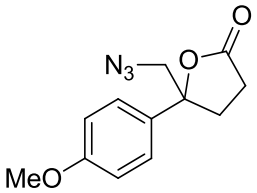
5-(Azidomethyl)-5-(p-tolyl)dihydrofuran-2(3H)-one (2b)



Starting from 4-(p-tolyl)pent-4-enoic acid **1b** (38 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2b** as pale yellow oil (38 mg, 0.16 mmol, 82 % yield). Rf: 0.40 (Pentane/Ethyl Acetate = 8:2) (Seebach

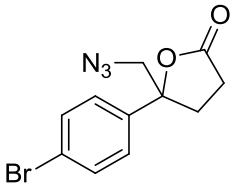
Stain).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.22 (d, *J* = 8.1 Hz, 2H, Ar*H*), 3.67 (d, *J* = 13.2 Hz, 1H, CH_2N_3), 3.52 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 2.80 – 2.62 (m, 2H, CH_2CH_2), 2.59 – 2.39 (m, 2H, CH_2CH_2), 2.36 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.0, 138.5, 137.5, 129.6, 124.7, 87.8, 60.0, 31.4, 28.8, 21.1. **IR** ν 3063 (w), 3030 (w), 2923 (w), 2105 (s), 1779 (s), 1516 (w), 1280 (m), 1075 (m), 937 (m). **HRMS (ESI)** calcd for $C_{12}H_{13}N_3NaO_2^+$ $[M+Na]^+$ 254.0900; found 254.0903.

5-(Azidomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3H)-one (2c)



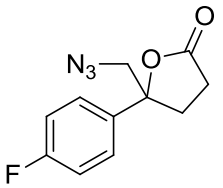
Starting from 4-(4-methoxyphenyl)pent-4-enoic acid **1c** (41 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2c** as white solid (43 mg, 0.17 mmol, 87 % yield). Rf: 0.60 (Pentane/Ethyl Acetate = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.5 Hz, 2H, Ar*H*), 6.92 (d, *J* = 8.5 Hz, 2H, Ar*H*), 3.81 (s, 3H, OCH_3), 3.66 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 3.48 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 2.80 – 2.61 (m, 2H, CH_2CH_2), 2.57 – 2.36 (m, 2H, CH_2CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 159.8, 132.5, 126.2, 114.3, 87.6, 60.2, 55.5, 31.4, 28.9. NMR data correspond to the reported values.[18]

5-(Azidomethyl)-5-(4-bromophenyl)dihydrofuran-2(3H)-one (2d)



Starting from 4-(4-bromophenyl)pent-4-enoic acid **1d** (51 g, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2d** as pale yellow oil (46 mg, 0.15 mmol, 78 % yield). Rf: 0.43 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 2H, Ar*H*), 7.29 – 7.21 (m, 2H, Ar*H*), 3.66 (d, *J* = 13.2 Hz, 1H, CH_2N_3), 3.52 (d, *J* = 13.2 Hz, 1H, CH_2N_3), 2.84 – 2.64 (m, 2H, CH_2CH_2), 2.53 (m, 1H, CH_2CH_2), 2.40 (m, 1H, CH_2CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$*d*) δ 175.4, 139.7, 132.1, 126.6, 122.8, 87.2, 59.8, 31.4, 28.7.NMR data correspond to the reported values.[18]

5-(Azidomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3H)-one (2e)



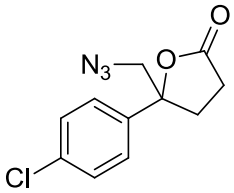
Starting from 4-(4-fluorophenyl)pent-4-enoic acid **1e** (39 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2e** as pale yellow solid (35 mg, 0.15 mmol, 74 % yield). Rf: 0.5 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H, Ar*H*), 7.13 – 7.05 (m, 2H, Ar*H*), 3.65

(d, *J* = 13.0 Hz, 1H, C*H*$_2$N$_3$), 3.51 (d, *J* = 13.2, 1H, C*H*$_2$N$_3$), 2.83 – 2.62 (m, 2H, *CH*$_2$*CH*$_2$), 2.57 – 2.48 (m, 1H, *CH*$_2$*CH*$_2$), 2.45 – 2.36 (m, 1H, *CH*$_2$*CH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.6, 162.7 (d, *J* = 248.0 Hz), 136.4 (d, *J* = 3.2 Hz), 126.8 (d, *J* = 8.2 Hz), 115.9 (d, *J* = 21.7 Hz), 87.3, 60.0, 31.5, 28.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.14 (m, 1F). **IR** 3078 (w), 3078 (w), 3078 (w), 2972 (w), 2932 (w), 2106 (s), 1783 (s), 1605 (w), 1512 (s), 1285 (m), 1232 (m). **HRMS** (ESI) calcd for $C_{11}H_{10}FN_3NaO_2^+$ $[M+Na]^+$ 258.0649; found 258.0650. **Melting point**: 71 °C.

Gram scale synthesis:

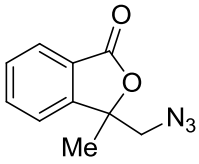
Starting from 4-(4-fluorophenyl)pent-4-enoic acid **1e** (1.00 g, 5.15 mmol, 1.0 equiv.), ABX **3a** (2.98 g, 10.30 mmol, 2.0 equiv.) and Cu[dap]$_2$Cl (2.3 mg, 2.50 µmol, 0.05 mol%). The crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2e** as pale yellow solid (990 mg, 4.21 mmol, 82 % yield). *(The flash SiO_2 column has to be deactivated by flashing mixture of pentane/Et_3N (95/5) before flashing 100% pentane).*

5-(Azidomethyl)-5-(4-chlorophenyl)dihydrofuran-2(3H)-one (2f)



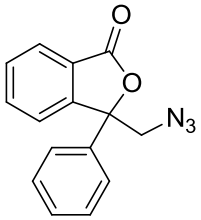
Starting from 4-(4-chlorophenyl)pent-4-enoic acid **1f** (42 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2f** as pale yellow solid (34 mg, 0.13 mmol, 68 % yield). Rf: 0.45 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.32 (d, *J* = 8.6 Hz, 2H, Ar*H*), 3.65 (d, *J* = 13.1, 1H, C*H*$_2$N$_3$), 3.51 (d, *J* = 13.2, 1H, C*H*$_2$N$_3$), 2.83 – 2.62 (m, 2H, *CH*$_2$*CH*$_2$), 2.52 (m, 1H, *CH*$_2$*CH*$_2$), 2.39 (m, 1H, *CH*$_2$*CH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.4, 139.1, 134.7, 129.2, 126.3, 87.2, 60.0, 31.5, 28.7. NMR data correspond to the reported values.[18]

3-(Azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)



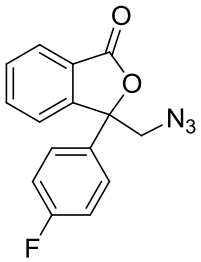
Starting from 2-(prop-1-en-2-yl)benzoic acid **1g** (32 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2g** as white solid (38 mg, 0.19 mmol, 94 % yield). Rf: 0.55 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.70 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.57 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.45 (d, *J* = 7.7 Hz, 1H, Ar*H*), 3.65 (m, 2H, C*H*$_2$N$_3$), 1.69 (s, 3H, C*H*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.1, 150.8, 134.5, 129.8, 126.1, 126.1, 121.3, 85.8, 58.1, 23.2. **IR** 3055 (w), 2985 (w), 2933 (w), 2105 (s), 1761 (s), 1468 (w), 1288 (m), 1035 (s). **HRMS** (ESI) calcd for $C_{10}H_9N_3NaO_2^+$ $[M+Na]^+$ 226.0587; found 226.0588. **Melting point** : 77 °C

3-(Azidomethyl)-3-phenylisobenzofuran-1(3H)-one (1h)



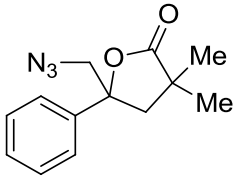
Starting from 2-(1-phenylvinyl)benzoic acid **1h** (50 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2h** as white solid (49 mg, 0.19 mmol, 92 % yield). Rf: 0.8 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.73 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.61 (m, 2H, Ar*H*), 7.53 (m, 2H, Ar*H*), 7.39 (m, 3H, Ar*H*), 4.07 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 3.99 (d, *J* = 13.1 Hz, 1H, CH_2N_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 149.6, 137.3, 134.7, 130.2, 129.3, 129.23, 126.4, 126.3, 125.5, 122.9, 88.7, 58.3. **IR** 3069 (w), 2925 (w), 2854 (w), 2102 (s), 1773 (s), 1600 (w), 1467 (m), 1288 (m), 1103 (m), 1017 (m). **HRMS** (ESI) calcd for $C_{15}H_{11}N_3NaO_2^+$ $[M+Na]^+$ 288.0743; found 288.0741. **Melting point** : 90 °C.

3-(Azidomethyl)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (2i)



Starting from 2-(1-(4-fluorophenyl)vinyl)benzoic acid **1i** (48 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2i** as yellow oil (51 mg, 0.18 mmol, 91 % yield). Rf: 0.55 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (m, 1H, Ar*H*), 7.75 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 7.62 (m, 2H, Ar*H*), 7.53(m, 2H, Ar*H*), 7.09 (m, 2H, Ar*H*), 4.03 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 3.96 (d, *J* = 13.1 Hz, 1H, CH_2N_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.0, 163.1 (d, *J* = 249.2 Hz), 149.4, 134.8, 133.2 (d, *J* = 3.3 Hz), 130.3, 127.7 (d, *J* = 8.4 Hz), 126.6, 126.3, 122.8, 116.2 (d, *J* = 21.7 Hz), 88.1, 58.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -112.12 (m, 1F). **IR** 3079 (w), 2930 (w), 2104 (s), 1770 (s), 1599 (w), 1512 (m), 1289 (m), 1242 (m). **HRMS** (ESI) calcd for $C_{15}H_{10}FN_3NaO_2^+$ $[M+Na]^+$ 306.0649; found 306.0648

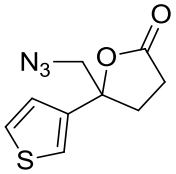
5-(Azidomethyl)-3,3-dimethyl-5-phenyldihydrofuran-2(3H)-one (2j)



Starting from 2,2-dimethyl-4-phenylpent-4-enoic acid **1j** (41 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2j** as brown oil (44 mg, 0.17 mmol, 90 % yield). Rf: 0.55 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NM**R (400 MHz, $CDCl_3$) δ 7.44 – 7.30 (m, 5H, Ar*H*), 3.62 (d, *J* = 13.1 Hz, 1H, CH_2N_3), 3.40

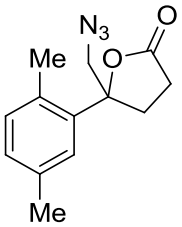
(d, *J* = 13.2 Hz, 1H, C*H*$_2$N$_3$), 2.61 (d, *J* = 13.0 Hz, 1H, C(CH$_3$)$_2$C*H*$_2$), 2.41 (d, *J* = 13.0 Hz, 1H, C(CH$_3$)$_2$C*H*$_2$), 1.36 (s, 3H, C*H*$_3$), 0.98 (s, 3H, C*H*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.0, 141.5, 129.0, 128.5, 124.7, 84.6, 60.2, 45.3, 40.6, 26.5, 26.0. **IR** 3065 (w), 2975 (w), 2933 (w), 2874 (w), 2103 (s), 1772 (s), 1450 (m), 1253 (m), 1157 (m), 1053 (s). **HRMS** (ESI) calcd for $C_{13}H_{15}N_3NaO_2^+$ $[M+Na]^+$ 268.1056; found 268.1056.

5-(Azidomethyl)-5-(thiophen-3-yl)dihydrofuran-2(3H)-one (2k)



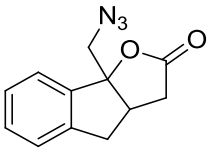
Starting from 4-(thiophen-3-yl)pent-4-enoic acid **1k** (25 mg, 0.12 mmol, 1.0 equiv.), ABX **3a** (70 mg, 0.24 mmol, 2.0 equiv.) and Cu[dap]$_2$Cl (0.5 mg, 0.6 µmol, 0.5 mol%), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2k** as pale yellow oil (22 mg, 0.10 mmol, 81 % yield). Rf: 0.45 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (m, 1H, Ar*H*), 7.31 (m, 1H, Ar*H*), 7.00 (m, 1H, Ar*H*), 3.71 (d, *J* = 13.1 Hz, 1H, C*H*$_2$N$_3$), 3.53 (d, *J* = 13.1 Hz, 1H, C*H*$_2$N$_3$), 2.78 – 2.51 (m, 3H, *CH*$_2$*CH*$_2$), 2.40 (m, 1H, *CH*$_2$*CH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$*d*) δ 175.7, 141.7, 127.6, 124.7, 121.9, 86.4, 59.2, 31.2, 28.8. NMR data correspond to the reported values. [18]

5-(Azidomethyl)-5-(2,5-dimethylphenyl)dihydrofuran-2(3H)-one (2l)



Starting from 4-(2,5-dimethylphenyl)pent-4-enoic acid **1l** (41 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2l** as pale yellow solid (35 mg, 0.14 mmol, 71 % yield). Rf: 0.48 (Pentane/ EtOAc = 8:2) (Seebach Stain). *Two rotamers are observed in NMR analysis, however they are not fully resolved. Only the major rotamer is described.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 1H, Ar*H*), 7.11 – 6.99 (m, 2H, Ar*H*), 3.67 (s, 2H, C*H*$_2$N$_3$), 2.86 – 2.69 (m, 2H, *CH*$_2$*CH*$_2$), 2.61 – 2.44 (m, 2H, *CH*$_2$*CH*$_2$), 2.37 (m, 3H, *CH*$_3$), 2.32 (m, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 138.3, 136.2, 132.7, 130.4, 129.3, 126.5, 88.8, 58.9, 31.3, 29.0, 21.2, 21.1. **IR** 3027 (w), 2955 (w), 2359 (w), 2108 (s), 1783 (s), 1299 (w), 1190 (m). **HRMS** (ESI) calcd for $C_{13}H_{15}N_3NaO_2^+$ $[M+Na]^+$ 268.1056; found 268.1064. **Melting point** : 61 °C.

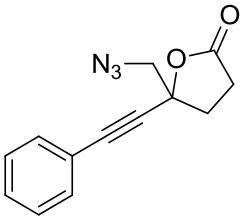
8b-(Azidomethyl)-3,3a,4,8b-tetrahydro-2H-indeno[1,2-b]furan-2-one (2m)



Starting from 2-(1-methylene-2,3-dihydro-1H-inden-2-yl)acetic acid **1m** (38 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2)

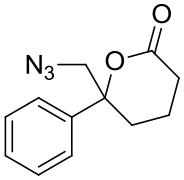
to afford **2m** as pale yellow oil (30 mg, 0.13 mmol, 65 % yield). Rf: 0.5 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 2H, Ar*H*), 7.34 – 7.24 (m, 2H, Ar*H*), 3.96 (d, *J* = 13.1 Hz, 1H, C*H*$_2$N$_3$), 3.52 (d, *J* = 13.1 Hz, 1H, C*H*$_2$N$_3$), 3.34 (dd, *J* = 16.5, 8.3 Hz, 1H, ArC*H*$_2$CH), 3.27 – 3.17 (m, 1H, C*H*), 3.05 (dd, *J* = 18.2, 10.0 Hz, 1H, OCOC*H*$_2$CH), 2.86 (dd, *J* = 16.6, 2.9 Hz, 1H, ArC*H*$_2$CH), 2.40 (dd, *J* = 18.2, 6.3 Hz, 1H, OCOC*H*$_2$CH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.7, 142.2, 138.9, 130.7, 128.0, 125.8, 124.8, 96.0, 56.2, 40.3, 37.4, 37.0. **IR** 3073 (w), 3030 (w), 2939 (w), 2860 (w), 2255 (w), 2108 (s), 1780 (s), 1194 (m), 956 (m), 911 (s). **HRMS** (ESI) calcd for $C_{12}H_{11}N_3NaO_2^+$ $[M+Na]^+$ 252.0743; found 252.0748.

5-(Azidomethyl)-5-(phenylethynyl)dihydrofuran-2(3H)-one (2n)



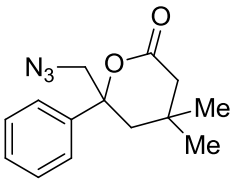
Starting from 4-methylene-6-phenylhex-5-ynoic acid **1n** (40 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2n** as pale yellow oil (23 mg, 0.095 mmol, 47 % yield). Rf: 0.70 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.42 (m, 2H, Ar*H*), 7.40 – 7.30 (m, 3H, Ar*H*), 3.77 (d, *J* = 13.0, 1H, C*H*$_2$N$_3$), 3.61 (d, *J* = 13.0, 1H, C*H*$_2$N$_3$), 2.89 – 2.78 (m, 1H, *CH*$_2$*CH*$_2$), 2.75 – 2.65 (m, 1H, *CH*$_2$*CH*$_2$), 2.59 – 2.48 (m, 2H, *CH*$_2$*CH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.27, 132.0, 129.5, 128.6, 121.1, 88.1, 85.3, 80.0, 57.9, 32.3, 28.8. NMR data correspond to the reported values.[18]

6-(Azidomethyl)-6-phenyltetrahydro-2H-pyran-2-one (2o)



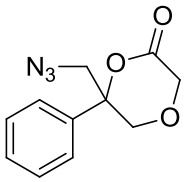
Starting from 5-phenylhex-5-enoic acid **1o** (38 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2o** as pale yellow oil (15 mg, 0.065 mmol, 33 % yield). Rf: 0.8 (Pentane/ EtOAc = 7:3) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.31 (m, 5H, Ar*H*), 3.61 (d, *J* = 13.0 Hz, 1H, C*H*$_2$N$_3$), 3.42 (d, *J* = 13.0 Hz, 1H, C*H*$_2$N$_3$), 2.50 (m, 2H, *CH*$_2$), 2.25 (m, 2H, *CH*$_2$), 1.83 (m, 1H, *CH*$_2$), 1.60 (m, 1H, *CH*$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 140.4, 129.2, 128.5, 125.3, 86.9, 60.8, 29.3, 29.1, 16.2. NMR data correspond to the reported values.[18]

6-(Azidomethyl)-4,4-dimethyl-6-phenyltetrahydro-2H-pyran-2-one (2p)



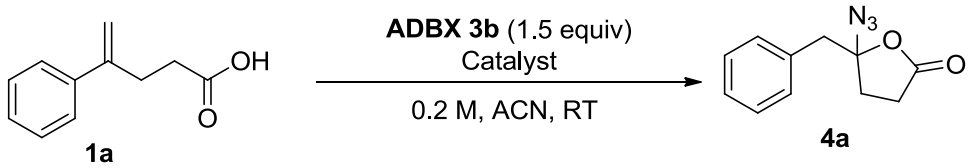
Starting from 3,3-dimethyl-5-phenylhex-5-enoic acid **1p** (44 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2p** as colorless oil (21 mg, 0.081 mmol, 42 % yield). Rf: 0.43 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.28 (m, 5H, Ar*H*), 3.50 (d, *J* = 12.9, 1H, C*H*$_2$N$_3$), 3.29 (d, *J* = 12.9 Hz, 1H, C*H*$_2$N$_3$), 2.35 – 2.16 (m, 4H, *CH*$_2$), 1.10 (s, 3H, *CH*$_3$), 0.78 (s, 3H *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 141.6, 129.0, 128.3, 125.1, 85.8, 62.0, 43.8, 41.7, 31.9, 30.7, 29.1. NMR data correspond to the reported values.[18]

6-(Azidomethyl)-6-phenyl-1,4-dioxan-2-one (2q)



Starting from 2-((2-phenylallyl)oxy)acetic acid **1q** (38 mg, 0.20 mmol, 1.0 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2q** as pale yellow oil (25 mg, 0.11 mmol, 54 % yield). Rf: 0.42 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 5H, Ar*H*), 4.44 (d, *J* = 17.7 Hz, 1H, CO_2CH_2O), 4.28 (d, *J* = 17.9 Hz, 1H, CO_2CH_2O), 4.24 (d, *J* = 12.7 Hz, 1H, CCH_2O), 4.03 (d, *J* = 12.7 Hz, 1H, CCH_2O), 3.78 (d, *J* = 13.0 Hz, 1H, C*H*$_2$N$_3$), 3.67 (d, *J* = 13.0 Hz, 1H, C*H*$_2$N$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 137.5, 129.2, 129.1, 125.1, 84.6, 67.9, 65.7, 57.3. **IR** 3065 (w), 2875 (w), 2109 (s), 1762 (s), 1451 (w), 1262 (s), 1129 (m), 954 (w), 908 (m). **HRMS** (ESI) calcd for $C_{11}H_{11}N_3NaO_3^+$ [M+Na]+ 256.0693; found 256.0690.

5. Optimization for the Lewis-acid catalyzed cascade functionalization of alkenes



1a

0.10 mmol
1.0 equiv

4a

Dry acetonitrile (0.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1** (0.10 mmol, 1.0 equiv), ADBX reagent **3b** (45 mg, 0.15 mmol, 1.5 equiv) and the catalyst. The resulting solution was stirred under N_2 at room temperature for mentioned time. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Then addition of 6 μL of CH_2Br_2 as internal standard gave NMR yield..

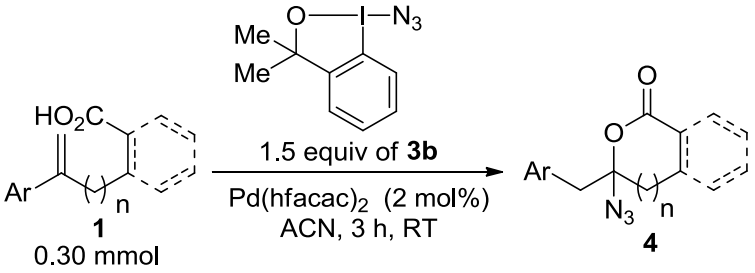
Entry	Catalyst (10 mol%)	Time	Concentration (M)	Conversion[a] (%)	Yield[b] (%)
1[c]	$Pd(OAc)_2$	15 h	0.040	90	34
2[c]	$Pd(TFA)_2$	15 h	0.040	90	32
3[c]	$Pd(OPiv)_2$	15 h	0.040	90	32
4	$AgBF_4$	15 h	0.040	>95	5
5	$Pd(OAc)_2$	15 h	0.040	>95	53
6	$Pd(acac)_2$	15 h	0.040	25	48
7	$Pd(tfacac)_2$	15 h	0.040	>95	47
8	$Pd(hfacac)_2$	15 h	0.040	>95	60
9[d]	$Pd(hfacac)_2$	15 h	0.040	>95	10
10	$Pd(hfacac)_2$	15 h	0.20	>95	63
11	$Pd(hfacac)_2$	15 h	0.40	>95	59
12	$Pd(hfacac)_2$	5 h	1.0	>95	60
13[e]	$Pd(hfacac)_2$	5 h	0.20	>95	57
14[f]	$Pd(hfacac)_2$	5 h	0.20	>95	54
15[g]	$Pd(hfacac)_2$	1 h	0.20	>95	60
16	$In(OTf)_3$	2 h	0.20	Low	45
17	$Sn(OTf)_2$	2 h	0.20	>95	85
18	$Zn(OTf)_2$	2 h	0.20	>95	58
19	$Zn(NTf_2)_2$	2 h	0.20	>95	<5

20	$Zn(BF_4)_2,H_2O$	2 h	0.20	>95	<10
21	$Sc(OTf)_3$	2 h	0.20	>95	35
22[h]	$Sn(OTf)_2$	2 h	0.20	>95	16
23[i]	$Sn(OTf)_2$	2 h	0.20	>95	75
24[g,i]	$Sn(OTf)_2$	2 h	0.20	>95	80[k]
25[h]	$Pd(hfacac)_2$	2 h	0.20	>95	58
26[j]	$Pd(hfacac)_2$	2 h	0.20	>95	75

[a] The conversion of **5a** by NMR is given. The reaction is stirred at RT unless otherwise noted. [b] NMR yield after using 6 µL CH_2Br_2 as internal standard. [c] In DCM [d] Using 1.5 equiv of ABX reagent. [e] At 50 °C. [f] At 0 °C. [g] Using 2.0 equiv of ADBX reagent. [h] 20 mol% catalyst [i] 5 mol% catalyst [j] 2 mol% catalyst [k] Issue of reproducibility using $Sn(OTf)_2$ as catalyst. Reactions were performed several times yielding always very different outcomes, ranging from about 20 to 80% NMR yield.

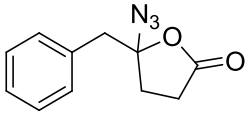
6. Lewis acid catalyzed azidolactonization.

General Procedure



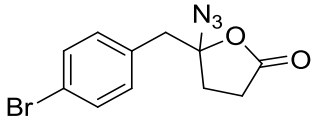
Dry acetonitrile (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1** (0.30 mmol, 1.0 equiv), ADBX reagent **3b** (136 mg, 0.450 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (3.1 mg, 6.0 μmol, 0.02 equiv.). The resulting solution was stirred under N_2 at room temperature for 2 h unless otherwise noted. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Then addition of 18 μL of CH_2Br_2 as internal standard gave NMR yield. Final purification was performed by column chromatography (Pentane/EtOAc : 100 to 90/10 to 80/20) over silica gel affording the corresponding azidolactone product **4**.

5-Azido-5-benzyldihydrofuran-2(3H)-one (4a)



Starting from **1a** (53 mg, 0.30 mmol), the crude product (75% NMR yield) was purified by column chromatography (Pentane/Ethyl Acetate = 9:1 then 8:2) to afford **4a** as colorless oil (34 mg, 0.16 mmol, 52%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 5H, Ar*H*), 3.34 (d, *J* = 14.1 Hz, 1H, ArC*H*$_2$), 3.23 (d, *J* = 14.1 Hz, 1H, ArC*H*$_2$), 2.74 – 2.55 (m, 1H, $O_2CCH_2CH_2$), 2.31 – 2.22 (m, 1H, $O_2CCH_2CH_2$), 2.23 – 2.16 (m, 1H, $O_2CCH_2CH_2$), 2.11 – 1.94 (m, 1H, $O_2CCH_2CH_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7, 133.1, 130.4, 128.7, 127.8, 99.4, 43.7, 31.3, 28.3. **IR** 3033 (w), 2928 (w), 2858 (w), 2602 (w), 2477 (w), 2118 (s), 1796 (s), 1718 (w), 1490 (w), 1456 (w), 1424 (w), 1332 (w), 1248 (m), 1167 (m), 1085 (w), 1031 (w), 916 (m), 875 (w). **HRMS** (APPI) calcd for $C_{11}H_{12}NO_2^+$ $[M-N_2+H]^+$ 190.0863; found 190.0863.

5-Azido-5-(4-bromobenzyl)dihydrofuran-2(3H)-one (4b)



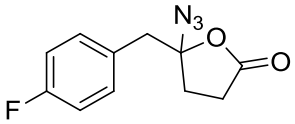
Starting from 4-(4-bromophenyl)pent-4-enoic acid **1d** (51 mg, 0.20 mmol, 1.0 equiv.), ADBX reagent **3b** (92 mg, 0.30 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.), the crude product (80% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4b** as pale orange oil (31 mg, 0.11 mmol, 53 % yield). Rf: 0.40 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (m, 2H, Ar*H*), 7.17 (m, 2H, Ar*H*), 3.29 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ar), 3.18 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ar), 2.68 (dt, *J* = 17.9, 9.7 Hz, 1H, $O_2CCH_2CH_2$), 2.33 (ddd, *J* = 17.9, 9.4, 3.2 Hz, 1H, $O_2CCH_2CH_2$), 2.15 (m, 1H, $O_2CCH_2CH_2$), 2.03 (ddd, *J* = 13.1, 9.5, 3.2 Hz, 1H, $O_2CCH_2CH_2$). **^{13}C NM**R (101 MHz, $CDCl_3$)

δ 174.7, 132.3, 132.2, 132.0, 122.2, 99.1, 43.3, 31.4, 28.3. **IR** 2990 (w), 2936 (w), 2116 (s), 1796 (s), 1493 (m), 1249 (m), 1165 (m), 1017 (m), 911 (s). **HRMS** (ESI) calcd for $C_{11}H_{11}BrNO_2^+$ [M-N_2+H]$^+$ 267.9973; found 267.9973.

1.5 mmol scale synthesis:

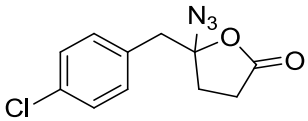
Starting from 4-(4-bromophenyl)pent-4-enoic acid **1d** (400 mg, 1.57 mmol, 1.0 equiv.), ADBX **3b** (713 mg, 2.35 mmol), 1.5 equiv.) and Pd(hfacac)$_2$ (16 mg, 0.031 mmol, 0.02 equiv.). The crude product (80% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4b** as pale orange oil (280 mg, 0.946 mmol, 60 % yield).

5-Azido-5-(4-fluorobenzyl)dihydrofuran-2(3H)-one (4c)



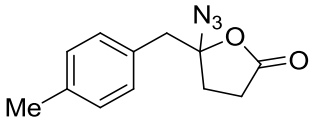
Starting from 4-(4-fluorophenyl)pent-4-enoic acid **1e** (39 mg, 0.20 mmol, 1.0 equiv.), ADBX reagent **3b** (92 mg, 0.30 mmol, 1.5 equiv) and Pd(hfacac)$_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.), the crude product (68% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4c** as pale yellow oil (22 mg, 0.094 mmol, 46 % yield). Rf: 0.40 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (m, 2H, Ar*H*), 7.04 (m, 2H, Ar*H*), 3.32 (d, *J* = 14.3 Hz, 1H, C*H*$_2$Ar), 3.21 (d, *J* = 14.3 Hz, 1H, C*H*$_2$Ar), 2.69 (dt, *J* = 17.8, 9.6 Hz, 1H, $O_2CCH_2CH_2$), 2.33 (ddd, *J* = 17.8, 9.4, 3.1 Hz, 1H, $O_2CCH_2CH_2$), 2.18 (m, 1H, $O_2CCH_2CH_2$), 2.04 (m, 1H, $O_2CCH_2CH_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.8, 162.6 (d, *J* = 247.0 Hz), 132.2 (d, *J* = 8.2 Hz), 129.0 (d, *J* = 3.3 Hz), 115.9 (d, *J* = 21.4 Hz), 99.3, 43.1, 31.5, 28.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.28 (m, 1F). **IR** 3048 (w), 2932 (w), 2116 (s), 1796 (s), 1607 (w), 1513 (s), 1227 (s), 1161 (s), 911 (s). **HRMS** (ESI) calcd for $C_{11}H_{10}FN_3NaO_2^+$ [M+Na]$^+$ 258.0649; found 258.0655

5-Azido-5-(4-chlorobenzyl)dihydrofuran-2(3H)-one (4d)



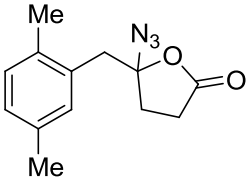
Starting from 4-(4-chlorophenyl)pent-4-enoic acid **1f** (42 mg, 0.20 mmol, 1.0 equiv.), ADBX reagent **3b** (92 mg, 0.30 mmol, 1.5 equiv) and Pd(hfacac)$_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.), the crude product (80% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4d** as pale yellow oil (32 mg, 0.13 mmol, 63 % yield). Rf: 0.38 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (m, 2H, Ar*H*), 7.22 (m, 2H, Ar*H*), 3.31 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ar), 3.19 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ar), 2.68 (dt, *J* = 17.9, 9.7 Hz, 1H, $O_2CCH_2CH_2$), 2.33 (ddd, *J* = 17.9, 9.4, 3.2 Hz, 1H, $O_2CCH_2CH_2$), 2.15 (m, 1H, $O_2CCH_2CH_2$), 2.03 (m, 1H, $O_2CCH_2CH_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.6, 134.0, 131.8, 131.6, 129.0, 99.1, 43.1, 31.3, 28.2. **IR** 2990 (w), 2936 (w), 2116 (s), 1796 (s), 1493 (m), 1249 (m), 1165 (m), 1017 (m), 911 (s). **HRMS** (ESI) calcd for $C_{11}H_{11}ClNO_2^+$ [M-N_2+H]$^+$ 224.0484; found 224.0480.

5-Azido-5-(4-methylbenzyl)dihydrofuran-2(3H)-one (4e)



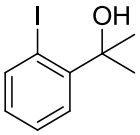
Starting from 4-(p-tolyl)pent-4-enoic acid **1b** (73 mg, 0.38 mmol, 1.0 equiv), using 4.0 mg of $Pd(hfacac)_2$ (2 mol%, 7.7 μmol) and 0.17 g of ADBX **3b** (1.5 equiv., 0.57 mmol) the crude product (64% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4e** as pale yellow oil (42 mg, 0.18 mmol, 48 % yield). Rf: 0.38 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.09 (m, 4H, Ar*H*), 3.30 (d, *J* = 14.1 Hz, 1H, C*H*$_2$Ar), 3.18 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ar), 2.70 – 2.55 (m, 1H, $O_2CCH_2CH_2$), 2.34 (s, 3H, *Me*), 2.30 – 2.14 (m, 2H, $O_2CCH_2CH_2$ + $O_2CCH_2CH_2$), 2.09 – 1.93 (m, 1H, $O_2CCH_2CH_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.8, 137.5, 130.3, 130.0, 129.4, 99.6, 43.2, 31.1, 28.3, 21.0. **IR** 3564 (w), 3330 (w), 3008 (w), 2925 (w), 2860 (w), 2454 (w), 2112 (s), 1785 (s), 1615 (w), 1516 (w), 1454 (w), 1419 (w), 1383 (w), 1330 (w), 1247 (s), 1159 (s), 1116 (w), 1067 (w), 1029 (m), 911 (s), 875 (w), 847 (w), 822 (w). **HRMS** (ESI) calcd for $C_{12}H_{13}N_3NaO_2^+$ $[M+Na]^+$ 254.0900; found 254.0903.

5-Azido-5-(2,5-dimethylbenzyl)dihydrofuran-2(3H)-one (4f)



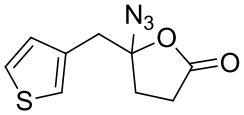
Starting from **1l** (61 mg, 0.30 mmol, 1.0 equiv.), the crude product (55% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4f** as a mixture (40/60 by ^{1}H-NMR) with 2-(2-iodophenyl)propan-2-ol (74 mg total, 30 mg of azidolactone calculated, 0.12 mmol, 40 % yield). Rf: 0.30 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). *Two rotamers are observed in NMR analysis, however they are not fully resolved. Only the major rotamer is described.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 – 6.96 (m, 3H, Ar*H*), 3.39 (d, *J* = 14.5 Hz, 1H, C*H*$_2$Ar), 3.19 (d, *J* = 14.4 Hz, 1H, C*H*$_2$Ar), 2.66 (dt, *J* = 17.5, 9.5 Hz, 1H, $O_2CCH_2CH_2$), 2.34 (s, 3H, *Me*), 2.30 (s, 3H, *Me*), 2.28 – 2.21 (m, 1H, $O_2CCH_2CH_2$), 2.21 – 2.13 (m, 1H, $O_2CCH_2CH_2$), 2.07 (ddd, *J* = 12.5, 9.2, 3.0 Hz, 1H, $O_2CCH_2CH_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7, 135.6, 134.2, 132.0, 131.3, 130.7, 128.6, 99.8, 40.0, 31.2, 28.2, 20.9, 19.6. **HRMS** (ESI) calcd for $C_{13}H_{16}N_3O_2^+$ $[M-N2+H]^+$ 218.1181; found 218.1180.

2-(2-Iodophenyl)propan-2-ol



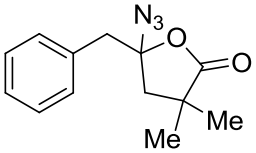
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar*H*), 7.63 (dd, *J* = 8.0, 1.7 Hz, 1H, Ar*H*), 7.33 (ddd, *J* = 7.9, 7.3, 1.4 Hz, 1H, Ar*H*), 6.96 – 6.80 (m, 1H, Ar*H*), 2.41 (s, 1H, O*H*), 1.76 (s, 6H, *Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) 148.5, 142.7, 128.6, 128.1, 126.7, 93.1, 73.6, 29.8. NMR data correspond to the reported values. [29]

5-Azido-5-(thiophen-3-ylmethyl)dihydrofuran-2(3H)-one (4g)



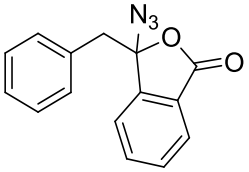
Starting from **1k** (55 mg, 0.30 mmol, 1.0 equiv.), the crude product (60% NMR yield) was purified by column chromatography (Pentane/Ethyl Acetate = 9:1 then 8:2) to afford **4g** as colorless oil (34 mg, 0.16 mmol, 52 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 5.0, 3.0 Hz, 1H, Ar*H*), 7.19 (dd, *J* = 2.9, 1.2 Hz, 1H, Ar*H*), 7.05 (dd, *J* = 4.9, 1.3 Hz, 1H, Ar*H*), 3.36 (d, *J* = 14.6 Hz, 1H, ArCH_2), 3.29 (d, *J* = 14.6 Hz, 1H, ArCH_2), 2.67 (dt, *J* = 17.7, 9.5 Hz, 1H, O_2CCH_2CH_2), 2.31 (ddd, *J* = 17.7, 9.5, 3.4 Hz, 1H, O_2CCH_2CH_2), 2.19 (dt, *J* = 13.3, 9.4 Hz, 1H, O_2CCH_2CH_2), 2.05 (ddd, *J* = 13.2, 9.6, 3.4 Hz, 1H, O_2CCH_2CH_2). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.7, 133.2, 129.1, 126.3, 124.7, 99.1, 38.4, 31.4, 28.3. **IR** 3106 (w), 2932 (w), 2863 (w), 2453 (w), 2254 (w), 2116 (s), 1793 (s), 1606 (w), 1451 (w), 1422 (w), 1242 (m), 1162 (s), 1075 (w), 1031 (m), 949 (w), 911 (s), 848 (w). **HRMS** (APCI) calcd for $C_9H_{10}NO_2S^+$ $[M\text{-}N_2\text{+}H]^+$ 196.0427; found 196.0426.

5-Azido-5-benzyl-3,3-dimethyldihydrofuran-2(3H)-one (4h)



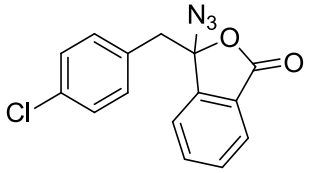
Starting from 2,2-dimethyl-4-phenylpent-4-enoic acid **1j** (61 mg, 0.30 mmol, 1.0 equiv.), the crude product (81% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4h** as pale orange oil (57 mg, 0.23 mmol, 77 % yield). Rf: 0.50 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 3.33 (d, *J* = 14.1 Hz, 1H, CH_2Ar), 3.20 (d, *J* = 14.1 Hz, 1H, CH_2Ar), 2.10 (d, *J* = 13.7 Hz, 1H, CCH_2CMe_2), 1.92 (d, *J* = 13.8 Hz, 1H, CCH_2CMe_2), 1.35 (s, 3H, CH_3), 0.99 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.6, 133.4, 130.7, 128.8, 127.9, 96.5, 44.9, 44.4, 40.4, 26.5, 26.0. **IR** 3065 (w), 2976 (w), 2934 (w), 2114 (s), 1785 (s), 1456 (w), 1258 (m), 1229 (s), 1129 (m), 1037 (m), 908 (s). **HRMS** (ESI) calcd for $C_{13}H_{15}N_3NaO_2^+$ $[M+Na]^+$ 268.1056; found 268.1056.

3-Azido-3-benzylisobenzofuran-1(3H)-one (4i)



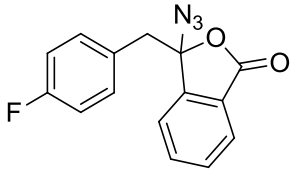
Starting from 2-(1-phenylvinyl)benzoic acid **1h** (67 mg, 0.30 mmol, 1.0 equiv.), the crude product (75% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4i** as a mixture (60/40 by ^{1}H-NMR) with 2-(2-iodophenyl)propan-2-ol (98 mg total, 59 mg of azidolactone calculated, 0.22 mmol, 74 % yield). Rf: 0.30 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain/UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.6, 0.9 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 7.56 (td, *J* = 7.5, 1.0 Hz, 1H, Ar*H*), 7.38 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.19 (dd, *J* = 5.0, 2.0 Hz, 3H, Ar*H*), 7.09 (dd, *J* = 6.7, 3.0 Hz, 2H, Ar*H*), 3.38 (s, 2H, CH_2Ar). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1, 148.5, 134.6, 132.3, 130.9, 130.7, 128.2, 127.5, 126.2, 125.7, 122.6, 98.8, 44.2. **HRMS** (ESI) calcd for $C_{15}H_{12}N_3O_2^+$ $[M\text{-}N2\text{+}H]^+$ 238.0868; found 238.0873.

3-Azido-3-(4-chlorobenzyl)isobenzofuran-1(3H)-one (4j)



Starting from 2-(1-(4-chlorophenyl)vinyl)benzoic acid **1w** (78 mg, 0.30 mmol, 1.0 equiv.), the crude product (78% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4j** as pale yellow oil (67 mg, 0.22 mmol, 74 % yield). Rf: 0.25 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain/UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.73 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 7.59 (td, *J* = 7.6, 0.9 Hz, 1H, Ar*H*), 7.41 (dd, *J* = 7.7, 0.9 Hz, 1H, Ar*H*), 7.17 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.03 (d, *J* = 8.4 Hz, 2H, Ar*H*), 3.41 – 3.26 (m, 2H, ArCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 145.9, 134.9, 133.7, 132.0, 131.2, 130.9, 128.5, 126.3, 126.0, 122.5, 98.5, 43.7. **IR** 3553 (w), 3064 (w), 2840 (w), 2433 (w), 2116 (s), 1784 (s), 1602 (w), 1493 (w), 1469 (w), 1435 (w), 1410 (w), 1349 (w), 1275 (m), 1239 (m), 1209 (w), 1160 (w), 1087 (m), 1014 (w), 956 (m), 906 (w), 844 (w), 817 (w). **HRMS** (ESI) calcd for $C_{15}H_{10}ClNO_2^+$ $[M\text{-}N2+H]^+$ 272.0478; found 272.0481.

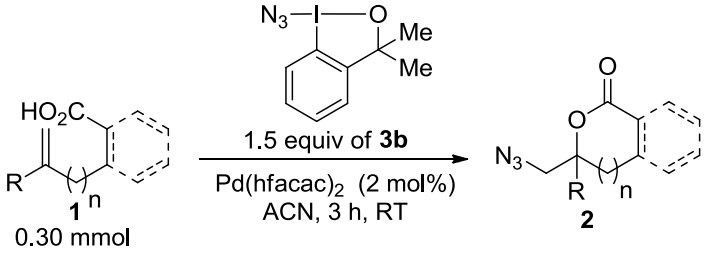
3-Azido-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (4k)



Starting from 2-(1-(4-Fluorophenyl)vinyl)benzoic acid **1i**, the crude product (75% NMR yield) was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **4k** as a mixture (40/60 by ^{1}H-NMR) with 2-(2-iodophenyl)propan-2-ol (122 mg total, 51 mg of azidolactone calculated, 0.18 mmol, 60 % yield). Rf: 0.30 (Pentane/ EtOAc = 8:2) ($KMnO_4$ Stain/UV). Always used directly as crude material for product modification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.73 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 7.57 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.40 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.11 – 7.01 (m, 2H, Ar*H*), 6.87 (d, *J* = 8.5 Hz, 2H, Ar*H*), 3.38 (d, *J* = 14.2 Hz, 1H, CH_2Ar), 3.32 (d, *J* = 14.2 Hz, 1H, CH_2Ar). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.0, 162.3 (d, *J* = 246.3 Hz), 145.9, 134.8, 132.3 (d, *J* = 8.1 Hz), 131.1, 128.1 (overlapping with 2-(2-iodophenyl)propan-2-ol), 126.3, 125.9, 122.5, 115.2 (d, *J* = 21.3 Hz), 98.7, 43.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ 114.51 (m, 1F). HRMS (ESI) calcd for $C_{15}H_{11}FNO_2^+$ $[M\text{-}N2+H]^+$ 256.0768; found 256.0779.

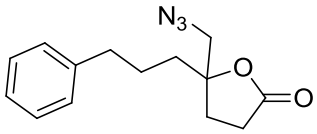
7. Pd-Catalyzed Synthesis of (1,2)-Azidolactones

General procedure



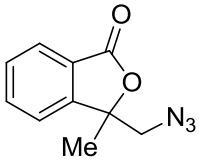
Dry acetonitrile (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1** (0.30 mmol, 1.0 equiv), ADBX reagent **3b** (136 mg, 0.450 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (3.1 mg, 6.0 μmol, 0.02 equiv.). The resulting solution was stirred under N_2 at room temperature for 2 h unless otherwise noted. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Final purification was performed by column chromatography (Pentane/EtOAc : 100 to 90/10 to 80/20) over silica gel affording the corresponding azidolactone product **2**.

5-(Azidomethyl)-5-(3-phenylpropyl)dihydrofuran-2(3H)-one (2s)



Starting from 4-Methylene-7-phenylheptanoic acid **1s** (55 mg, 0.25 mmol, 1.0 equiv.), $Pd(hfacac)_2$ (2.6 mg, 5.0 μmol, 0.02 equiv), ADBX **3b** (115 mg, 0.378 mmol, 1.5 equiv), the crude product (40 % NMR yield, using 5 μL of CH_2Br_2 as internal standard) was purified by column chromatography (Pentane/Ethyl Acetate = 9:1 then 8:2) to afford **2s** as colorless oil (13 mg, 0.050 mmol, 20 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.1, 6.6 Hz, 2H, Ar*H*), 7.24 – 7.18 (m, 1H, Ar*H*), 7.18 – 7.13 (m, 2H, Ar*H*), 3.51 (d, *J* = 12.8 Hz, 1H, C*H*$_2$N$_3$), 3.35 (d, *J* = 12.8 Hz, 1H, C*H*$_2$N$_3$), 2.76 – 2.66 (m, 1H, $O_2CCH_2CH_2$), 2.66 – 2.61 (m, 2H, $ArCH_2CH_2CH_2$), 2.55 (ddd, *J* = 18.2, 10.6, 5.9 Hz, 1H, $O_2CCH_2CH_2$), 2.16 (ddd, *J* = 13.3, 10.7, 5.9 Hz, 1H, $O_2CCH_2CH_2$), 1.99 (ddd, *J* = 13.3, 10.6, 7.4 Hz, 1H, $O_2CCH_2CH_2$), 1.78 – 1.64 (m, 4H, $ArCH_2CH_2CH_2$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 141.2, 128.5, 128.3, 126.1, 86.6, 57.7, 37.2, 35.7, 28.9, 28.6, 25.0. **IR** 3061 (w), 3028 (w), 2945 (w), 2869 (w), 2108 (s), 1777 (s), 1604 (w), 1495 (w), 1455 (w), 1281 (m), 1241 (m), 1198 (m), 1168 (m), 1083 (w), 1027 (w), 946 (m), 917 (w), 847 (w). **HRMS** (ESI) calcd for $C_{14}H_{17}N_3NaO_2^+$ $[M+Na]^+$ 282.1213; found 282.1215.

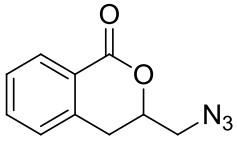
3-(Azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)



Starting from 2-(prop-1-en-2-yl)benzoic acid **1g** (32 mg, 0.20 mmol, 1.0 equiv.), ADBX reagent **3b** (92 mg, 0.30 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.), the crude

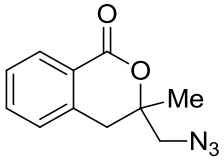
product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2g** as white solid (20 mg, 0.104 mmol, 50 % yield). Rf: 0.55 (Pentane/ EtOAc = 8:2) (Seebach Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.70 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.57 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.45 (d, *J* = 7.7 Hz, 1H, Ar*H*), 3.65 (m, 2H, CH_2N_3), 1.69 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.1, 150.8, 134.5, 129.8, 126.1, 126.1, 121.3, 85.8, 58.1, 23.2. **IR** 3055 (w), 2985 (w), 2933 (w), 2105 (s), 1761 (s), 1468 (w), 1288 (m), 1035 (s). **HRMS** (ESI) calcd for $C_{10}H_9N_3NaO_2^+$ $[M+Na]^+$ 226.0587; found 226.0588. **Melting point** : 77 °C.

3-(Azidomethyl)isochroman-1-one (2t)



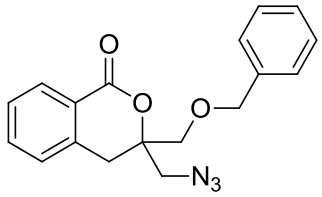
Starting from 2-allylbenzoic acid **1t** (32 mg, 0.20 mmol, 1.0 equiv.), ADBX reagent **3b** (92 mg, 0.30 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.), the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2t** as pale yellow oil (29 mg, 0.14 mmol, 71 % yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 – 8.00 (m, 1H, Ar*H*), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.35 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.22 (d, *J* = 7.5 Hz, 1H, Ar*H*), 4.69 – 4.53 (m, 1H, C*H*), 3.67 – 3.49 (m, 2H, CH_2N_3), 3.12 (dd, *J* = 16.3, 11.8 Hz, 1H, ArCH_2CH), 2.87 (dd, *J* = 16.3, 3.2 Hz, 1H, ArCH_2CH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.6, 138.3, 134.3, 130.6, 128.1, 127.8, 124.7, 76.8, 53.8, 30.5. **IR** 3614 (s), 3075 (w), 3074 (w), 3038 (w), 3038 (w), 2930 (w), 2929 (w), 2928 (w), 2920 (w), 2104 (m), 1726 (m), 1609 (w), 1462 (w), 1362 (w), 1271 (m), 1228 (w), 1126 (m), 1086 (m), 1033 (w), 950 (w), 935 (w), 905 (w). **HRMS** (ESI) calcd for $C_{10}H_9N_3NaO_2^+$ $[M+Na]^+$ 226.0587; found 226.0591.

