

Supporting Information

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A Zinc(II) Catalyst System for the Conia-Ene Reaction of Alkynyl Aminomalonates Applicable to 5-*Endo*-Dig Reactions

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Introduction

¹H and ¹³C NMR spectra were recorded on Bruker DPX-400, DRX-400, AVC-500 or AVB-500 using deutero chloroform as an internal deuterium lock. Chemical shifts are quoted in units of δ relative to tetramethylsilane (δ=0). Multiplets are indicated as s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; dd, double doublet; m, multiplet; br, broad, etc. Coupling constants J are quoted in Hz. ¹³C spectra were recorded with proton decoupling; HMQC, were recorded to assist assignment.

Infrared spectra were recorded on a Tensor 27 FTIR spectrometer. The samples were prepared as a thin film and the intensity of the peak is indicated with w, weak, m, medium, and s, strong.

Mass spectra were recorded by the Mass Spectrometry Service at the Chemical Research Laboratory, University of Oxford.

Flash chromatography was carried out on silica gel [Merck 9385 Kieselgel 60 (230-400 ASTM)]. Analytical TLC was carried out on 0.25 mm thick plates precoated with Merck Kieselgel F₂₅₄ silica gel and visualised by UV and aqueous potassium permanganate solution, ethanolic phosphomolybdic acid solution or ninhydrin in ethanol.

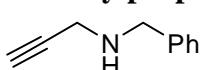
Solvents were purified by standard techniques. Ether refers to diethyl ether. Petroleum ether (PE) refers to the fraction boiling at 40-60 °C.

The cyclization precursors for the 5-exo cyclization reaction as well as diethyl *N*-benzyl-amino malonate were synthesised according to procedures described by us before.^[1] The butynoic amido malonates were generated according to a procedure of Hatakeyama.^[2] The general procedure for the cyclization reaction was based on the Conia-ene reaction described by Li.^[3]

1. Synthesis of the cyclization precursors

1. 1. Synthesis of propargyl amino malonates

N-Benzylprop-2-yn-1-amine

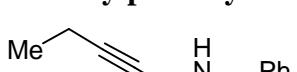


Propargyl bromide (3.34 mL, 80% in toluene, 30 mmol, 1.0 eq.) was added dropwise to benzylamine (19.66 mL, 180 mmol, 6.0 eq.). The reaction was stirred 15 h at room temperature and then 2 M NaOH (100 mL) and Et₂O (100 mL) were added. The organic layer was separated and the aqueous layer was extracted with Et₂O (2 × 50 mL). The combined organic layers were dried (MgSO₄) and the solvent removed. Purification by FC (EtOAc) yielded *N*-benzylprop-2-yn-1-amine (3.36 g, 23.1 mmol, 77%) as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.38-7.31 (*m*, 4H, H_{ar}), 7.29-7.25 (*m*, 1H, H_{ar}), 3.90 (*s*, 2H, CH₂Ph), 3.44 (*d*, 2H, *J* = 2.4 Hz, CH₂CC), 2.27 (*t*, 1H, *J* = 2.4 Hz, CCH), 1.51 (*s*, 1H, NH).

The ¹H-NMR data is in accordance to the literature.^[4]

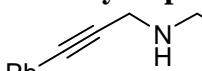
N-Benzylpent-2-yn-1-amine



1-Bromopent-2-yne (1.53 mL, 15.0 mmol, 1.0 eq.) was added dropwise to benzylamine (9.83 mL, 90 mmol, 6.0 eq.). After complete addition the reaction was stirred at room temperature for 15 h. Then 2 M NaOH (100 mL) and Et₂O (100 mL) were added. The organic layer was separated and the aqueous layer was extracted twice with Et₂O (50 mL). The combined organic layers were dried (MgSO₄) and the solvent was evaporated. Purification by FC (PE/EtOAc 1:2) afforded *N*-benzylpent-2-yn-1-amine (1.96 g, 11.3 mmol, 76%) as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.37-7.24 (*m*, 5H, H_{ar}), 3.87 (*s*, 2H, CH₂Ph), 3.41 (*t*, 2H, *J* = 2.2 Hz, CCCH₂N), 2.23 (*qt*, 2H, *J* = 7.5, 2.2 Hz, CCCH₂CH₃), 1.16 (*t*, 3H, *J* = 7.5 Hz, CCCH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 139.7 (C_{ar}), 128.4 (4×CH_{ar}), 127.0 (CH_{ar}), 85.3 (C), 77.3 (C), 52.5 (CH₂), 37.9 (CH₂), 14.1 (CH₃), 12.4 (CH₂). IR(film): 3317m, 3062w, 3027w, 2975m, 2935m, 2917m, 2877w, 2843w, 1495w, 1453s, 1359w, 1318w, 1130w, 1101w, 1028w, 738s, 698s. MS (ESI+): 174.13 (100, [M+H]⁺). HRMS (ESI): calculated for C₁₂H₁₆N ([M+H]⁺) 174.1277, found 174.1281.