3-(Azidomethyl)-3-methylisochroman-1-one (2u)



Starting from 2-(2-methylallyl)benzoic acid **1u** (53 mg, 0.30 mmol, 1.0 equiv.), $Pd(hfacac)_2$ (3 mg, 6 μmol, 2 mol %), and ADBX **3b** (137 mg, 0.450 mmol, 1.5 equiv.) and 20 hours of reaction, the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2u** as pale yellow oil (44 mg, 0.20 mmol, 68% yield) as a dark yellow viscous oil. Rf: 0.25 (Pentane/EtOAc 7/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.56 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.40 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.25 (d, *J* = 7.7 Hz, 1H, Ar*H*), 3.54 (d, *J* = 12.7 Hz, 1H, ArCH_2), 3.40 (d, *J* = 12.7 Hz, 1H, ArCH_2), 3.31 (d, *J* = 16.4 Hz, 1H, N_3CH_2), 2.88 (d, *J* = 16.4 Hz, 1H, N_3CH_2), 1.43 (d, *J* = 1.6 Hz, 3H, CH_3).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.9, 137.0, 134.2, 130.1, 128.1, 127.7, 124.2, 81.6, 58.1, 34.8, 23.4. **IR** 3432 (w), 3070 (w), 2983 (w), 2937 (w), 2108 (s), 1721 (s), 1607 (w), 1459 (w), 1389 (w), 1289 (s), 1236 (m), 1168 (w), 1114 (m), 1080 (m), 1036 (w), 950 (w), 841 (w). **HRMS** (ESI) calcd for $C_{11}H_{11}N_3NaO_2^+$ $[M+Na]^+$ 240.0743; found 240.0748

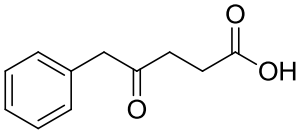
3-(Azidomethyl)-3-((benzyloxy)methyl)isochroman-1-one (2v)



Starting from 2-(2-((benzyloxy)methyl)allyl)benzoic acid **1v** (85 mg, 0.30 mmol, 1.0 equiv.), $Pd(hfacac)_2$ (15.0 mg, 0.029 mmol, 10 mol %), and ADBX **3b** (137 mg, 0.450 mmol, 1.5 equiv.) and 20 h of reaction, the crude product was purified by column chromatography (Pentane/EtOAc = 9:1 to 8/2) to afford **2v** as pale yellow oil (50.8 mg, 0.141 mmol, 90% purity, 45% yield). A ≥ 95% pure sample was obtained through preparative TLC (20 x 20 sqcm plate; pentane/DCM/EtOAc 18/1/1). Rf = 0.56 (pentane/EtOAc 5/1) ($KMnO_4$ Stain). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.8, 1.3 Hz, 1H, Ar*H*), 7.56 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.39 (td, *J* = 7.7, 1.2 Hz, 1H, Ar*H*), 7.35 – 7.27 (m, 3H, Ar*H* + Ph*H*), 7.25 – 7.21 (m, 3H, Ph*H*), 4.56 (d, *J* = 12.0 Hz, 1H, PhCH_2O), 4.49 (d, *J* = 12.0 Hz, 1H, PhCH_2O), 3.63 (d, *J* = 9.7 Hz, 1H, CCH_2O), 3.59 (d, *J* = 9.9 Hz, 2H, aliphatic CH_2), 3.52 (d, *J* = 9.8 Hz, 1H, CCH_2O), 3.20 (d, *J* = 16.7 Hz, 1H, aliphatic CH_2), 3.14 (d, *J* = 16.7 Hz, 1H, aliphatic CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 137.2, 136.6, 134.2, 130.2, 128.4, 128.1, 127.9, 127.7, 127.6, 124.2, 82.6, 73.6, 70.6, 54.8, 30.6. **IR** 3065 (w), 3035 (w), 2921 (w), 2868 (w), 2105 (s), 1727 (s), 1607 (w), 1488 (w), 1455 (w), 1360 (w), 1283 (s), 1107 (s), 1024 (w), 959 (w), 920 (w), 919 (w). **HRMS** (ESI) calcd for $C_{18}H_{17}N_3NaO_3^+$ $[M+Na]^+$ 346.1162; found 346.1161.

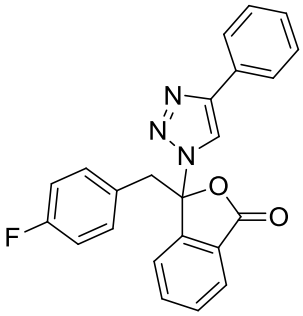
8. Derivatizations

4-Oxo-5-phenylpentanoic acid (5)



Dry acetonitrile (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1a** (53 mg, 0.30 mmol, 1.0 equiv), ADBX reagent **3b** (136 mg, 0.450 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (3.1 mg, 6.0 μmol, 0.02 equiv.). The resulting solution was stirred under N_2 at room temperature for 3 h. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Then addition of 18 μL of CH_2Br_2 as internal standard showed 80-85% NMR yield. Evaporation of $CDCl_3$ and CH_2Br_2 under reduced pressure gave back the crude material, which was directly used without any purification. Pd/C (32 mg, 15 μmol, 5 mol%, loading 5% in Pd) and EtOAc (1.5 mL, 0.2 M) were introduced. After bubbling H_2 (with balloon) for 5 min, the solution was stirred for 48h at rt under 1 atmosphere of H_2. Then the reaction mixture was filtered using HPLC filter to remove solid Pd/C, before being concentrated under reduced pressure. The crude material was purified by column chromatography, affording **6** (43 mg, 0.22 mmol) in 75% yield over two steps. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 2H, Ar*H*), 7.30 – 7.25 (m, 1H, Ar*H*), 7.21 (m, 2H, Ar*H*), 3.74 (s, 2H, ArCH_2), 2.75 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$), 2.61 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2CO_2H$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 177.9, 134.0, 129.6, 128.9, 127.3, 50.1, 36.3, 27.9. NMR data correspond to the reported values.[30]

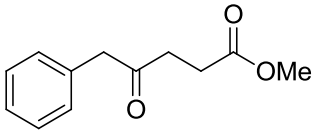
3-(4-Fluorobenzyl)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)isobenzofuran-1(3H)-one (6)



Dry acetonitrile (1.0 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1i** (48 mg, 0.20 mmol, 1.0 equiv), ADBX reagent **3b** (91 mg, 0.30 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (2.1 mg, 4.0 μmol, 0.02 equiv.). The resulting solution was stirred under N_2 at room temperature for 2 h. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Then addition of 6 μL of CH_2Br_2 as internal standard showed 75% NMR yield. Evaporation of $CDCl_3$ and CH_2Br_2 under reduced pressure gave back the crude material which was directly used without any purification. Quantities of triethylamine (42 μL, 0.30 mmol, 2.0 equiv) and copper iodide (2.9 mg, μmol, 0.10 equiv), ethynylbenzene (33 μl, 0.30 mmol, 2.0 equiv) and THF (0.75 mL, 0.20 M) were calculated considering 75% yield, meaning 0.15 mmol of azidolactone. All the reagents were introduced under nitrogen and the reaction mixture was stirred overnight (16h) at room

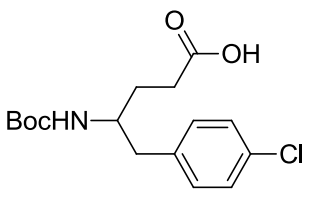
temperature. After completion of the reaction, the resulting mixture was concentrated under reduced pressure and purified by preparative TLC using 60/40 pentane/ethylacetate as eluent system, affording **8** in 65% isolated yield after two steps. (50 mg, 0.13 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.7, 1.0 Hz, 1H, Ar*H*), 7.81 (ddd, *J* = 7.5, 4.7, 1.1 Hz, 2H, Ar*H*), 7.79 – 7.72 (m, 3H, Ar*H* + NC*H*), 7.62 (td, *J* = 7.5, 0.9 Hz, 1H, Ar*H*), 7.44 – 7.36 (m, 2H, Ar*H*), 7.36 – 7.28 (m, 1H, Ar*H*), 7.01 (dd, *J* = 8.6, 5.4 Hz, 2H, Ar*H*), 6.84 (t, *J* = 8.6 Hz, 2H, Ar*H*), 4.09 (d, *J* = 14.4 Hz, 1H, ArCH_2), 3.88 (d, *J* = 14.3 Hz, 1H, ArCH_2). **^{13}C NMR** (100 MHz, $CDCl_3$) 166.5, 162.3 (d, *J* = 247.1 Hz), 147.56, 146.5, 135.3, 132.2 (d, *J* = 8.3 Hz), 131.4, 129.8, 128.8, 128.5, 127.3 (d, *J* = 3.4 Hz), 126.0, 125.7, 125.0, 124.2, 117.9, 115.3 (d, *J* = 21.5 Hz), 95.8, 44.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.07 (m, 1F). **IR** 3145 (w), 3065 (w), 2885 (w), 2253 (w), 2148 (w), 1894 (w), 1789 (s), 1607 (w), 1512 (m), 1475 (w), 1464 (w), 1415 (m), 1353 (w), 1279 (m), 1228 (m), 1160 (w), 1075 (m), 1029 (w), 971 (s), 915 (m), 840 (m). **HRMS** (ESI) calcd for $C_{23}H_{16}FN_3NaO_2^+$ $[M+Na]^+$ 408.1119; found 408.1111. **Melting point:** 141.7-148.5 °C (decomp.).

Methyl 4-oxo-5-phenylpentanoate (7)



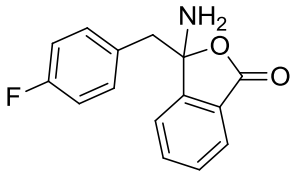
Dry acetonitrile (1.5 mL) was added in a flame dried 4 mL test tube containing a teflon coated stirring bar, the enoic acid **1a** (53 mg, 0.30 mmol, 1.0 equiv), ADBX reagent **3b** (136 mg, 0.450 mmol, 1.5 equiv) and $Pd(hfacac)_2$ (3.1 mg, 6.0 μmol, 0.02 equiv.). The resulting solution was stirred under N_2 at room temperature for 3 h. After completion of the reaction, the crude mixture was obtained after concentration under reduced pressure. Then addition of 18 μL of CH_2Br_2 as internal standard showed 80-85% NMR yield. Evaporation of $CDCl_3$ and CH_2Br_2 under reduced pressure gave back the crude material, which was directly used without any purification. Pd/C (16 mg, 7.5 μmol, 2.5 mol%, loading 5% in Pd) and Methanol (1.5 mL, 0.2 M) were introduced. After bubbling H_2 (with balloon) for 5 min, the solution was stirred for 24h at rt under 1 atmosphere of H_2. Full conversion was confirmed by TLC (90/10 pentane/ethylacetate), then the reaction mixture was filtered using HPLC filter to remove solid Pd/C. The vial was rinsed 3 times using EtOAc before being concentrated under reduced pressure and purified by preparative column chromatography over silicagel, using 90/10 pentane/ethylacetate as eluent system, affording **8** as a pale yellow oil in 70% isolated yield after two steps. (43 mg, 0.21 mmol).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 - 7.30 (m, 2H, Ar*H*), 7.30 - 7.16 (m, 3H, Ar*H*), 3.74 (s, 2H, CH_2Ar), 3.65 (s, 3H, *Me*), 2.76 (t, J = 6.6 Hz, 2H, C$H_2$$CH_2$COOMe), 2.56 (t, J = 6.6 Hz, 2H, CH_2CH_2COOMe).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 173.1, 134.0, 129.4, 128.7, 127.0, 51.7, 50.0, 36.4, 27.7. NMR data correspond to the reported values.[21]

4-((tert-Butoxycarbonyl)amino)-5-(4-chlorophenyl)pentanoic acid (8)



In a flame dried 4 mL test-tube were introduced azido lactone **4d** (25 mg, 0.10 mmol) and THF (1.0 mL, 0.10 M) under nitrogen. To this solution was added black platinum (2.0 mg, 10 mmol, 0.10 equiv) and Boc_2O (44 mg, 0.20 mmol, 2.0 equiv.), before being placed under H_2 pressure (1atm, balloon). The resulting solution was stirred for 18h at room temperature. Filtration using HPLC filter and evaporation of the solvent under reduced pressure gave the crude mixture as a solid-oil mixture. Final precipitation was obtained by adding chloroform. After two washing sequence with chloroform, the expected product **9** was isolated as colorless solid (16 mg, 0.048 mmol, 48 % yield). NB: Mixture of rotamers not fully resolved (M stands for major rotamer, m stands for minor rotamer). (NMR ratio: 86:14). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.01 (s, 1H, COO*H* (M+m)), 7.38 (d, *J* = 8.4 Hz, 0.13H, Ar*H* (m)), 7.32 (d, *J* = 8.3 Hz, 1.87H, Ar*H* (M)), 7.23 – 7.15 (d, *J* = 8.3 Hz, 2H, Ar*H* (M+m)), 6.72 (d, *J* = 8.9 Hz, 0.86H, N*H* (M)), 6.31 (d, *J* = 9.2 Hz, 0.14H, N*H* (m)), 3.66 – 3.49 (m, 1H, NC*H* (M+m)), 2.65 (m, 2H, ArCH_2 (M+m)), 2.30 – 2.13 (m, 2H, CH_2CH_2COOH (M+m)), 1.67 (m, 1H, CH_2CH_2COOH (M+m)), 1.52 (m, 1H, CH_2CH_2COOH (M+m)), 1.32 (s, 7.5H, Boc (M)), 1.23 (s, 1.5H, Boc (m)). **^{13}C NMR** (100 MHz, DMSO-d_6) (only major rotamer) δ 174.2, 155.2, 138.1, 131.0, 130.5, 127.9, 77.3, 51.0, 40.1, 30.4, 29.5, 28.2. **IR** 3359 (w), 2975 (m), 2934 (m), 2605 (w), 2260 (w), 2118 (w), 1902 (w), 1695 (s), 1521 (m), 1448 (w), 1402 (m), 1363 (m), 1257 (m), 1170 (s), 1093 (w), 1024 (s), 900 (w), 818 (w). **HRMS** (ESI) calcd for $C_{16}H_{21}ClNO_4^-$ $[M-H]^-$ 326.1165; found 326.1156; **Melting point**: 146.9 – 147.9 °C.

3-Amino-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (9)

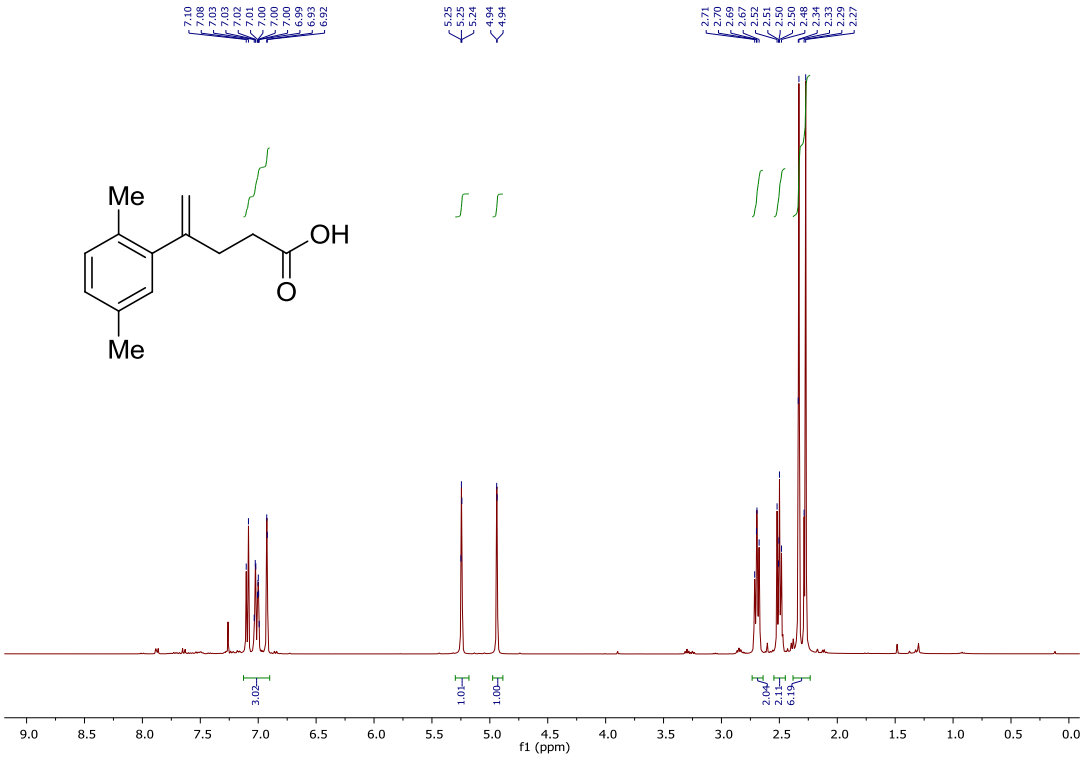


In a flame dried 4 mL test-tube were introduced unseparated iodoalcohol and azido lactone **4k** (51 mg, 0.18 mmol, based on NMR yield) and THF (1.8 mL, 0.10 M) under nitrogen. To this solution was added black platinum (3.5 mg, 18 μmol, 0.10 equiv) and Boc_2O (79 mg, 0.36 mmol, 2.0 equiv), before being placed under H_2 pressure (1atm, balloon). The resulting solution was stirred for 15h at room temperature. Filtration using HPLC filter and evaporation of the solvent under reduced pressure gave the crude mixture. Purification using preparative TLC using 55/45 pentane/ethyl acetate as eluant afforded primary amine product **10** as colorless solid (37 mg, 0.14 mmol, 80 % yield). No N-Boc protected amine was observed. The reaction was scaled up to 420 mg of azidolactone **4k** (1.48 mmol) dissolved in 14 mL of THF and using only black platinum catalyst (29 mg, 0.15 mmol, 0.10 equiv). In this case, 80% conversion and 53% yield of **9** was obtained (203 mg, 0.789 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.1 Hz, 1H, Ar*H*), 7.67 (td, *J* = 7.3, 1.1 Hz, 1H, Ar*H*), 7.52 (t, *J* = 7.3 Hz, 2H, Ar*H*), 7.20 – 7.12 (m, 2H, Ar_FH), 6.97 – 6.87 (m (app tt), 2H, Ar_FH), 3.26 (s, 2H, Ar_FCH_2), 2.52 (brs, 2H, NH_2). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5, 162.2 (d, *J* = 246.0 Hz), 149.3, 134.0, 132.3 (d, *J* = 8.0 Hz), 130.2, 129.6 (d, *J* = 3.3 Hz), 127.7, 125.3, 122.8, 115.1 (d, *J* = 21.3 Hz), 98.7, 45.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.15 (m, 1F). **IR** 3403 (w), 3337 (w), 3235 (w), 3059 (w), 2927 (w), 2857 (w), 2254 (w), 1751 (s), 1611 (w), 1511 (m), 1475 (w), 1429 (w), 1383 (w), 1284 (m), 1229 (m), 1156 (w), 1120 (m), 1088 (w), 1010 (w), 942 (w), 867 (m), 838 (w). **HRMS** (ESI) calcd for $C_{15}H_{12}FNNaO_2^+$ $[M+Na]^+$ 280.0744; found 280.0741. **Melting point:** 132.7-135.7 °C (decomp.).

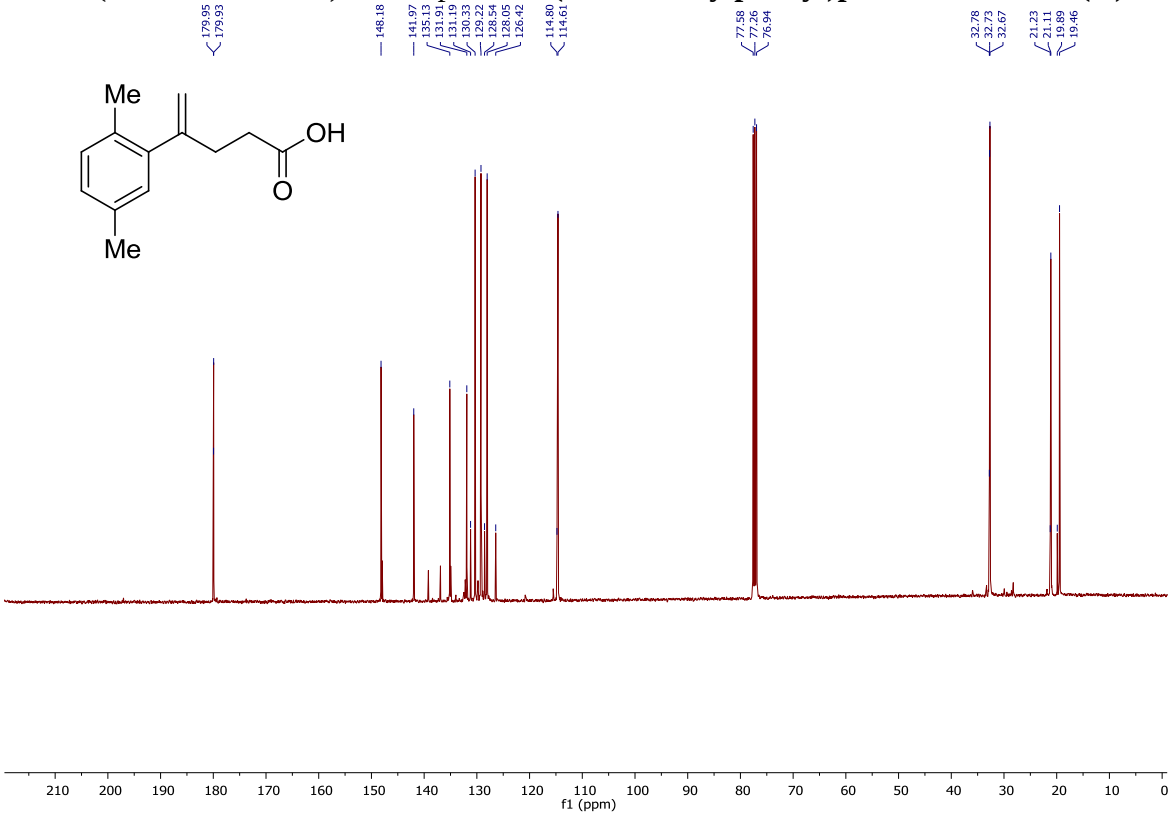
9. Spectra of compounds

a. Spectra of new compounds of starting materials

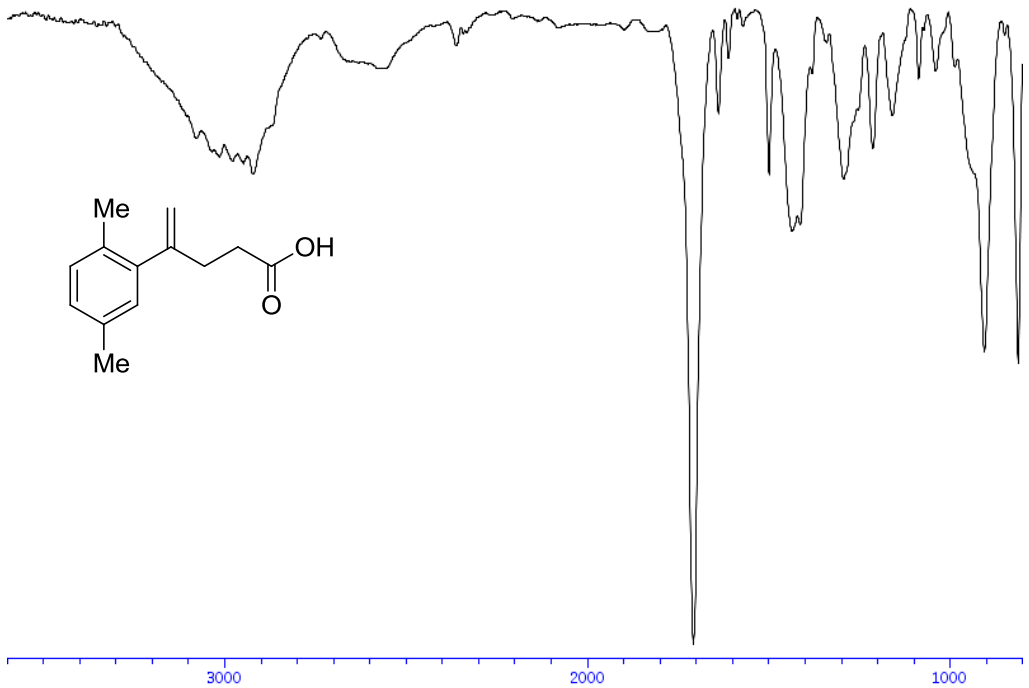
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4-(2,5-dimethylphenyl)pent-4-enoic acid (1l)**



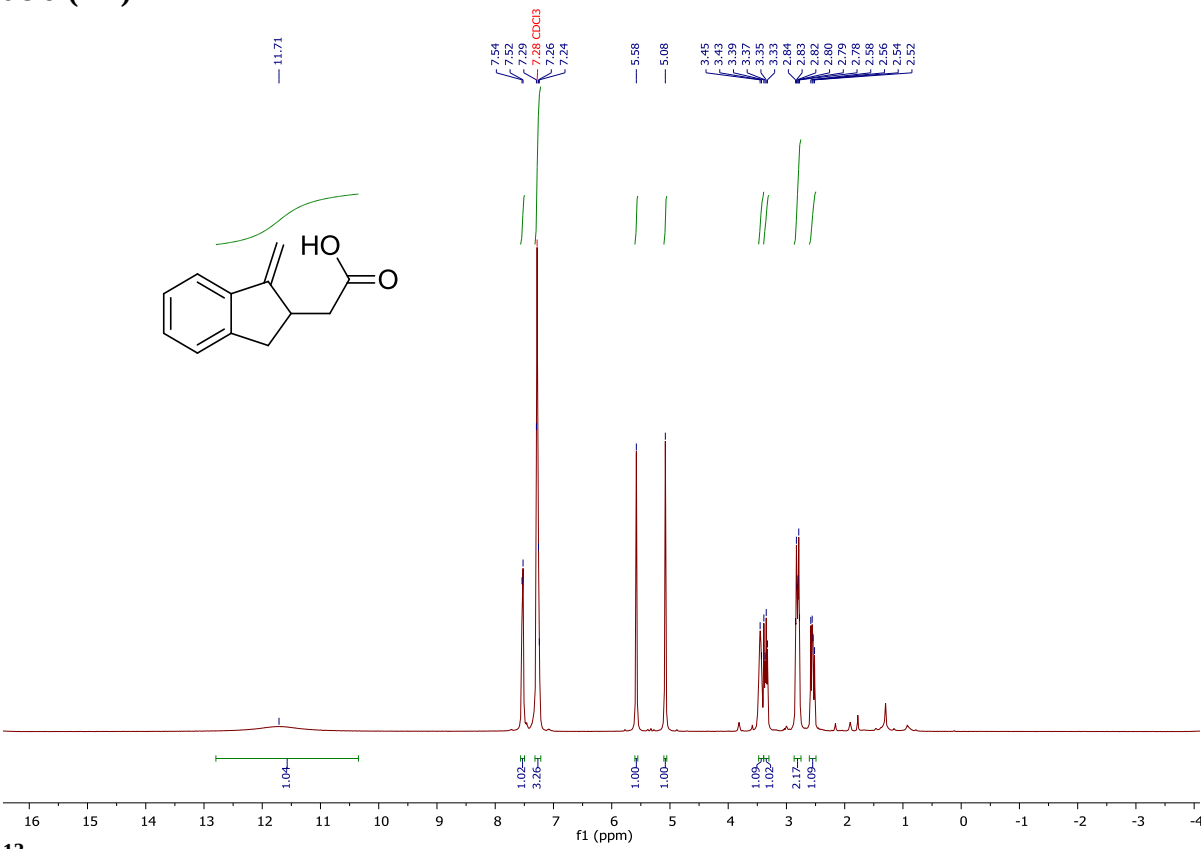
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4-(2,5-dimethylphenyl)pent-4-enoic acid (1l)**



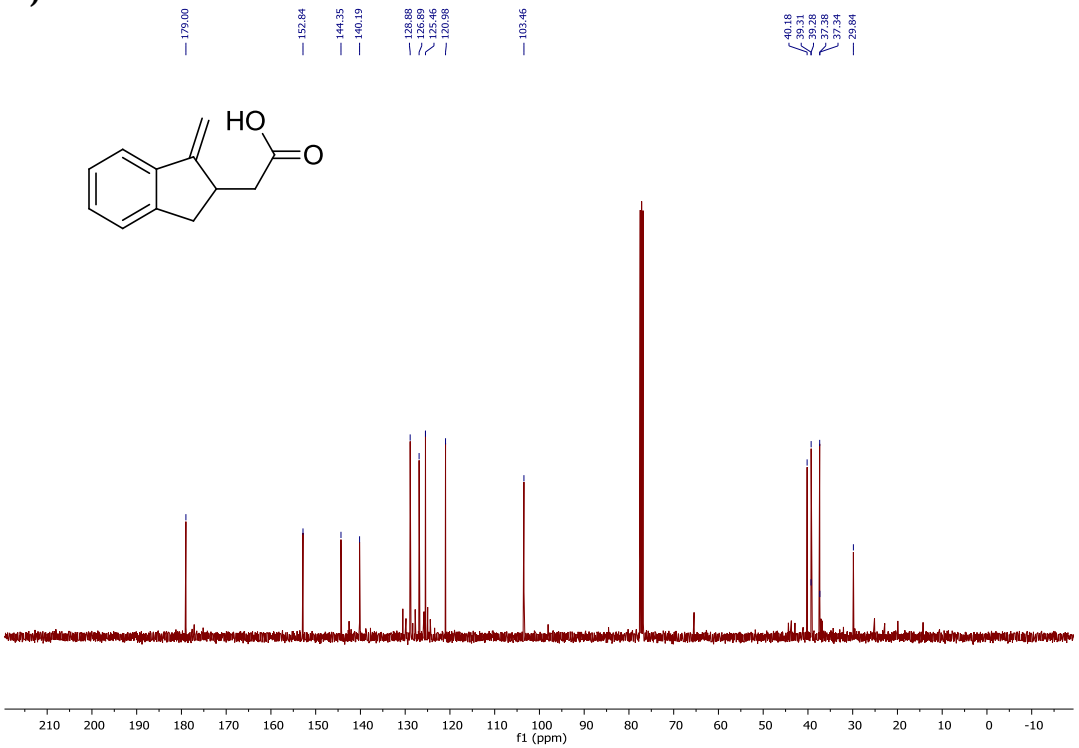
IR of compound **4-(2,5-dimethylphenyl)pent-4-enoic acid (1l)**



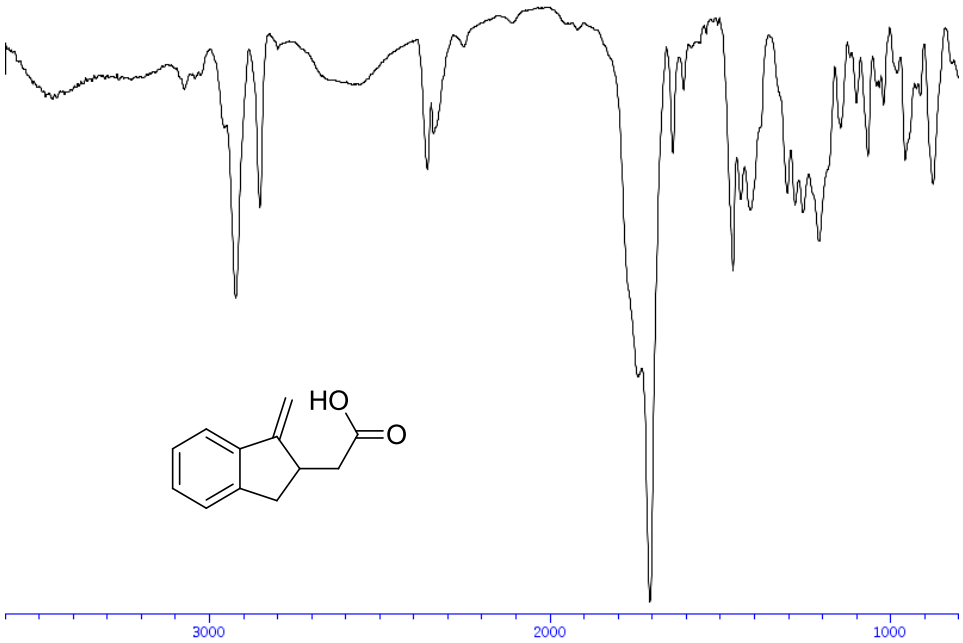
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2-(1-methylene-2,3-dihydro-1H-inden-2-yl)acetic acid (1m)**



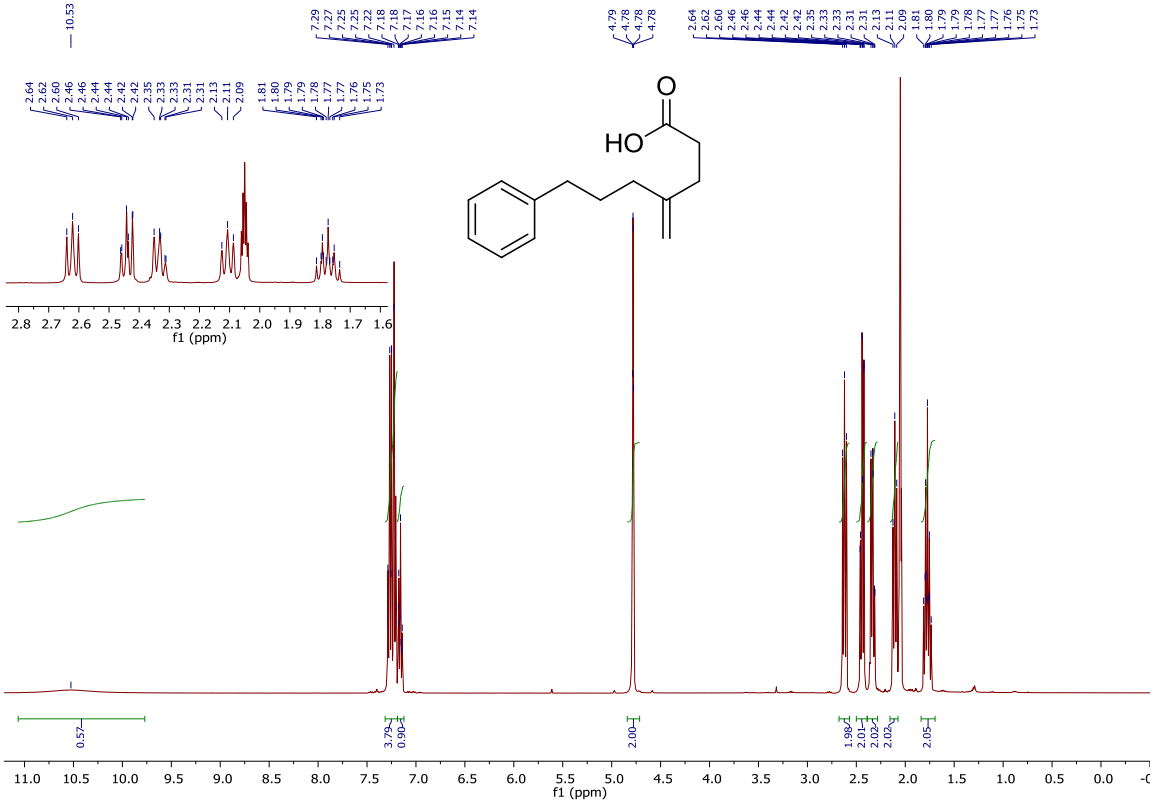
^{13}C NMR (101 MHz, $CDCl_3$) of compound **2-(1-methylene-2,3-dihydro-1H-inden-2-yl)acetic acid (1m)**



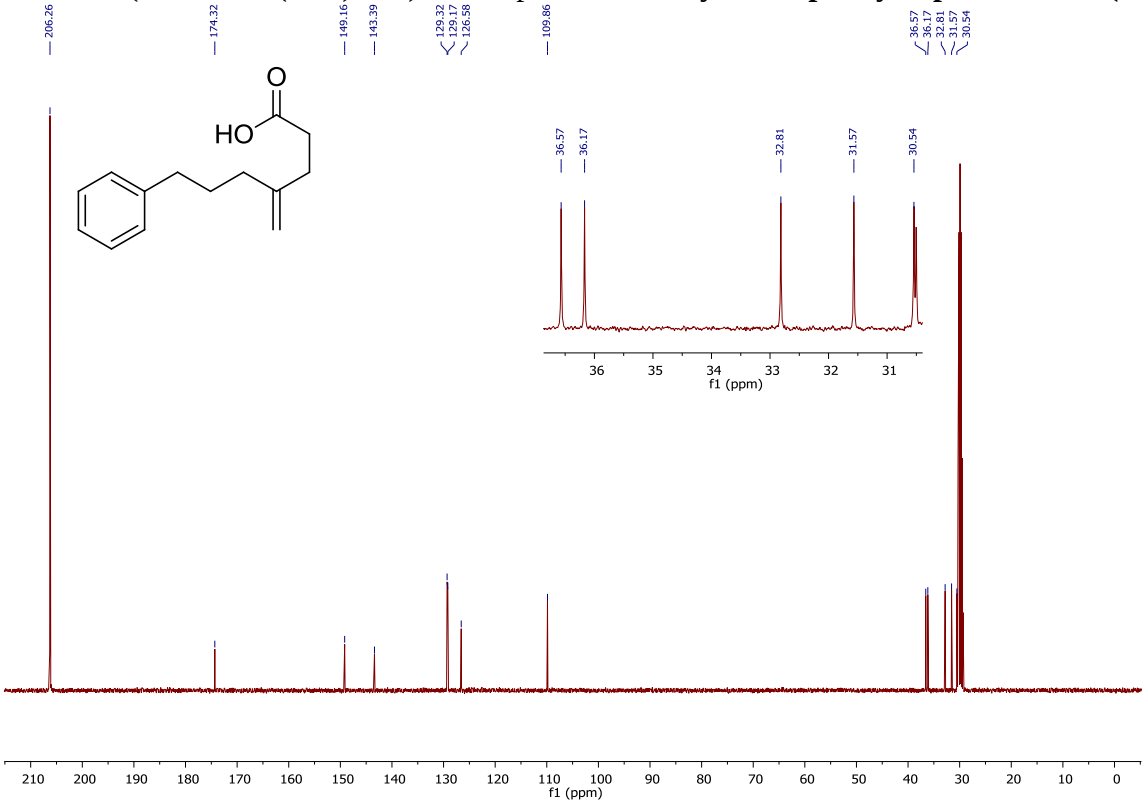
IR of compound **2-(1-methylene-2,3-dihydro-1H-inden-2-yl)acetic acid (1m)**



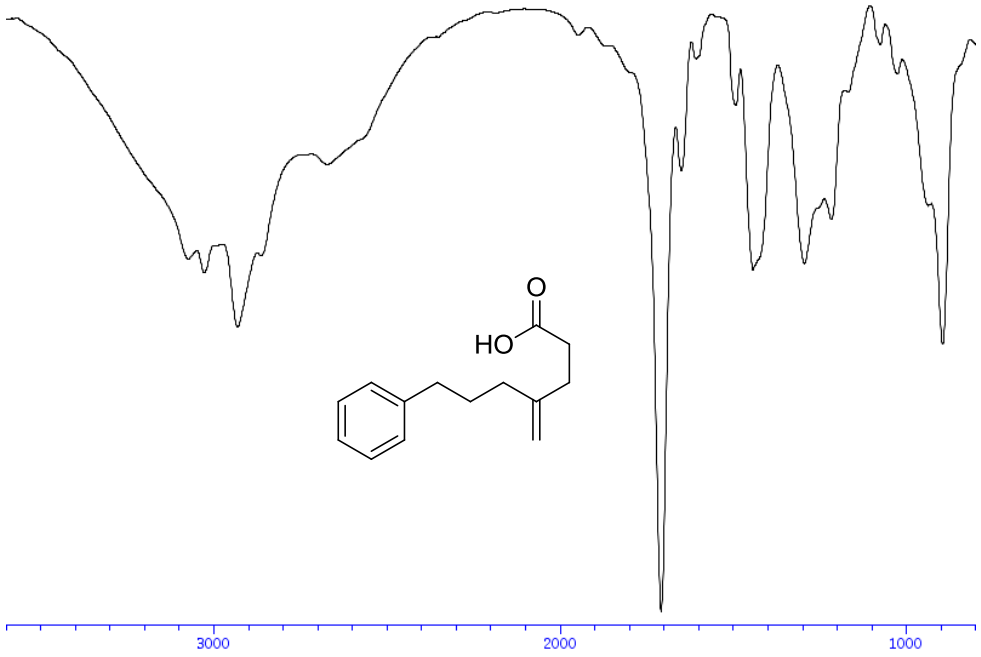
^{1}H-NMR (400 MHz, $(CD_3)_2CO$) of compound **4-methylene-7-phenylheptanoic acid (1s)**



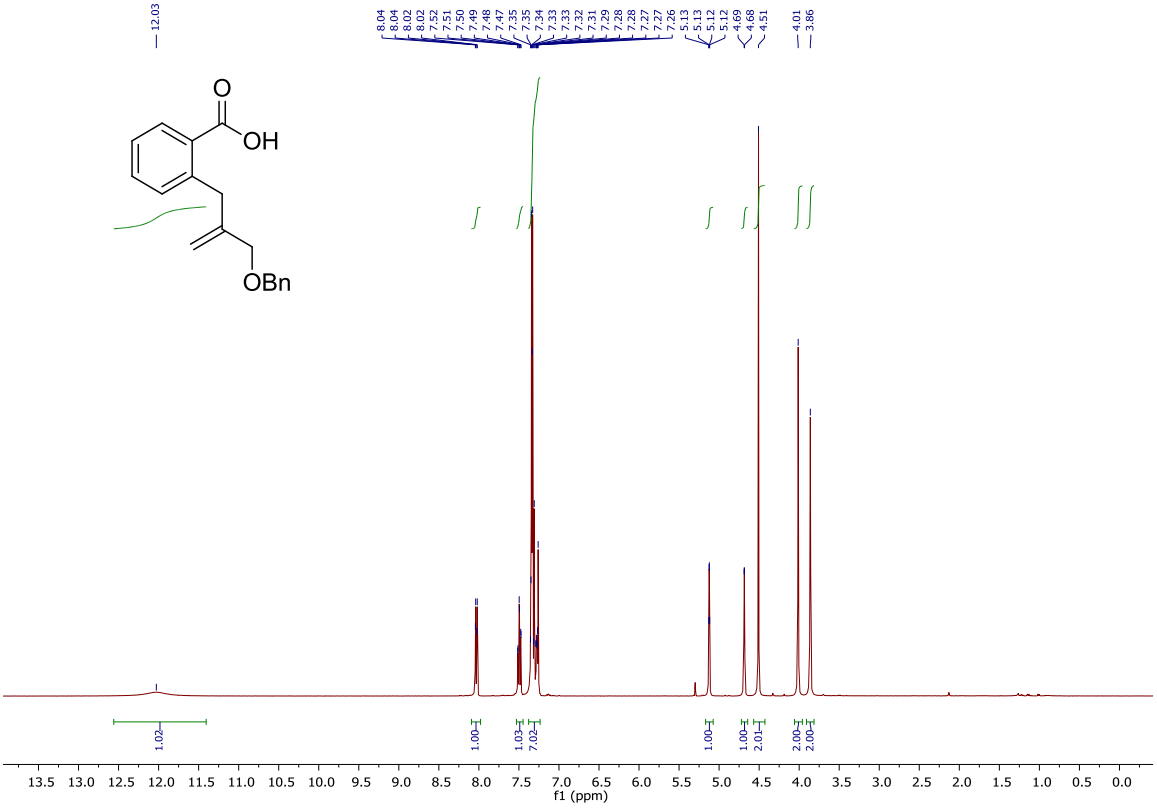
^{13}C-NMR (101 MHz, $(CD_3)_2CO$) of compound **4-methylene-7-phenylheptanoic acid (1s)**



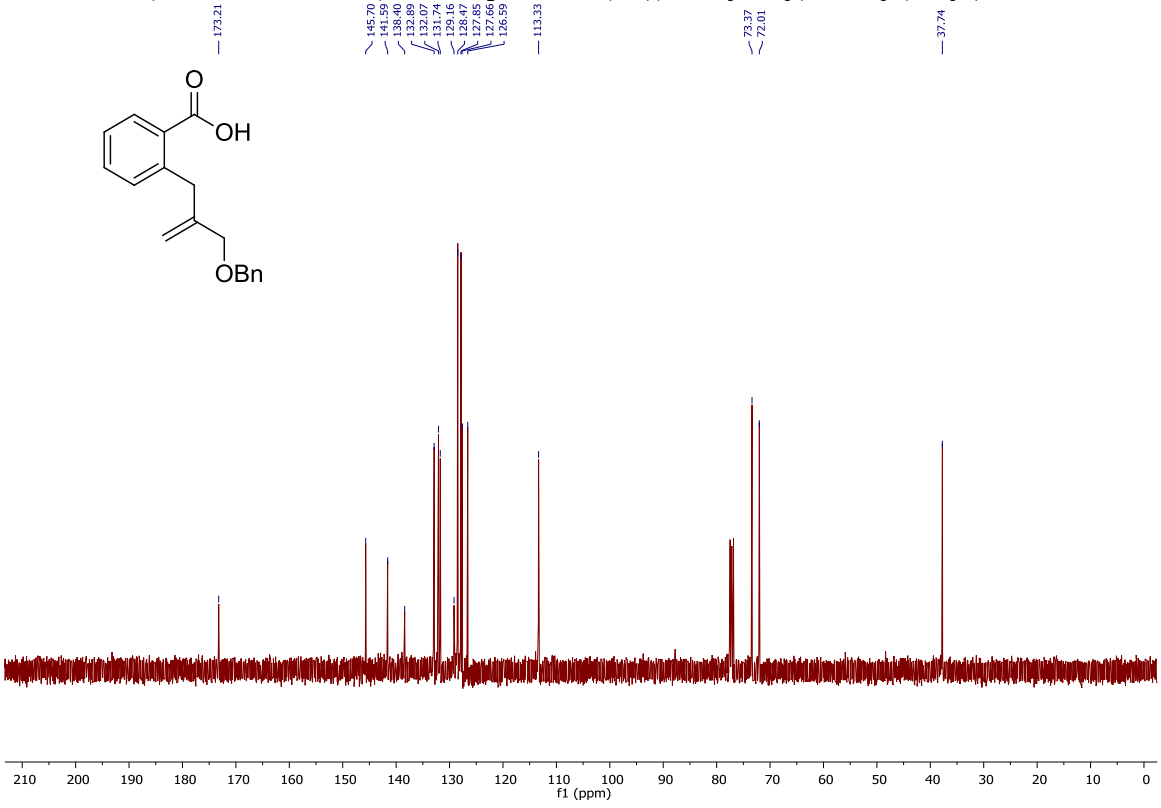
IR of compound **4-methylene-7-phenylheptanoic acid (1s)**



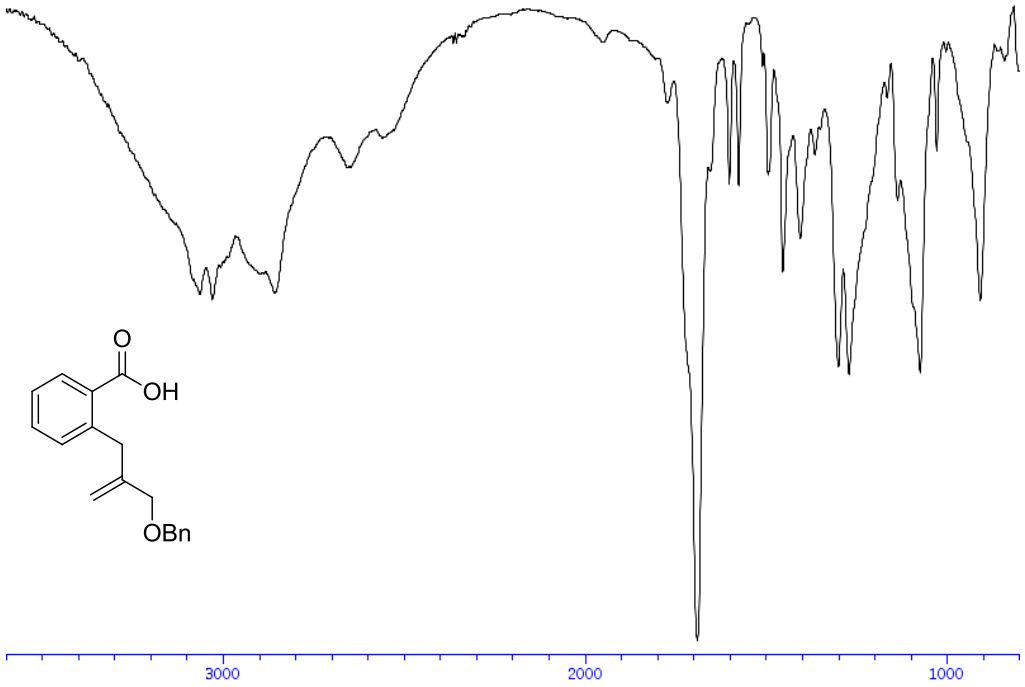
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **2-(2-((Benzyloxy)methyl)allyl)benzoic acid (1v)**



^{13}C-NMR (101 MHz, $CDCl_3$) of compound **2-(2-((Benzyloxy)methyl)allyl)benzoic acid (1v)**