N-Benzyl-3-phenylprop-2-yn-1-amine

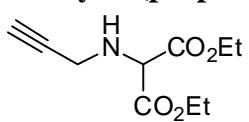


3-Phenyl propargyl chloride (2.06 mL, 15 mmol, 1.0 eq.) was added dropwise to benzylamine (9.89 mL, 90 mmol, 6.0 eq.). After complete addition the reaction was stirred for 15 h. Aqueous 2 M NaOH and Et₂O were added (100 mL) and the organic layer was separated. The aqueous layer was extracted twice with Et₂O (75 mL), the combined organic layers were dried (MgSO₄) and the solvent removed. After purification by FC (PE/Et₂O 1:2) *N*-benzyl-3-phenylprop-2-yn-1-amine (3.09 g, 14.0 mmol, 93%) was obtained as a yellow oil.

¹H-NMR (400 MHz, CDCl₃): 7.46-7.44 (*m*, 2H, H_{ar}), 7.40-7.26 (*m*, 8H, H_{ar}), 3.96 (*s*, 2H, CH₂Ph), 3.67 (*s*, 2H, CH₂CC). The NH proton is not resolved.

The NMR data is in accordance with the literature.^[4]

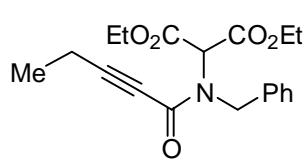
Diethyl 2-(prop-2-ynylamino)malonate **4c**



Propargylamine (1.92 mL, 30 mmol, 1.5 eq.), NEt₃ (418 mL, 30 mmol, 1.5 eq.) and diethyl bromomalonate (3.71 mL, 92% pure (ex-Aldrich), 20 mmol, 1.0 eq.) were dissolved in CHCl₃ (50 mL) and heated to reflux for 3 d. Then water (100 mL) was added and the organic layer was separated. The aqueous layer was extracted twice with Et₂O (75 mL), the combined organic layers were dried (MgSO₄) and the solvent was evaporated. Purification by FC (PE/Et₂O 2:1) afforded diethyl 2-(prop-2-ynylamino)malonate **4c** (1.11 g, approx. 90% pure, 4.68 mmol, 23%) as a yellow oil.

¹H-NMR (400 MHz, CDCl₃): 4.31-4.20 (*m*, 4H, 2 × CH₂O), 4.25 (*s*, 1H, NHCH), 3.52 (*d*, 2H, *J* = 2.5 Hz, CH₂), 2.25 (*t*, 1H, *J* = 2.5 Hz, CCH), 1.30 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 168.1 (2 × CO), 80.32 (C_{sp}), 72.5 (CH_{sp}), 63.3 (C), 61.9 (2 × CH₂), 36.5 (CH₂), 14.0 (2 × CH₃). IR (film): 3223s, 2984m, 2940w, 2908w, 1788s, 1735s, 1467w, 1448w, 1371m, 1302m, 1219m, 1180m, 1155m, 1096w, 1028w, 860w, 669w. MS (ESI+): 214.12 (32, [M+H]⁺), 236.08 (100, [M+Na]⁺), 307.19 (16), 329.15 (93), 449.21 (36, [2M+Na]⁺), 518.26 (78), 731.38 (20). HRMS (ESI): calculated for C₁₀H₁₆NO₄ ([M+H]⁺) 214.1074 found 214.1079.

Diethyl 2-(*N*-benzylpent-2-ynamido)malonate **14a**

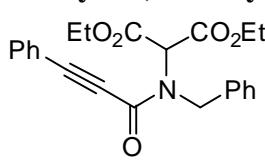


According to a procedure by Hatakeyama:^[2] 2-Pentynoic acid (471 mg, 4.8 mmol, 1.2 eq.) was dissolved in DCM (12 mL). A few drops of DMF were added and then dropwise oxalyl chloride (372 μL, 4.4 mmol, 1.1 eq.). After complete addition the reaction was stirred for 1 h at room temperature.

In a separate flask diethyl 2-(benzylamino)malonate (1.06 g, 4.0 mmol, 1.0 eq.) was dissolved in a mixture of DCM (8 mL) and sat. NaHCO₃ solution (8 mL). To this vigorously stirred solution was added the crude acid chloride. The reaction was stirred 30 min at room temperature and the filtered through a plug of silica (eluent: Et₂O). Then the solvent was removed. Purification by FC (PE/Et₂O 4:3) afforded diethyl 2-(*N*-benzylpent-2-ynamido)malonate **14a** (1.16 g, 3.35 mmol, 84%) as a slightly yellow oil.