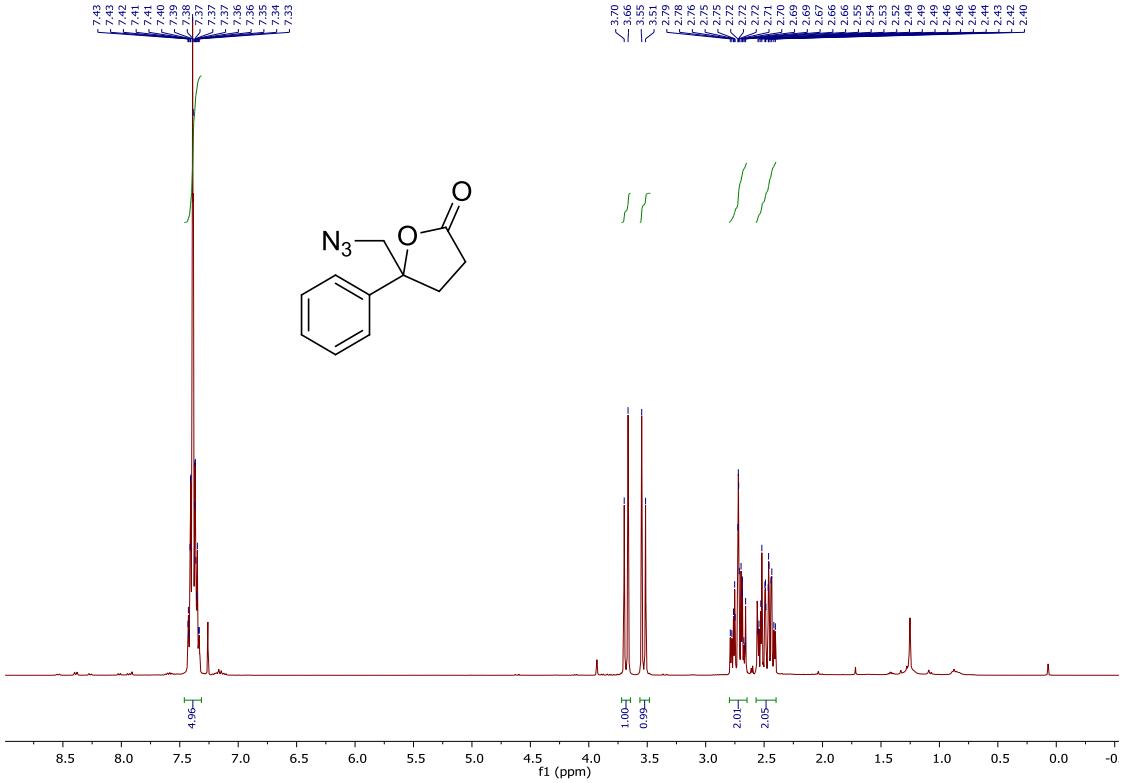


IR of compound **2-(2-((Benzyloxy)methyl)allyl)benzoic acid (1v)**

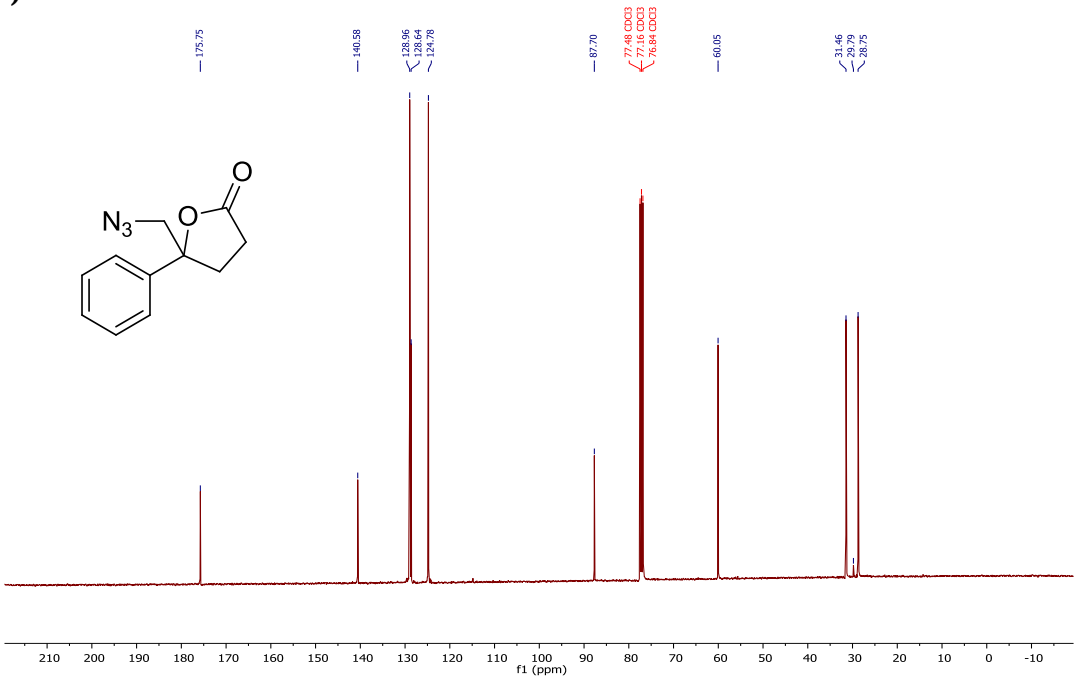


b. Spectra of compounds from photoredox catalysis

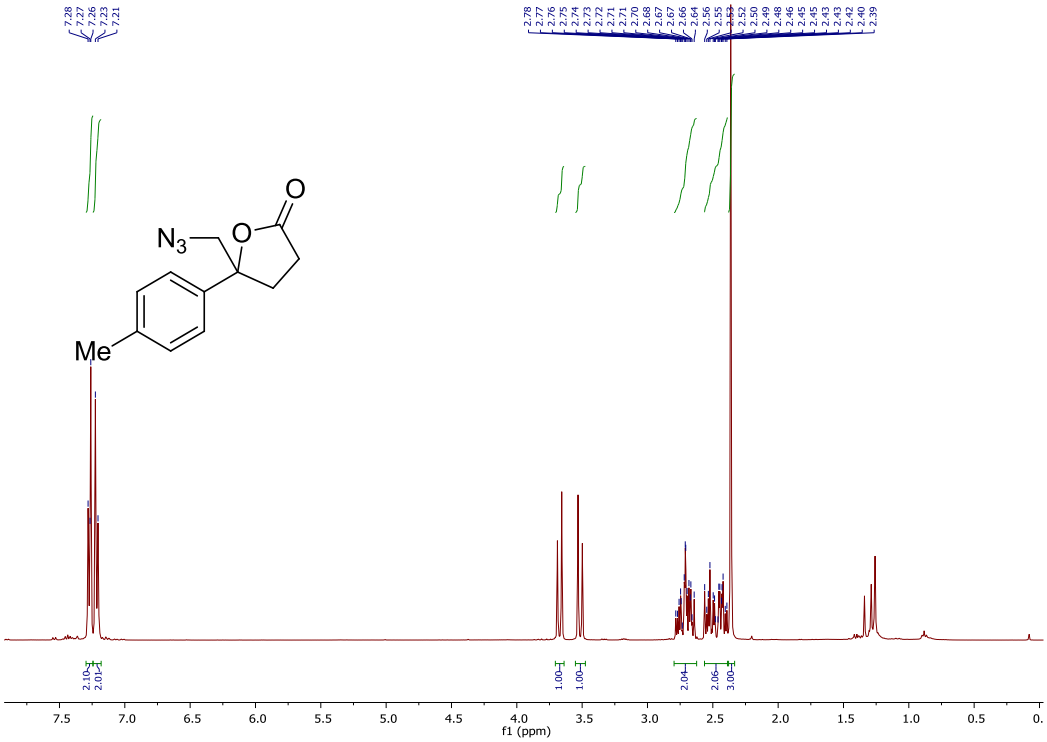
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-phenyldihydrofuran-2(3H)-one (2a)**



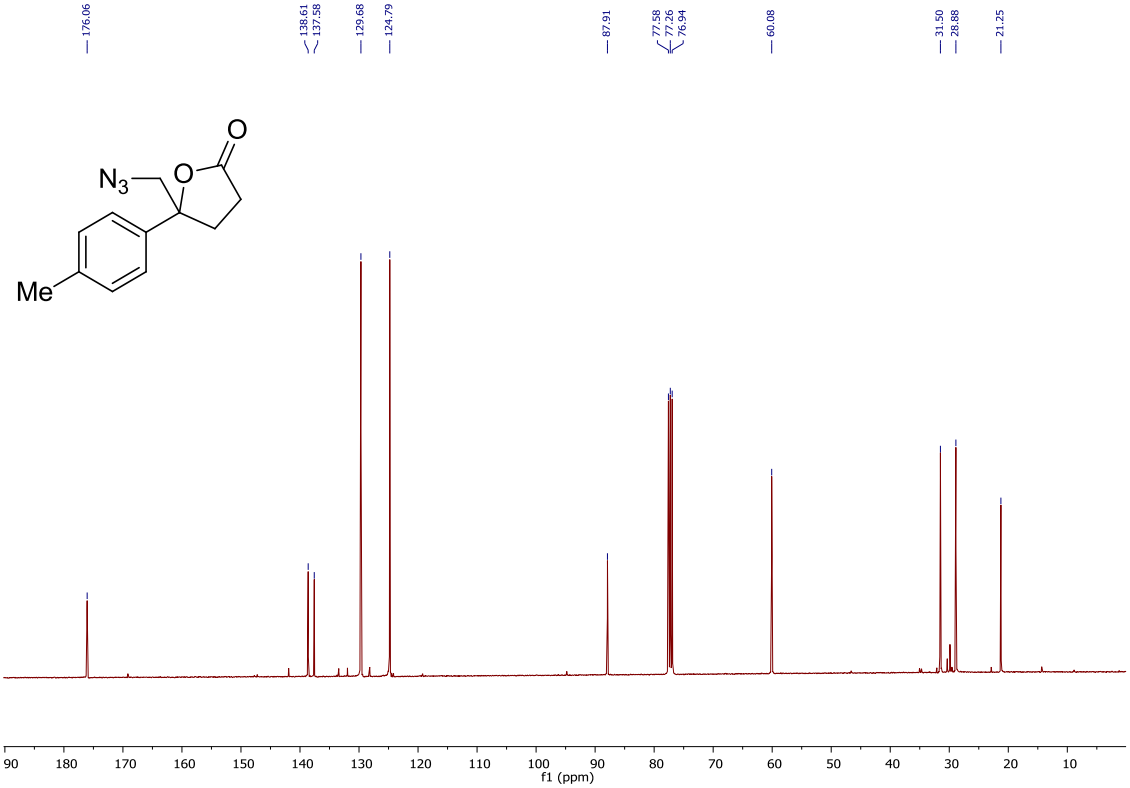
^{13}C NMR (101 MHz, $CDCl_3$) of compound 5-(azidomethyl)-5-phenyldihydrofuran-2(3H)-one (2a)



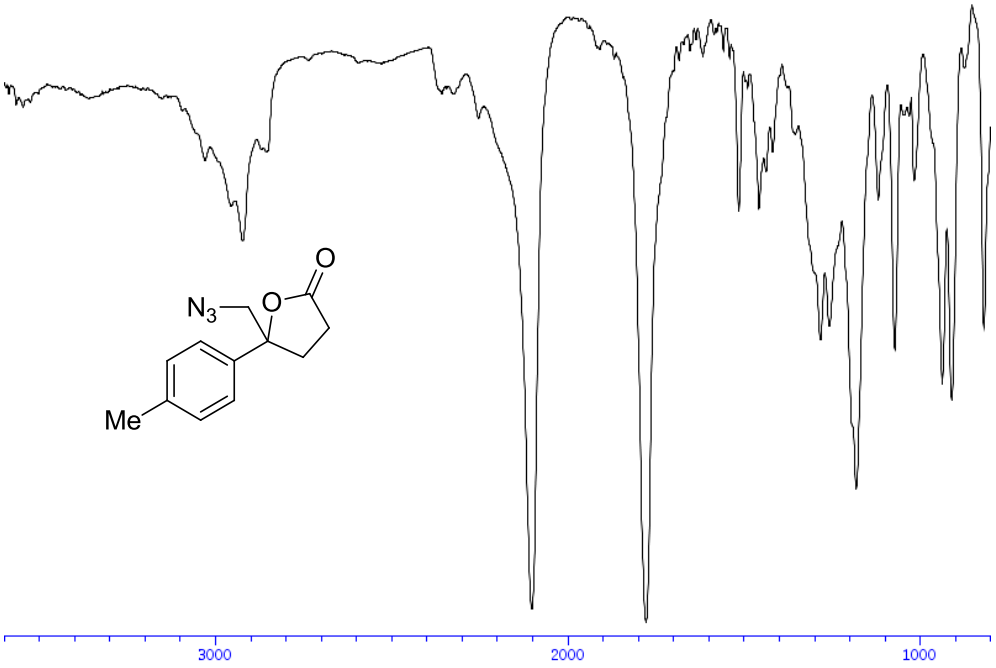
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(p-tolyl)dihydrofuran-2(3H)-one (2b)**



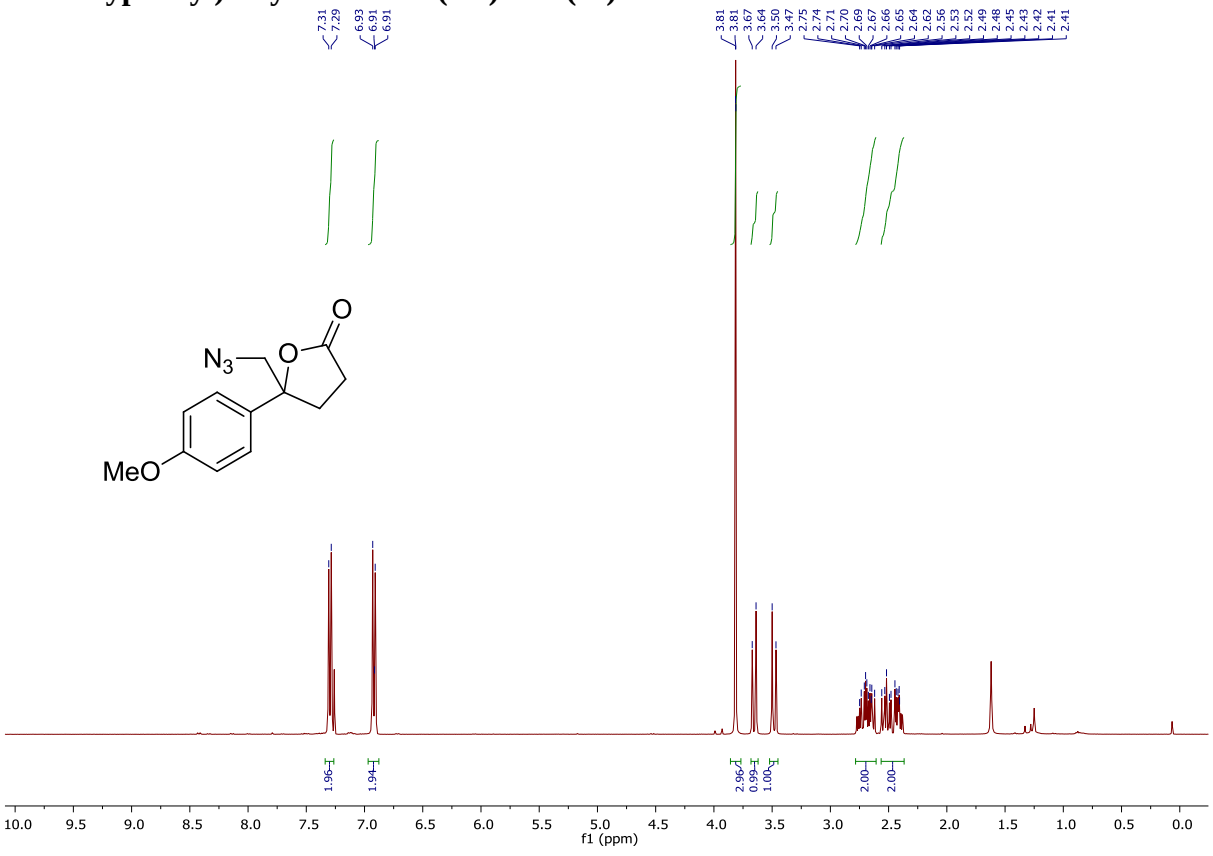
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(p-tolyl)dihydrofuran-2(3H)-one (2b)**



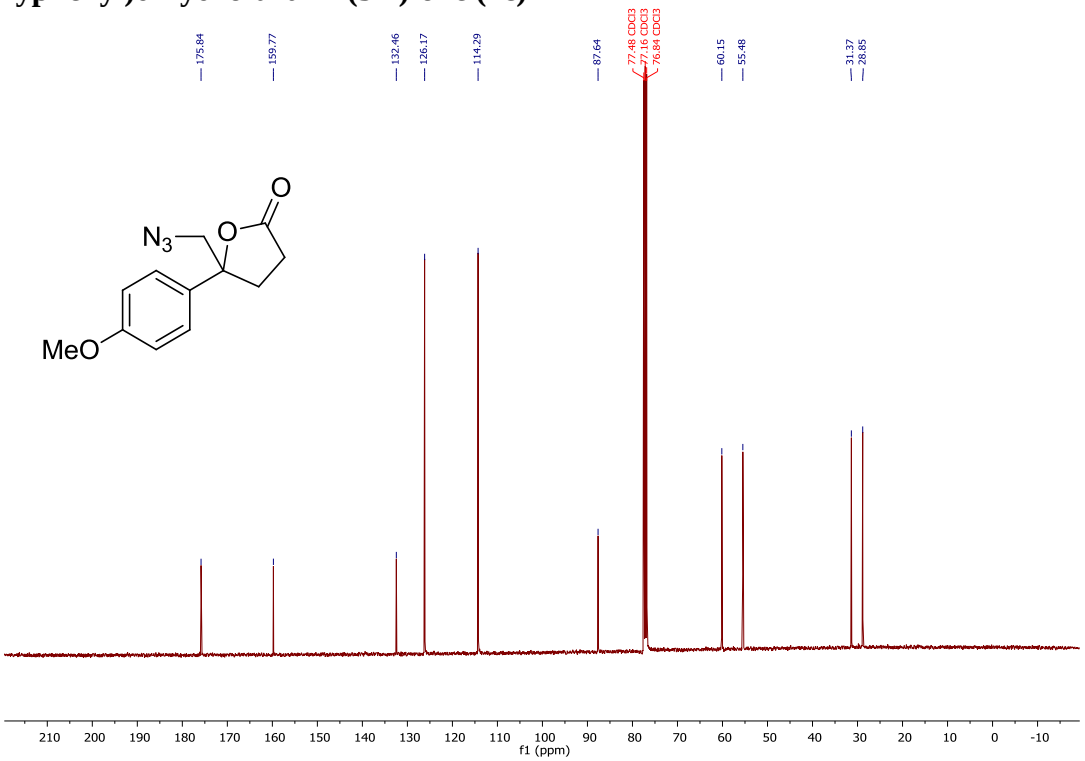
IR of compound **5-(azidomethyl)-5-(p-tolyl)dihydrofuran-2(3H)-one (2b)**



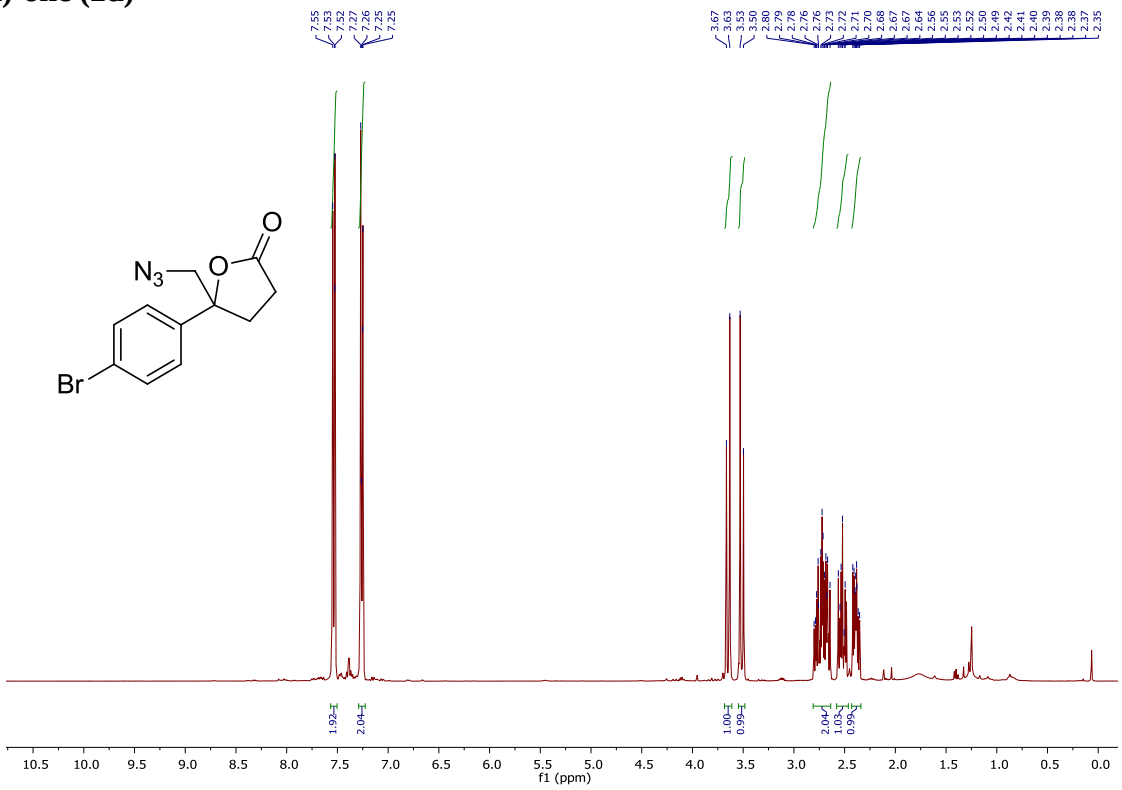
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3H)-one (2c)**



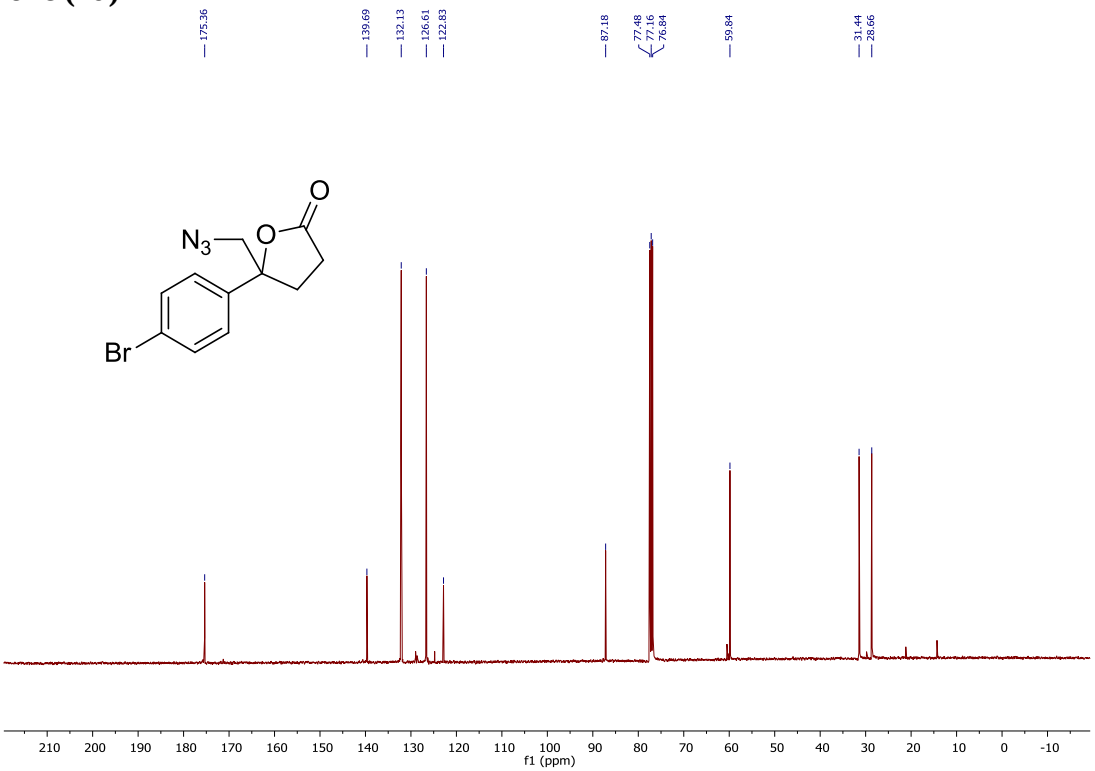
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3H)-one (2c)**



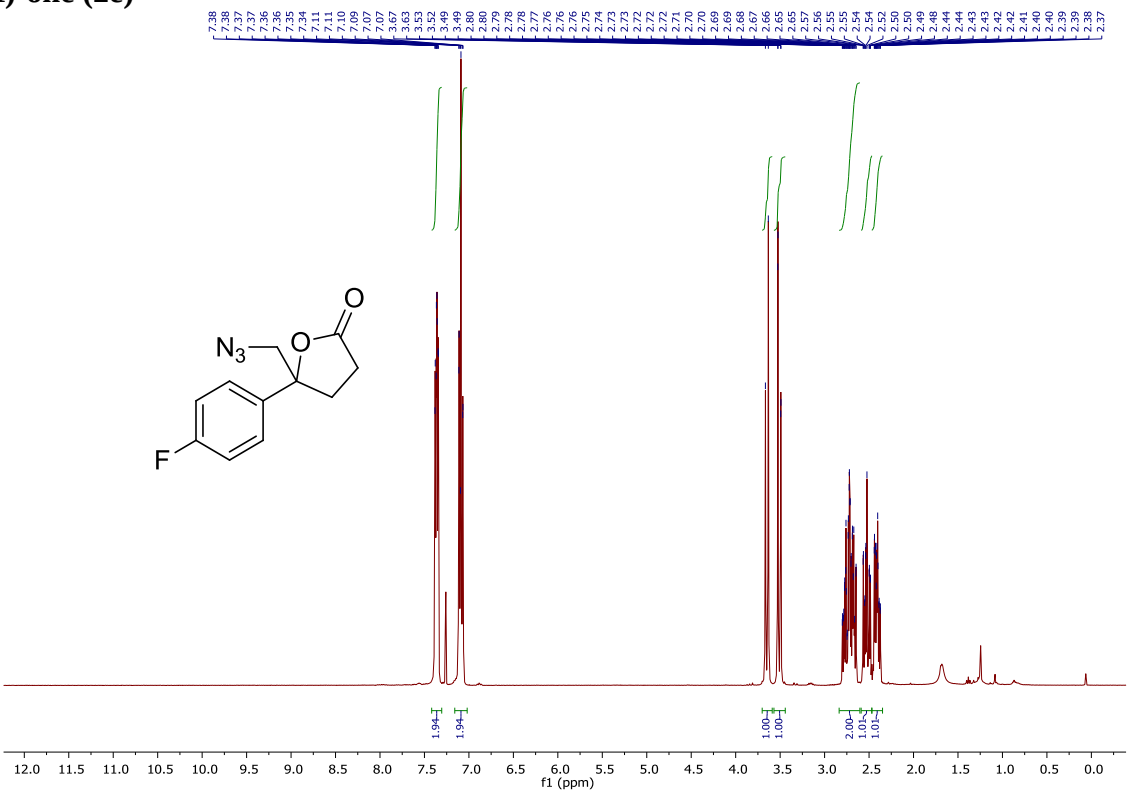
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-bromophenyl)dihydrofuran-2(3H)-one (2d)**



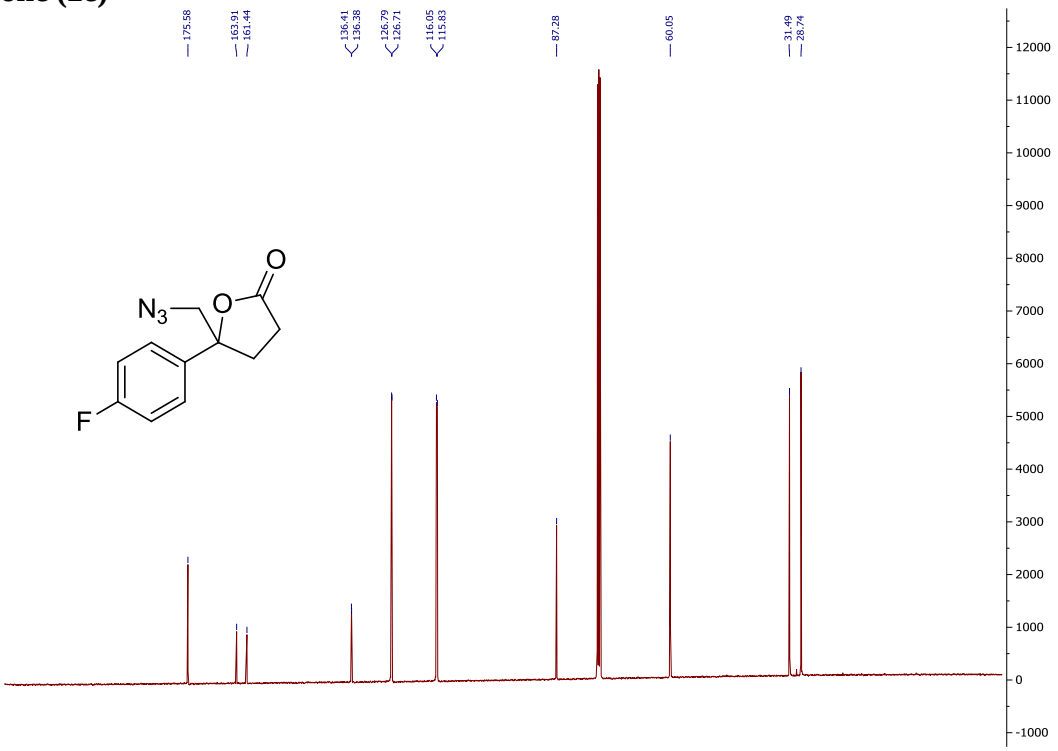
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-bromophenyl)dihydrofuran-2(3H)-one (2d)**



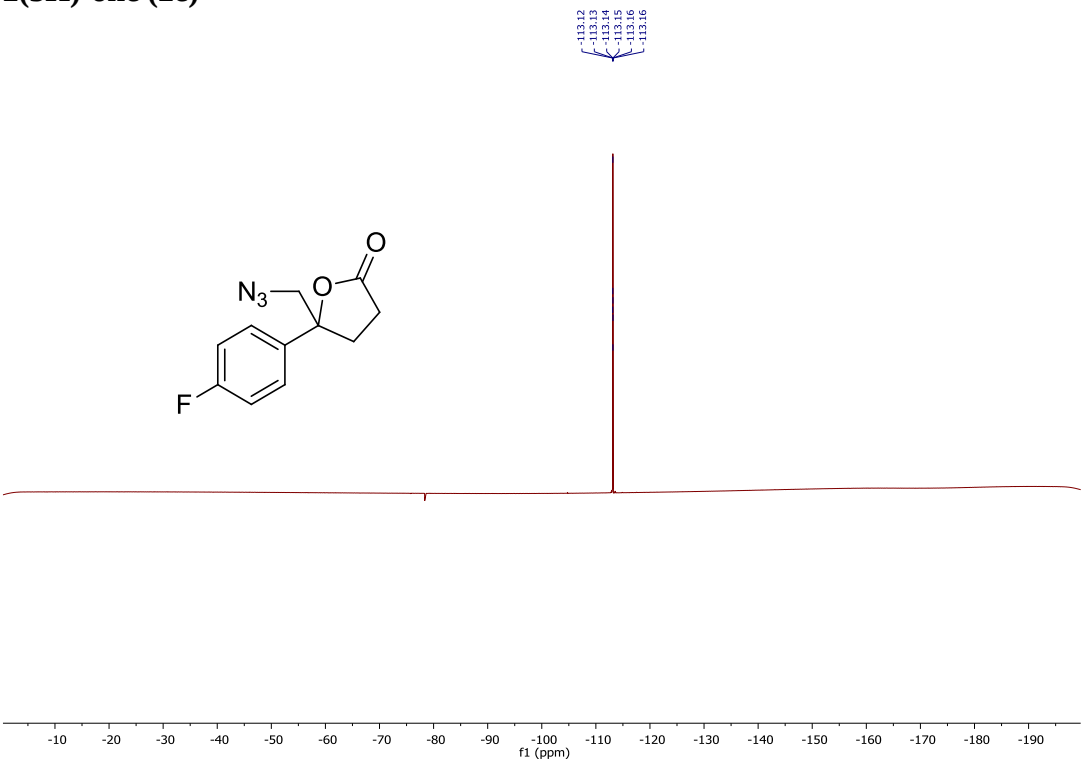
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3H)-one (2e)**



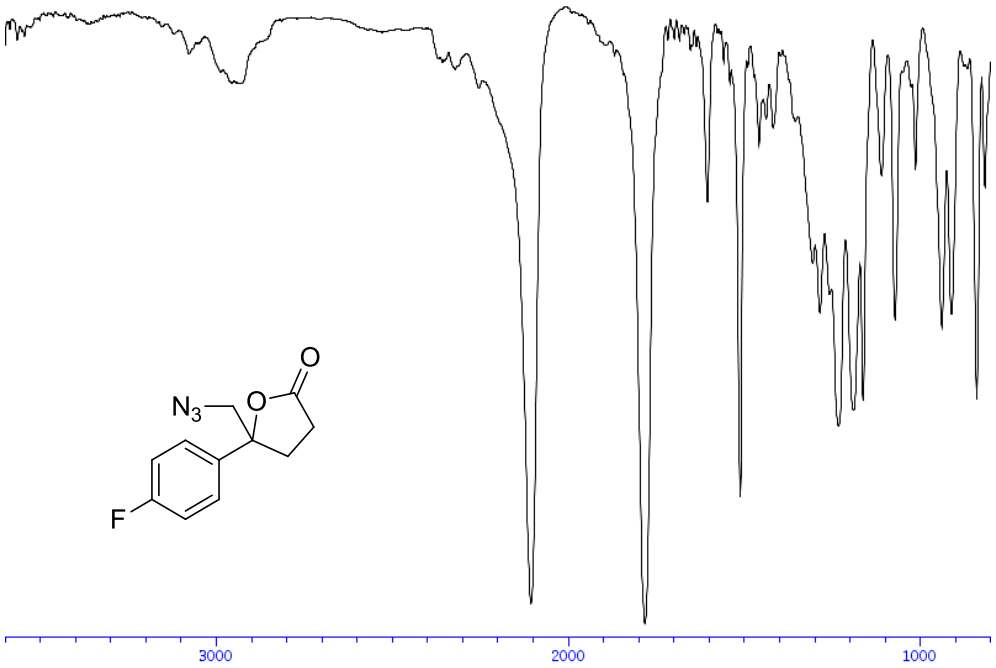
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3H)-one (2e)**



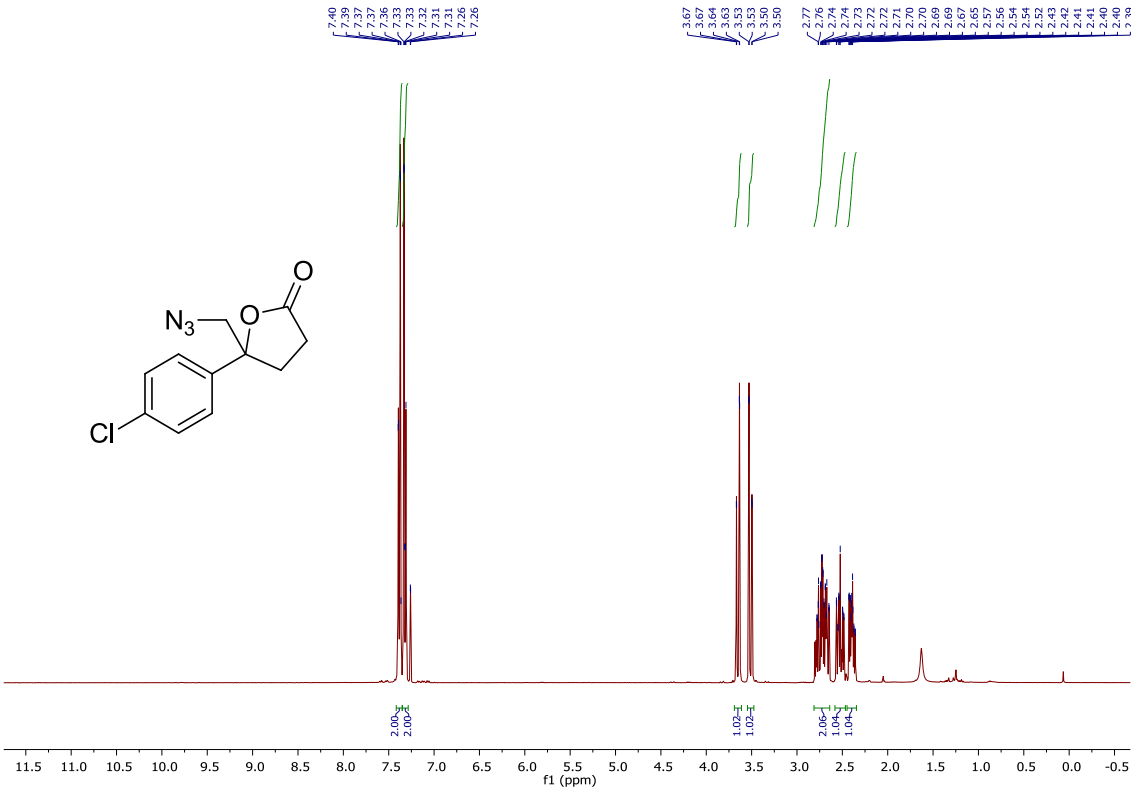
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3H)-one (2e)**



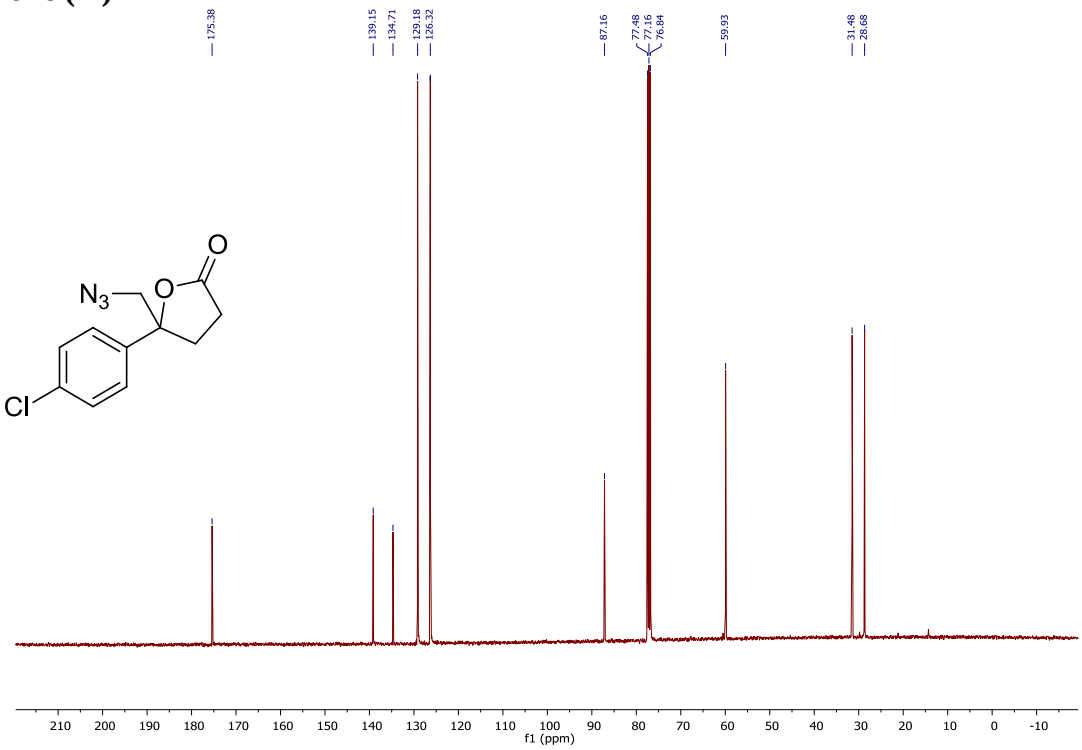
IR of compound **5-(azidomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3H)-one (2e)**



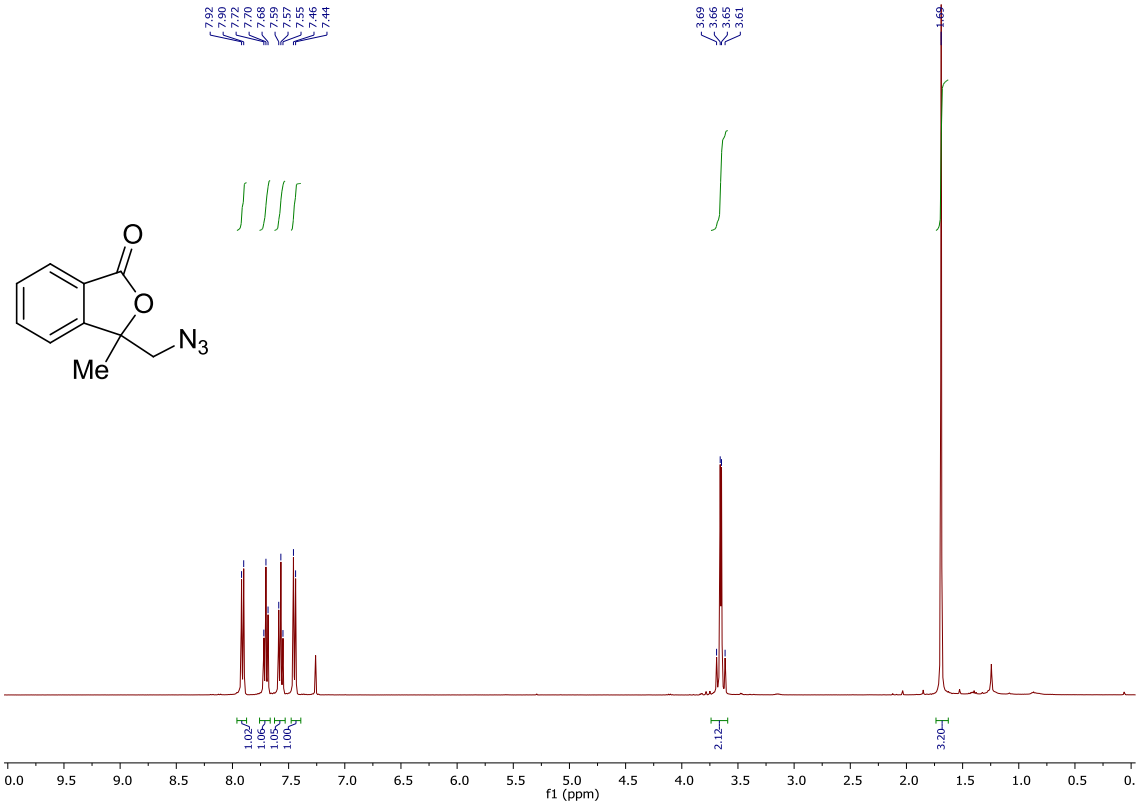
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-chlorophenyl)dihydrofuran-2(3H)-one (2f)**



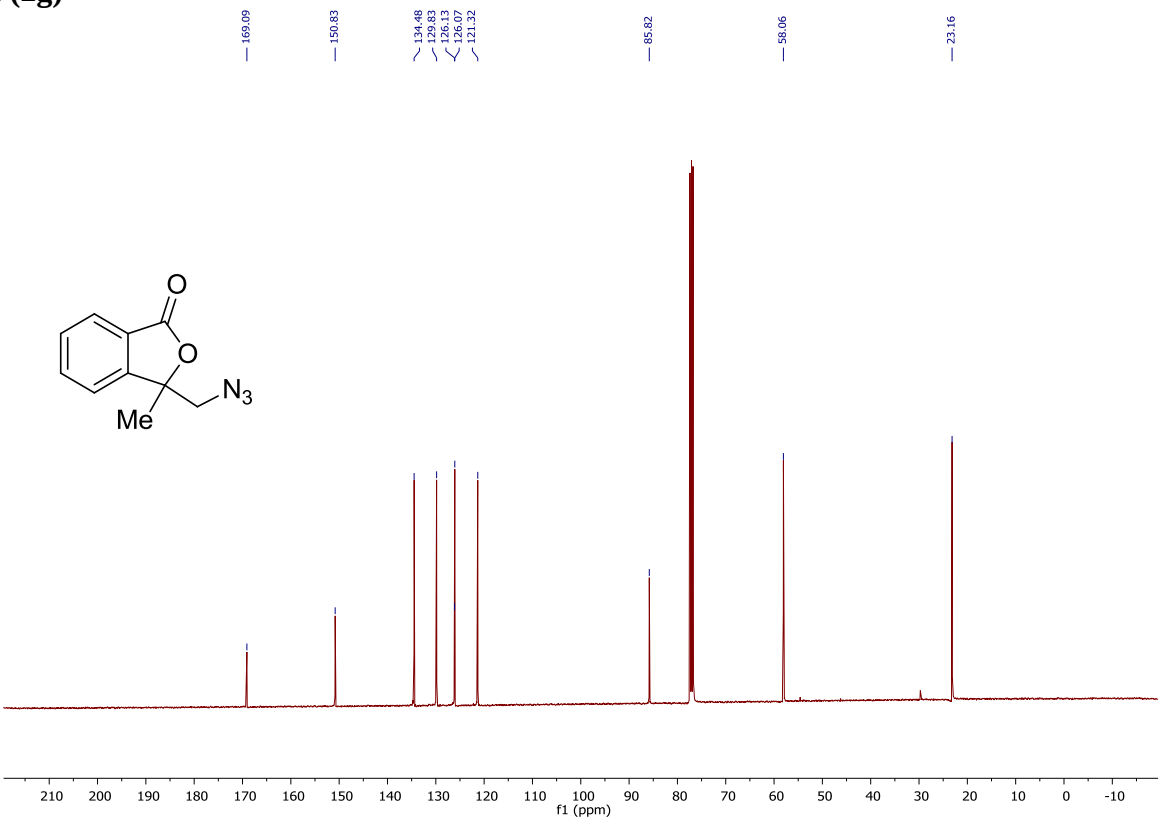
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(4-chlorophenyl)dihydrofuran-2(3H)-one (2f)**



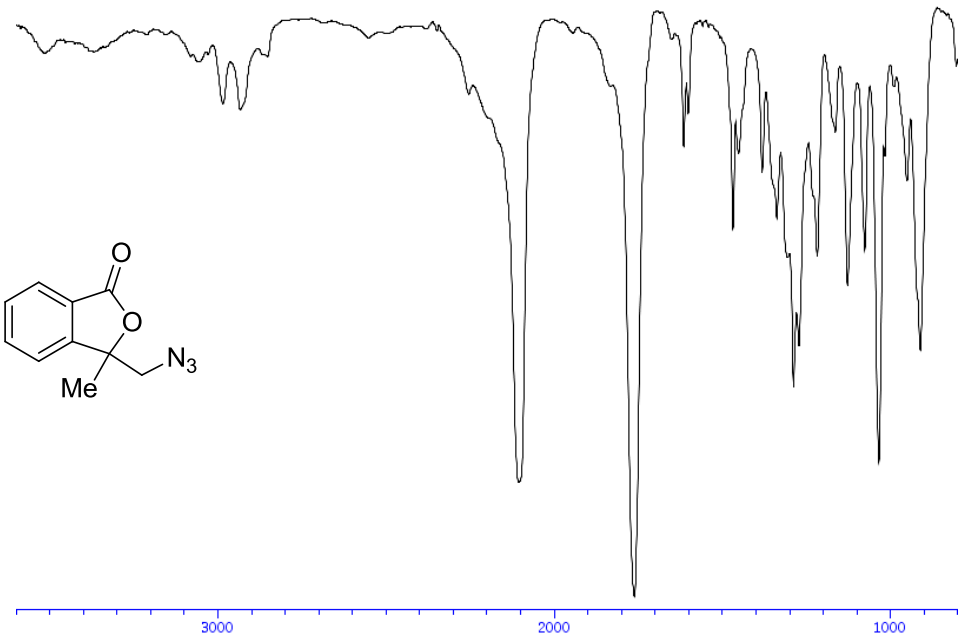
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



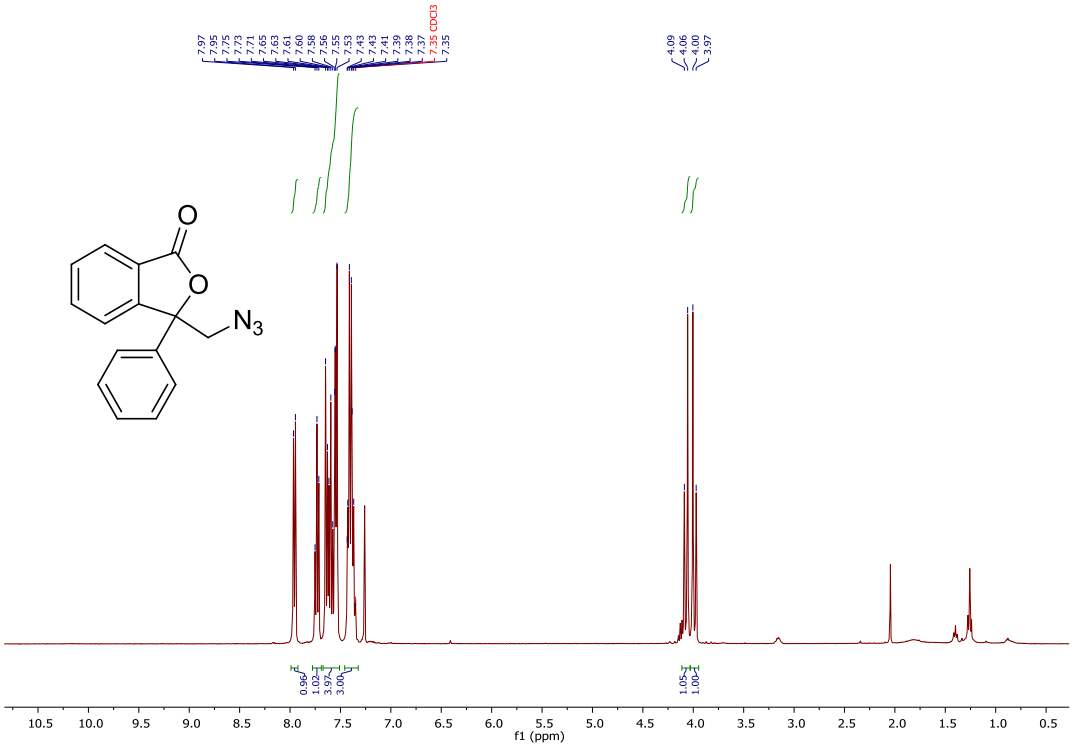
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



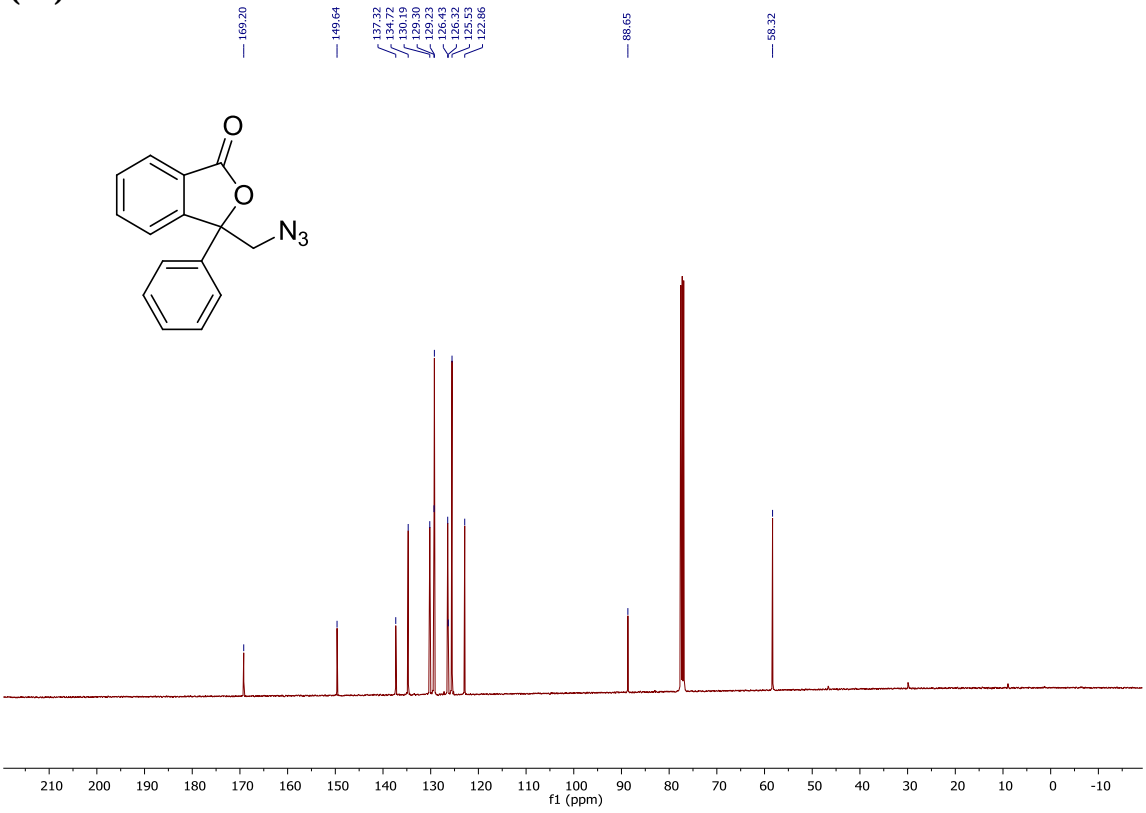
IR of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



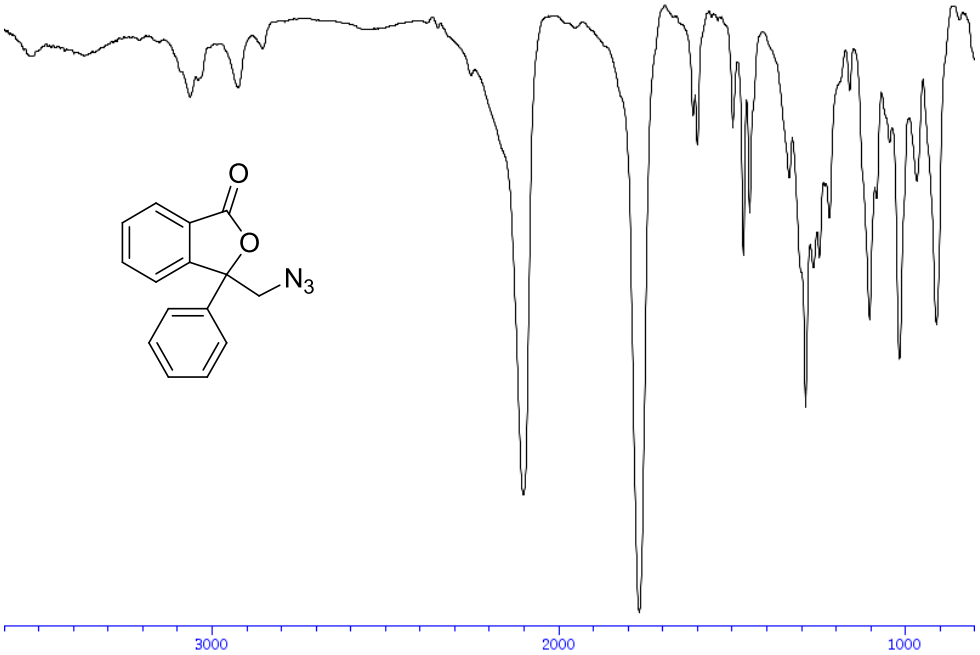
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-phenylisobenzofuran-1(3H)-one (2h)**



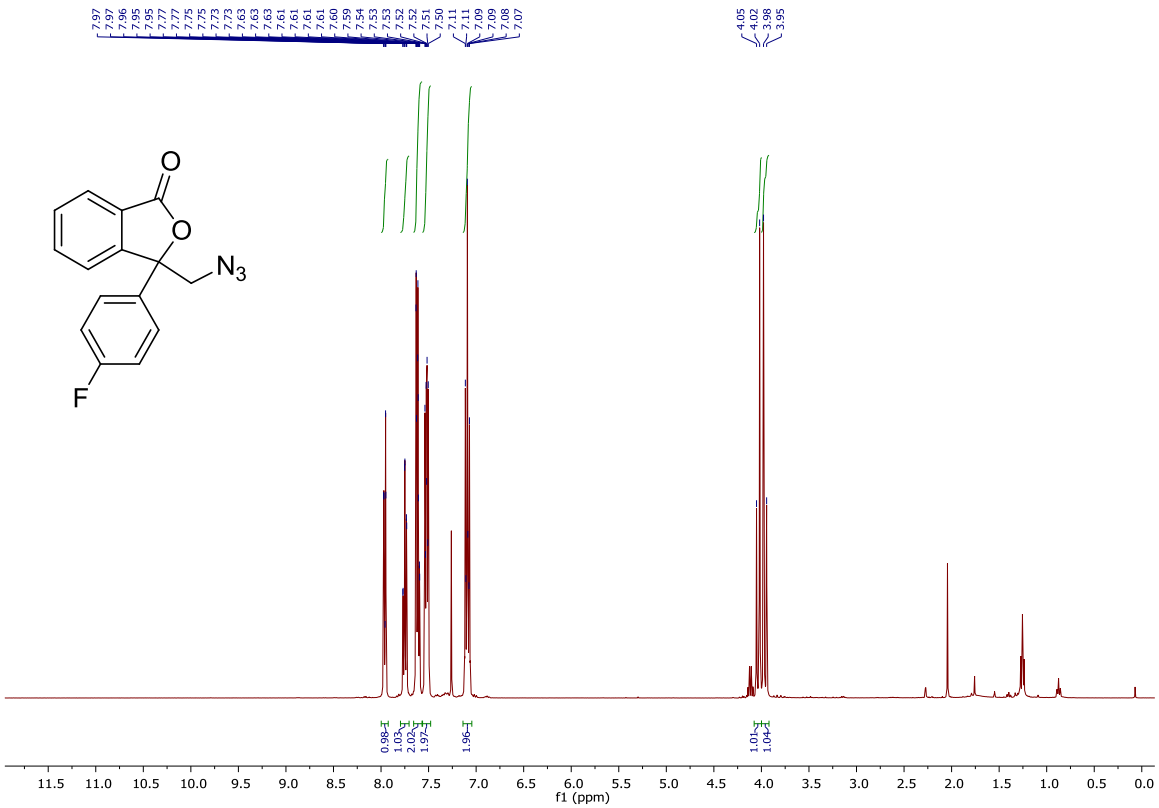
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-phenylisobenzofuran-1(3H)-one (2h)**



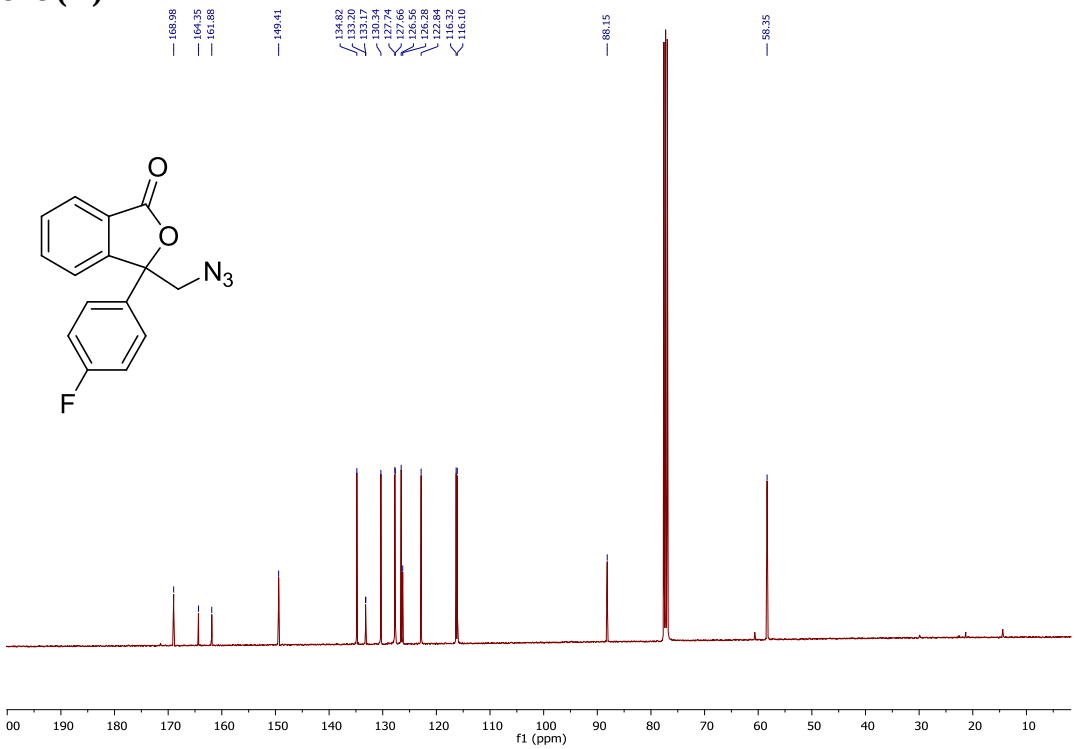
IR of compound **3-(azidomethyl)-3-phenylisobenzofuran-1(3H)-one (2h)**



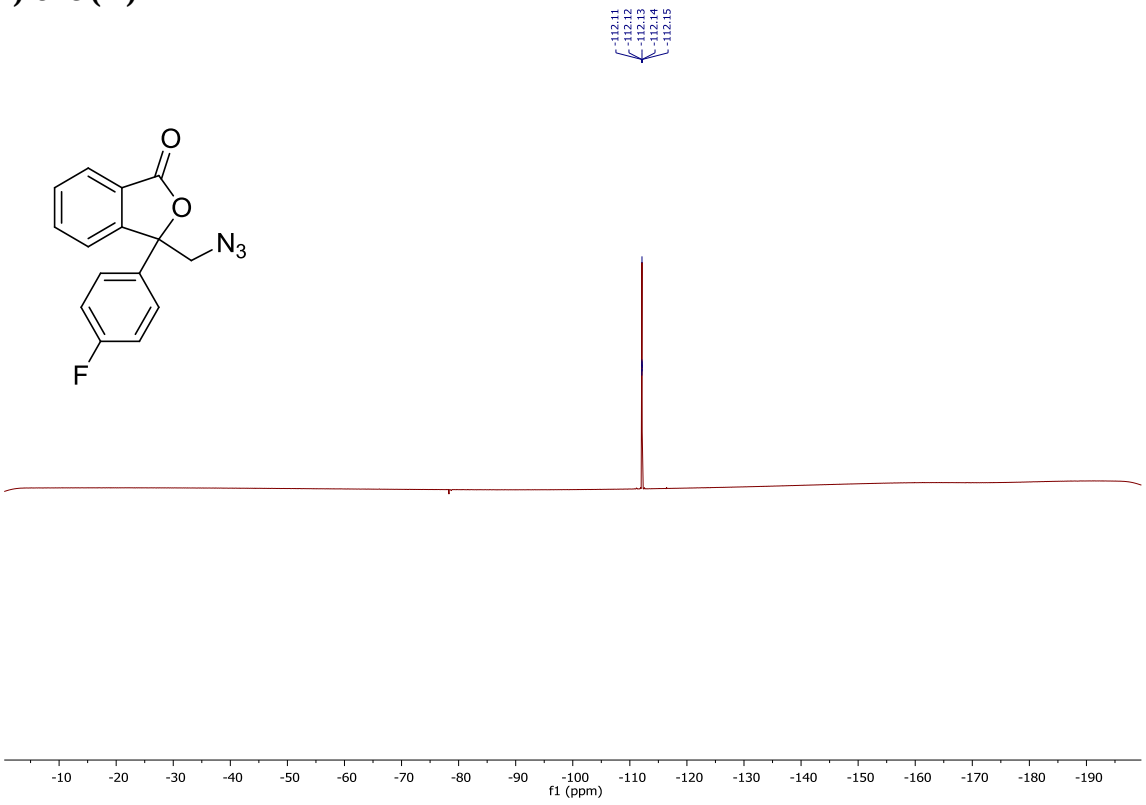
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (2i)**



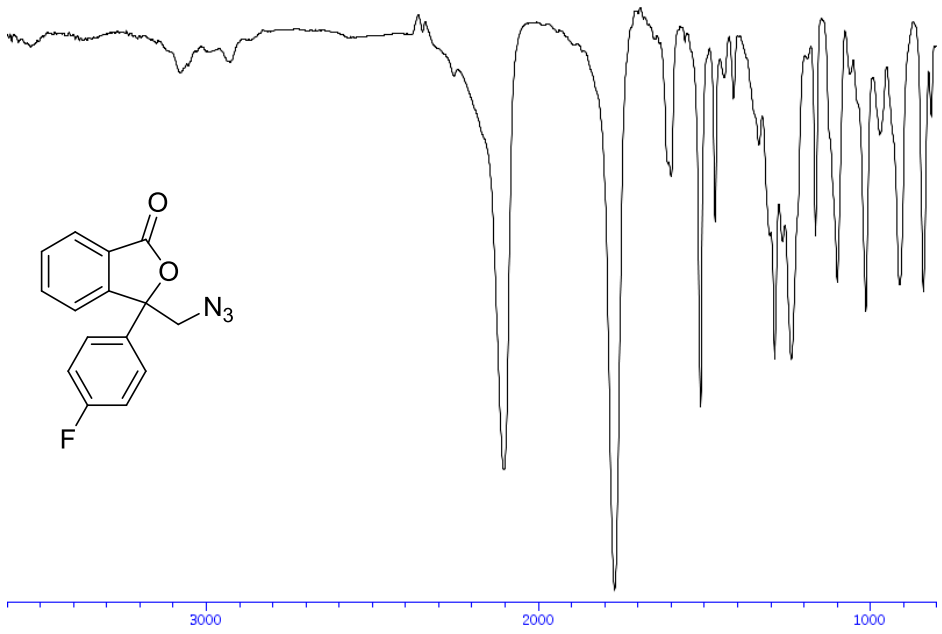
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (2i)**



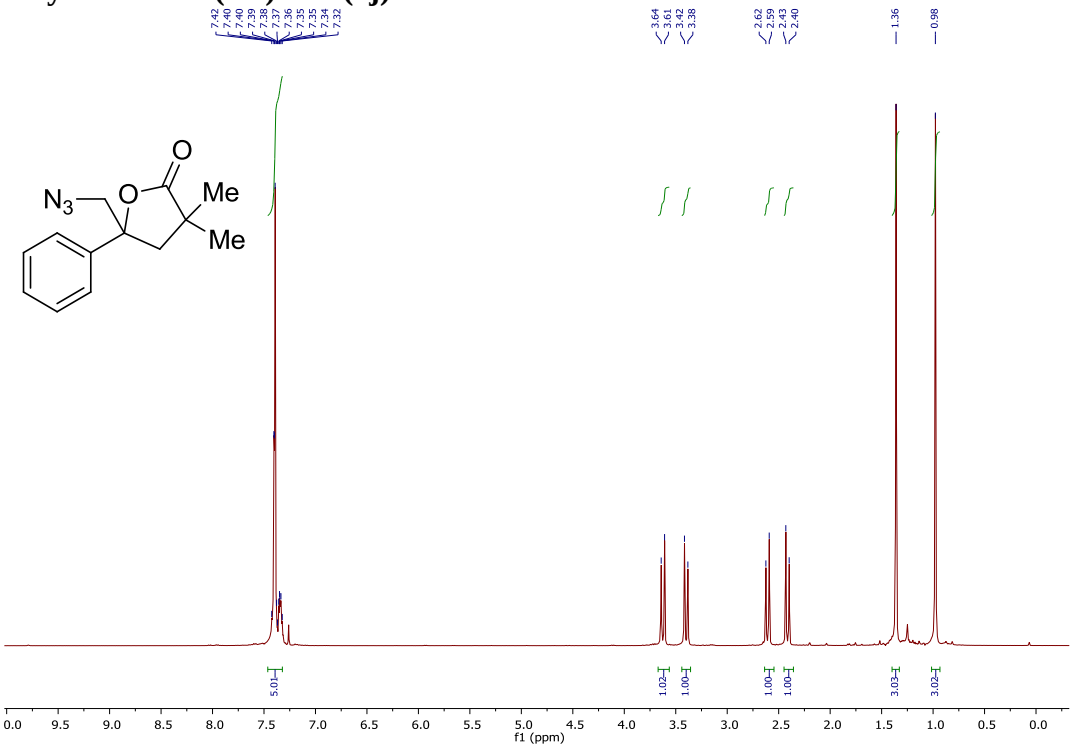
^{19}F NMR (376 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (2i)**



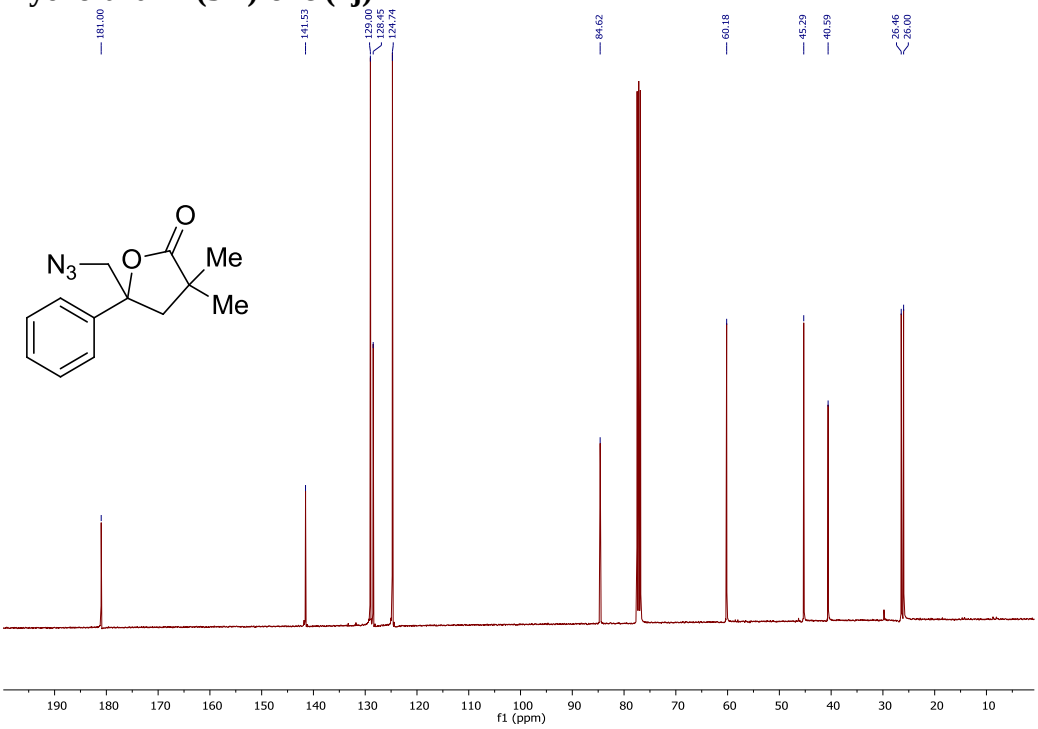
IR of compound **3-(azidomethyl)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (2i)**



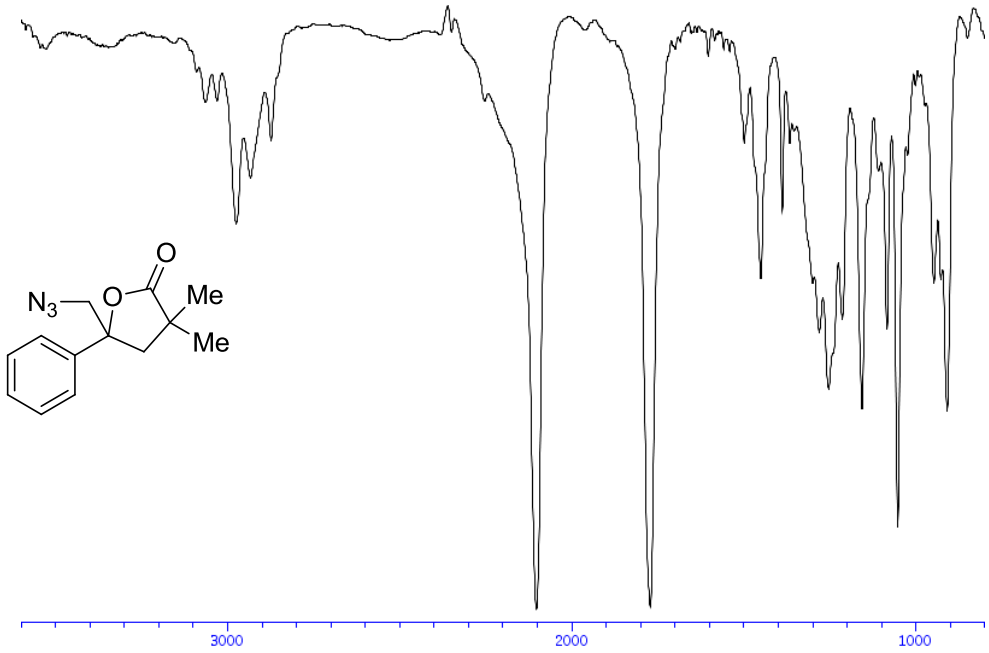
^{1}H NMR (400 MHz, $CDCl_3$) of compound**5-(azidomethyl)-3,3-dimethyl-5-phenyldihydrofuran-2(3H)-one (2j)**



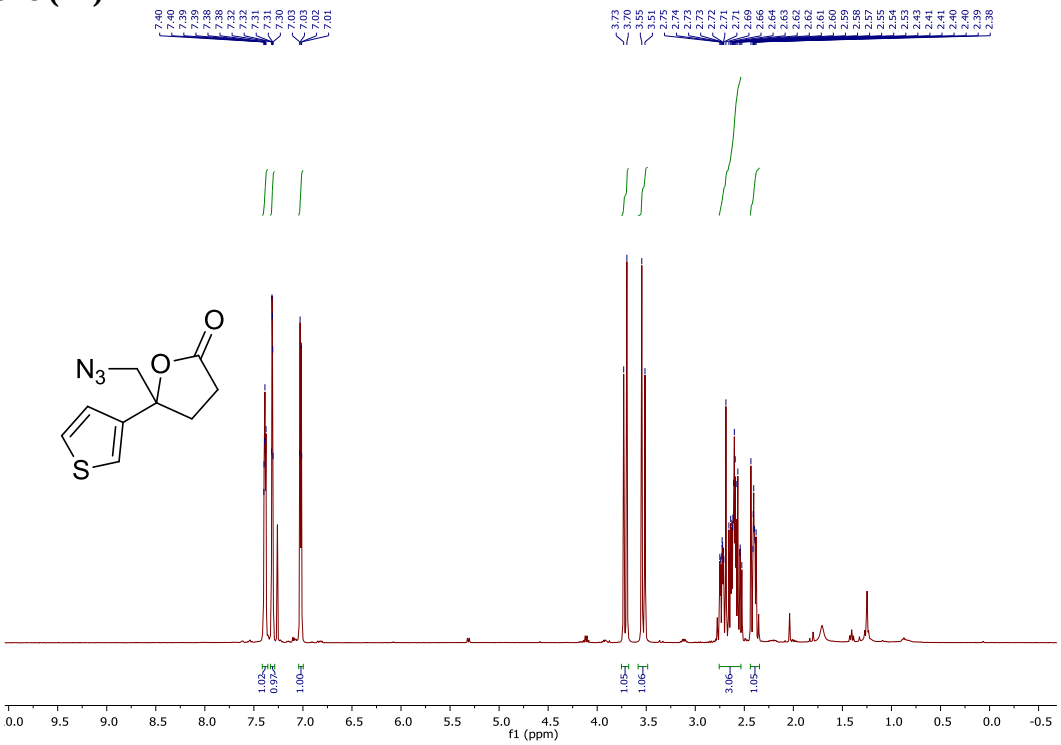
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-3,3-dimethyl-5-phenyldihydrofuran-2(3H)-one (2j)**



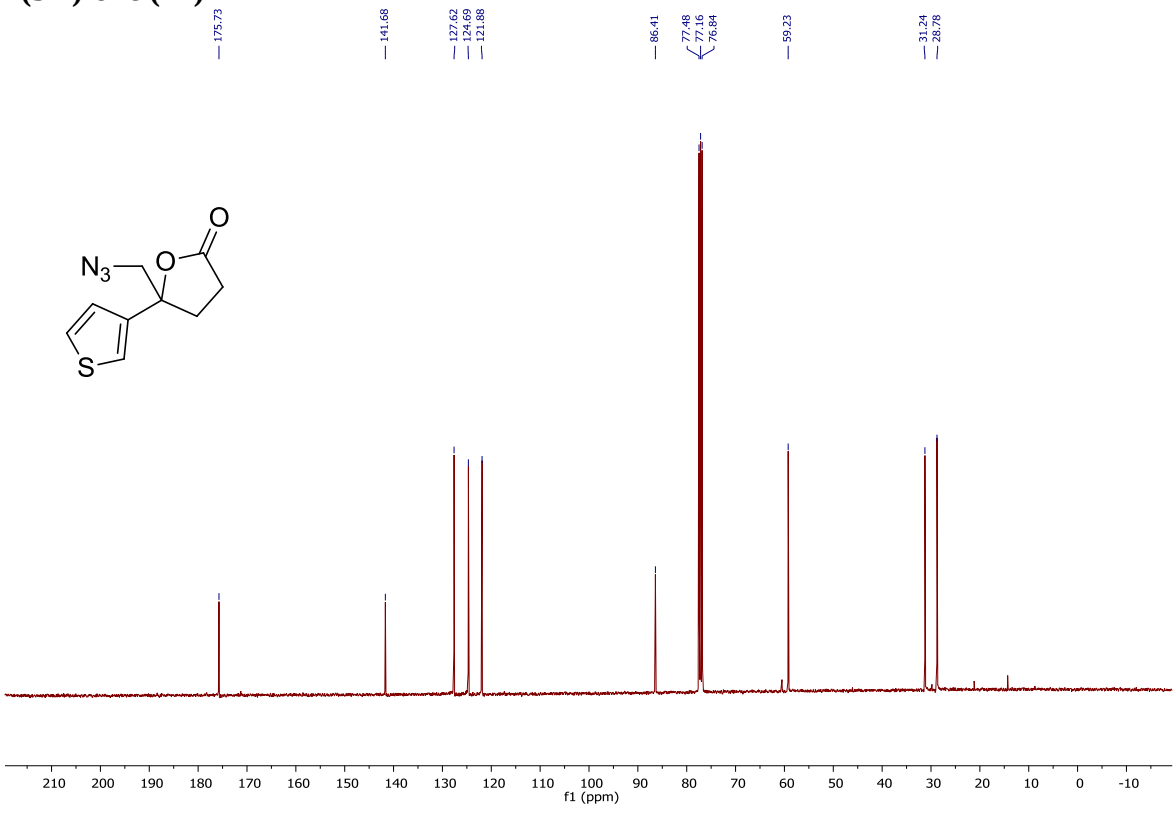
IR of compound **5-(azidomethyl)-3,3-dimethyl-5-phenyldihydrofuran-2(3H)-one (2j)**



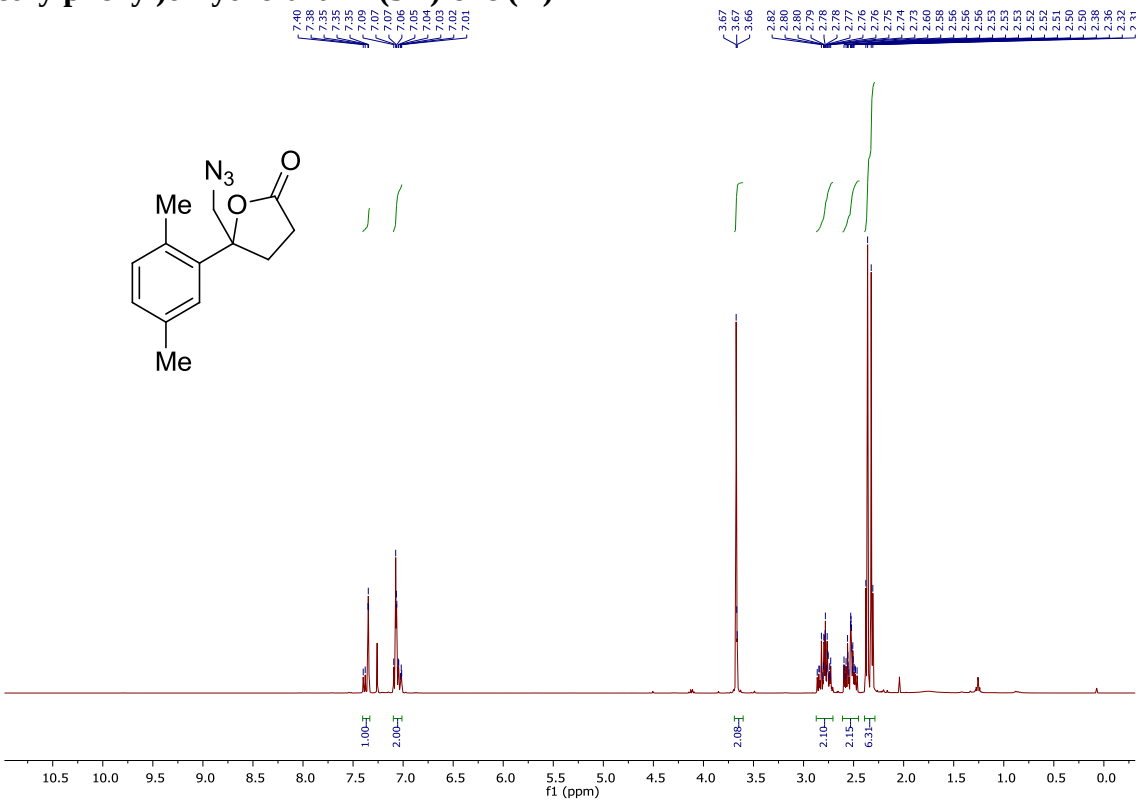
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(thiophen-3-yl)dihydrofuran-2(3H)-one (2k)**



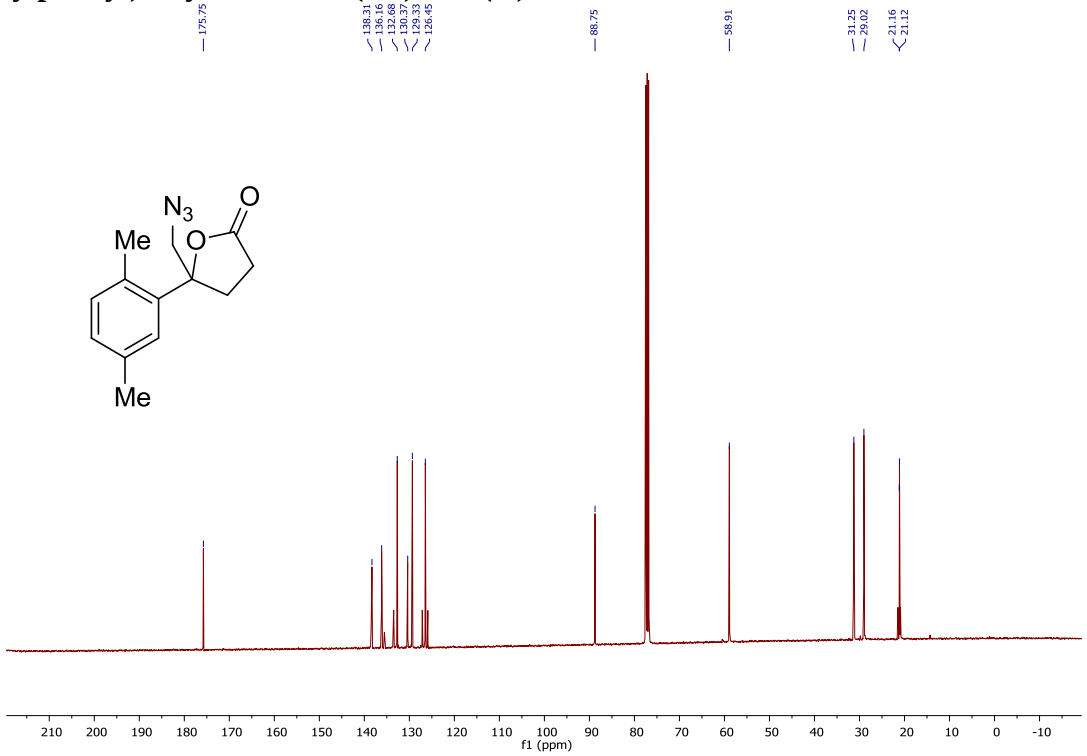
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(thiophen-3-yl)dihydrofuran-2(3H)-one (2k)**



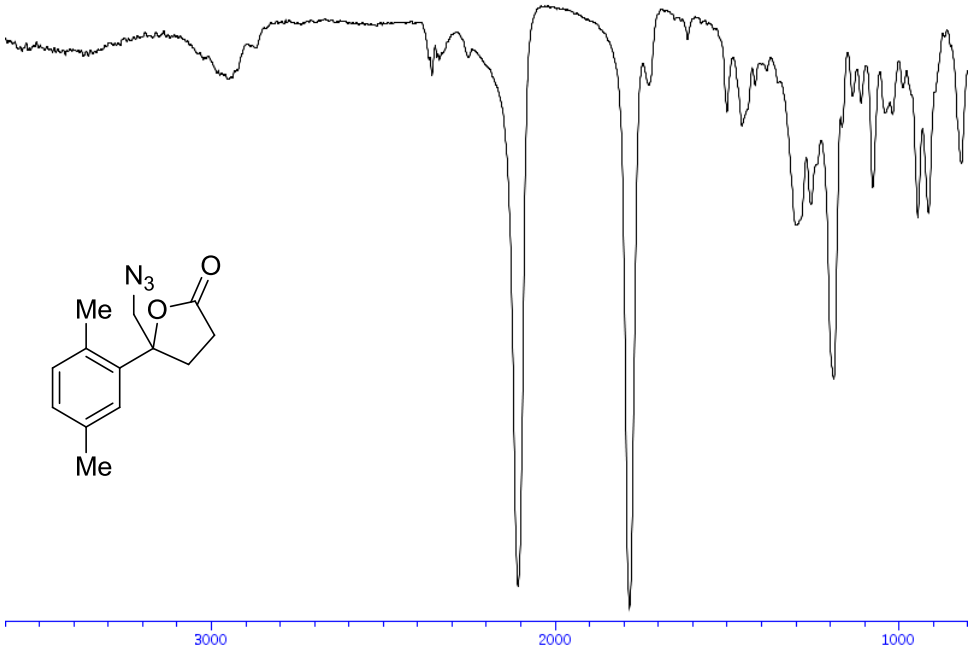
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(2,5-dimethylphenyl)dihydrofuran-2(3H)-one (2l)**



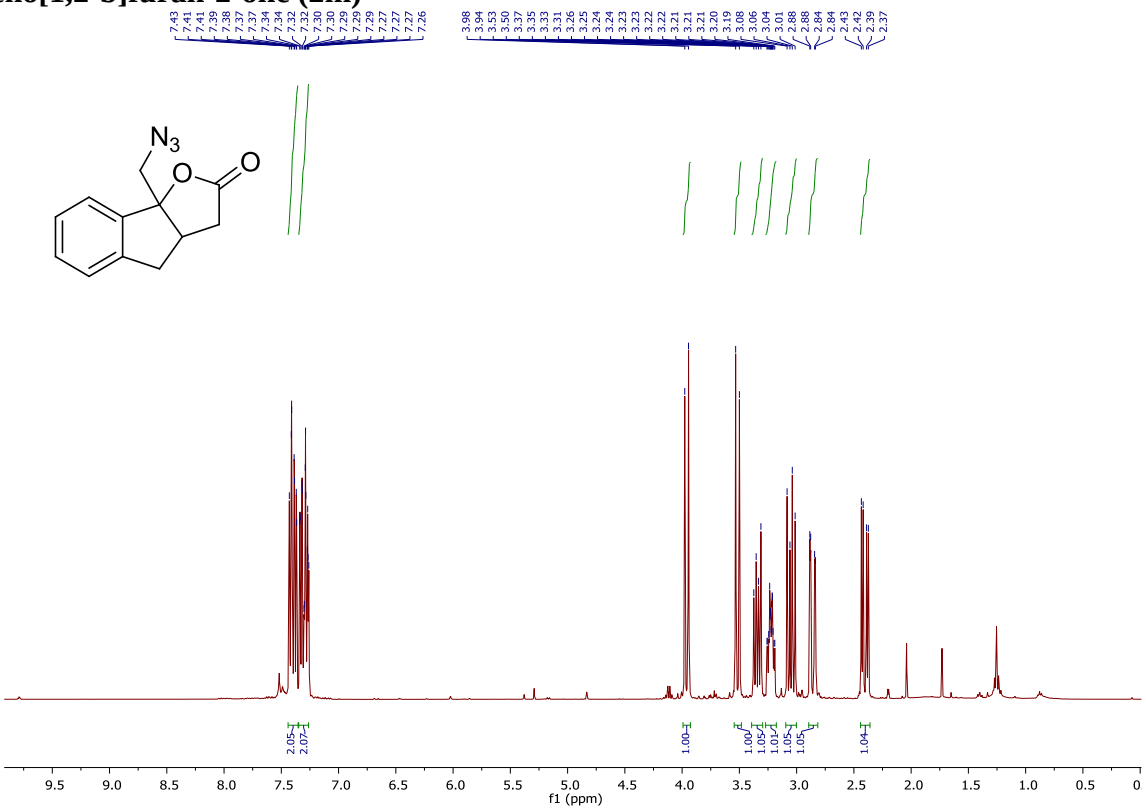
^{13}C NMR (101 MHz, $CDCl_3$) of compound **-(azidomethyl)-5-(2,5-dimethylphenyl)dihydrofuran-2(3H)-one (2l)**



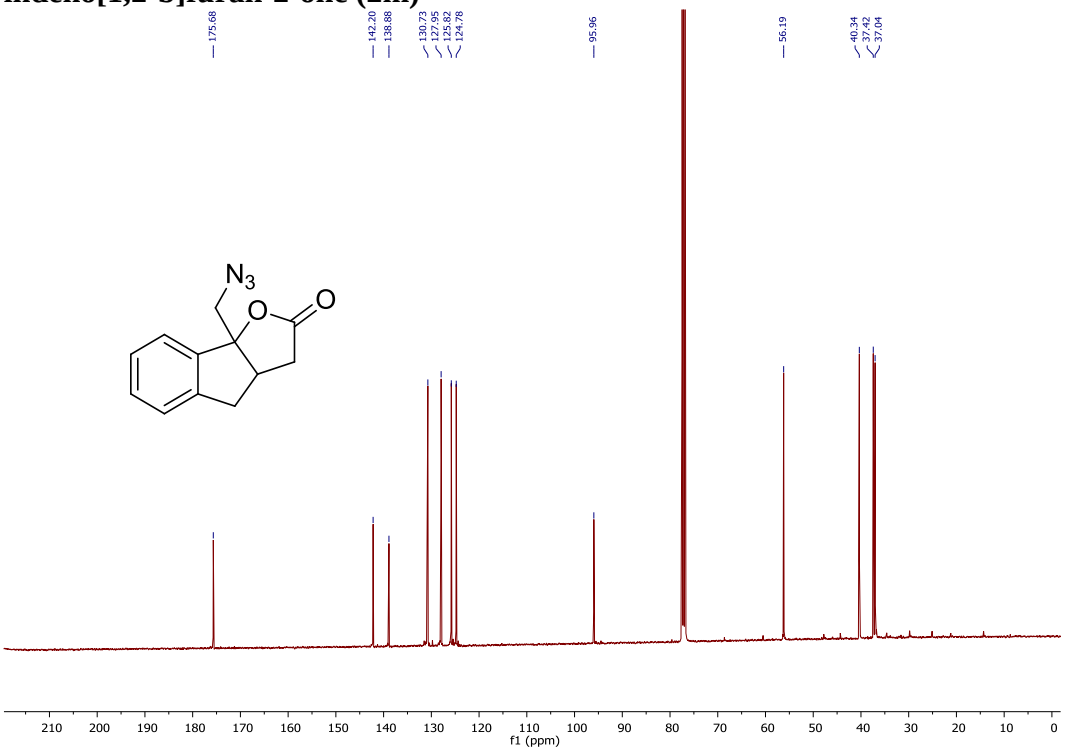
IR of compound **-(azidomethyl)-5-(2,5-dimethylphenyl)dihydrofuran-2(3H)-one (2l)**



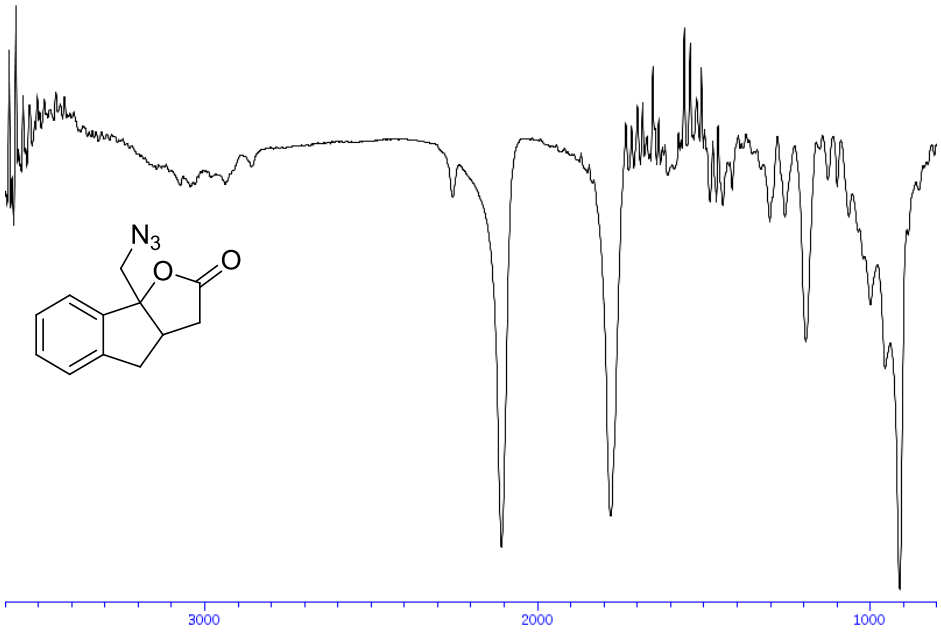
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8b-(azidomethyl)-3,3a,4,8b-tetrahydro-2H-indeno[1,2-b]furan-2-one (2m)**



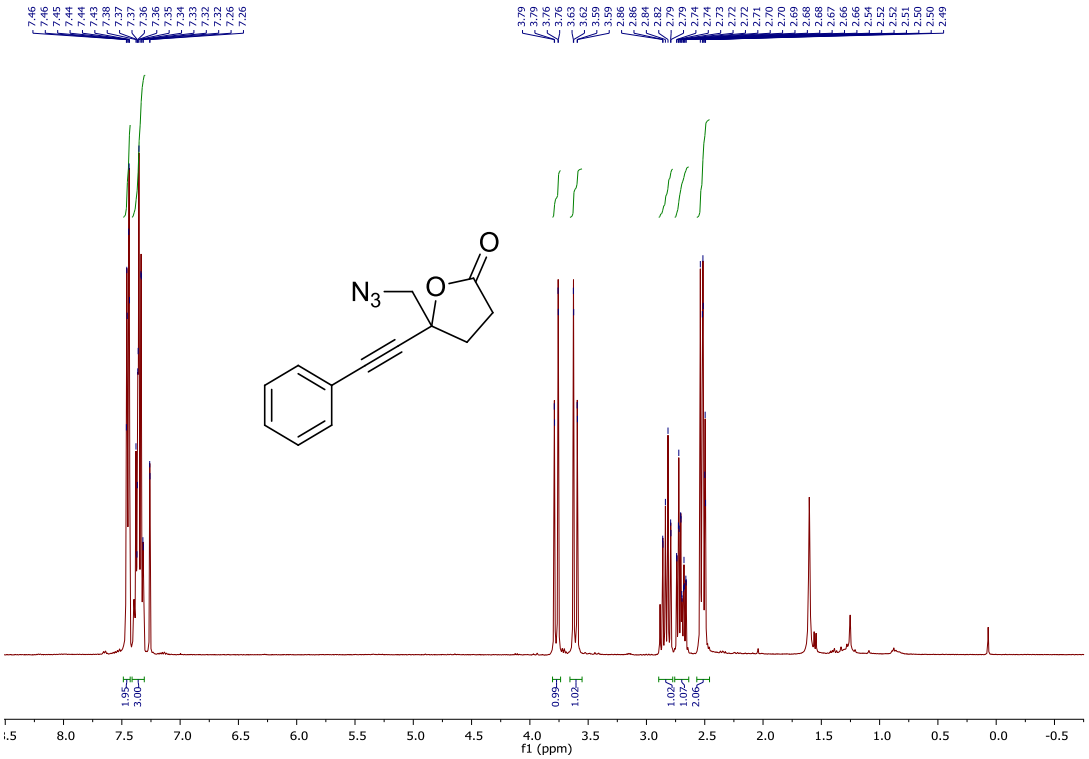
^{13}C NMR (101 MHz, $CDCl_3$) of compound **8b-(azidomethyl)-3,3a,4,8b-tetrahydro-2H-indeno[1,2-b]furan-2-one (2m)**



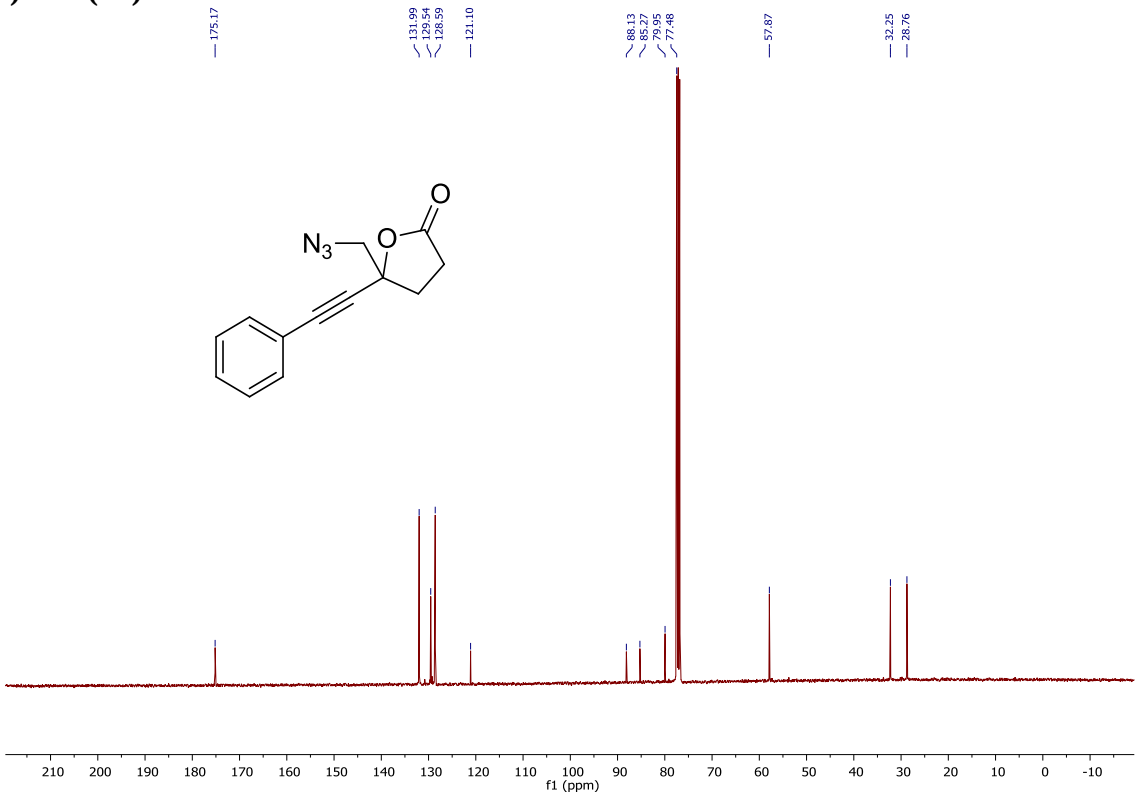
IR of compound **8b-(azidomethyl)-3,3a,4,8b-tetrahydro-2H-indeno[1,2-b]furan-2-one (2m)**