Mixture of rotamers: ¹H-NMR (400 MHz, CDCl₃): 7.36-7.21 (*m*, 5H, H_{ar}), 5.62/5.34 (*s*, 1H, NCH), 4.98/4.82 (*s*, 2H, PhCH₂), 4.12-4.04 (*m*, 2H, OCH₂), 3.95-3.87 (*m*, 2H, CH₂O), 2.39/2.32 (*q*, 2H, *J* = 7.5 Hz, CH₂CC), 1.22/1.12 (*t*, 3H, *J* = 7.5 Hz, CCCH₂CH₃), 1.16/1.15 (*t*, 6H, 2 × OCH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 165.7/165.5 (2 × CO), 155.7/155.7 (CO), 136.5/136.1 (C_{ar}), 128.4/128.1 (2 × CH_{ar}), 127.8/127.5 (2 × CH_{ar}), 127.6/127.2 (CH_{ar}), 96.5/96.3 (C_{sp}), 72.9/72.6 (C_{sp}), 64.1 /59.7 (CH), 62.3/62.1 (2 × CH₂), 52.2/48.0 (CH₂), 13.8 (2 × CH₃), 12.7/12.7 (CH₃), 12.6/12.5 (CH₂). IR (film): 2983m, 2941w, 2238m, 1743s, 1643s, 1497m, 1449m, 1421m, 1369m, 1307m, 1249m, 1181s, 1031m, 970w, 859w, 741m, 701m. MS (ESI+): 346.17 (90, [M+H]⁺), 368.12 (100, [M+Na]⁺), 713.26 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₁₉H₂₃NNaO₅ ([M+Na]⁺) 368.1468 found 368.1468.

Diethyl 2-(*N*-benzyl-3-phenylpropiolamido)malonate **14b**

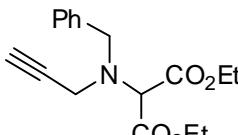


According to a procedure by Hatakeyama:^[2] 3-Phenylpropiolic acid (702 mg, 4.8 mmol, 1.2 eq.) was dissolved in DCM (12 mL). A few drops of DMF were added and then dropwise oxalyl chloride (372 μL, 4.4 mmol, 1.1 eq.). After complete addition the reaction was stirred for 1 h at room temperature. In a separate flask diethyl 2-(benzylamino)malonate (1.06 g, 4.0 mmol, 1.0 eq.) was

dissolved in a mixture of DCM (8 mL) and sat. NaHCO_3 solution (8 mL). To this vigorously stirred solution was added the crude acid chloride. The reaction was stirred 30 min at room temperature and the filtered through a plug of silica (eluent: Et_2O). Then the solvent was removed. Purification by FC (PE/ Et_2O 1:1) afforded diethyl 2-(*N*-benzyl-3-phenylpropiolamido)malonate **14b** (1.41 g 3.57 mmol, 89%) as a slightly yellow oil.

Mixture of rotamers: $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.57-7.23 (*m*, 10H, H_{ar}), 5.59/5.41 (*s*, 1H, NCH), 5.07/4.88 (*s*, 2H, CH_2Ph), 4.14-4.08 (*m*, 2H, CH_2O), 4.00-3.92 (*m* 2H, CH_2O), 1.18/1.15 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, C_6D_6): 165.60/165.5 (2 \times CO), 155.7/155.6 (CO), 136.28/136.00 (C_{ar}), 132.6 (2 \times CH_{ar}), 130.5/130.4 (CH_{ar}), 128.5 (4x CH_{ar}), 127.8 (CH_{ar}), 127.5/127.4 (2 \times CH_{ar}), 119.92/119.85 (C_{ar}), 92.5/92.0 (C_{sp}), 81.1/80.8 (C_{sp}), 64.1/62.5 (C), 62.2/59.9 (2 \times CH_2), 52.3/48.5 (CH_2), 13.8/13.8 (2 \times CH_3). IR(film): 3064w, 3033w, 2983m, 2939w, 2218m, 1743s, 1641s, 1492m, 1445m, 1420m, 1369m, 1302s, 1179s, 1096w, 1029m, 970w, 760m, 738w, 691m. MS (ESI+): 394.17 (86, $[\text{M}+\text{H}]^+$), 416.13 (100, $[\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{23}\text{H}_{23}\text{NNaO}_5$ ($[\text{M}+\text{Na}]^+$) 416.1468, found 416.1468.

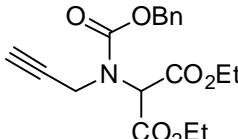
Diethyl 2-(benzyl(prop-2-ynyl)amino)malonate **14c**

 *N*-Benzyl propargyl amine (4.42 g, 30 mmol, 1.5 eq.), NEt_3 (2.79 mL, 30 mmol, 1.0 eq.) and diethyl bromomalonate (3.70 mL, 92% pure (ex-Aldrich), 20 mmol, 1.0 eq.) were dissolved in CHCl_3 (100 mL). The reaction was heated to 80 °C for 48 h.

After cooling, water (100 mL) was added and the layers were separated. The aqueous layer was extracted twice with Et_2O (75 mL). The combined organic layers were dried (MgSO_4) and the solvent was removed. After purification by FC (PE/ Et_2O 5:1, R_f (PE/ Et_2O 5:1) = 0.40) diethyl 2-(benzyl(prop-2-ynyl)amino)malonate **14c** (2.89 g, 9.54 mmol, 48%) was obtained as a pale yellow oil.

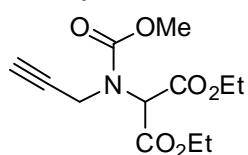
$^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.45-7.43 (*m*, 2H, H_{ar}), 7.35-7.31 (*m*, 2H, H_{ar}), 7.29-7.25 (*m*, 1H, H_{ar}), 4.40 (*s*, 1H, NCH), 4.30-4.22 (*m*, 4H, 2 \times CH_2O), 3.98 (*s*, 2H, CH_2Ph), 3.56 (*d*, 2H, $J = 2.4$ Hz, CH_2CC), 2.25 (*t*, 1H, $J = 2.4$ Hz, CCH), 1.31 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 167.7 (2 \times CO), 138.1 (C_{ar}), 129.0 (2 \times CH_{ar}), 128.4 (2 \times CH_{ar}), 127.4 (CH_{ar}), 79.4 (C_{sp}), 73.1 (CH_{sp}), 66.8 (CH), 61.4 (2 \times CH_2), 54.8 (CH_2), 40.6 (CH_2), 14.1 (2 \times CH_3). IR (film): 3283s, 2983m, 2938w, 2906w, 1755s, 1733s, 1495w, 1454m, 1396m, 1301m, 1250m, 1222s, 1030s, 743m, 699m. MS (ESI+): 304.16 (81, $[\text{M}+\text{H}]^+$), 326.12 (100, $[\text{M}+\text{Na}]^+$), 629.27 (100, $[2\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{17}\text{H}_{21}\text{NaNO}_4$ ($[\text{M}+\text{Na}]^+$) 326.1363 found 326.1364.

Diethyl 2-((benzyloxycarbonyl)(prop-2-ynyl)amino)malonate **14d**

 Diethyl 2-(prop-2-yn-1-ylamino)malonate (426 mg, 2.0 mmol, 1.0 eq.) was dissolved in a mixture of DCM (4 mL) and aq. sat. NaHCO_3 solution (4 mL). To this vigorously stirred mixture was added dropwise benzyl chloroformate (430 μL , 3.0 mmol, 1.5 eq.). After complete addition the reaction was stirred 30 min at room temperature and was filtered through a plug of silica (eluent: Et_2O). The solvent was removed and after purification by FC (PE/ Et_2O 3:1) diethyl 2-((benzyloxycarbonyl)(prop-2-ynyl)amino)malonate **14d** (512 mg, 95% pure, 1.40 mmol, 70%) was obtained as a colorless oil.

Mixture of rotamers: $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.41-7.29 (*m*, 5H, H_{ar}), 5.45/5.12 (*s*, 1H, CH), 5.23/5.17 (*s*, 2H, CH_2Ph), 4.29-5.15 (*m*, 4H, 2 \times CH_2O), 2.27-2.25/2.23-2.21 (*m*, 1H, CCH), 1.30/1.22 (*t*, 6H, $J = 7.0$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 166.1/165.8 (2 \times CO), 155.6/154.9 (CO) 135.9/135.6 (C_{ar}), 128.5 (2 \times CH_{ar}), 128.4/128.2 (CH_{ar}), 128.1/127.8 (2 \times CH_{ar}), 79.1/78.5 (CH_{sp}), 72.4/71.7 (C), 68.3/62.2 (2 \times CH_2), 61.8/61.4 (CH_2), 37.0/36.0 (CH_2), 13.9/13.9 (2 \times CH_3). IR (film): 3280m, 3066w, 3034w, 2983m, 2941w, 2907w, 1743s, 1713s, 1498w, 1449m, 1412m, 1369m, 1258s, 1196m, 1192m, 1029m, 980w, 770w, 738w, 698w. MS (ESI+): 370.11 (100, $[\text{M}+\text{Na}]^+$), 717.24 (77, $[2\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{18}\text{H}_{21}\text{NNaO}_6$ ($[\text{M}+\text{Na}]^+$) 370.1261 found 370.1258.

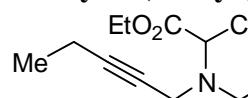
Diethyl 2-(methoxycarbonyl(prop-2-ynyl)amino)malonate **14e**



Diethyl 2-(prop-2-yn-1-ylamino)malonate (426 mg, 2.0 mmol, 1.0 eq.) was dissolved in a mixture of DCM (4 mL) and aq. sat. NaHCO_3 solution (4 mL). To this vigorously stirred mixture was added dropwise methyl chloroformate (232 μL , 3.0 mmol, 1.5 eq.). After complete addition the reaction was stirred for 30 min at room temperature and was filtered through a plug of silica (eluent: Et_2O). The solvent was removed and after purification by FC (three times PE/ Et_2O 2:1) diethyl 2-(methoxycarbonyl-(prop-2-ynyl)amino)malonate **14e** (314 mg, 1.16 mmol, 58%) was obtained as a colorless oil.

Mixture of rotamers: $^1\text{H-NMR}$ (400 MHz, CDCl_3): 5.44/5.16 (*s*, 1H, $\text{CH}(\text{CO})_2$), 4.34-4.22 (*m*, 6H, 2 \times CH_2O and CH_2N), 3.82/3.75 (*s*, 3H, CH_3O), 2.25-2.20 (*m*, 1H, CCH), 1.31 (*t*, 6H, $J = 7.2$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 166.1/165.9 (2 \times CO), 156.2/155.4 (CO), 79.1/78.7 (C), 72.0/71.5 (CH), 62.2 (2 \times CH_2), 61.6/61.3 (CH), 53.7/53.4 (CH_3), 36.6/35.8 (CH_2), 13.9 (2 \times CH_3). IR (film): 3274m, 2984m, 1743s, 1717s, 1460m, 1405w, 1370w, 1264s, 1196s, 1110w, 1097w, 1031s, 914w, 864w, 773w, 670w. MS (ESI+): 272.13 (30, $[\text{M}+\text{H}]^+$), 294.10 (100, $[\text{M}+\text{Na}]^+$), 565.24 (29, $[2\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{12}\text{H}_{17}\text{NNaO}_6$ ($[\text{M}+\text{Na}]^+$) 294.0948 found 294.0945.