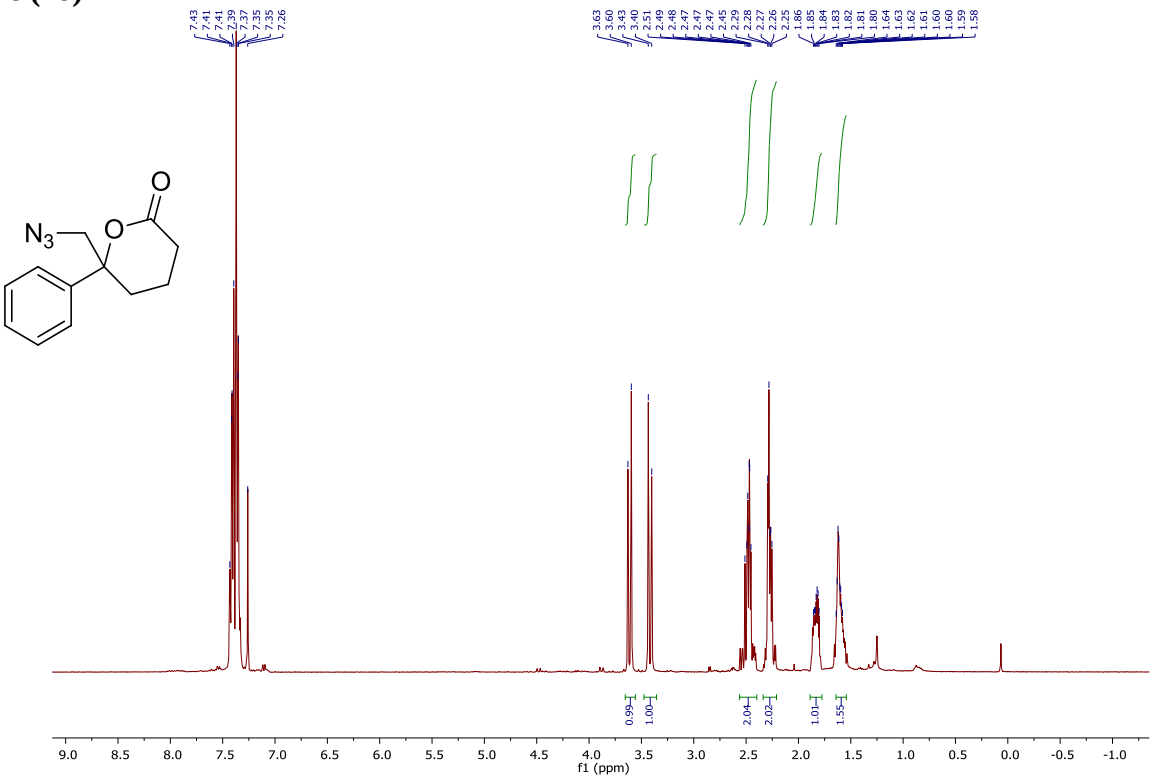
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(phenylethynyl)dihydrofuran-2(3H)-one (2n)**



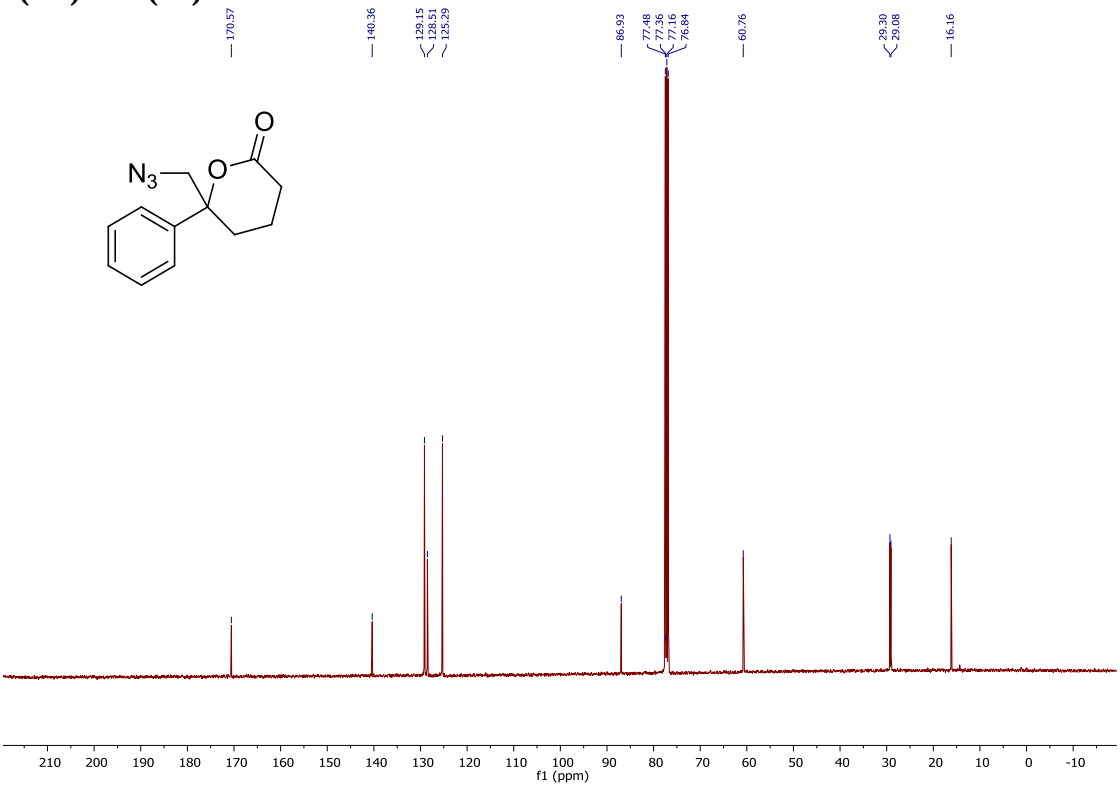
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(phenylethynyl)dihydrofuran-2(3H)-one (2n)**



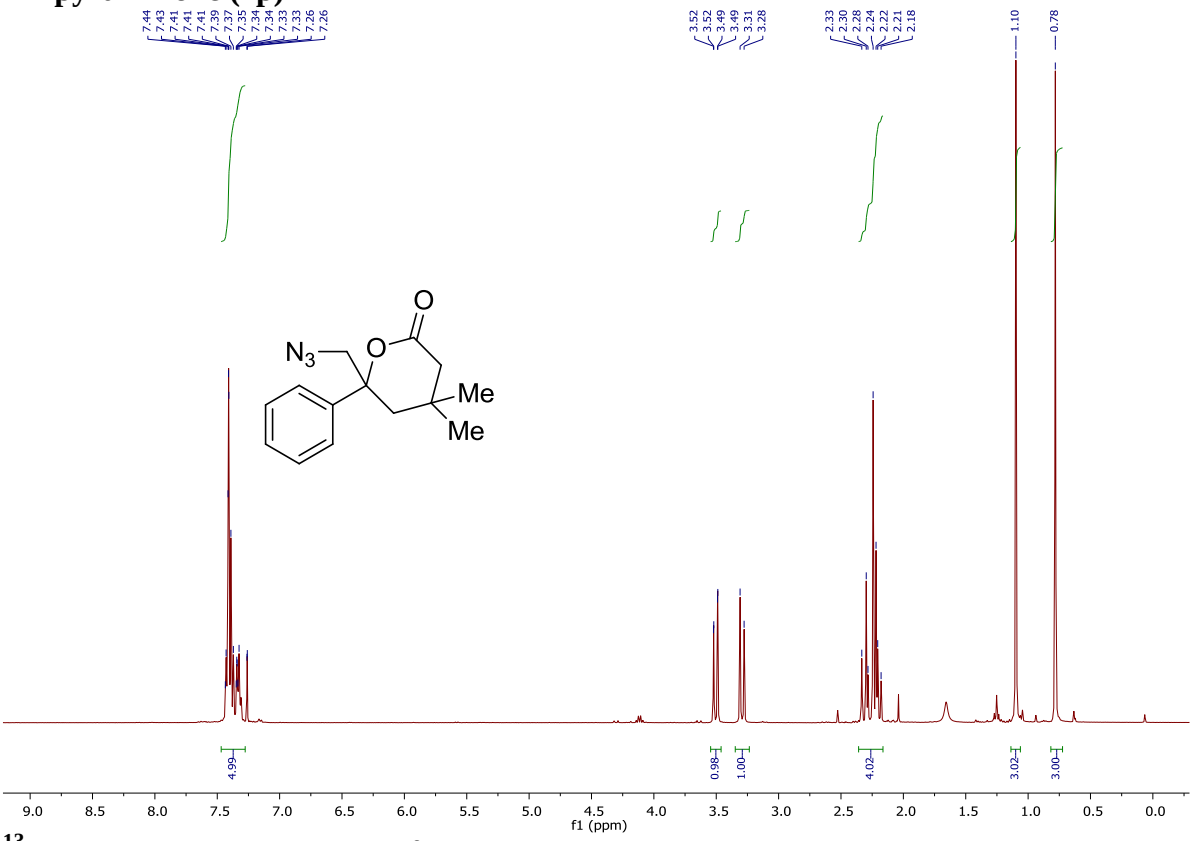
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6-(azidomethyl)-6-phenyltetrahydro-2H-pyran-2-one (2o)**



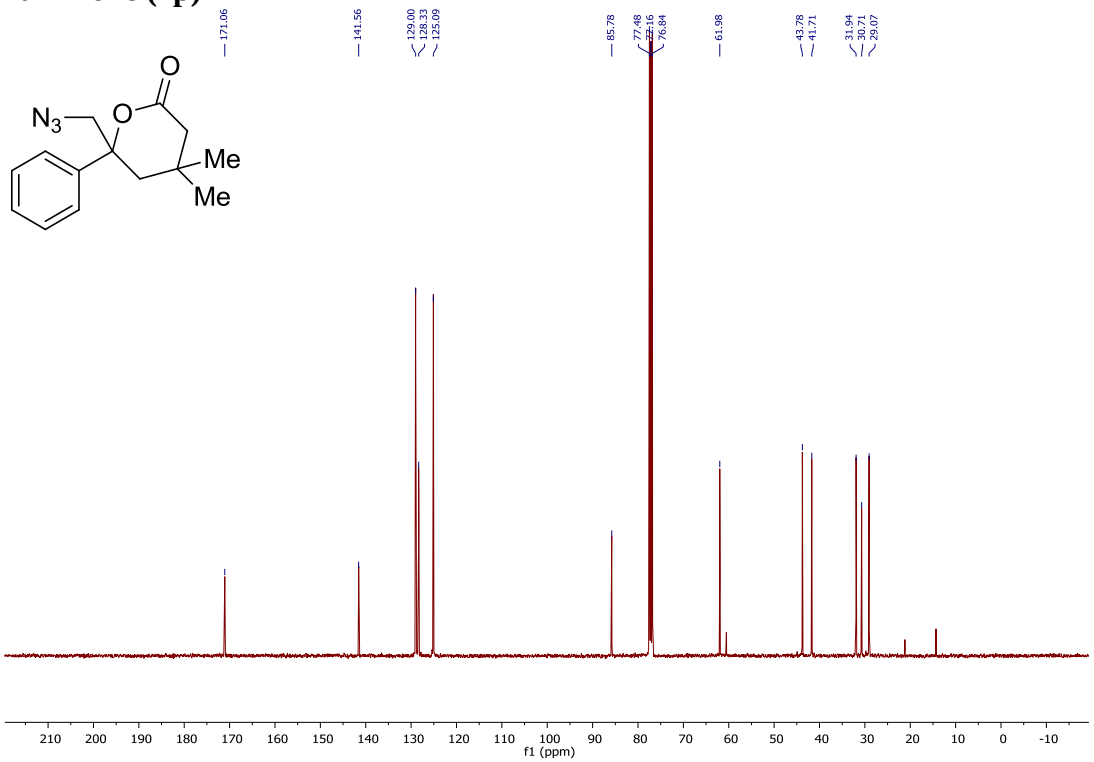
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(phenylethynyl)dihydrofuran-2(3H)-one (2n)**



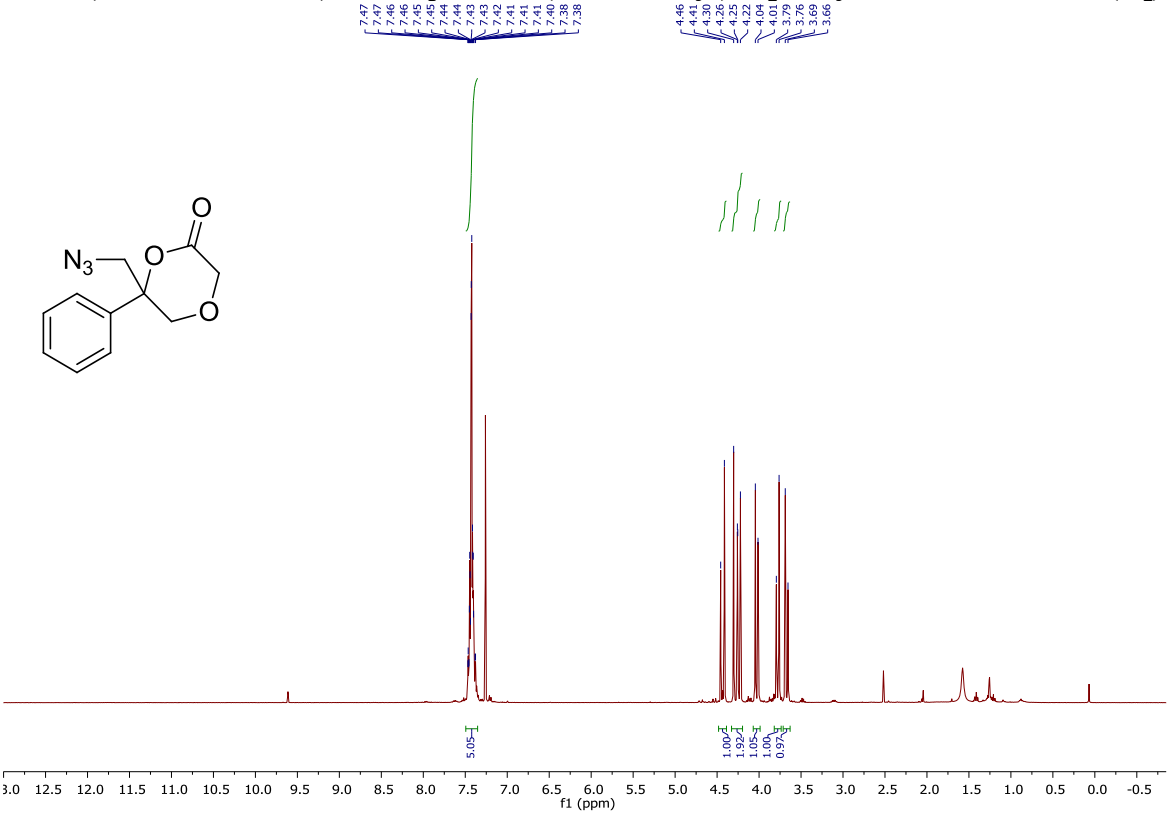
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6-(azidomethyl)-4,4-dimethyl-6-phenyltetrahydro-2H-pyran-2-one (2p)**



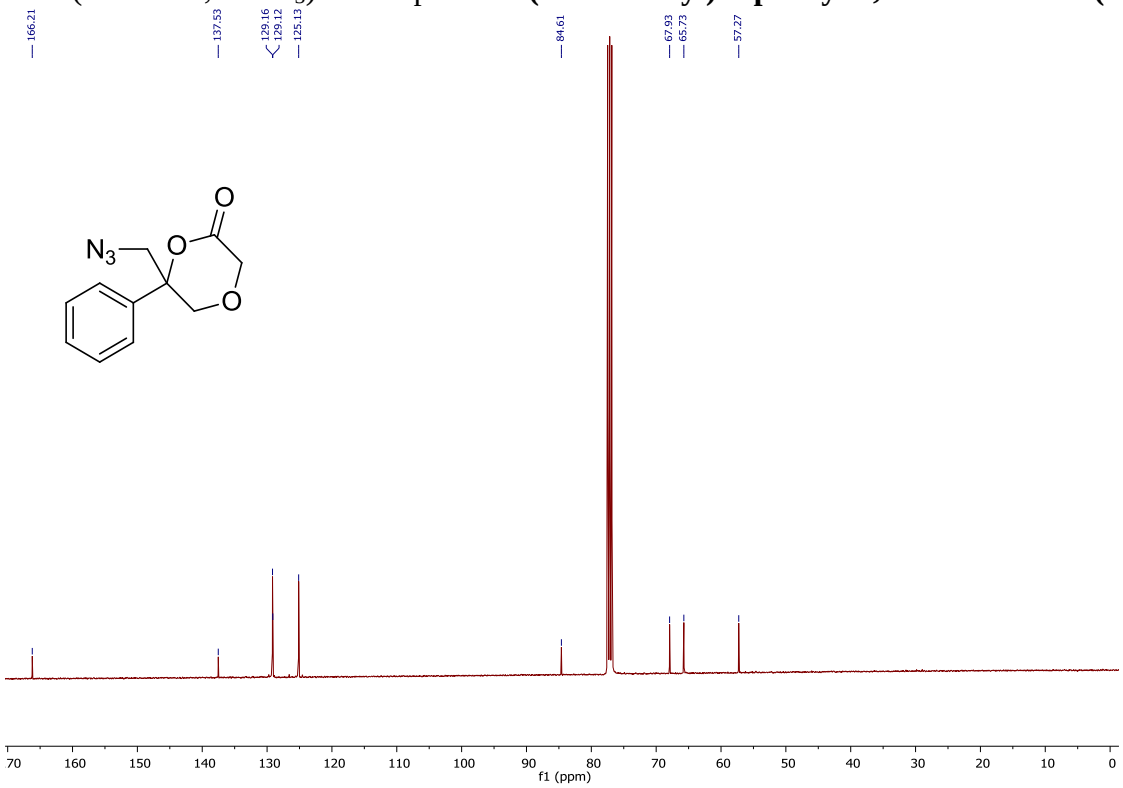
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6-(azidomethyl)-4,4-dimethyl-6-phenyltetrahydro-2H-pyran-2-one (2p)**



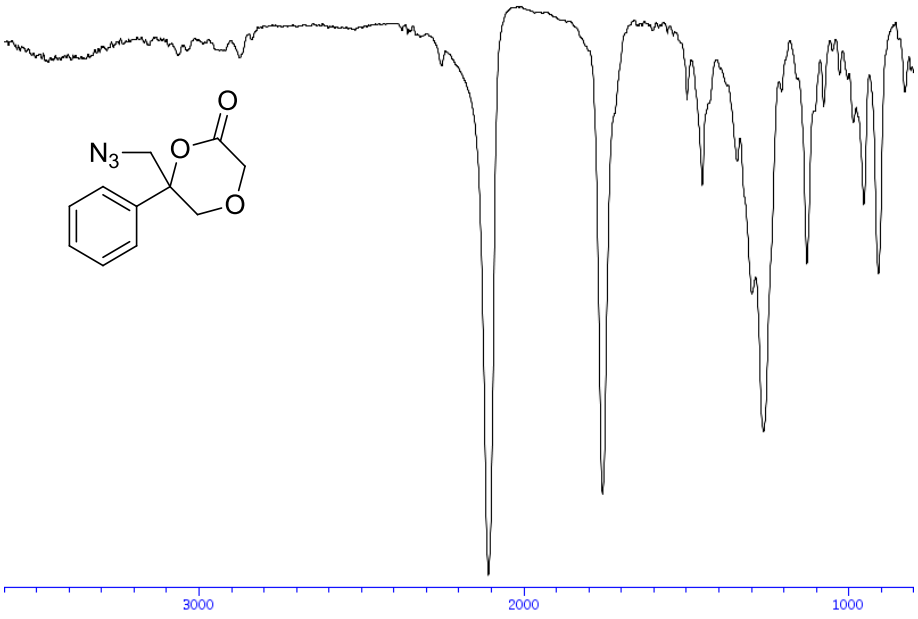
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6-(azidomethyl)-6-phenyl-1,4-dioxan-2-one (2q)**



^{13}C NMR (101 MHz, $CDCl_3$) of compound **6-(azidomethyl)-6-phenyl-1,4-dioxan-2-one (2q)**

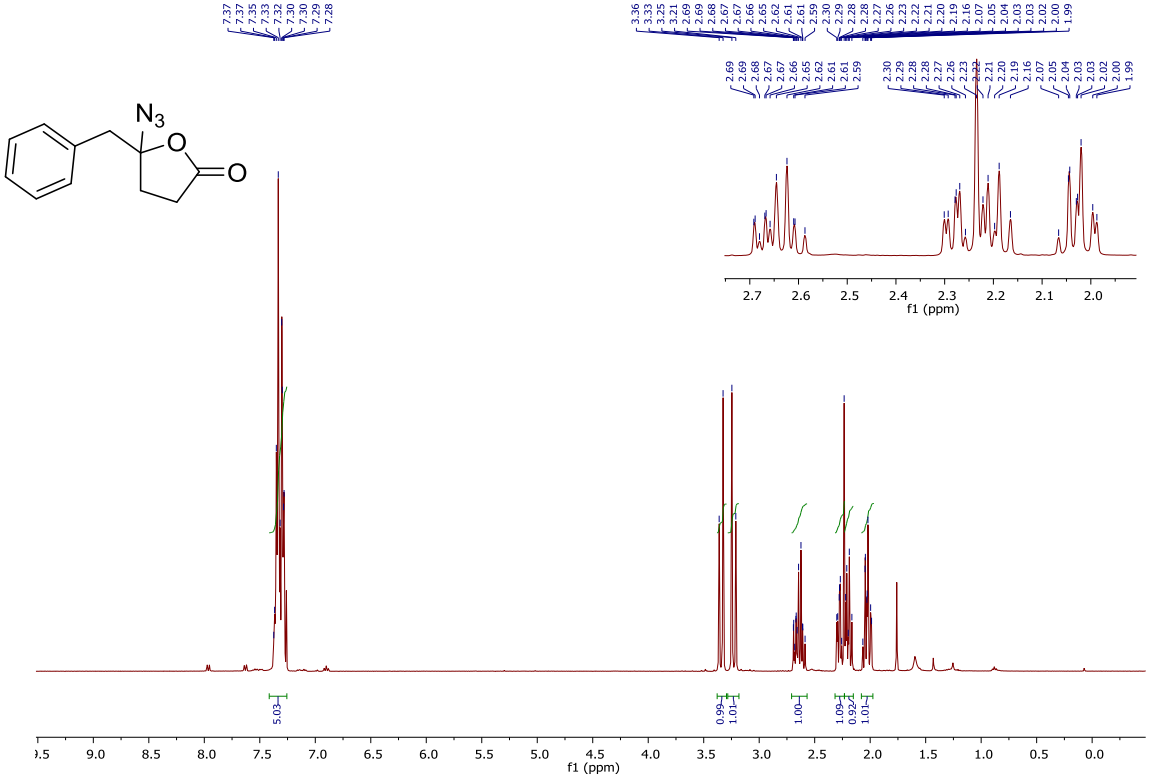


IR of compound **6-(azidomethyl)-6-phenyl-1,4-dioxan-2-one (2q)**

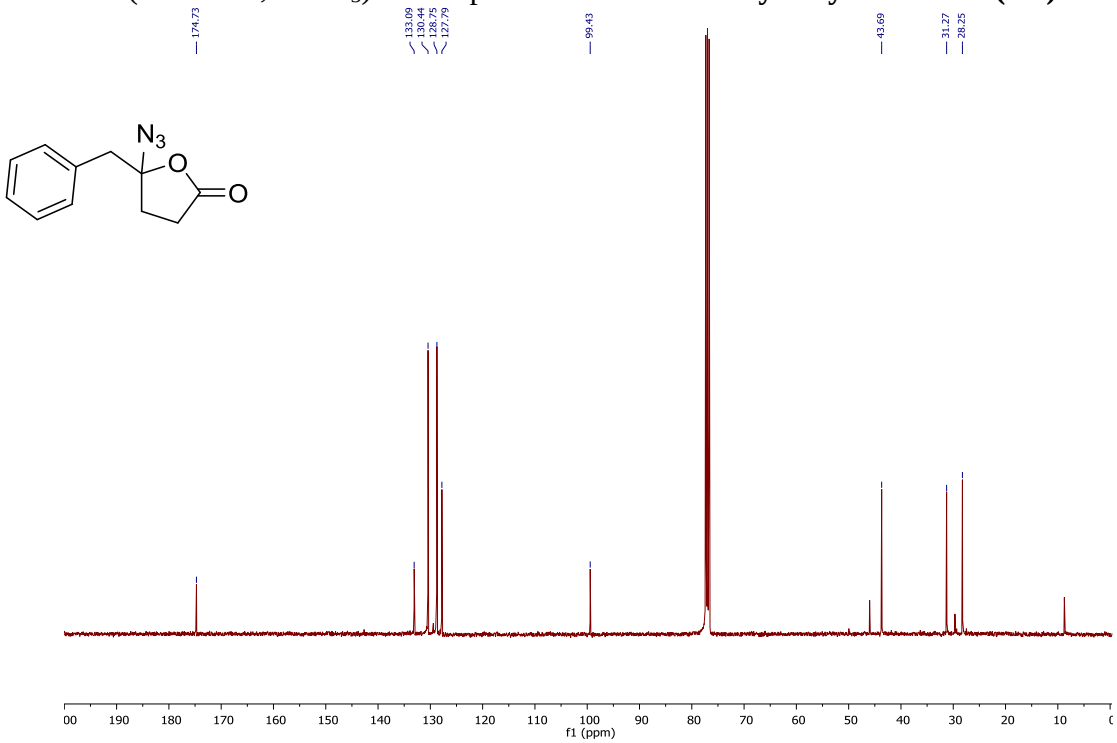


c. Spectra of new compounds for Lewis acid catalyzed aryl migration

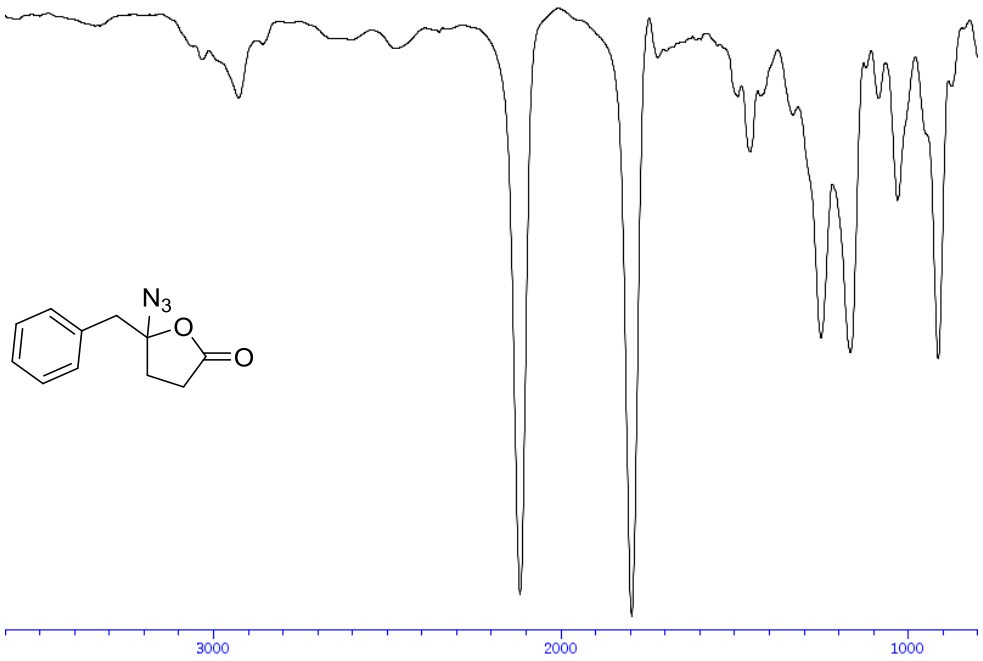
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-benzyldihydrofuran-2(3H)-one (4a)**



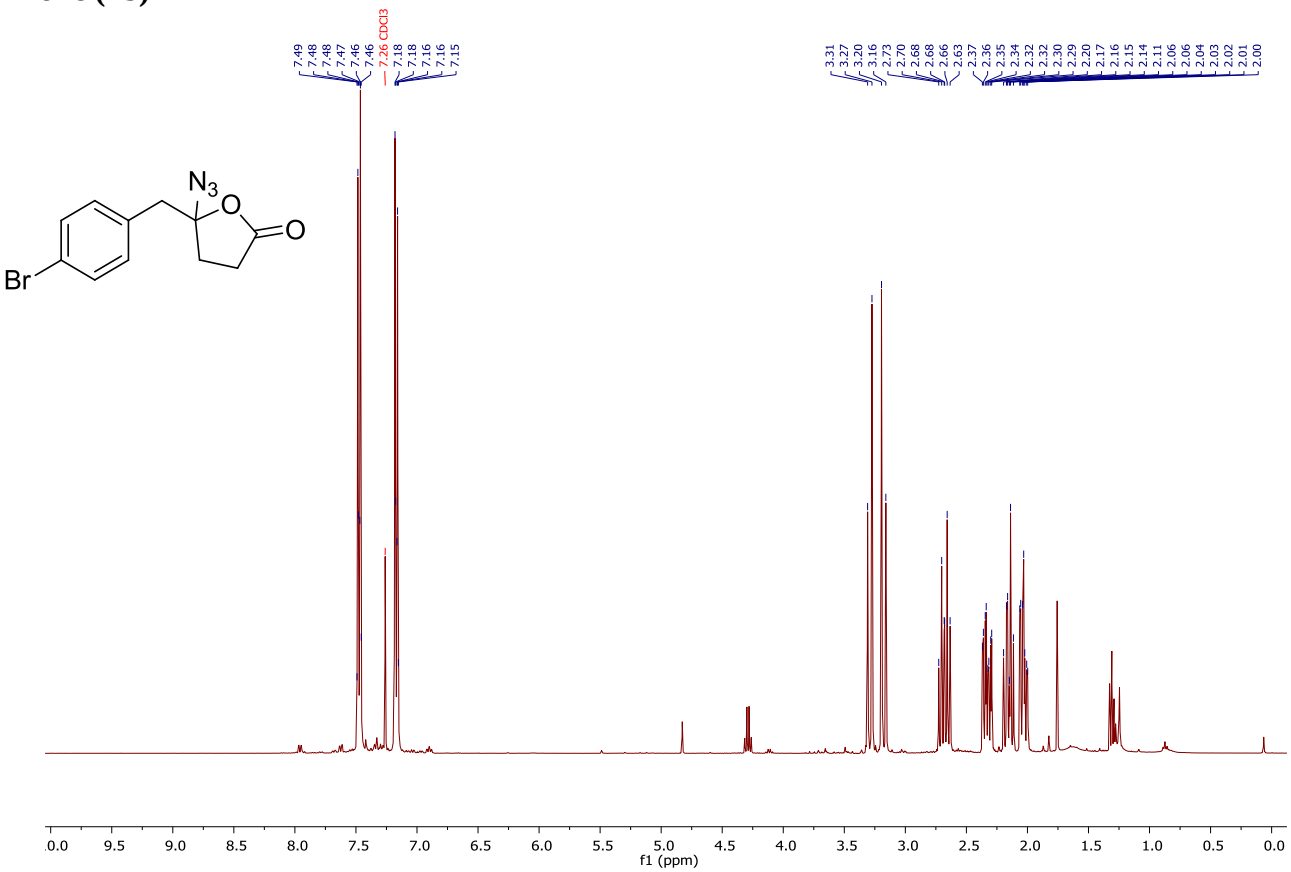
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-benzyldihydrofuran-2(3H)-one (4a)**



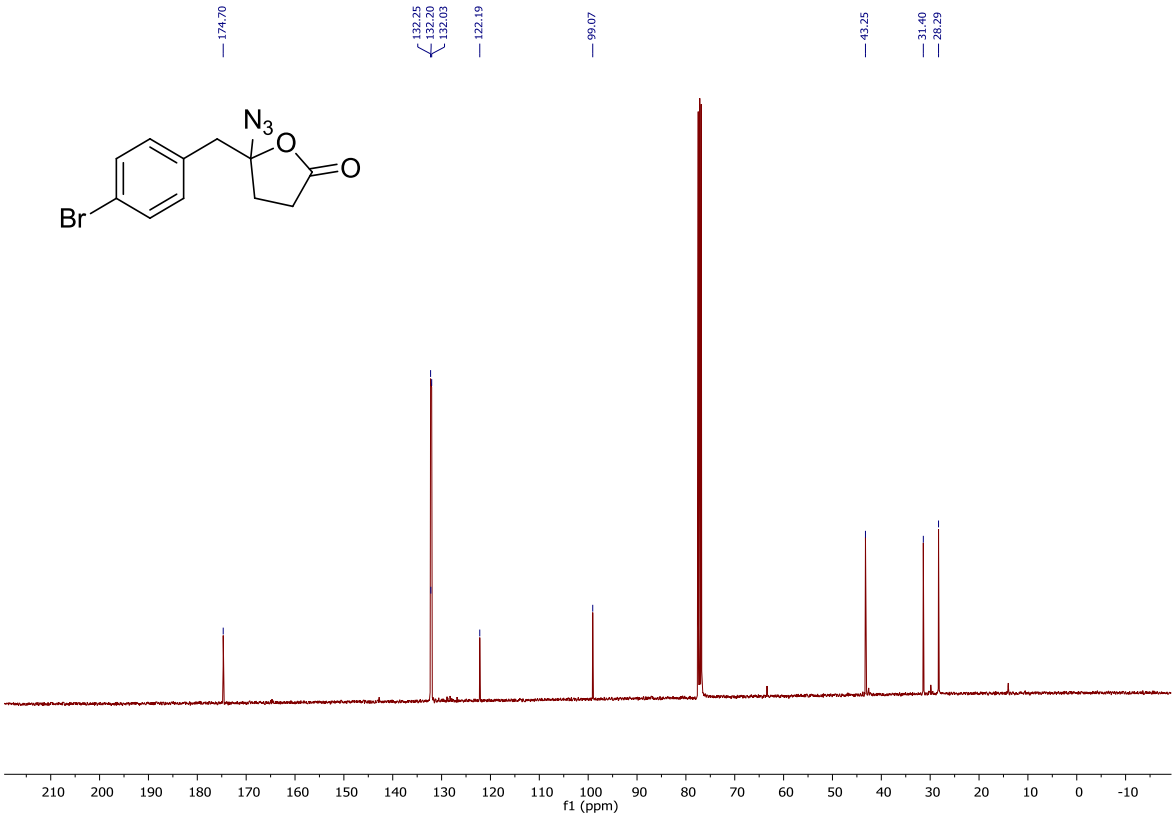
IR of compound **5-azido-5-benzyldihydrofuran-2(3H)-one (4a)**



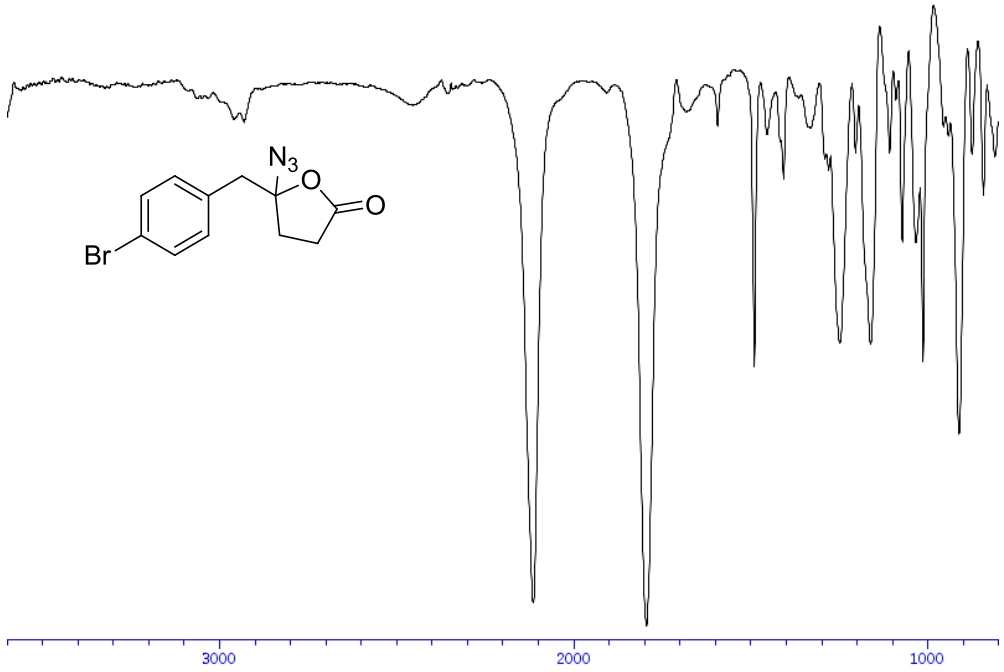
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(4-bromobenzyl)dihydrofuran-2(3H)-one (4b)**



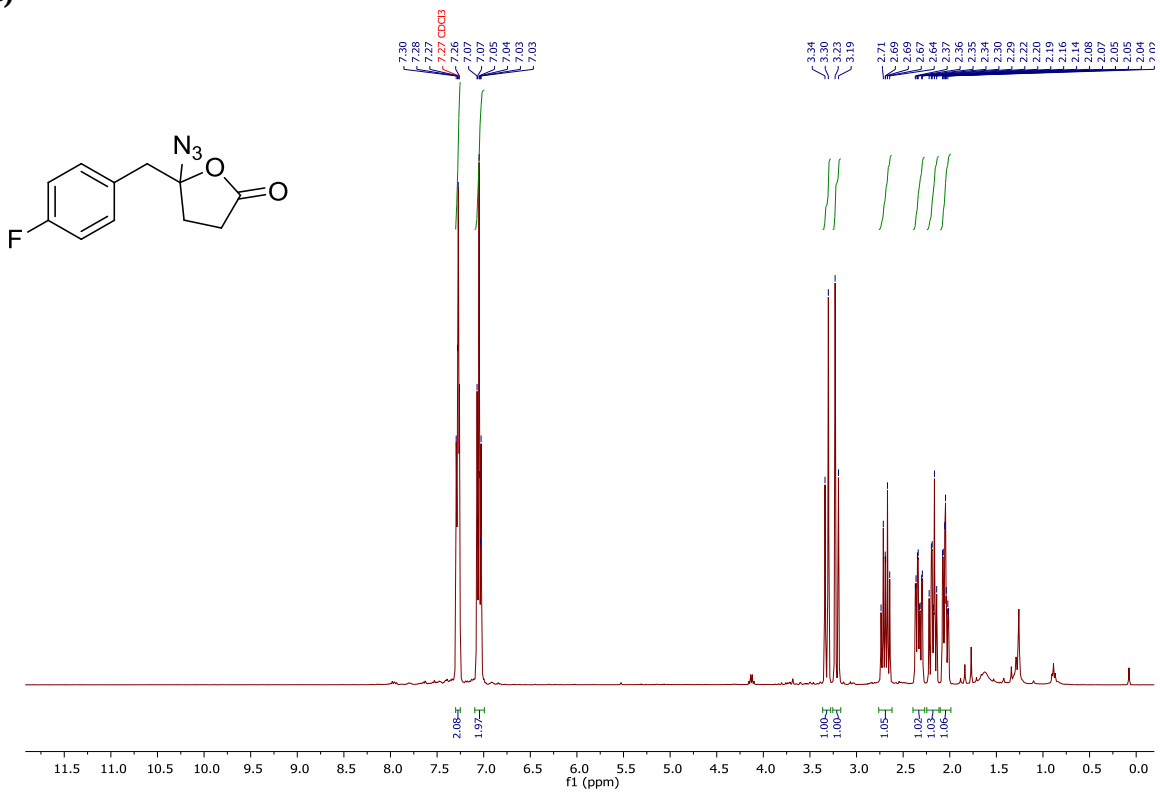
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(4-bromobenzyl)dihydrofuran-2(3H)-one (4b)**



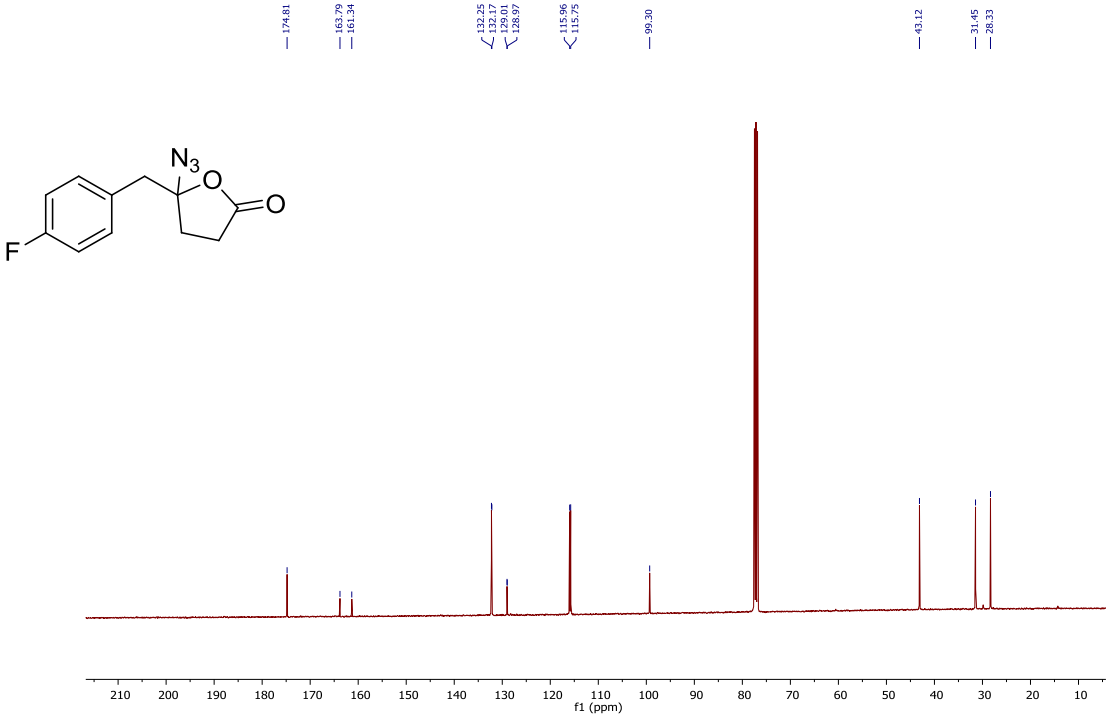
IR of compound **5-azido-5-(4-bromobenzyl)dihydrofuran-2(3H)-one (4b)**



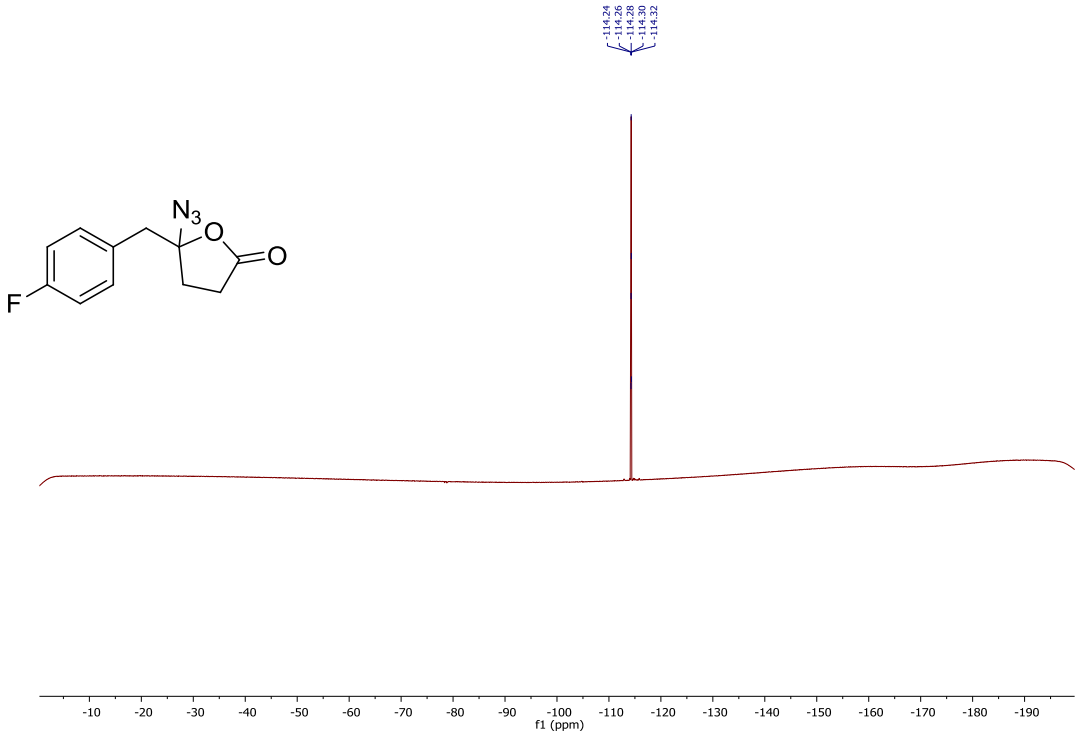
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(4-fluorobenzyl)dihydrofuran-2(3H)-one (4c)**



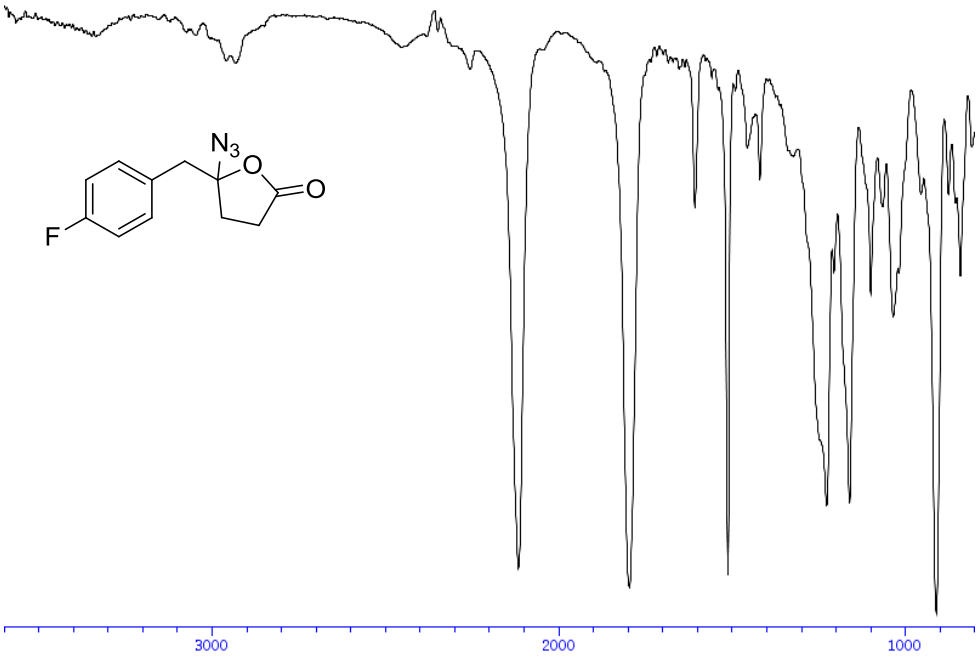
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(4-fluorobenzyl)dihydrofuran-2(3H)-one (4c)**



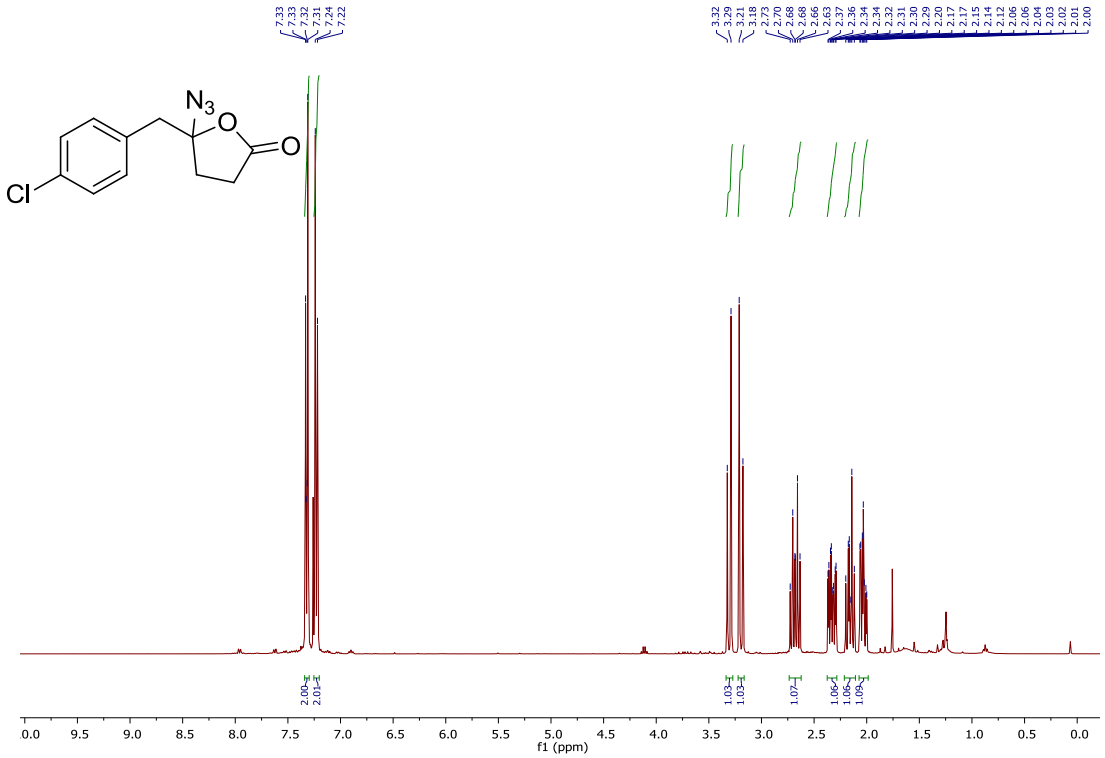
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5-azido-5-(4-fluorobenzyl)dihydrofuran-2(3H)-one (4c)**