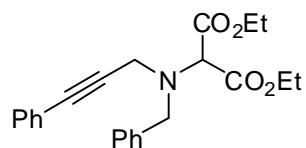
Diethyl 2-(benzyl(pent-2-ynyl)amino)malonate **14f**



N-Benzylpent-2-yn-1-amine (1.96 g, 11.3 mmol, 1.5 eq.), diethyl bromomalonate (1.39 g, 7.5 mmol, 1.0 eq.) and NEt_3 (2.09 mL, 15.0 mmol, 2.0 eq.) were dissolved in CHCl_3 (100 mL) and heated to reflux for 3 d. To the cooled reaction mixture was added water (100 mL) and the organic layer was separated. The aqueous layer was extracted twice with EtOAc (75 mL) and the combined organic layers dried (MgSO_4). After evaporation the crude product was purified by FC (PE/ Et_2O 6:1). Diethyl 2-(benzyl(pent-2-ynyl)amino)malonate **14f** (1.46 g, 4.4 mmol, 59%) was obtained as slightly yellow oil. $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.44 (*d*, 2H, $J = 7.1$ Hz, H_{ar}), 7.32 (*t*, 2H, $J = 7.3$ Hz, H_{ar}), 7.28-7.24 (*m*, 1H, H_{ar}), 4.47 (*s*, 1H, NCH), 4.31-4.22 (*m*, 4H, 2 \times CH_2O), 3.95 (*s*, 2H, CH_2Ph), 3.49 (*t*, 1H, $J = 2.0$ Hz, CCCH_2N), 2.20 (*tq*, 2H, $J = 7.4$, 2.0 Hz, $\text{CH}_3\text{CH}_2\text{CC}$), 1.31 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3), 1.14 (*t*, 3H, $J = 7.4$ Hz, $\text{CH}_3\text{CH}_2\text{CC}$). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 167.9 (2 \times CO), 138.5 (C_{ar}), 129.0 (2 \times CH_{ar}), 128.3 (2 \times CH_{ar}), 127.2 (CH_{ar}), 86.9 (C_{sp}), 74.6 (C_{sp}), 66.8 (CH), 61.3 (2 \times CH_2), 54.8 (CH_2), 41.1 (CH_2), 14.1 (2 \times CH_3), 14.0 (CH_3), 12.5 (CH_2). IR(film): 2980m, 2938w, 1758s, 1734s, 1495w, 1454m, 1370m, 1301m, 1223m, 1149s, 1099w,

1031s, 742m, 699m. MS (ESI+): 332.16 (100, $[M+H]^+$). HRMS (ESI): calculated for $C_{19}H_{25}NNaO_4$ ($[M+Na]^+$) 354.1676, found 354.1672.

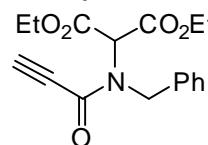
Diethyl 2-(benzyl(3-phenylprop-2-ynyl)amino)malonate **14g**



N-Benzyl-3-phenylprop-2-yn-1-amine (3.09 g 14.0 mmol, 1.5 eq.), NEt₃ (2.60 mL, 18.7 mmol, 2.0 eq.) and diethyl bromomalonate (1.72 mL, 92% pure (ex-Aldrich), 9.3 mmol, 1.0 eq.) were dissolved in CHCl₃ (100 mL) and heated to reflux for 3 d. After cooling, water was added (100 mL) and the organic layer was separated. The aqueous layer was extracted twice with Et₂O (75 mL), the combined organic layers dried (MgSO₄) and the solvent was removed. Purification by FC (PE/Et₂O 8:1) afforded diethyl 2-(benzyl(3-phenylprop-2-ynyl)amino)malonate **14g** (1.11 g, 2.94 mmol, 32%) as a yellow oil.

¹H-NMR (400 MHz, CDCl₃): 7.49-7.43 (m, 4H, H_{ar}), 7.37-7.26 (m, 6H, H_{ar}), 4.47 (s, 1H, NCH), 4.29-4.21 (m, 4H, 2 × CH₂), 4.05 (s, 2H, CH₂Ph), 3.77 (s, 2H, CH₂CC), 1.29 (t, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 167.8 (2 × CO), 138.3 (C_{ar}), 131.7 (2 × CH_{ar}), 129.1 (2 × CH_{ar}), 128.4 (2 × CH_{ar}), 128.2 (2 × CH_{ar}), 128.1 (CH_{ar}), 127.4 (CH_{ar}), 123.1 (C_{ar}), 85.3 (C_{sp}), 84.9 (C_{sp}), 67.2 (CH), 61.5 (2 × CH₂), 55.0 (CH₂), 41.5 (CH₂), 14.1 (2 × CH₃). IR (film): 3062w, 3029w, 2982m, 2937w, 2905w, 1756s, 1733s, 1599w, 1491m, 1454w, 1444m, 1369m, 1301m, 1248m, 1221m, 1147s, 1114w, 1074w, 1030m, 758m, 693m. MS (ESI+): 380.22 (72, $[M+H]^+$), 403.22 (100, $[M+Na]^+$), 781.39 (100, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{23}H_{25}NO_4$ ($[M+H]^+$) 380.1856 found 380.1651.

Diethyl 2-(*N*-benzylpropiolamido)malonate **14h**



Diethyl 2-(benzylamino)malonate (1.06 g, 4.0 mmol, 1.0 eq.) and propionic acid (246 μ L, 4.0 mmol, 1.0 eq.) were dissolved in DCM (50 mL). DCC (867 mg, 4.2 mmol, 1.05 eq.) was added in one portion and the reaction was stirred at room temperature over night.

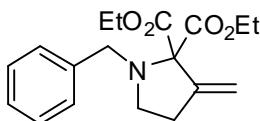
A precipitate appeared. The solvent was removed and the residue suspended in Et₂O (20 mL) and filtered through a plug of silica (eluent: Et₂O). The solvent was subsequently removed. After two purification steps by FC (PE/Et₂O 3:2) diethyl 2-(*N*-benzylpropiolamido)malonate **14h** (372.5 mg, 1.03 mmol, 26%) was obtained as a colorless oil.

Mixture of rotamers: ¹H-NMR (400 MHz, CDCl₃): 7.37-7.21 (m, 5H, H_{ar}), 5.63/5.25 (s, 1H, CHN), 5.01/4.84 (s, 2H, CH₂Ph), 4.14-4.05 (m, 2H, CH₂O), 3.96-3.88 (m, 2H, CH₂O), 3.22/3.17 (s, 1H, CCH), 1.17/1.16 (t, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 165.4/165.1 (2 × CO), 154.4/154.4 (CO), 136.0/135.4 (C_{ar}), 128.5/128.2 (2 × CH_{ar}), 127.9/127.4 (CH_{ar}), 127.8/127.6 (CH_{ar}), 80.8/80.6 (CH_{sp}), 75.1/74.8 (C_{sp}), 63.9/59.8 (C), 62.5/62.2 (2 × CH₂), 52.3/48.1 (CH₂), 13.8/13.7 (2 × CH₃). IR(film): 3241w, 2985w, 2939w, 2108m, 1743s, 1646s, 1497w, 1449m, 1424m, 1370m, 1301m, 1240m, 1221m, 1181s, 1096w, 1029m, 971w, 862w, 747m, 701m. MS (ESI+): 318.17 (30, $[M+H]^+$), 340.12 (100, $[M+Na]^+$), 657.26 (76, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{17}H_{19}NNaO_5$ ($[M+Na]^+$) 340.1155, found 340.1163.

2. Cyclization reactions

2. 1. 5-exo-Cyclizations (Conia-ene reactions)

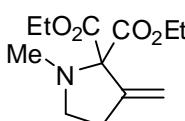
Diethyl 1-benzyl-3-methylenepyrrolidine-2,2-dicarboxylate **5a**^[1]



Diethyl 2-(benzyl(but-3-ynyl)amino)malonate **4a** (159 mg, 0.5 mmol, 1.0 eq.) and zinc chloride (7 mg, 0.05 mmol, 10 mol%) were dissolved in DCE (5 mL) and heated in a sealed tube to 100 °C for 15 h. The cooled reaction mixture was filtered through silica (Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O 5:1) diethyl 1-benzyl-3-methylenepyrrolidine-2,2-dicarboxylate **5a** (120.9 mg, 0.38 mmol, 76%) was obtained as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.43-7.39 (*m*, 2H, H_{ar}), 7.33-7.29 (*m*, 2H, H_{ar}), 7.27, 7.23 (*m*, 1H, H_{ar}), 5.40 (*t*, 1H, *J* = 2.2 Hz, CHH=C), 5.21 (*t*, 1H, *J* = 2.2 Hz, CHH=), 4.32 (*dq*, 2H, *J* = 10.7, 7.1 Hz, OCHH), 4.24 (*dq*, 2H, *J* = 10.7, 7.1 Hz, OCHH), 3.90 (*s*, 2H, CH₂Ph), 2.84 (*t*, 2H, *J* = 6.7 Hz, CH₂N), 2.58 (*tt*, 1H, *J* = 6.7, 2.2 Hz, CH₂C=C), 1.31 (*t*, 6H, *J* = 7.1 Hz, CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.0 (2 × CO), 147.1 (C_{ar}), 139.5 (C_{olef}), 128.5 (2 × CH_{ar}), 128.2 (2 × CH_{ar}), 126.9 (C_{Char}), 111.0 (CH₂olef), 77.5 (C(CO)₂), 61.4 (2 × CH₂), 54.7 (CH₂Ph), 49.0 (CH₂N), 31.1 (CH₂), 14.2 (2 × CH₃). IR(film): 2980m, 2935w, 2831m, 1729s, 1454w, 1367w, 1227s, 1137m, 1051s, 903w, 743w, 699w. MS (ESI+): 318 (45, [M+H]⁺), 657 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₁₈H₂₄NO₄ ([M+H]⁺) 318.1700, found 318.1703. HMQC was used for assignment. Cyclization of a closely related substrate under indium(III) catalysis was reported by Hatakeyama and co-workers.^[2]