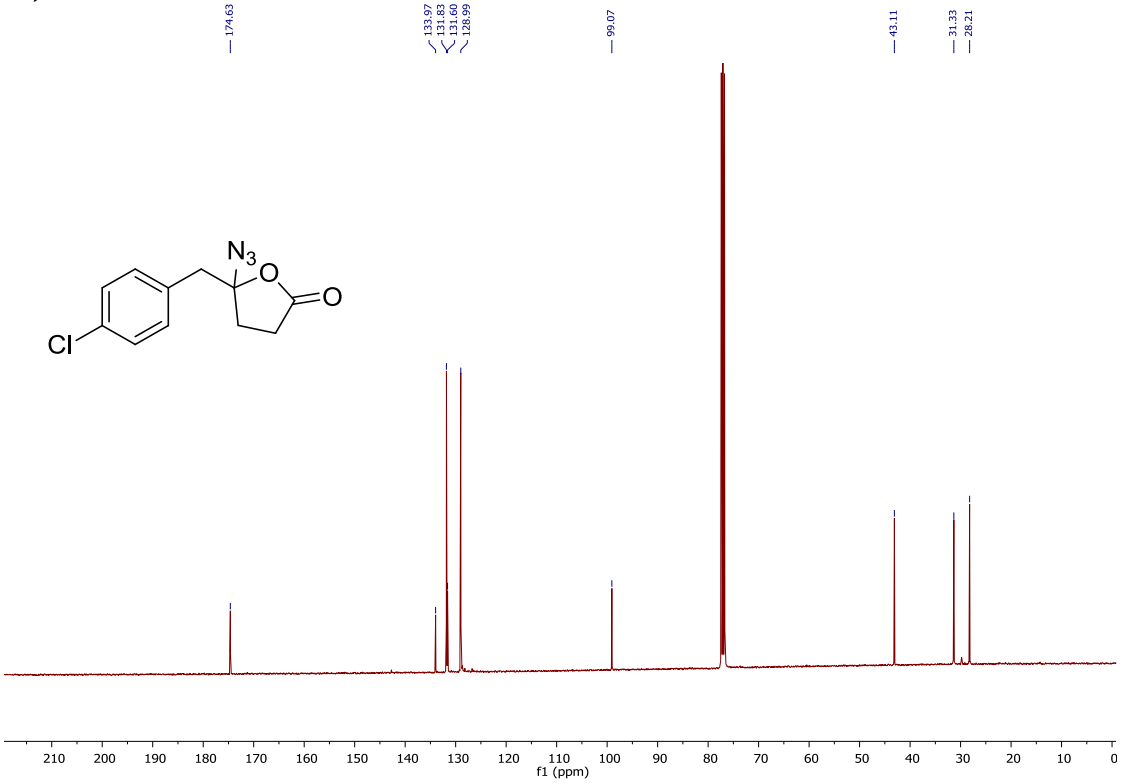
IR of compound **5-azido-5-(4-fluorobenzyl)dihydrofuran-2(3H)-one (4c)**



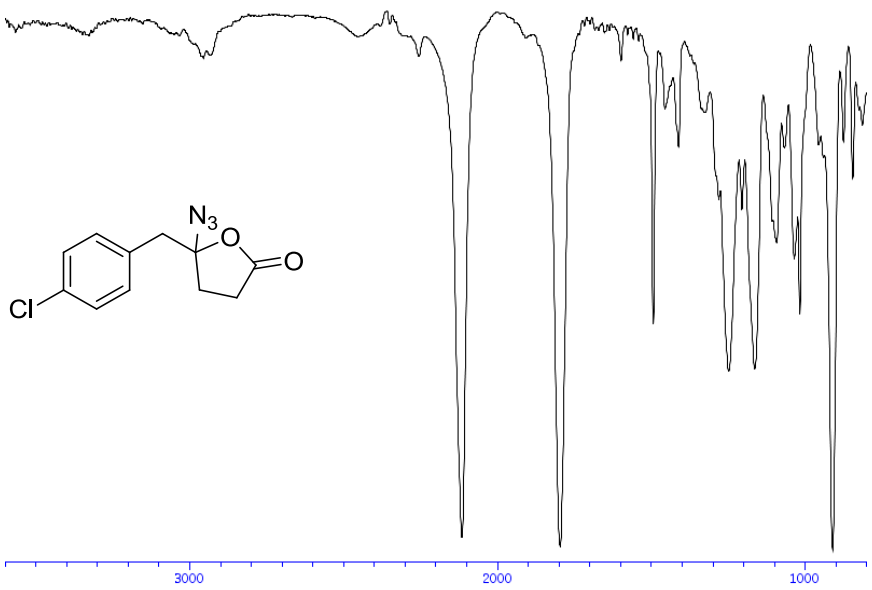
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(4-chlorobenzyl)dihydrofuran-2(3H)-one (4d)**



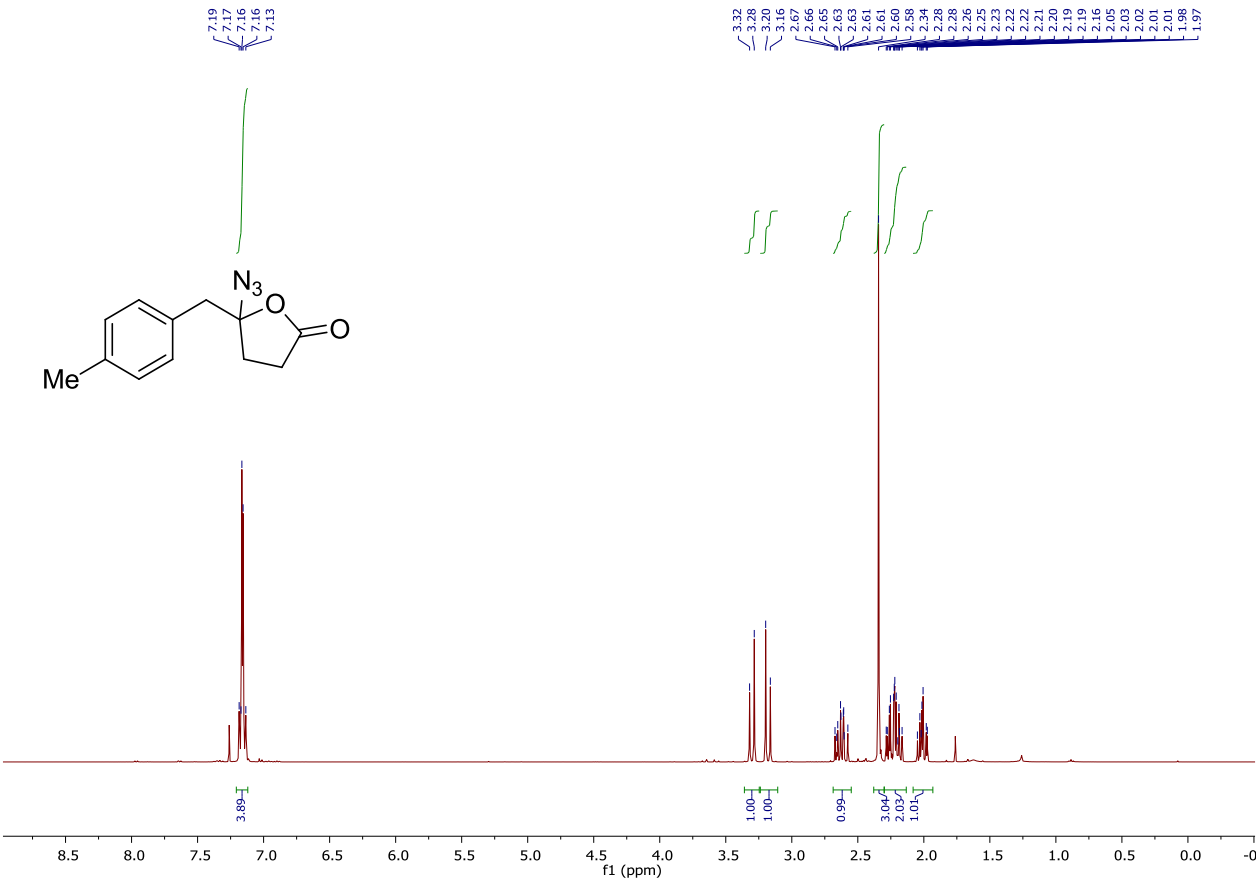
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(4-chlorobenzyl)dihydrofuran-2(3H)-one (4d)**



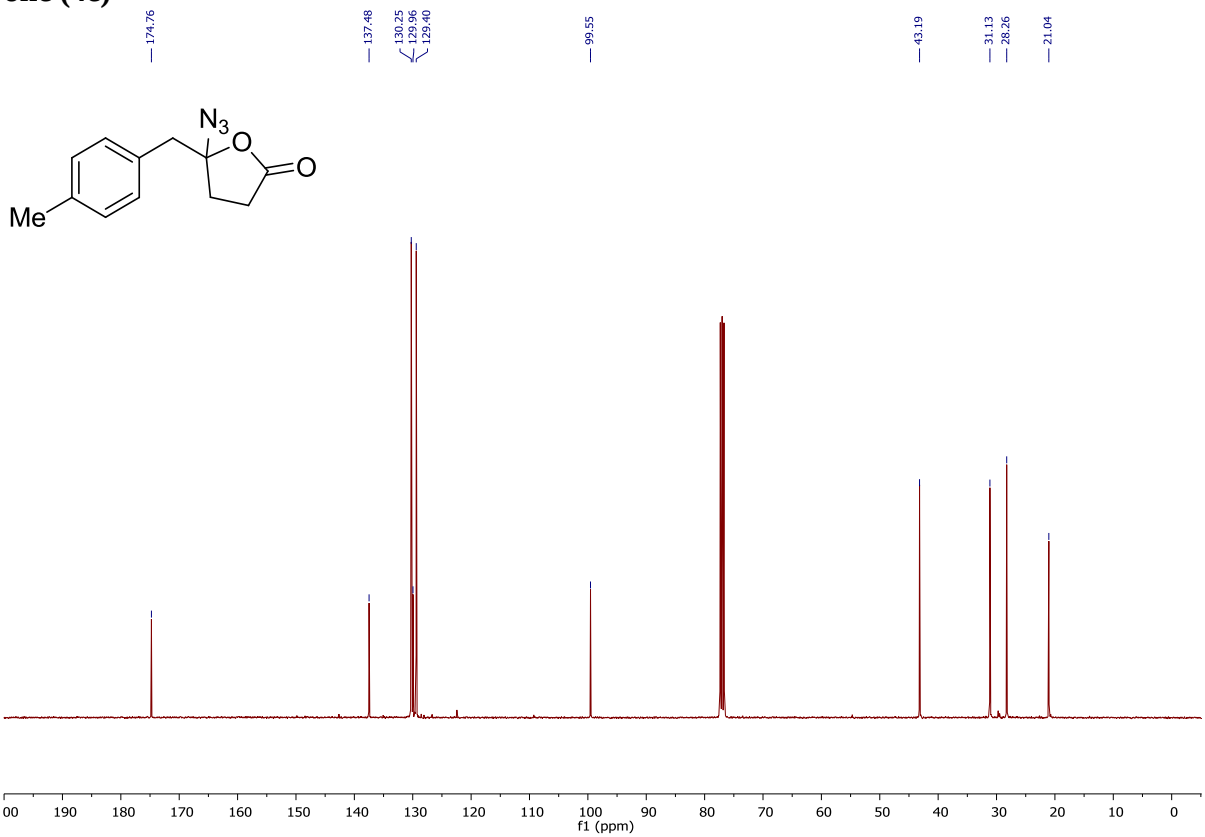
IR of compound **5-azido-5-(4-chlorobenzyl)dihydrofuran-2(3H)-one (4d)**



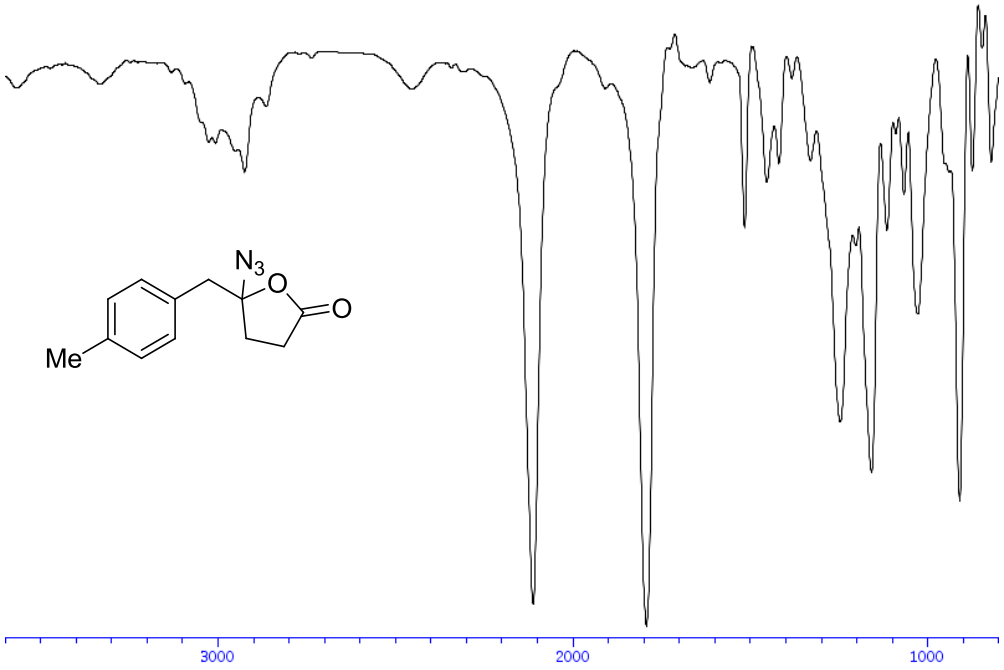
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(4-methylbenzyl)dihydrofuran-2(3H)-one (4e)**



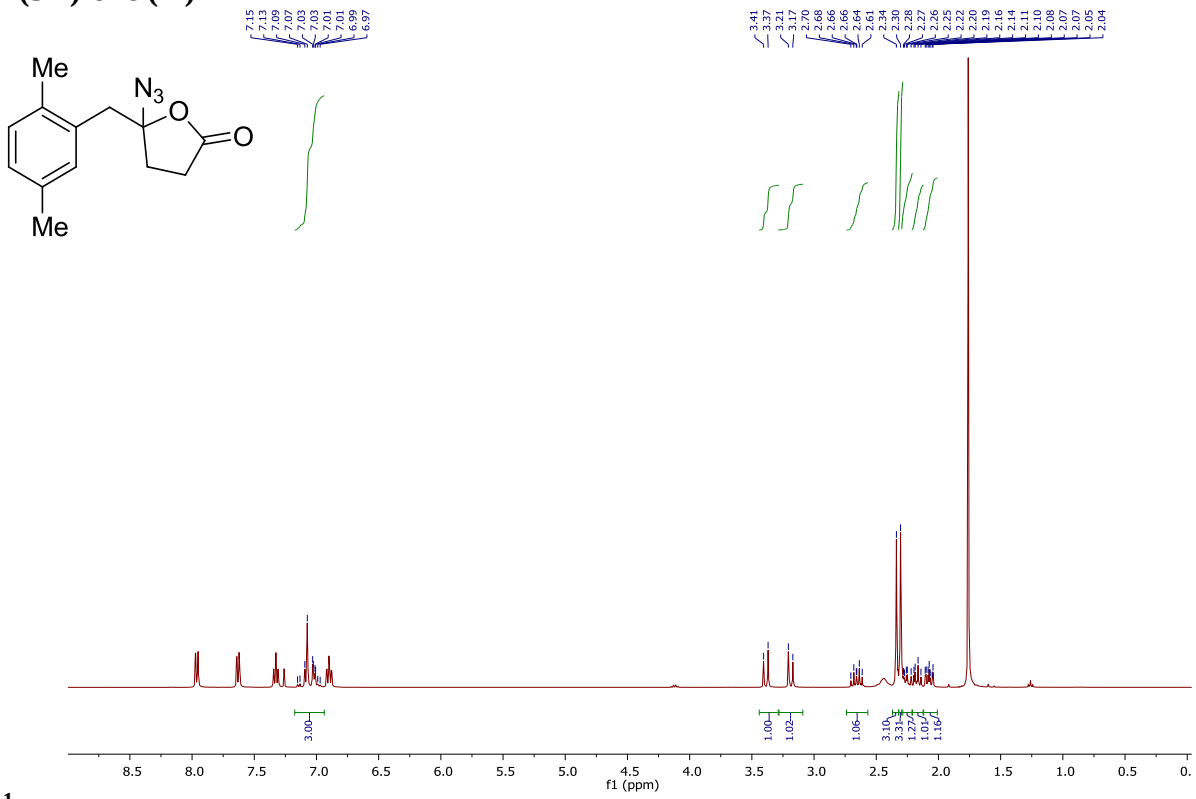
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(4-methylbenzyl)dihydrofuran-2(3H)-one (4e)**



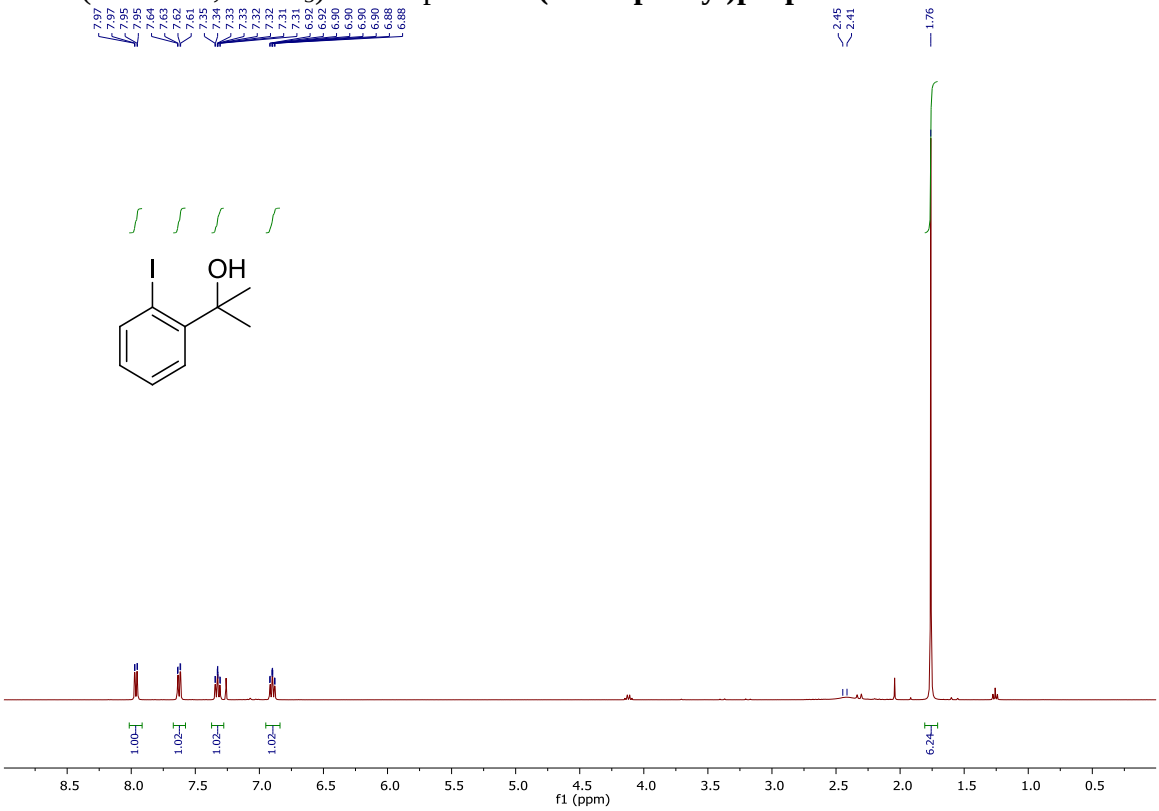
IR of compound **5-azido-5-(4-methylbenzyl)dihydrofuran-2(3H)-one (4e)**



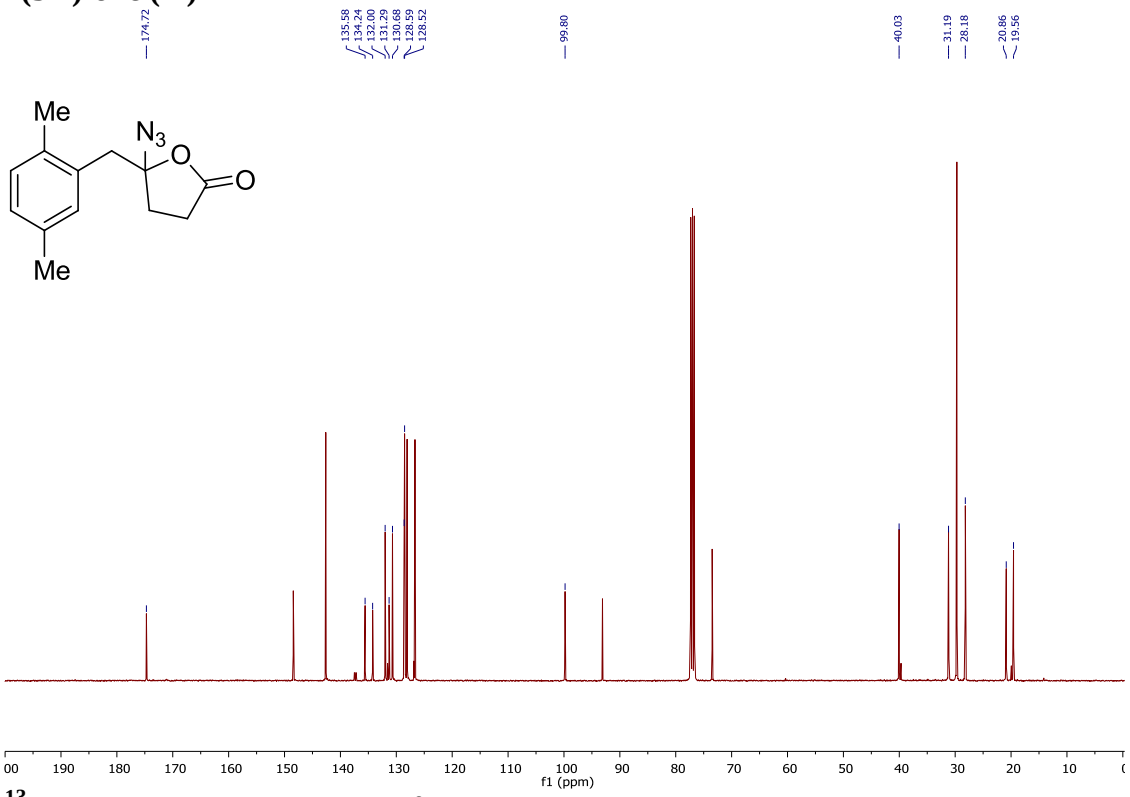
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(2,5-dimethylbenzyl)dihydrofuran-2(3H)-one (4f)**



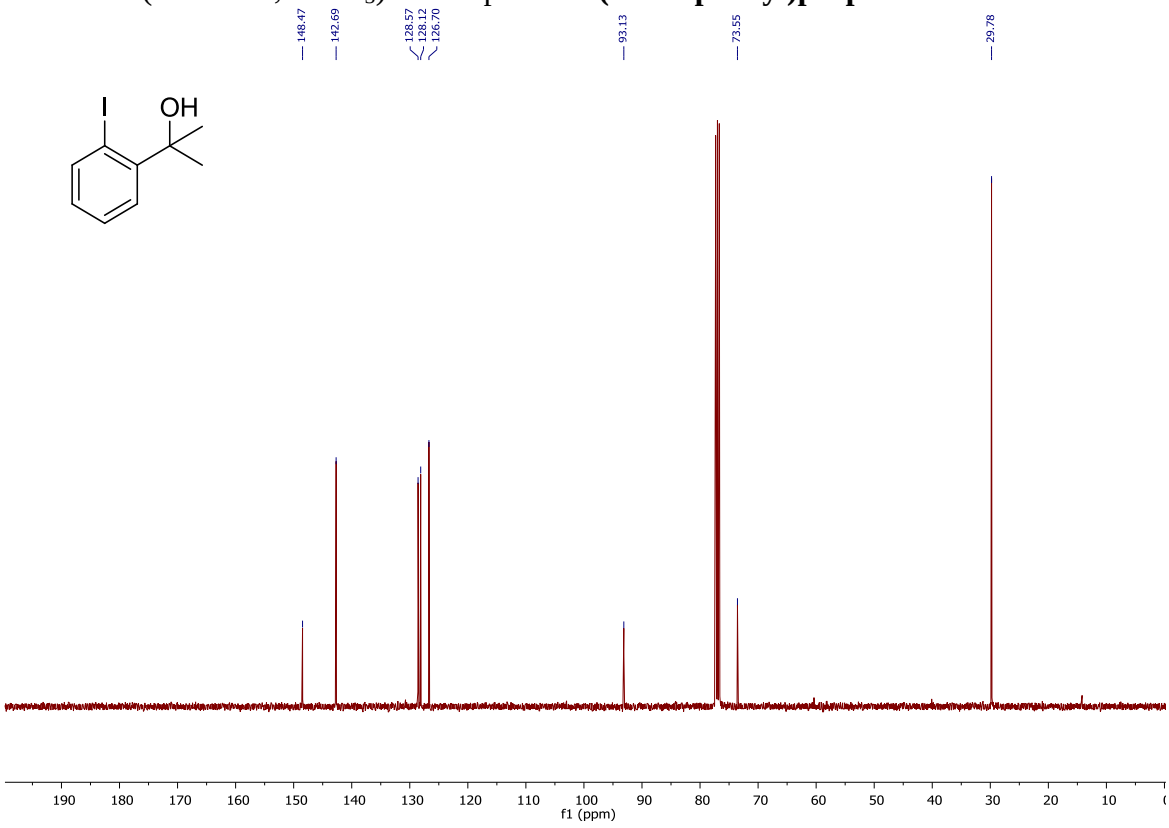
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2-(2-iodophenyl)propan-2-ol**



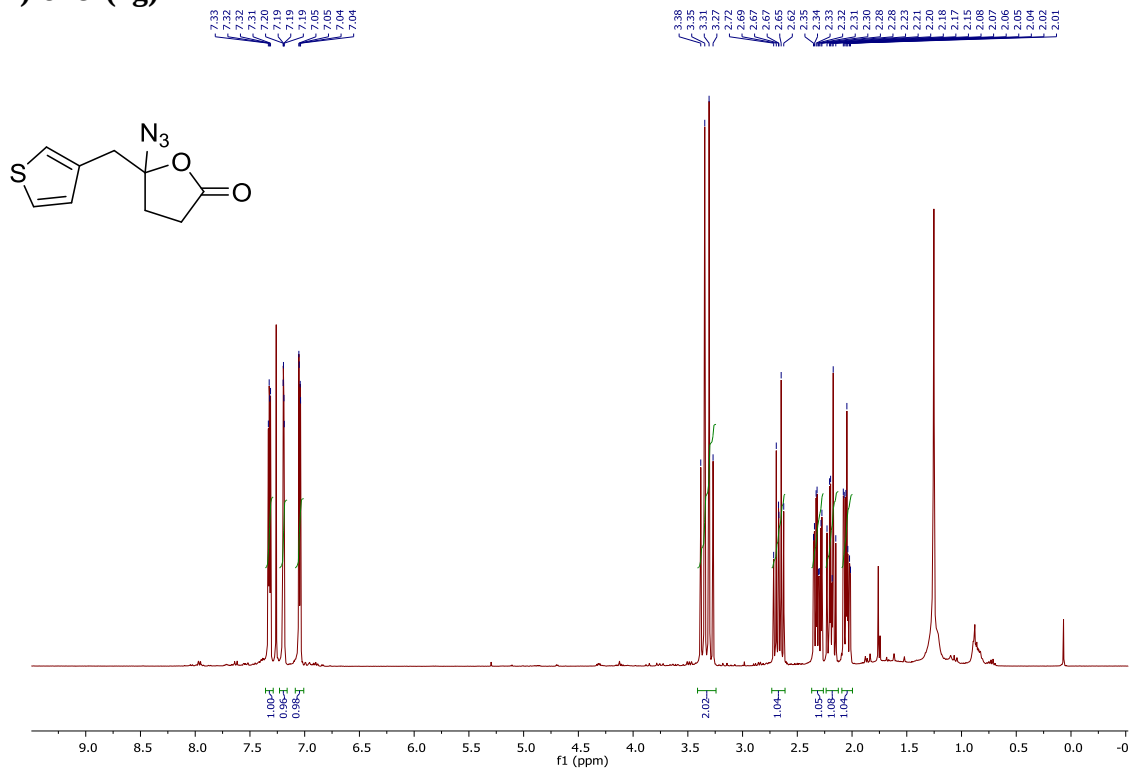
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(2,5-dimethylbenzyl)dihydrofuran-2(3H)-one (4f)**



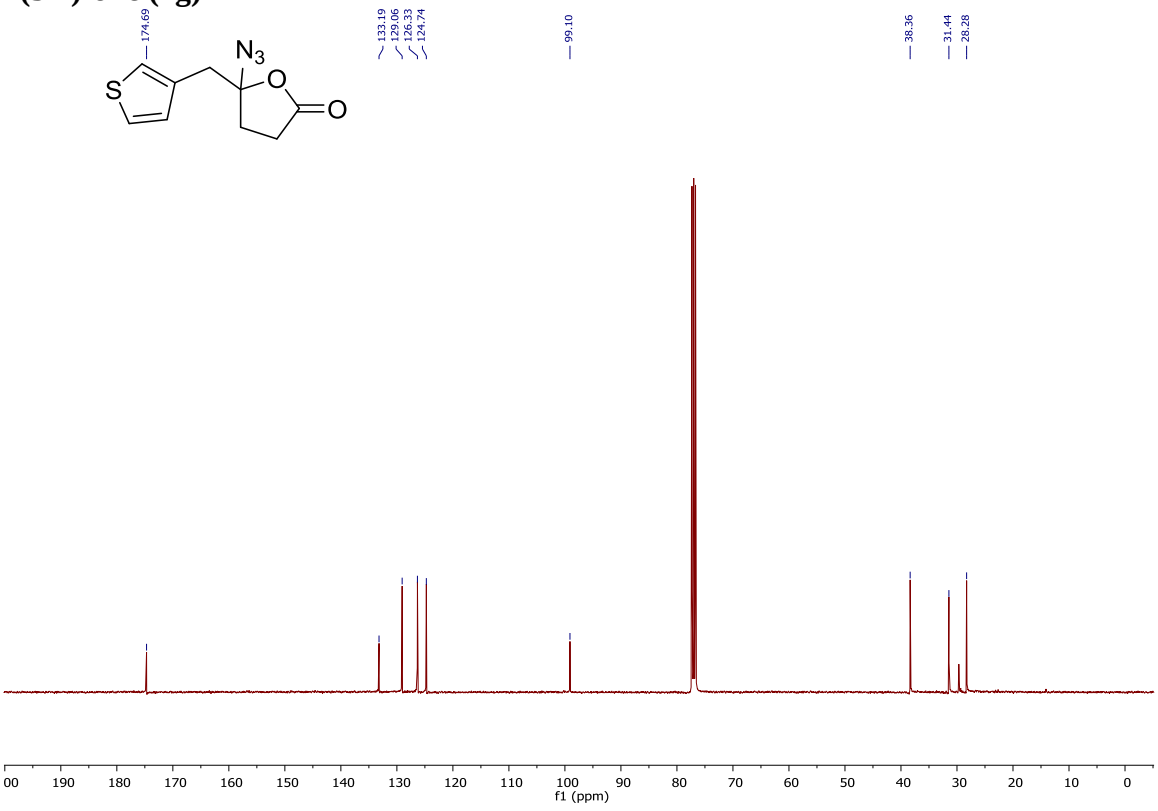
^{13}C NMR (101 MHz, $CDCl_3$) of compound **2-(2-iodophenyl)propan-2-ol**



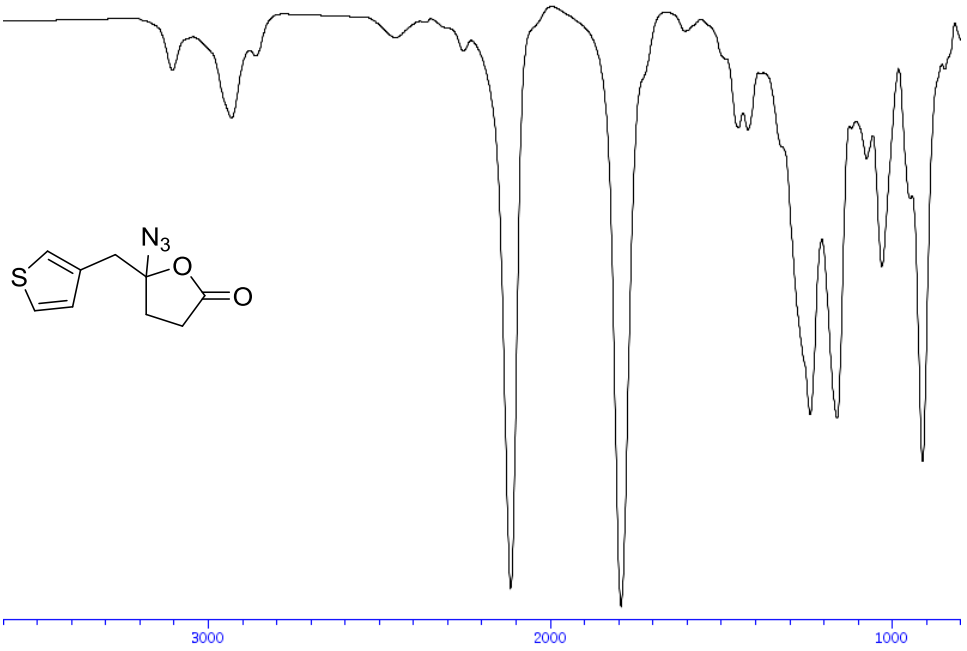
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-(thiophen-3-ylmethyl)dihydrofuran-2(3H)-one (4g)**



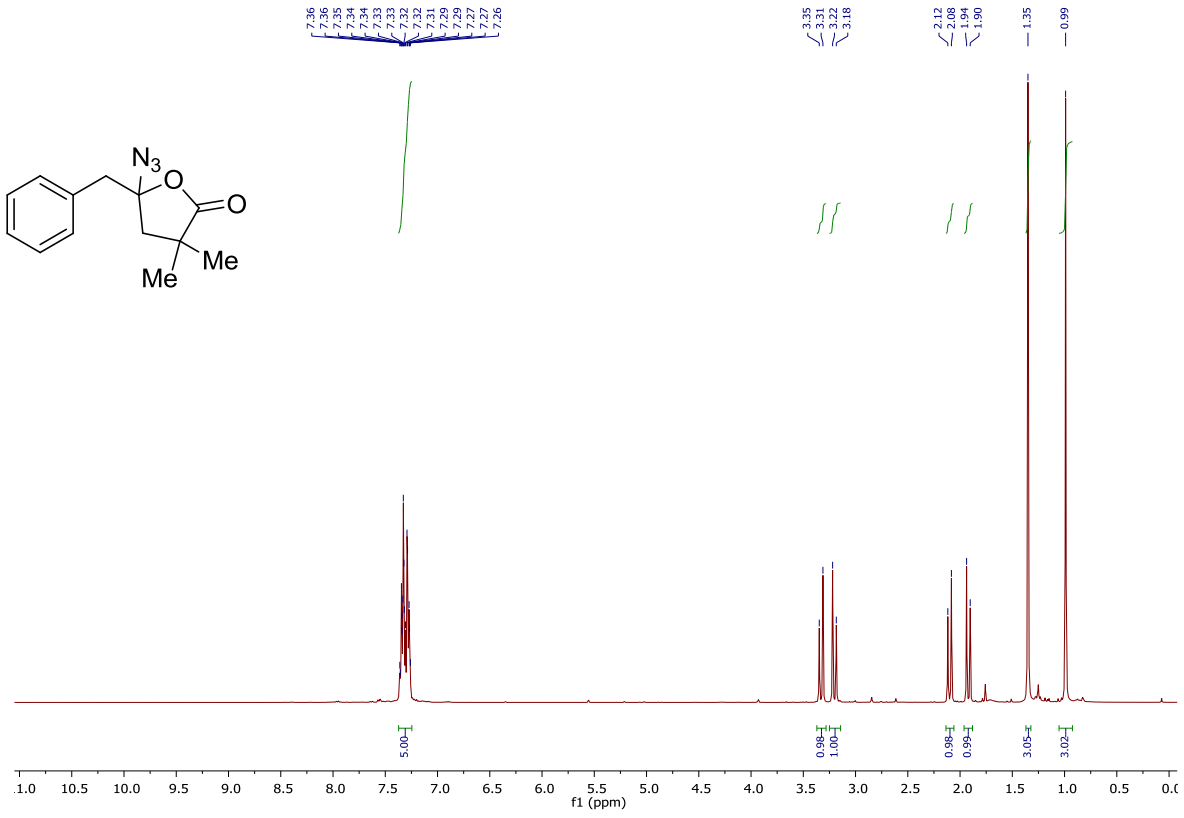
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-(thiophen-3-ylmethyl)dihydrofuran-2(3H)-one (4g)**



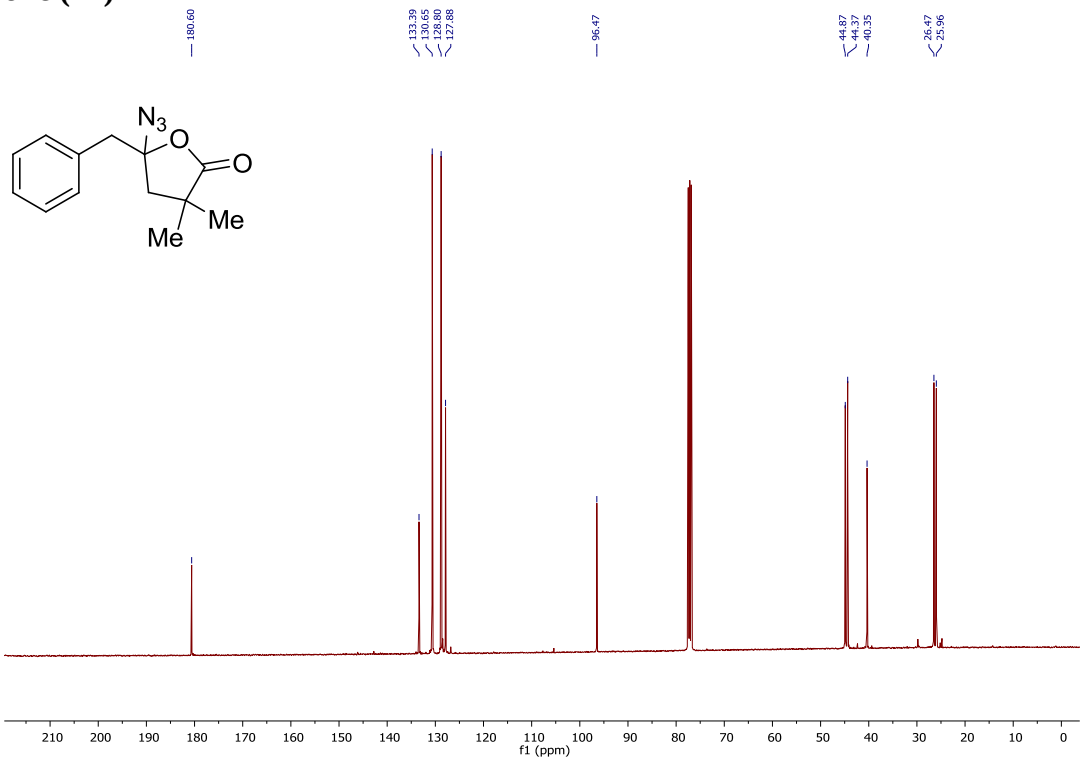
IR of compound **5-azido-5-(thiophen-3-ylmethyl)dihydrofuran-2(3H)-one (4g)**



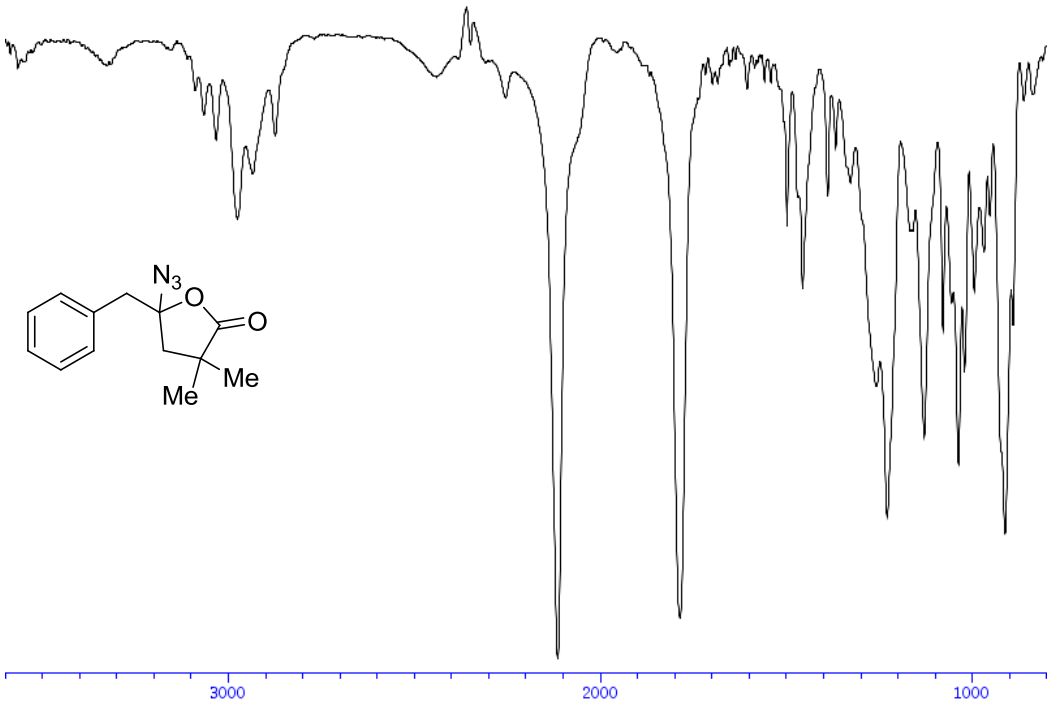
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5-azido-5-benzyl-3,3-dimethyldihydrofuran-2(3H)-one (4h)**



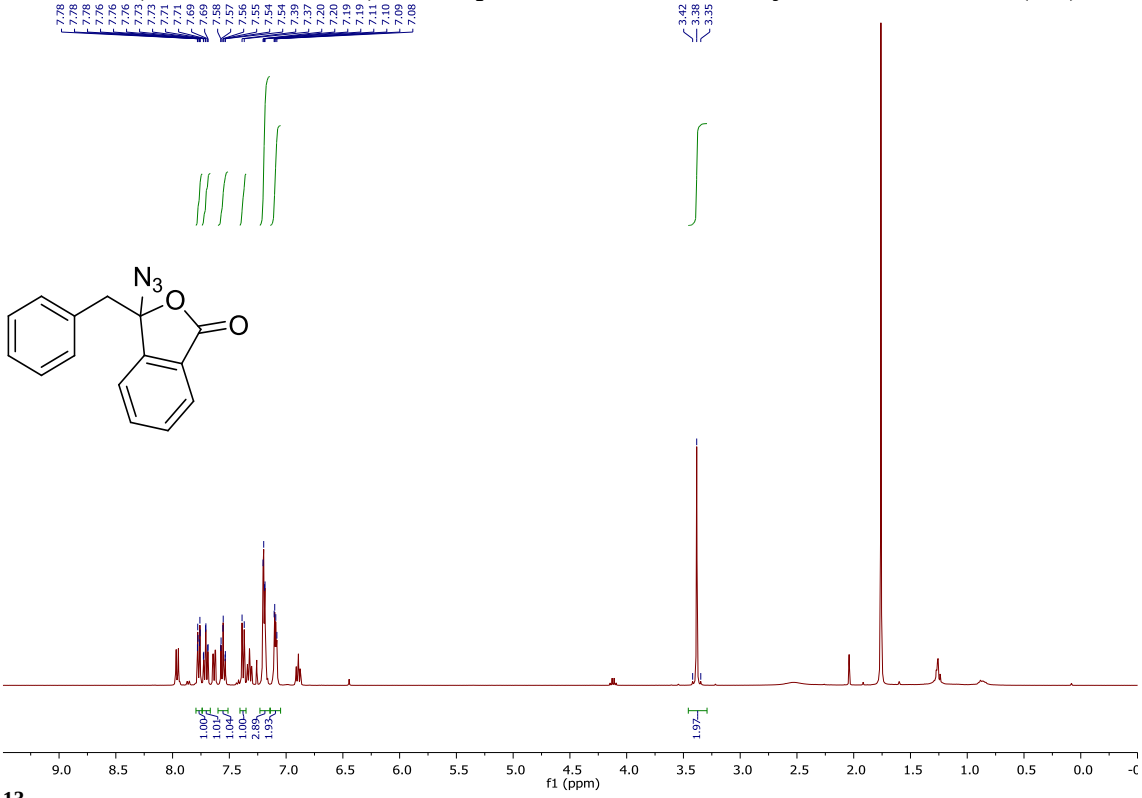
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5-azido-5-benzyl-3,3-dimethyldihydrofuran-2(3H)-one (4h)**



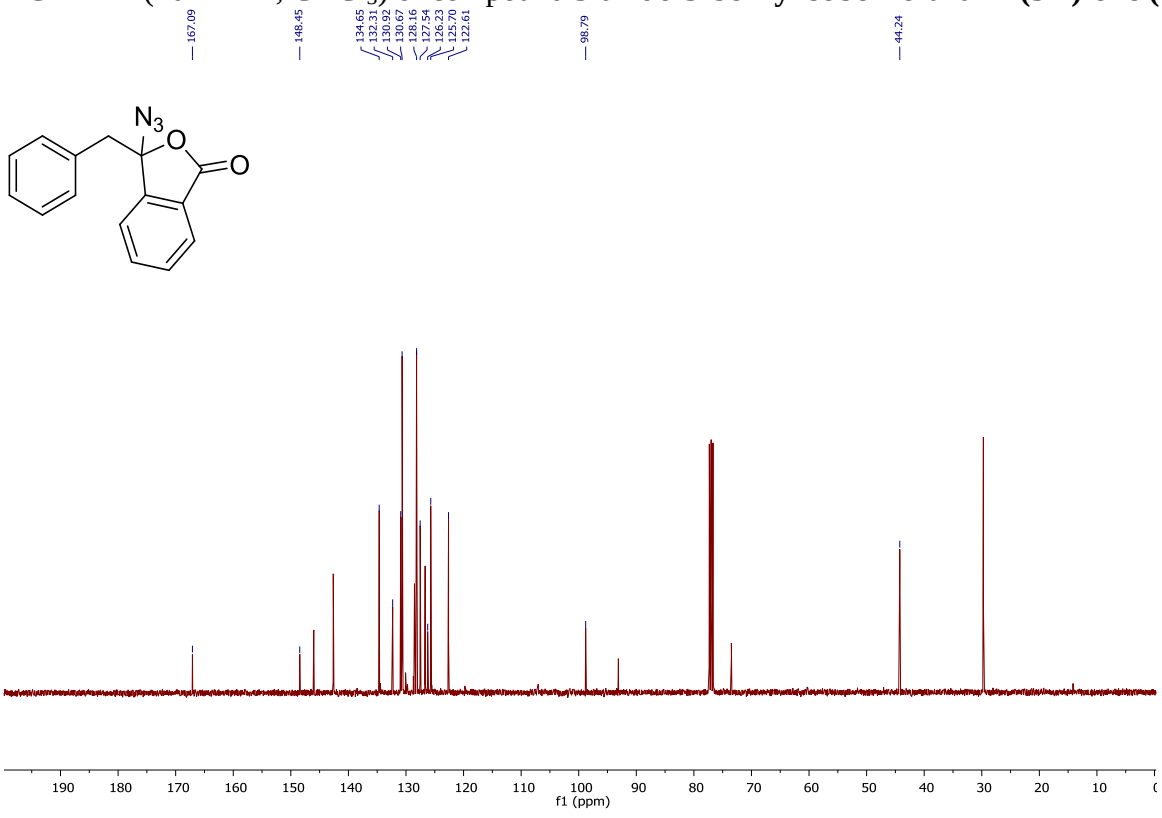
IR of compound **5-azido-5-benzyl-3,3-dimethyldihydrofuran-2(3H)-one (4h)**



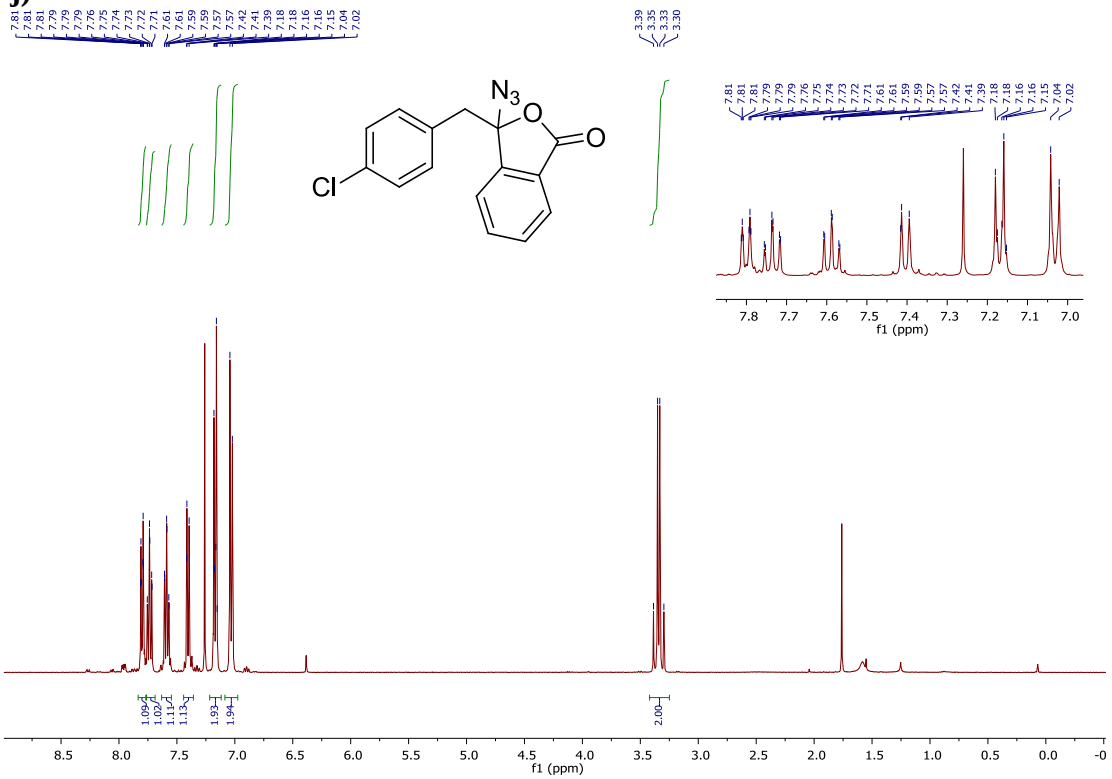
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3-azido-3-benzylisobenzofuran-1(3H)-one (4i)**