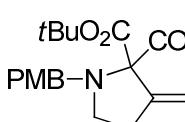
Diethyl 1-methyl-3-methylenepyrrolidine-2,2-dicarboxylate **5b**



Diethyl 2-(but-3-ynyl(methyl)amino)malonate **4b** (121 mg, 0.5 mmol, 1.0 eq.) and 7 mg zinc chloride (0.05 mmol, 10 mol%) were dissolved in 5 mL DCE and heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through silica (Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O 1:1) diethyl 1-methyl-3-methylenepyrrolidine-2,2-dicarboxylate **5b** (104.3 mg, 0.43 mmol, 86%) was obtained as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 5.38 (*t*, 1H, *J* = 2.2 Hz, H_{olef}), 5.19 (*t*, 1H, *J* = 2.2 Hz, H_{olef}), 4.33-4.19 (*m*, 4H, 2 × CH₂O), 2.98 (*t*, 2H, *J* = 6.7 Hz, CH₂N), 2.63 (*tt*, 2H, *J* = 6.7, 2.2 Hz, CH₂C=C), 2.53 (*s*, 3H, NCH₃), 1.30 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 168.5 (2 × CO), 147.2 (C_{olef}), 110.8 (CH₂olef), 77.4 (C), 61.3 (2 × CH₂), 53.0 (CH₂), 36.8 (CH₃), 31.1 (CH₂), 14.2 (2 × CH₃). IR(film): 2982m, 2939w, 2829w, 1730s, 1660w, 1447w, 1277s, 1250s, 1211m, 1067s, 1045w, 950w, 902w. MS (ESI+): 242.13 (81, [M+H]⁺), 264.10 (100, [M+Na]⁺), 505.20 (78, [2M+Na]⁺). HRMS (ESI): calculated for C₁₂H₂₀NO₄ ([M+H]⁺) 242.1387, found 242.1387. HMQC was used for assignment.

Di-*tert*-butyl 1-(4-methoxybenzyl)-3-methylenepyrrolidine-2,2-dicarboxylate **5d**

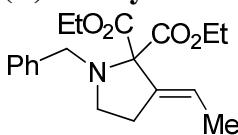


Di-*tert*-butyl 2-(but-3-yn-1-yl(4-methoxybenzyl)amino)malonate **4d** (194 mg, 0.5 mmol, 1.0 eq.) and zinc iodide (16 mg, 0.05 mmol, 10 mol%) were dissolved in DCE (4 mL) and heated to 100 °C for 15 h in a sealed tube. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O). After purification by FC (PE/Et₂O 8:1) a 3.8 : 1 mixture (total 0.37 mmol) of di-*tert*-butyl 1-

(4-methoxybenzyl)-3-methylenepyrrolidine-2,2-dicarboxylate (0.29 mmol, 58%) and starting material (0.08 mmol, 15%) was obtained as a colorless oil.

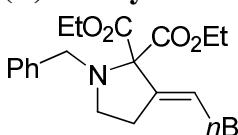
¹H-NMR (400 MHz, CDCl₃): 7.35 (*d*, 2H, *J* = 8.5 Hz, H_{ar}), 6.87-6.84 (*m*, 2H, H_{ar}), 5.39 (*t*, 1H, *J* = 2.1 Hz, CH_{olef}), 5.21 (*t*, 1H, *J* = 2.0 Hz, CH_{olef}), 3.93 (*s*, 2H, CH₂Ar), 3.80 (*s*, 3H, OCH₃), 2.81 (*t*, 2H, *J* = 6.4 Hz, CH₂N), 2.55 (*tt*, 2H, *J* = 6.4, 2.2 Hz, CH₂C=C), 1.51 (*s*, 18H, C(CH₃)₃). ¹³C-NMR (100 MHz, CDCl₃): 168.0 (CO), 158.5 (C_{ar}), 147.7 (C_{ar}), 129.5 (CH_{olef}), 113.5 (4xCH_{ar}), 110.5 (C_{olef}), 81.9 (C), 78.1 (2 × C), 55.2 (CH₃), 54.1 (CH₂), 49.5 (CH₂), 31.1 (CH₂), 28.0 (6 × CH₃). IR (film): 2977m, 2933w, 2835w, 1725s, 1612w, 1512s, 1457w, 1393w, 1368m, 1283w, 1248s, 1150s, 1034m, 985w, 901w, 839m. MS (ESI+): 404.23 (100, [M+H]⁺), 426.21 (70, [M+Na]⁺). HRMS (ESI): calculated for C₂₃H₃₃NNaO₅ ([M+Na]⁺) 426.2251, found 426.2239.