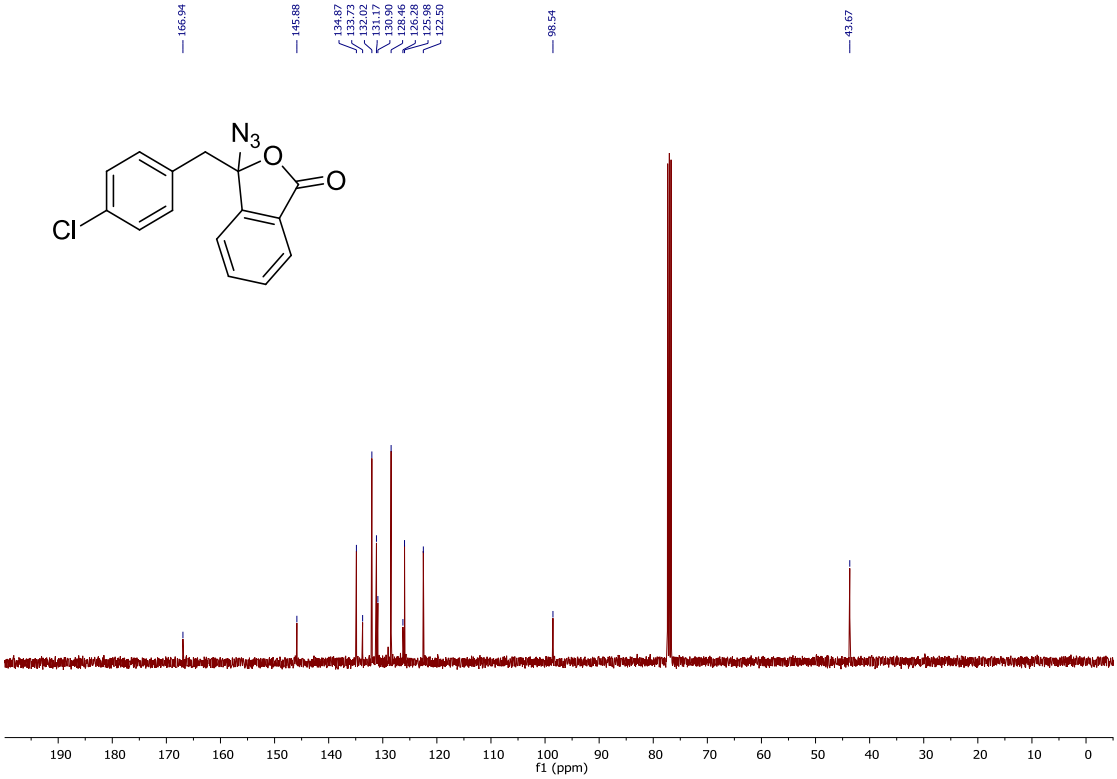
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-azido-3-benzylisobenzofuran-1(3H)-one (4i)**



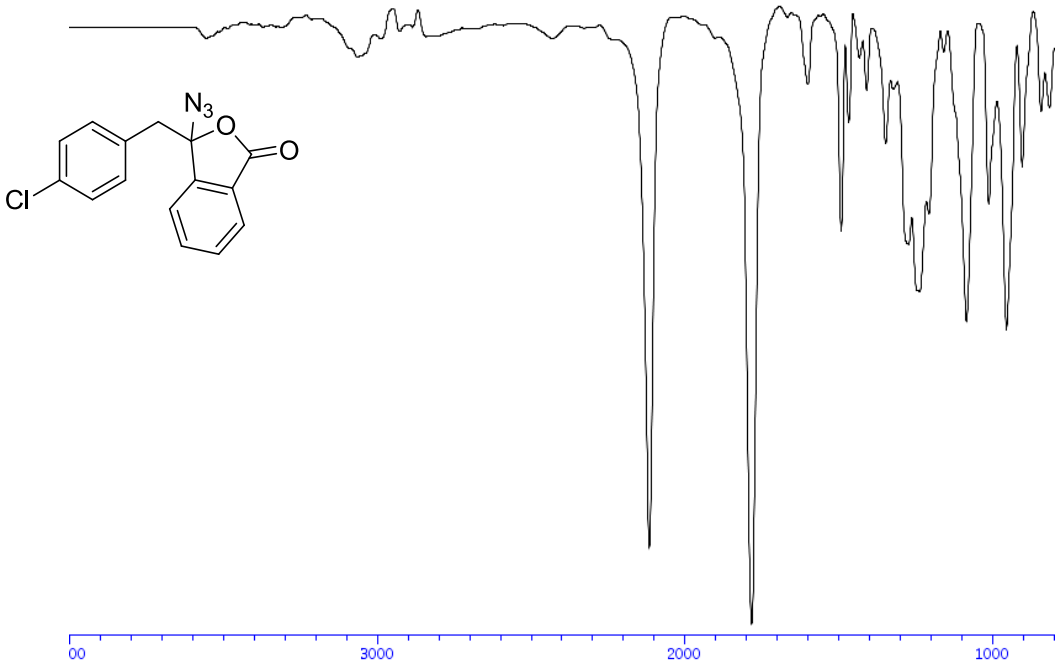
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3-azido-3-(4-chlorobenzyl)isobenzofuran-1(3H)-one (4j)**



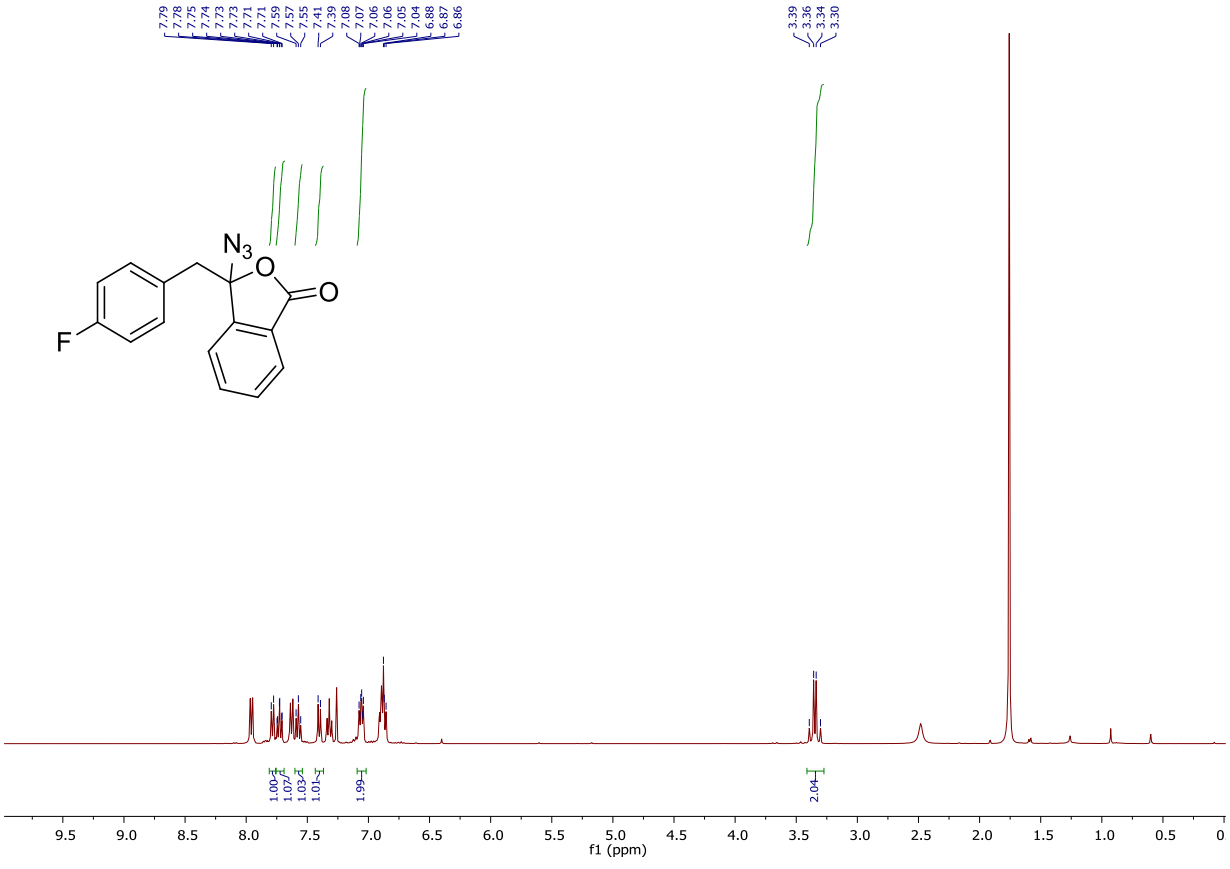
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-azido-3-(4-chlorobenzyl)isobenzofuran-1(3H)-one (4j)**



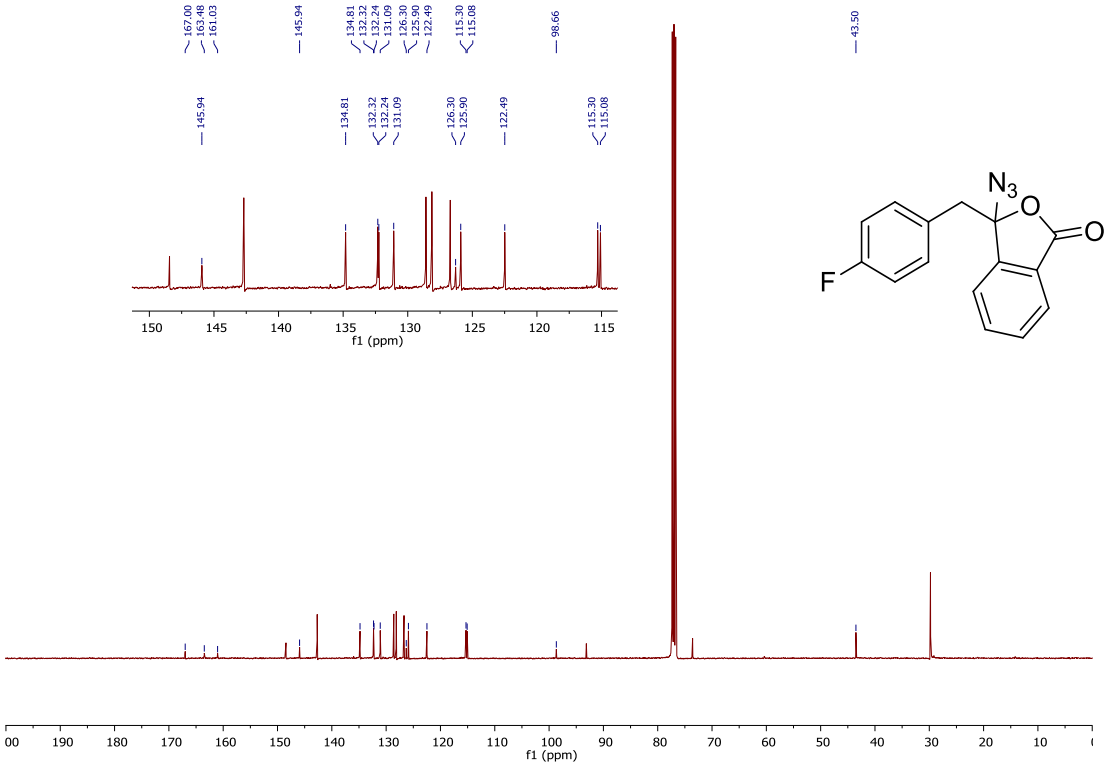
IR of compound **3-azido-3-(4-chlorobenzyl)isobenzofuran-1(3H)-one (4j)**



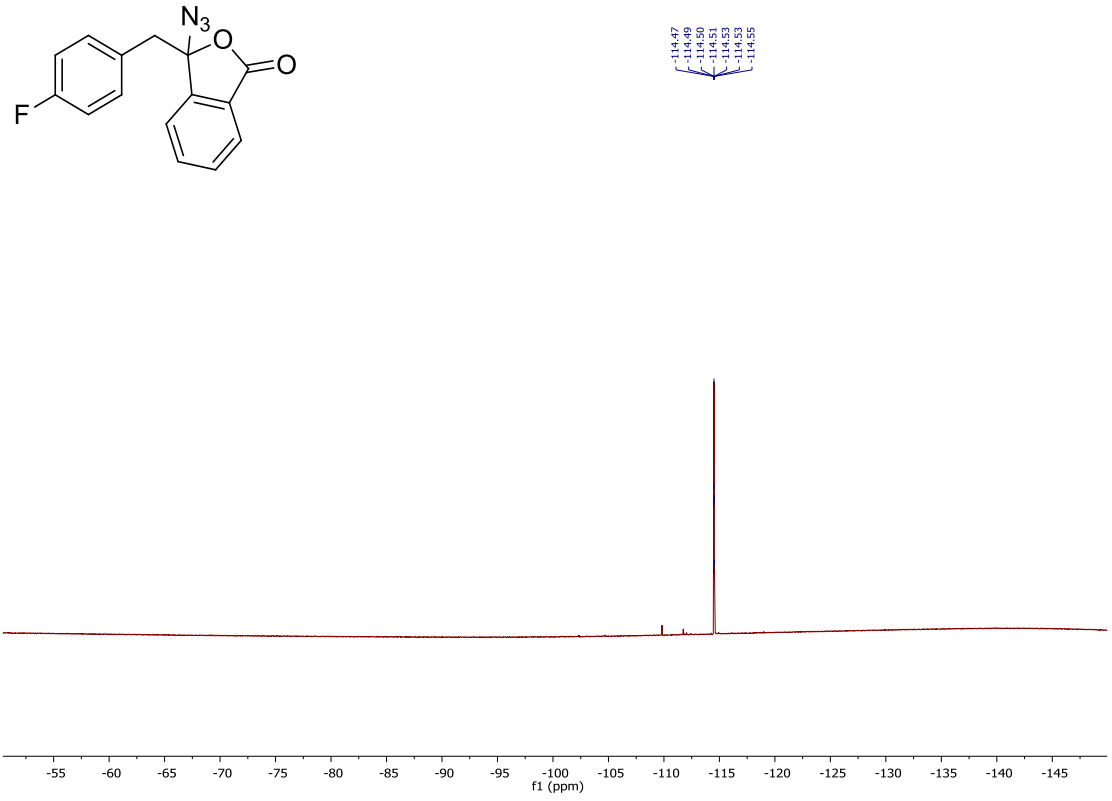
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3-azido-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one**



^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-azido-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one**

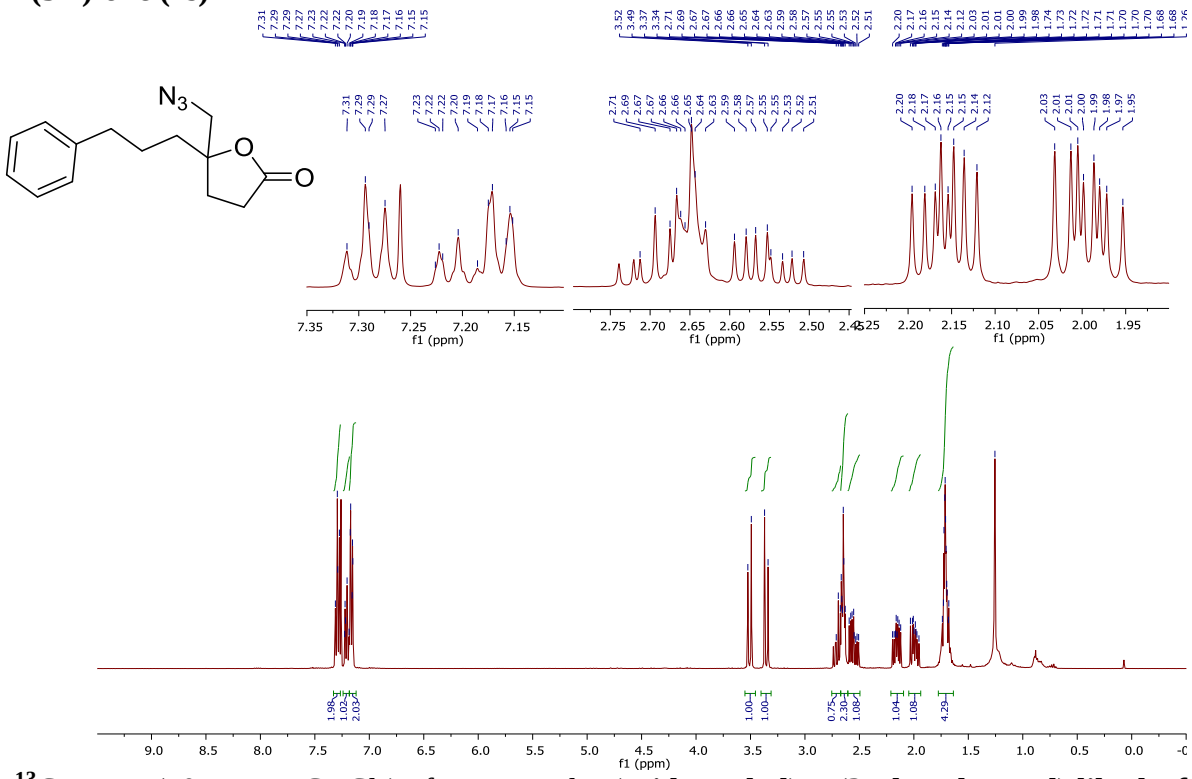


^{19}F NMR (376 MHz, $CDCl_3$) of compound **3-azido-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one**

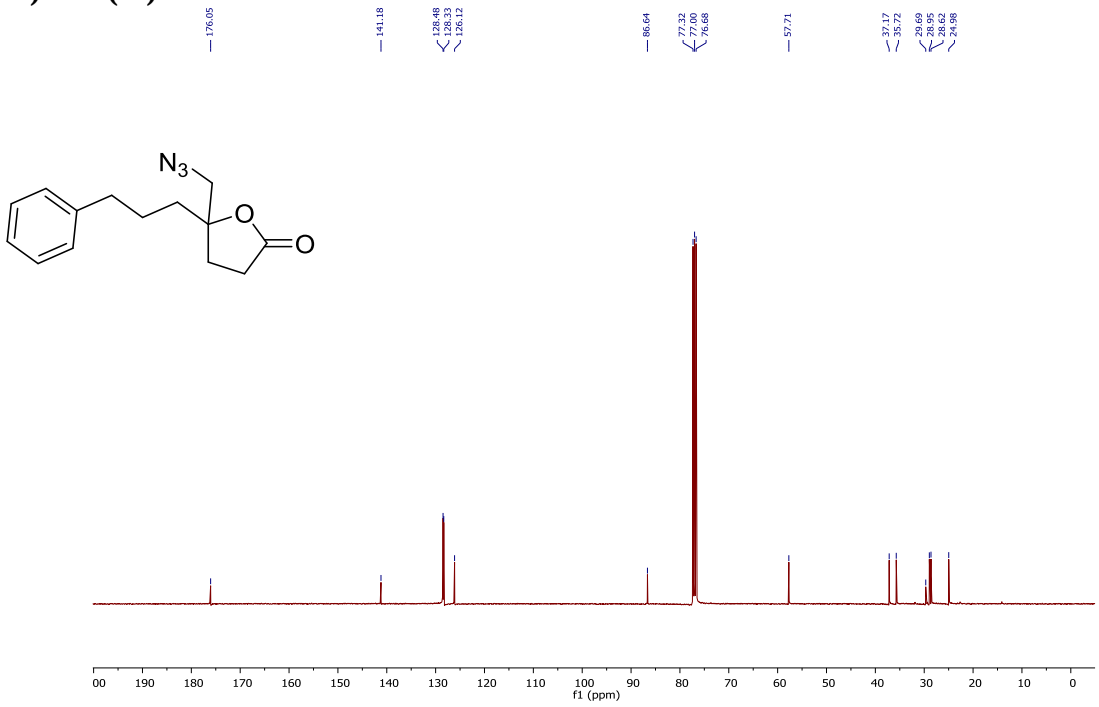


d. spectra of new compounds from the Pd catalysis.

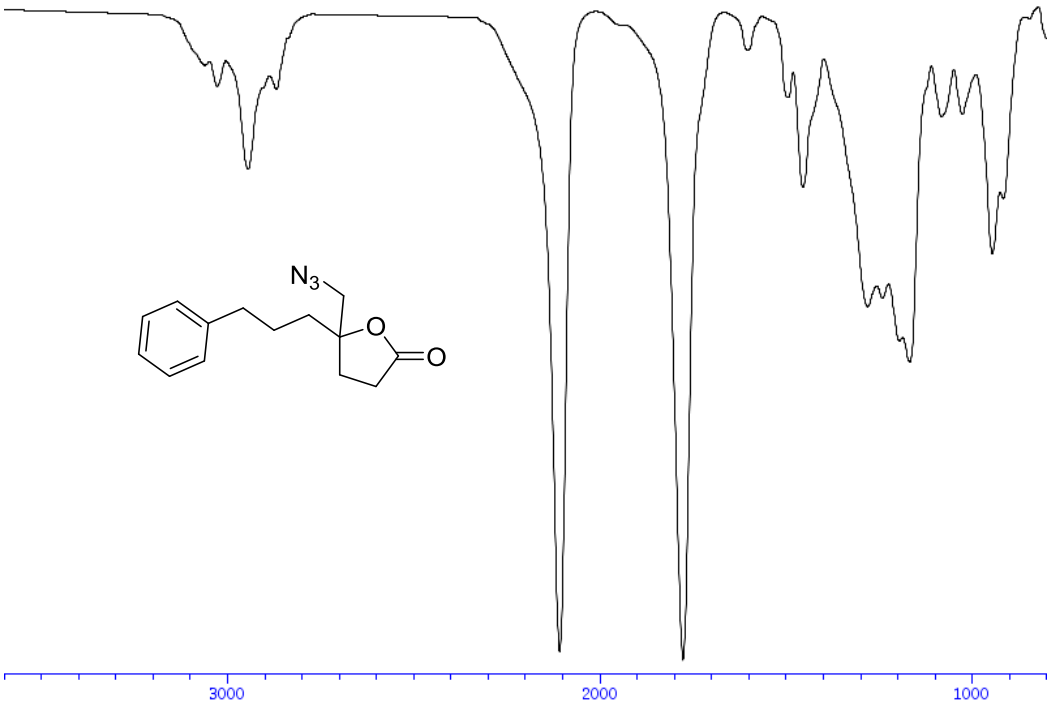
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(3-phenylpropyl)dihydrofuran-2(3H)-one (2s)**



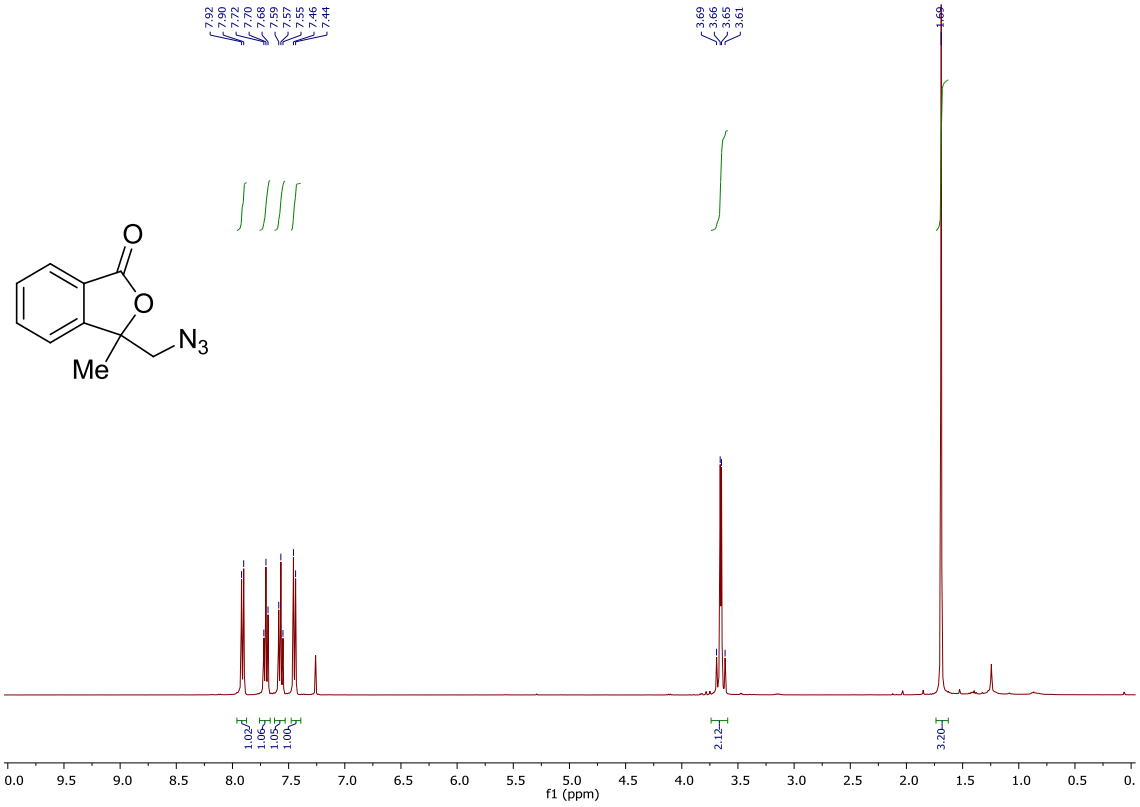
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **5-(azidomethyl)-5-(3-phenylpropyl)dihydrofuran-2(3H)-one (2s)**



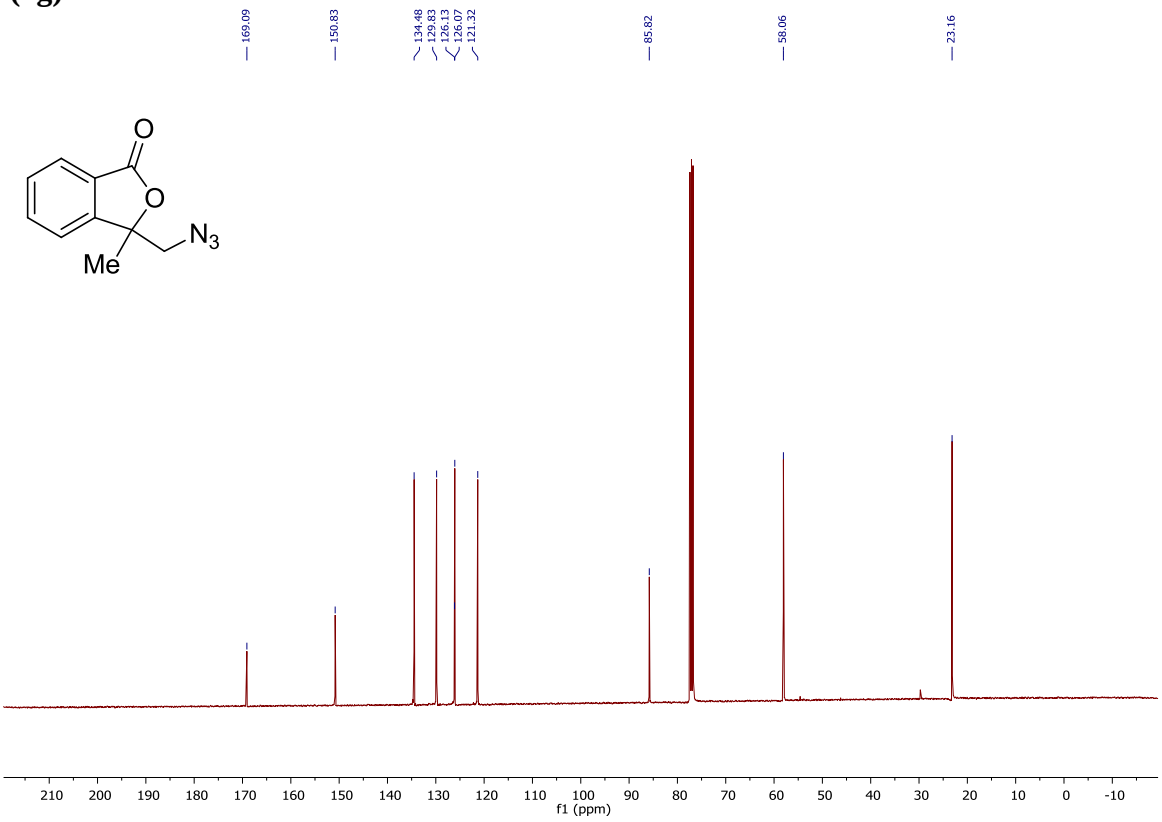
IR of compound **5-(azidomethyl)-5-(3-phenylpropyl)dihydrofuran-2(3H)-one (s)**



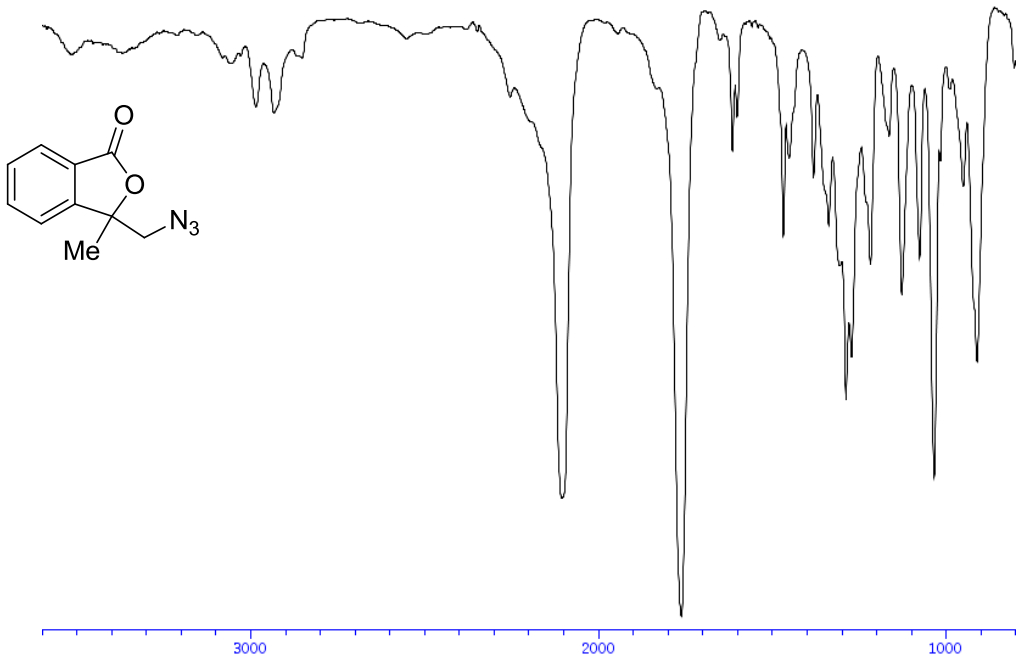
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



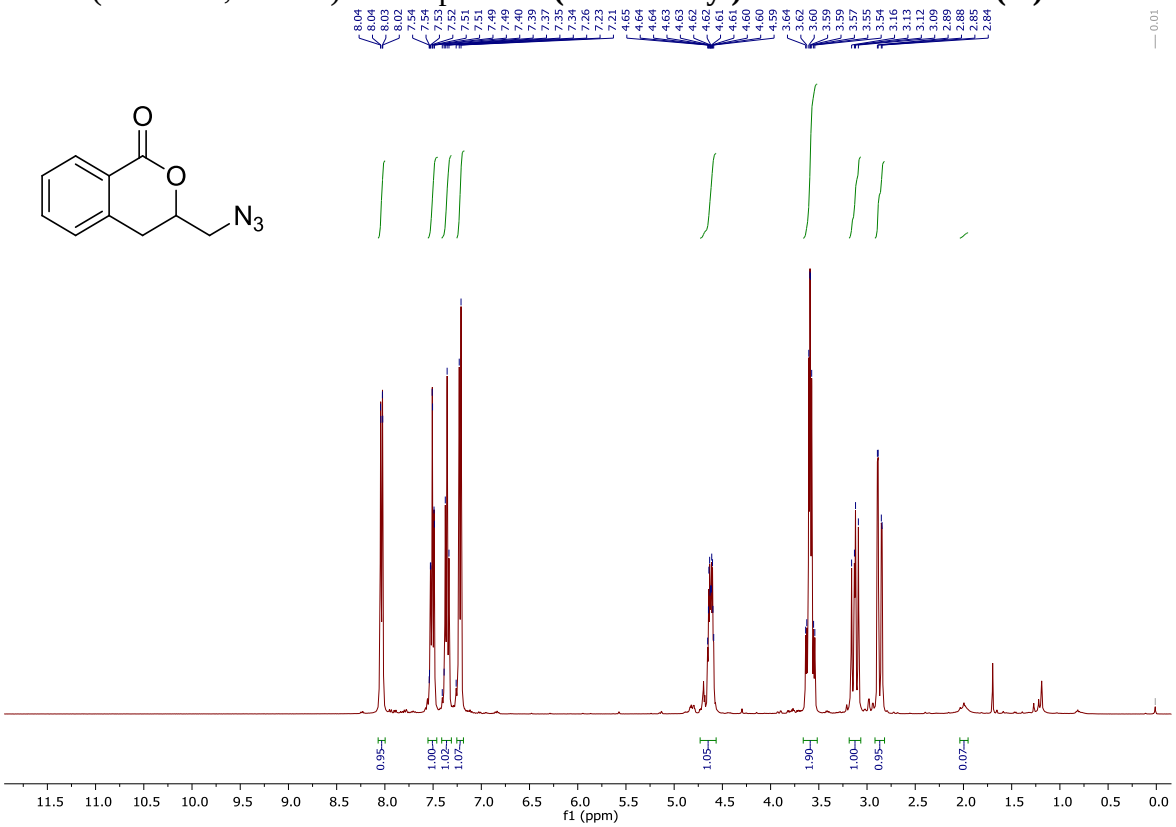
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



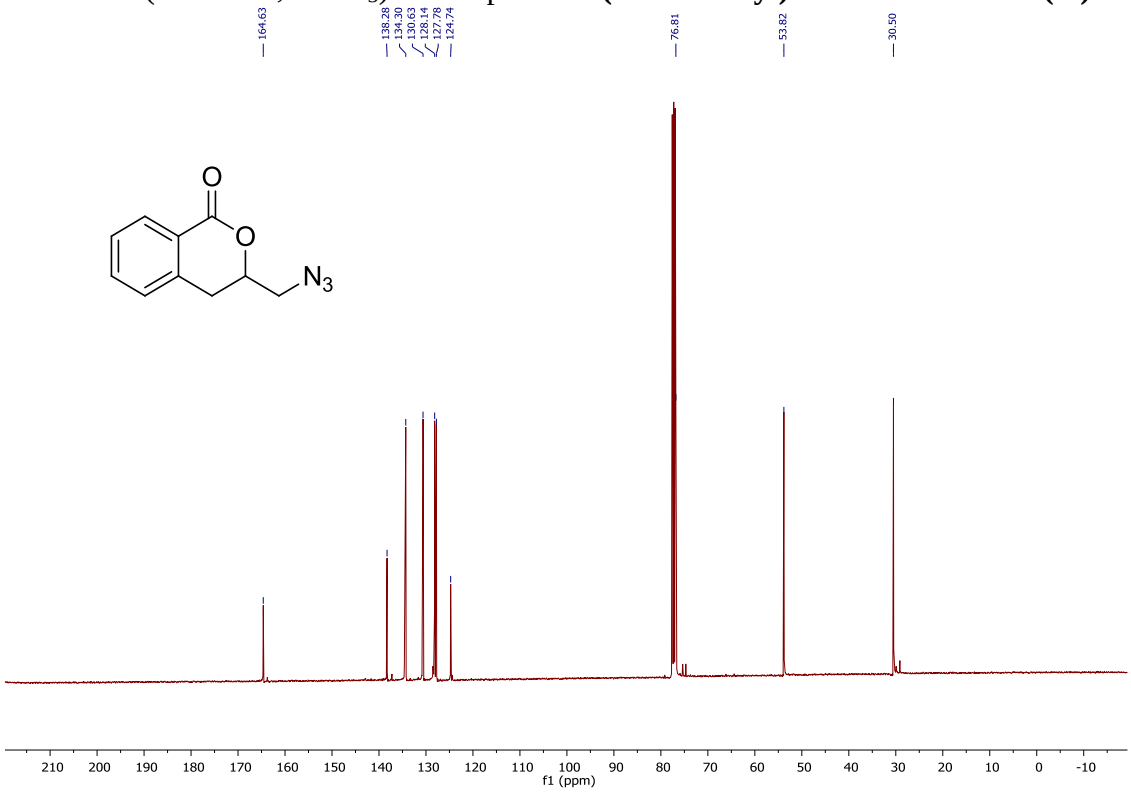
IR of compound **3-(azidomethyl)-3-methylisobenzofuran-1(3H)-one (2g)**



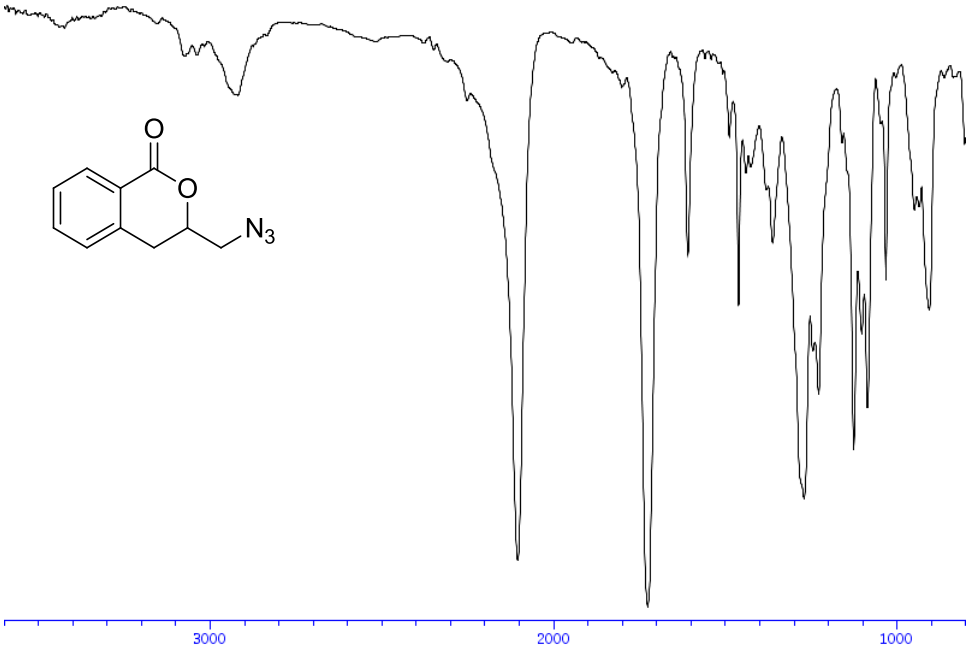
^{1}H-NMR (400 MHz, CDCl3) of compound **3-(azidomethyl)isochroman-1-one (2t)**



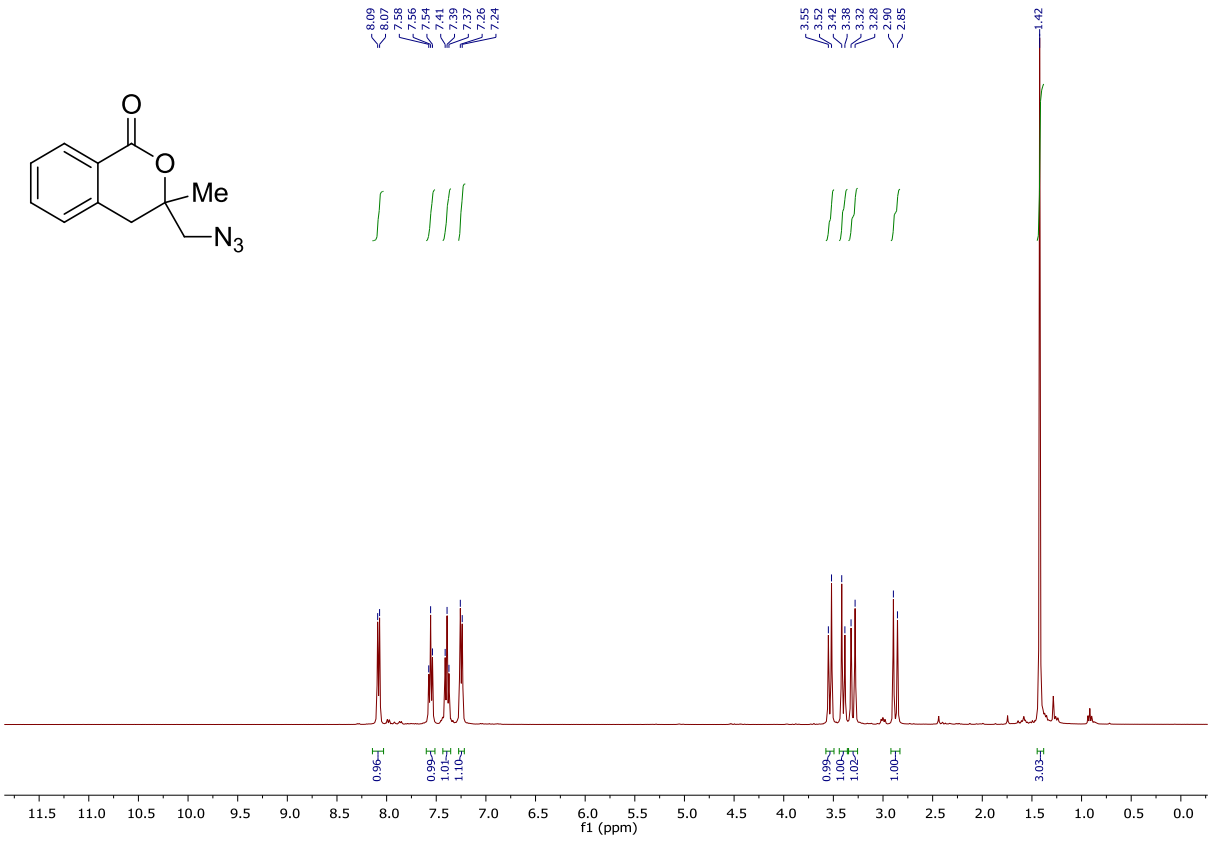
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-(azidomethyl)isochroman-1-one (2t)**



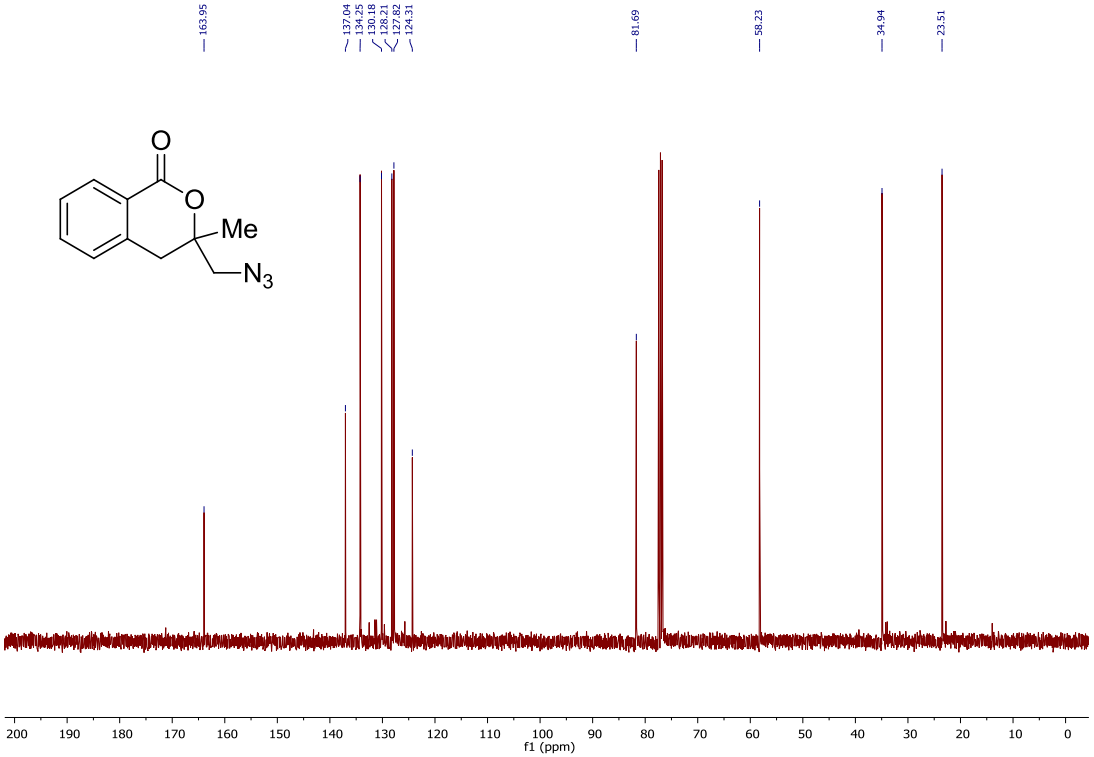
IR of compound **3-(azidomethyl)isochroman-1-one (2t)**



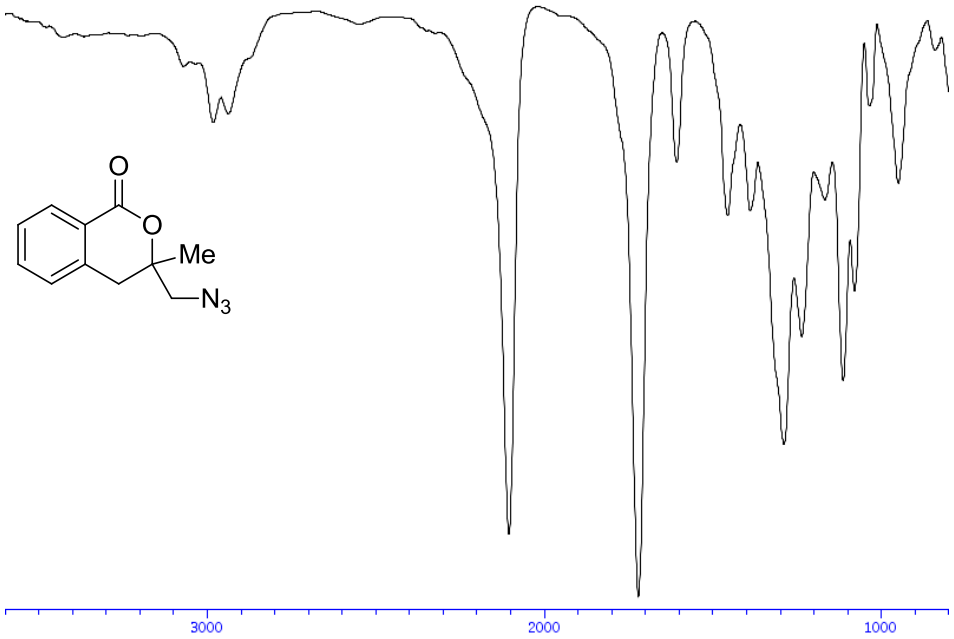
^{1}H-NMR (400 MHz, CDCl3) of compound **3-(Azidomethyl)-3-methylisochroman-1-one (2u)**



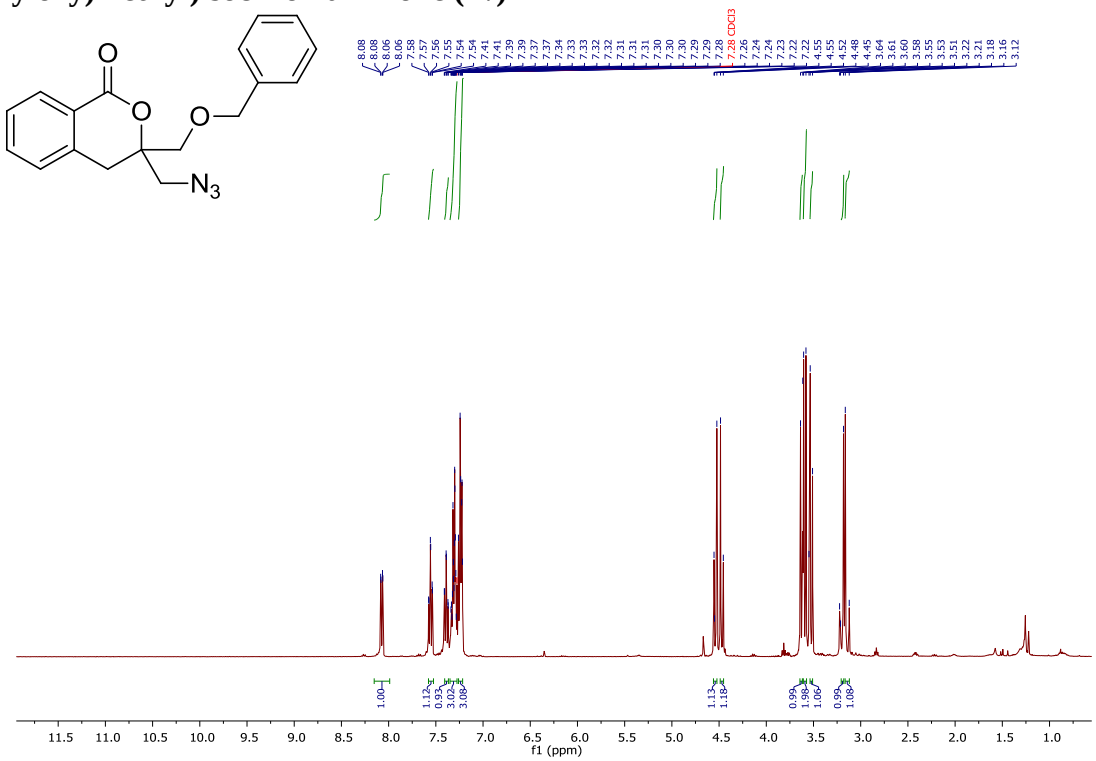
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-(Azidomethyl)-3-methylisochroman-1-one (2u)**



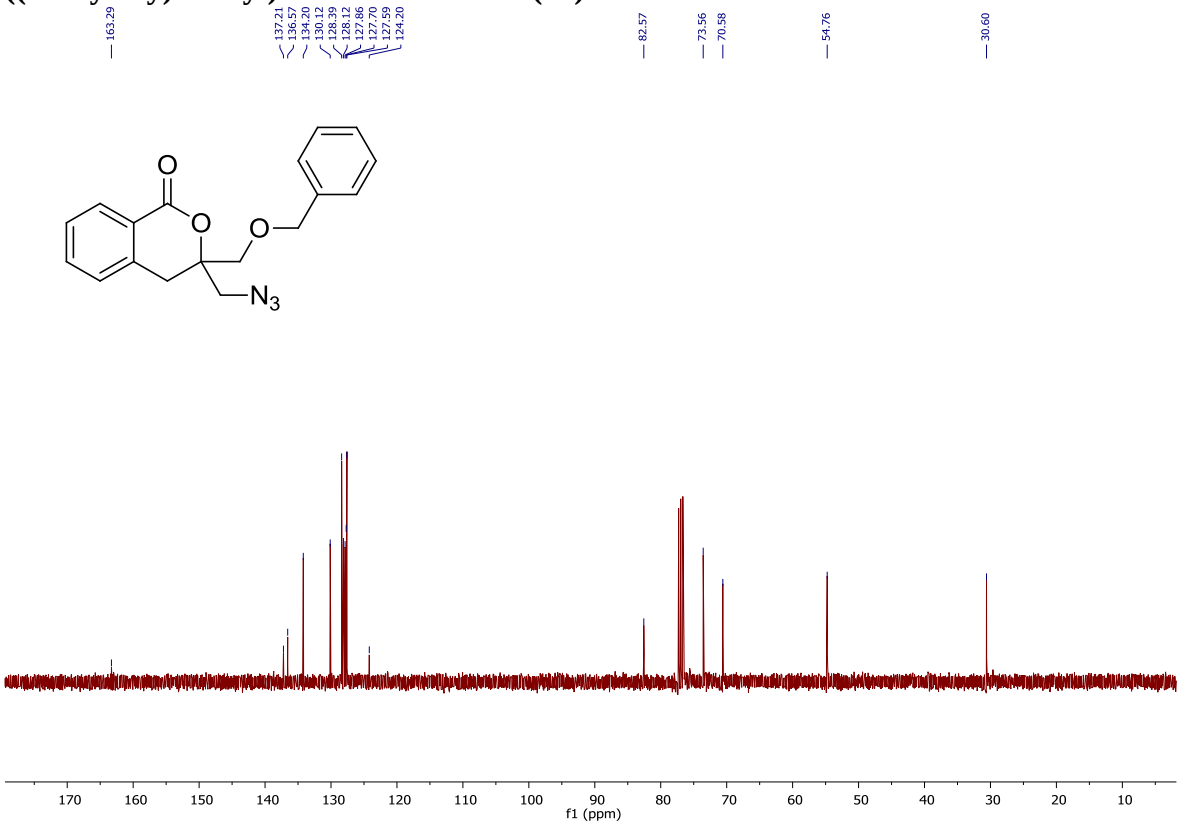
IR of compound **3-(Azidomethyl)-3-methylisochroman-1-one (2u)**



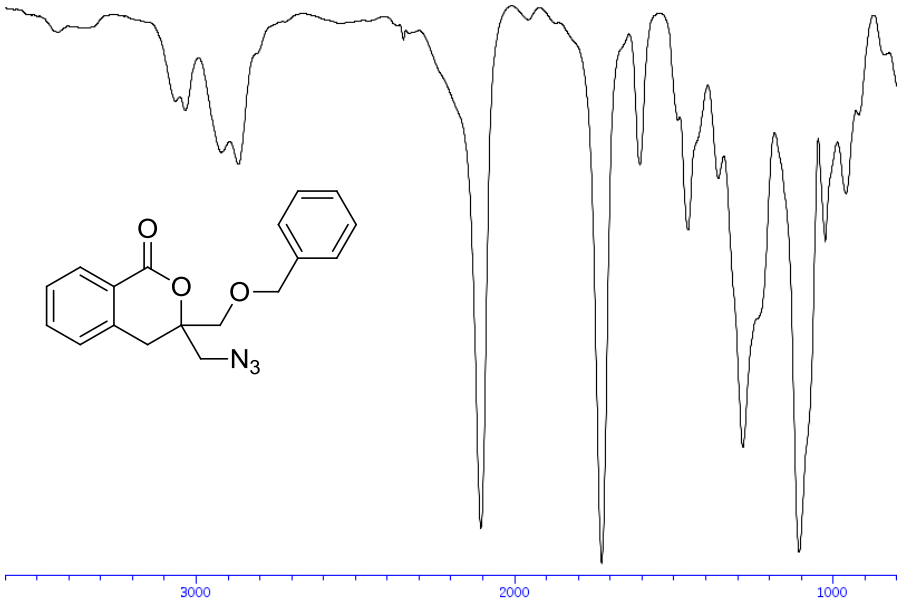
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3-(Azidomethyl)-3-((benzyloxy)methyl)isochroman-1-one (2v)**



^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-(Azidomethyl)-3-((benzyloxy)methyl)isochroman-1-one (2v)**

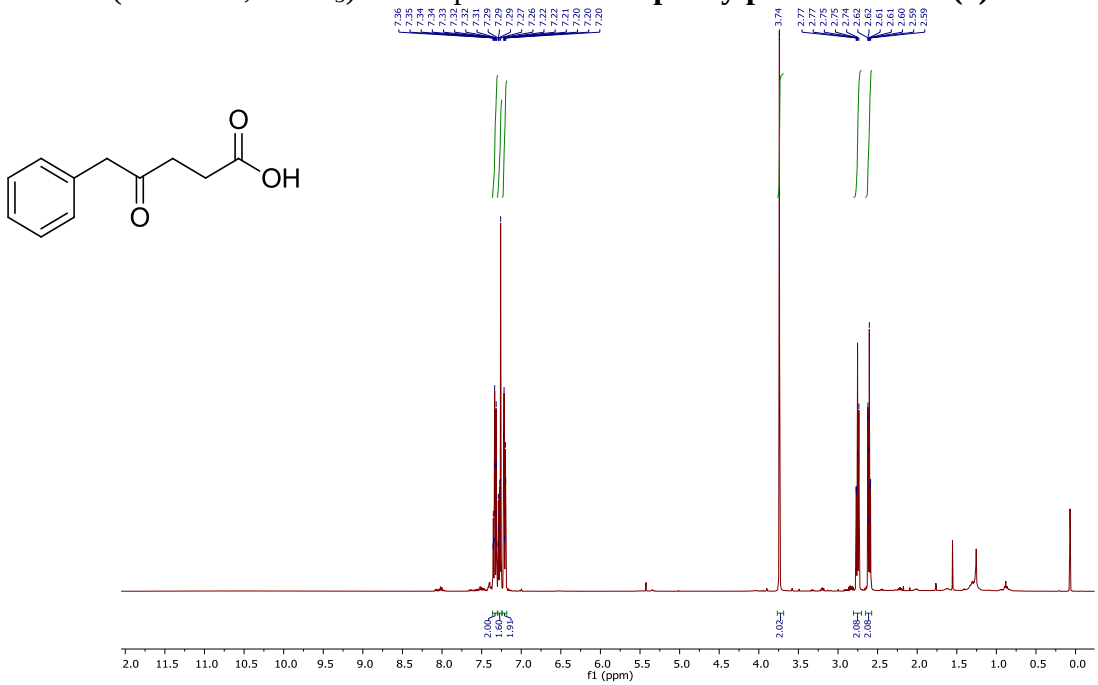


IR of compound **3-(Azidomethyl)-3-((benzyloxy)methyl)isochroman-1-one (XX)**

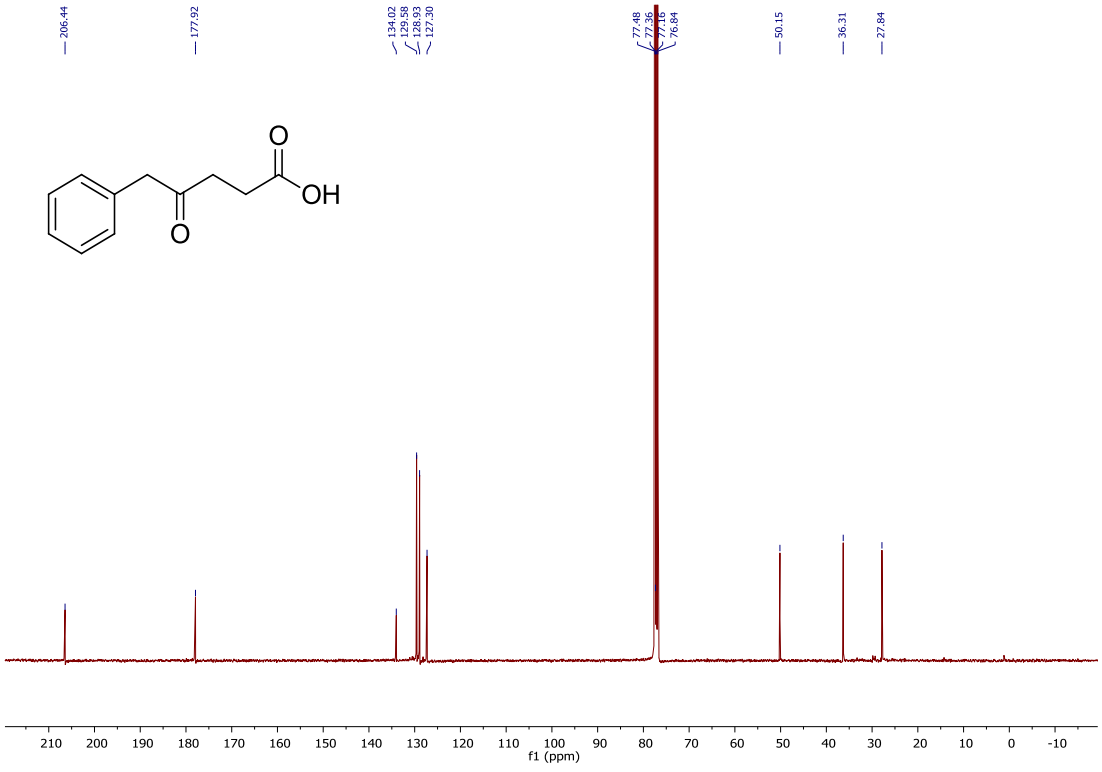


e. Spectra of new compounds from derivatization.

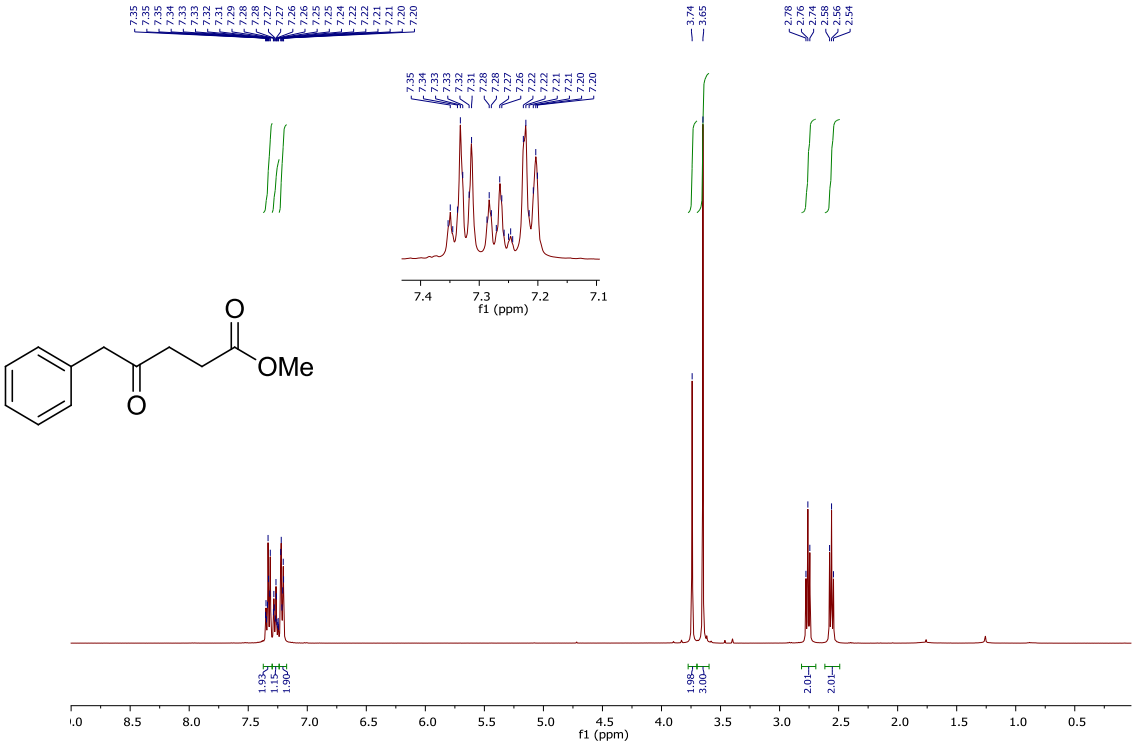
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **4-oxo-5-phenylpentanoic acid (6)**



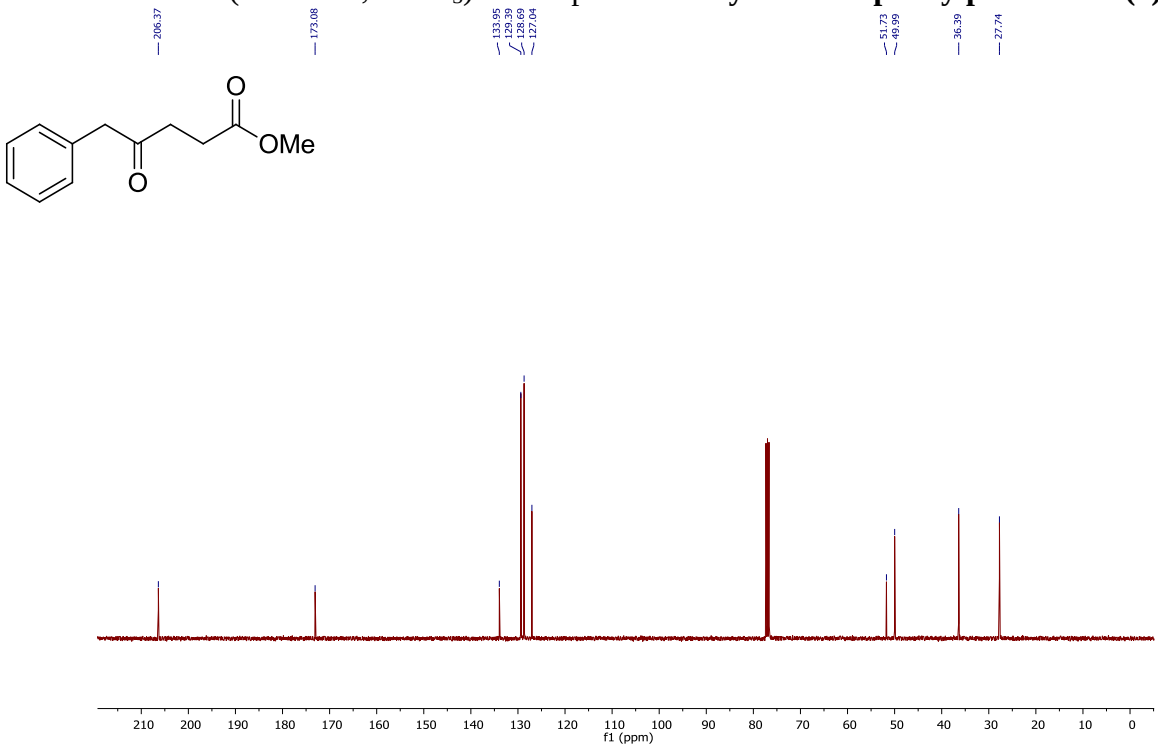
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **4-oxo-5-phenylpentanoic acid (6)**



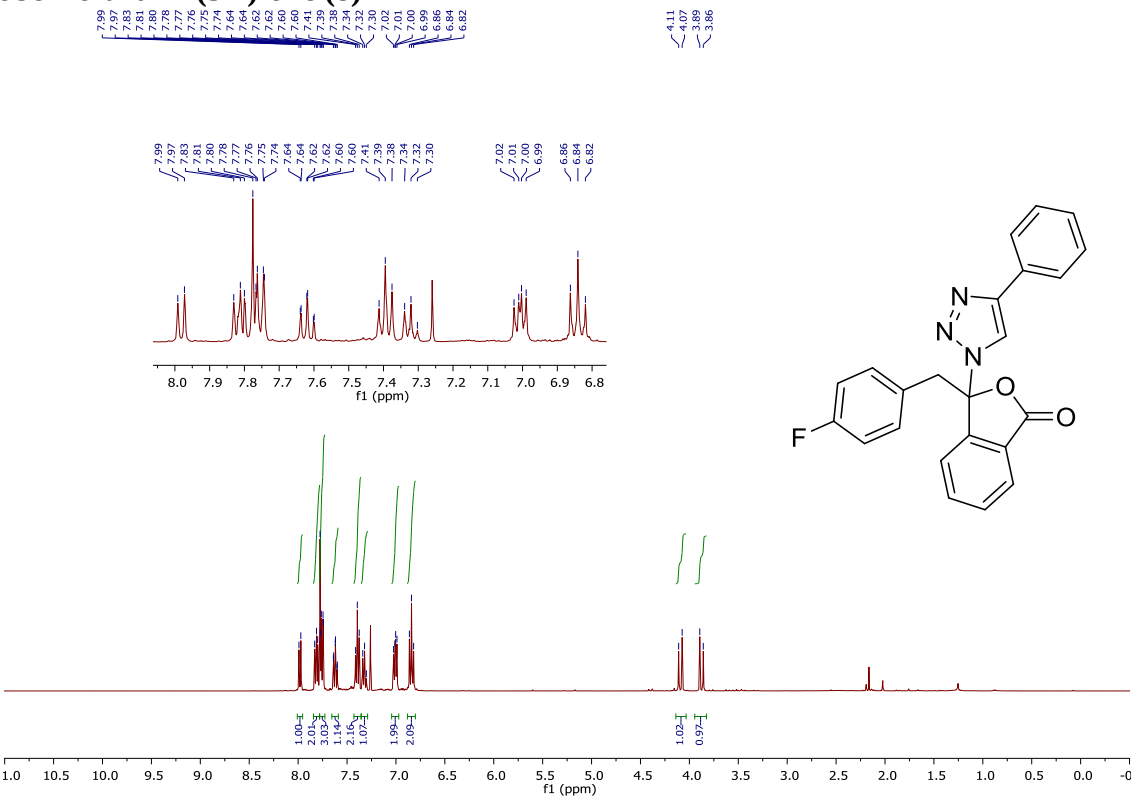
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **methyl 4-oxo-5-phenylpentanoate (7)**



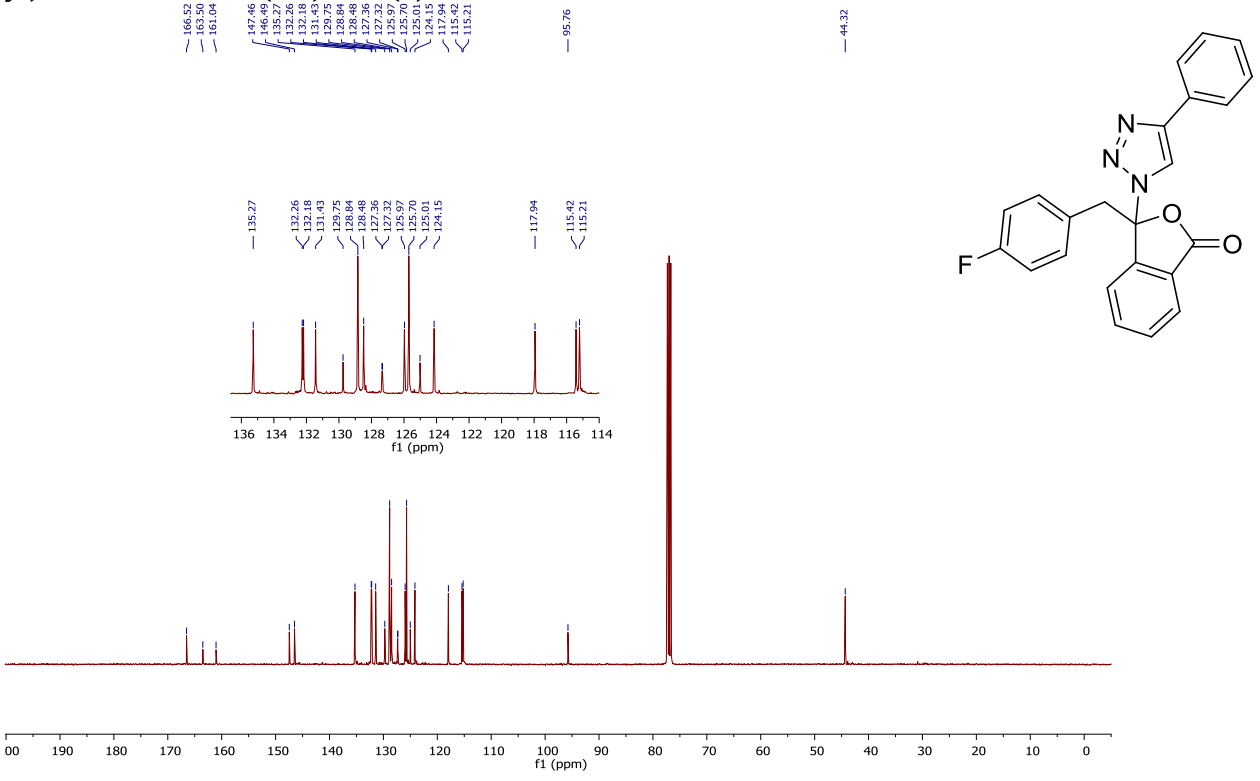
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **methyl 4-oxo-5-phenylpentanoate (7)**



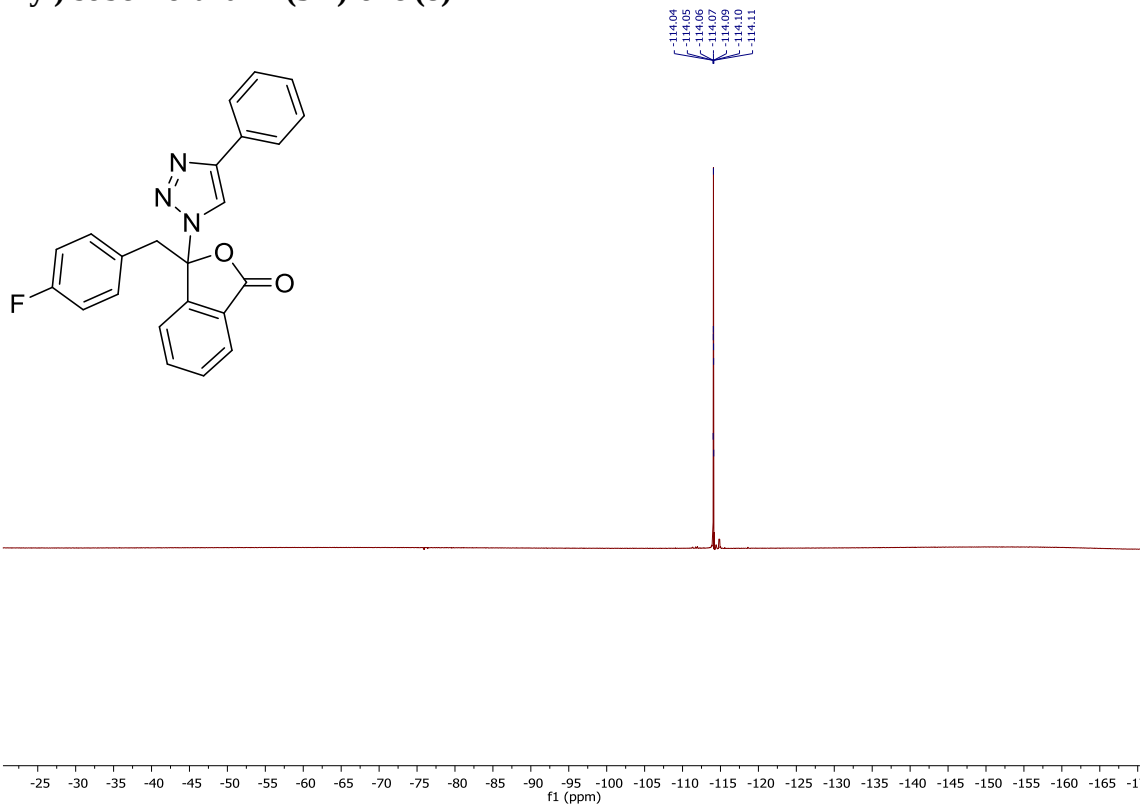
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3-(4-fluorobenzyl)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)isobenzofuran-1(3H)-one (8)**



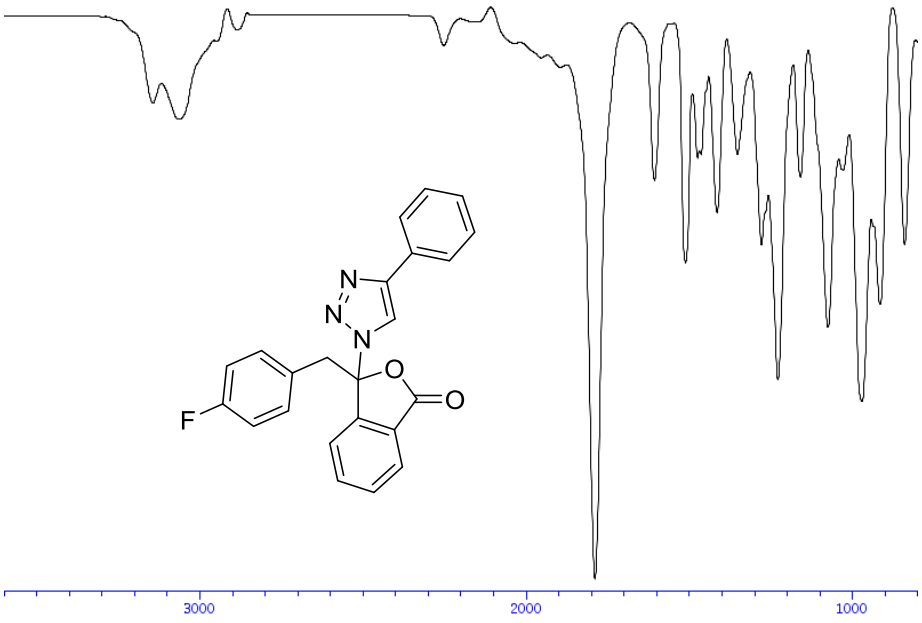
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-(4-fluorobenzyl)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)isobenzofuran-1(3H)-one (8)**



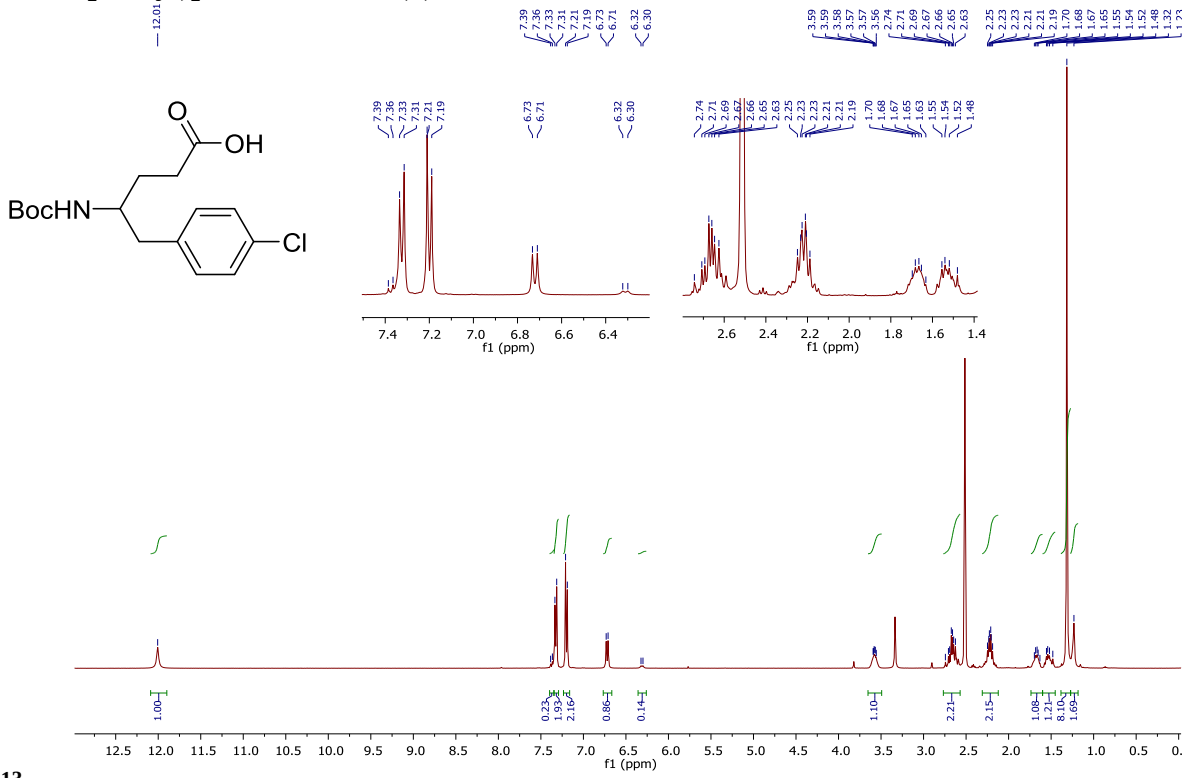
^{19}F NMR (376 MHz, $CDCl_3$) of compound **3-(4-fluorobenzyl)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)isobenzofuran-1(3H)-one (8)**



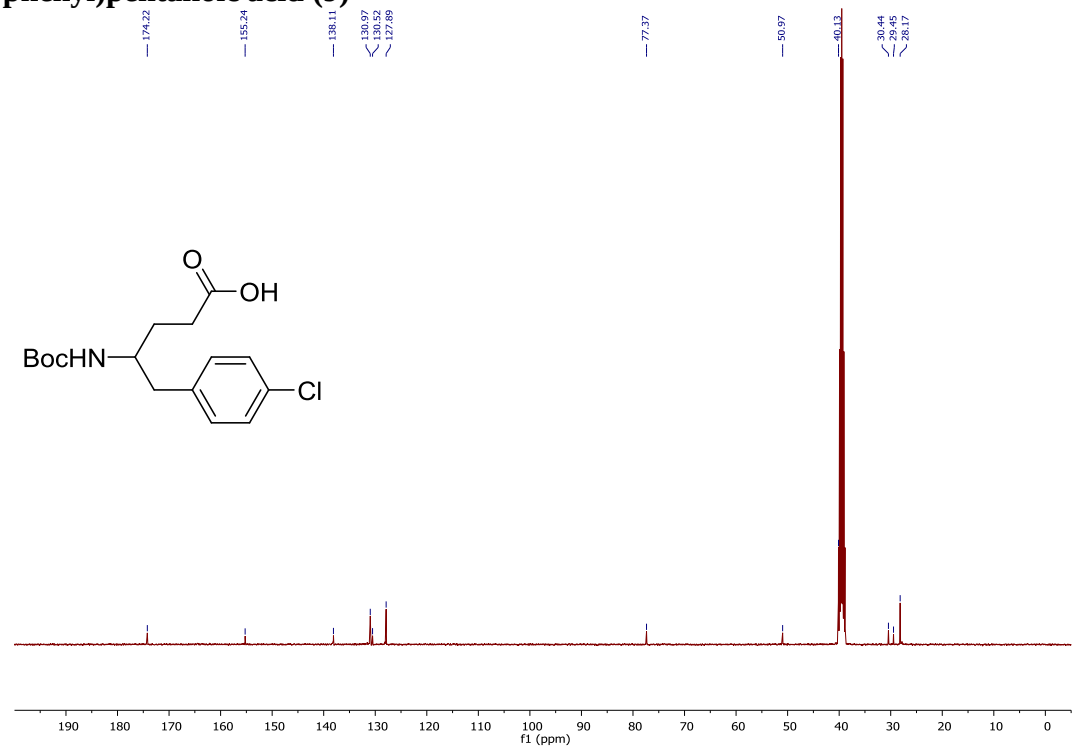
IR of compound **3-(4-fluorobenzyl)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)isobenzofuran-1(3H)-one (8)**



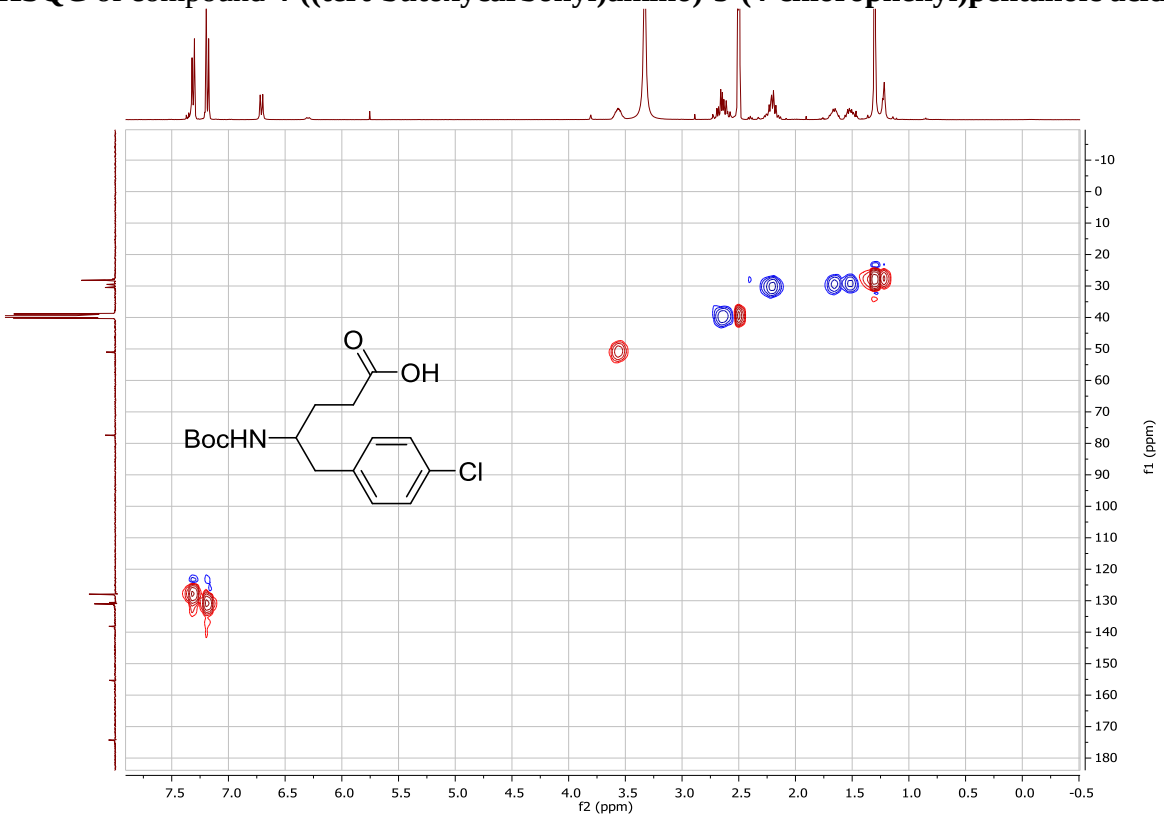
^{1}H-NMR (400 MHz, CDCl3) of compound **4-((tert-butoxycarbonyl)amino)-5-(4-chlorophenyl)pentanoic acid (9)**



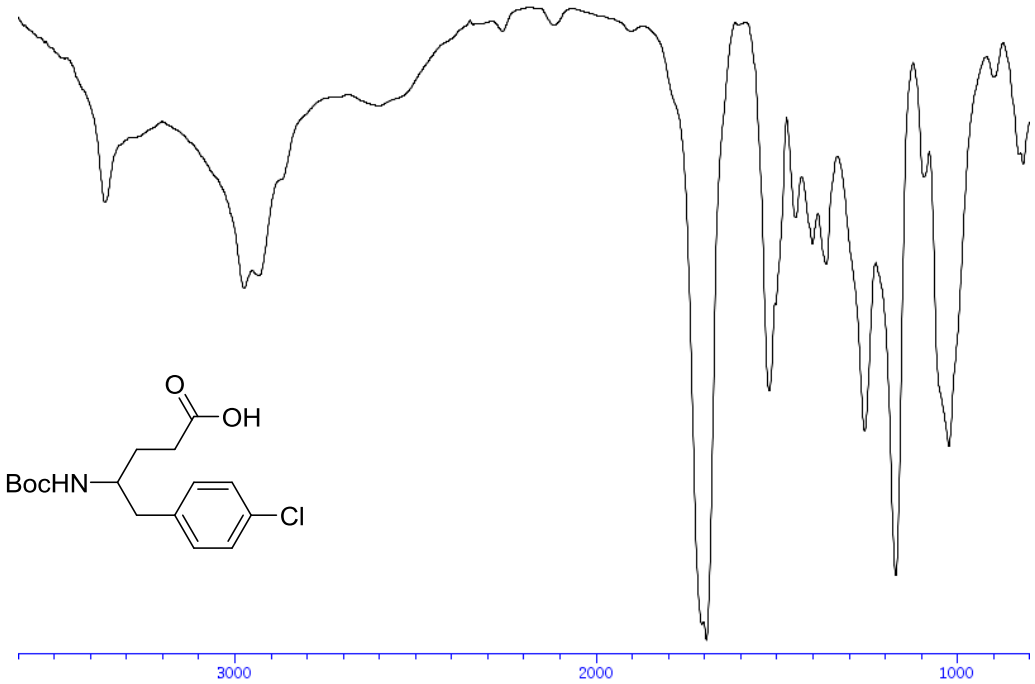
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **4-((tert-butoxycarbonyl)amino)-5-(4-chlorophenyl)pentanoic acid (9)**



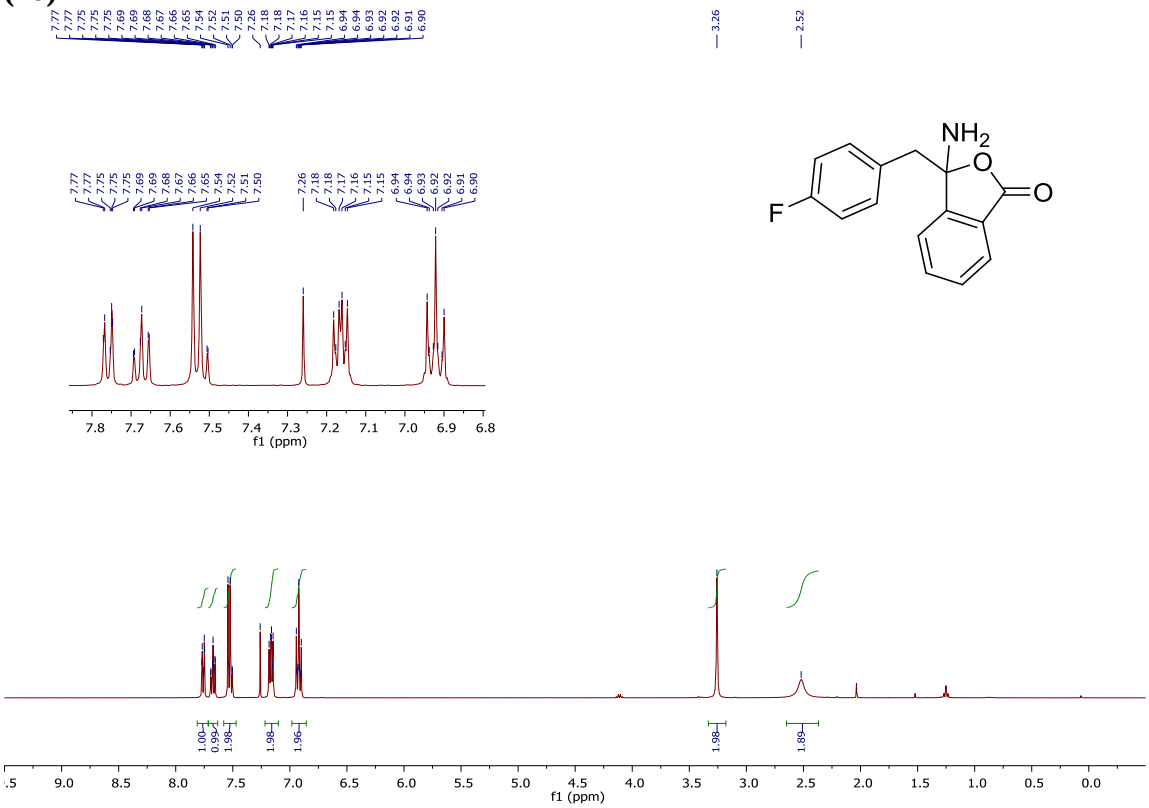
HSQC of compound **4-((tert-butoxycarbonyl)amino)-5-(4-chlorophenyl)pentanoic acid (9)**



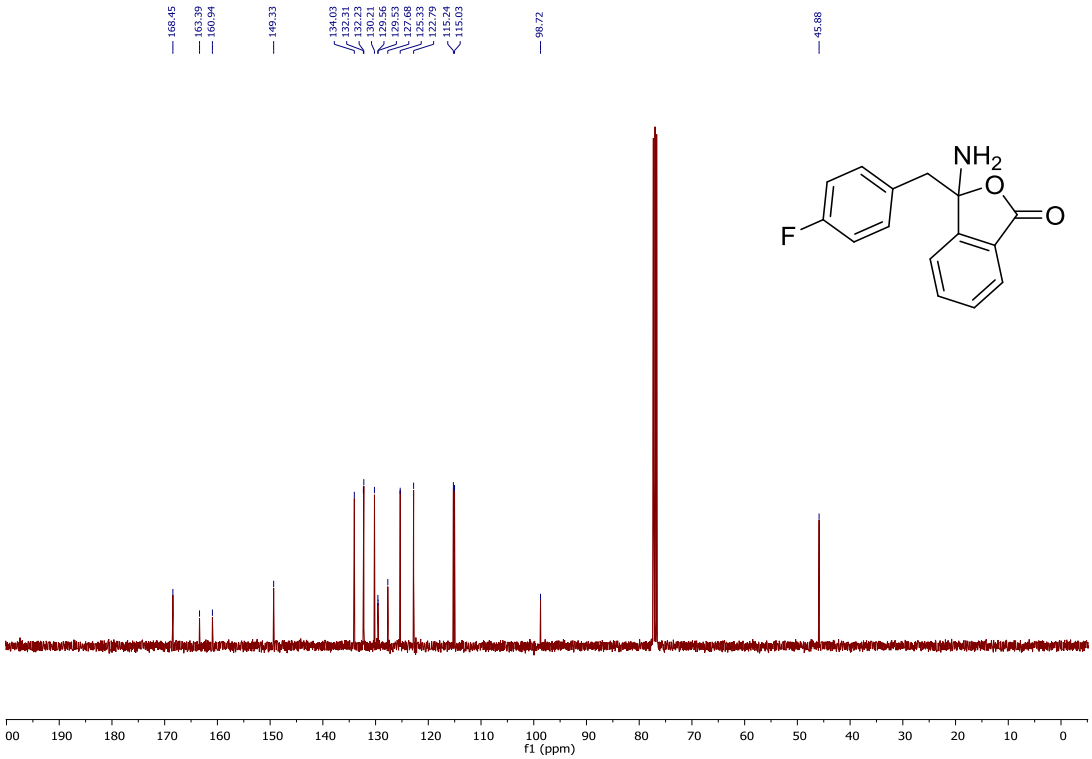
IR of compound **4-((tert-butoxycarbonyl)amino)-5-(4-chlorophenyl)pentanoic acid (9)**



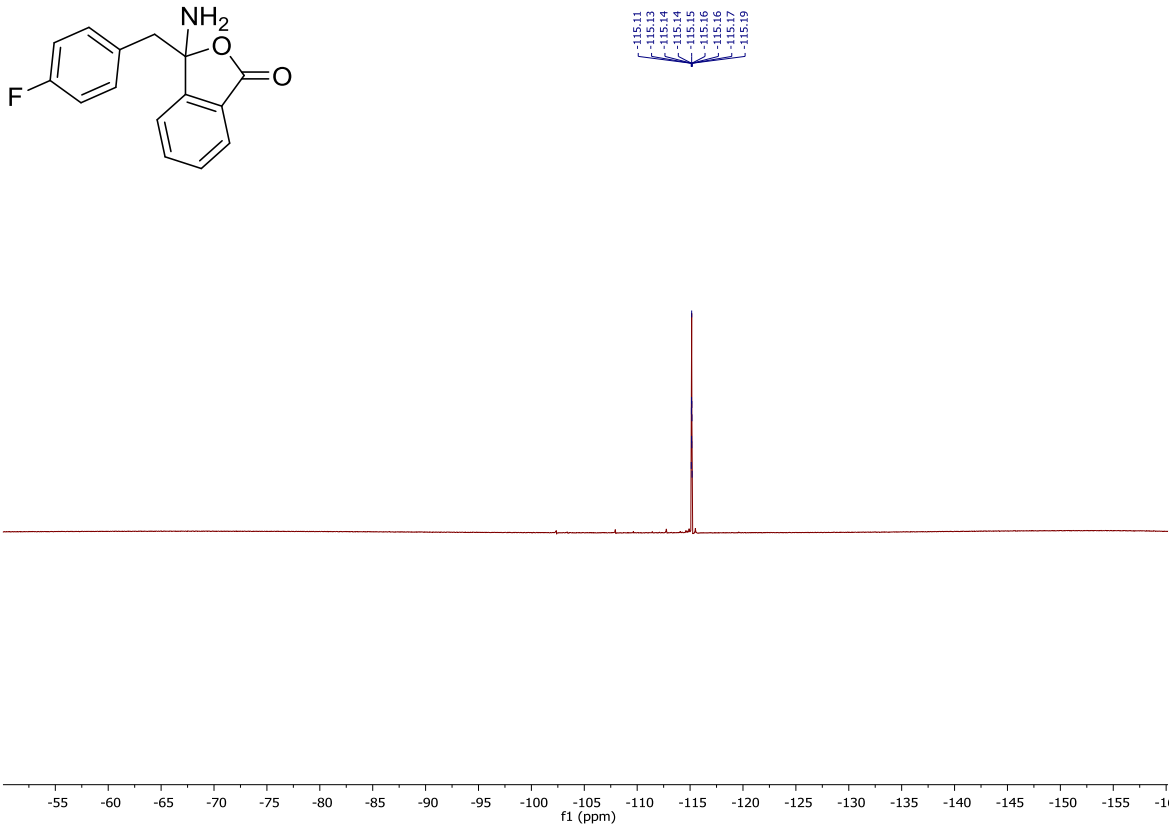
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 3-**amino-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (10)**



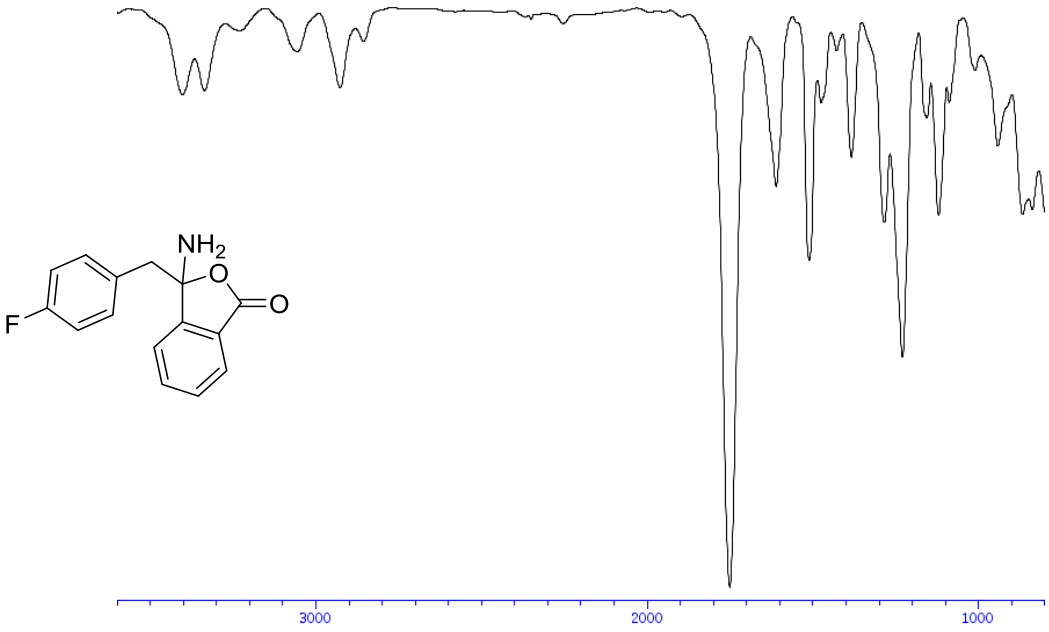
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **3-amino-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (10)**



^{19}F NMR (376 MHz, $CDCl_3$) of compound **3-amino-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (10)**



IR of compound **-amino-3-(4-fluorobenzyl)isobenzofuran-1(3H)-one (10)**



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