(E)-Diethyl 1-benzyl-3-ethylidenepyrrolidine-2,2-dicarboxylate 5e

 Diethyl 2-(benzyl(pent-3-ynyl)amino)malonate **4e** (166 mg, 0.5 mmol, 1.0 eq.) and zinc chloride (7 mg, 0.05 mmol, 10 mol%) were dissolved in DCE (5 mL) and heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through silica (Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O 5:1) (E)-diethyl 1-benzyl-3-ethylidenepyrrolidine-2,2-dicarboxylate **5e** (150.7 mg, *E/Z* 38:1, 0.45 mmol, 91%) was obtained as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.42-7.41 (*m*, 2H, H_{ar}), 7.33-7.30 (*m*, 2H, H_{ar}), 7.27-7.23 (*m*, 1H, H_{ar}), 5.84 (*qt*, 1H, *J* = 6.9, 2.5 Hz, CH_{olef}), 4.28 (2 × *dq*, 4H, *J* = 10.8, 7.1 Hz, 2 × CH₂O), 3.87 (*s*, 2H, CH₂Ph), 2.86 (*t*, 1H, *J* = 6.7 Hz, CH₂N), 2.52-2.47 (*m*, 2H, CH₂C=C), 1.67 (*dt*, 3H, *J* = 6.9, 1.5 Hz, C=CCH₃), 1.31 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.2 (2 × CO), 139.5 (C_{olef}), 138.5 (C_{ar}), 128.5 (2 × CH_{ar}), 128.2 (2 × CH_{ar}), 126.9 (CH_{ar}), 120.7 (CH_{olef}), 77.5 (C), 61.3 (CH₂), 54.8 (CH₂), 49.5 (CH₂), 27.5 (CH₂), 14.8 (CH₃), 14.3 (2 × CH₃). IR (film): 2981m, 2937w, 2831w, 1728s, 1453w, 1367w, 1250s, 1230s, 1139m, 1076w, 1044m, 860w, 743m, 700m. MS (ESI+): 332.16 (97, [M+H]⁺), 354.12 (100, [M+Na]⁺), 685.24 (94, [2M+Na]⁺). HRMS (ESI): calculated for C₁₉H₂₆NO₄ ([M+H]⁺) 332.1856 found 332.1856. COSY, HMBC and NOE were used for assignment.

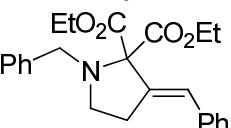
(E)-Diethyl 1-benzyl-3-pentylidenepyrrolidine-2,2-dicarboxylate 5f

 Diethyl 2-(benzyl(oct-3-ynyl)amino)malonate **4f** (187 mg, 0.5 mmol, 1.0 eq.) and zinc chloride (7 mg, 0.05 mmol, 10 mol%) were dissolved in DCE (5 mL) and heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through silica (Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O 5:1) (E)-diethyl 1-benzyl-3-pentylidenepyrrolidine-2,2-dicarboxylate **5f** (161.2 mg, 0.45 mmol, 86%) was obtained as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.42-7.40 (*m*, 2H, H_{ar}), 7.33-7.29 (*m*, 2H, H_{ar}), 7.27-7.22 (*m*, 1H, H_{ar}), 5.77 (*tt*, 1H, *J* = 7.1, 2.5 Hz, H_{olef}) 4.34-4.21 (*m*, 4H, 2 × CH₂O), 3.87 (*s*, 2H, CH₂Ph), 2.85 (*t*, 2H, *J* = 6.7 Hz, CH₂N), 2.51-2.47 (*m*, 2H, CH₂CH₂N), 2.05 (*q*, 2H, *J* = 7.1 Hz, C=CHCH₂), 1.41-1.27 (*m*, 4H, CH₂CH₂CH₃), 1.31 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃), 0.89 (*t*, 3H, *J* = 7.1 Hz, CH₂CH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.4 (2 × CO), 139.6 (C_{olef}), 137.6 (C_{ar}), 128.5 (2 × CH_{ar}), 128.2 (2 × CH_{ar}), 126.9 (CH_{ar}), 126.6 (CH_{olef}), 77.5 (C), 61.2 (2 × CH₂), 54.8 (CH₂), 49.6 (CH₂), 31.1 (CH₂), 29.1 (CH₂), 27.6 (CH₂), 22.2 (CH₂), 14.2 (2 × CH₃), 14.0 (CH₃). IR

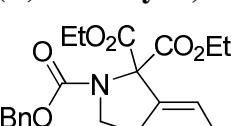
(film): 2958m, 2931m, 2857w, 1730s, 1454w, 1367w, 1229w, 1043m, 743w, 700w. MS (ESI+): 374.21 (75, [M+H]⁺), 396.19 (78, [M+Na]⁺), 769.38 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₂₂H₃₁NaNO₄ ([M+Na]⁺) 396.2145 found 396.2145. COSY, HMQC, HMBC and NOE were used for assignment.

(E)-Diethyl 1-benzyl-3-benzylidenepyrrolidine-2,2-dicarboxylate 5g^[1]

 Diethyl 2-(benzyl(4-phenylbut-3-ynyl)amino)malonate **4g** (98 mg, 0.25 mmol, 1.0 eq.) and zinc chloride (3 mg, 10 mol%) was dissolved in DCE (1.5 mL) and heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through silica (Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O 6:1) ((E)-diethyl 1-benzyl-3-benzylidenepyrrolidine-2,2-dicarboxylate **5g** (83.2 mg, 0.21 mmol, 85%) was obtained as a clear oil.

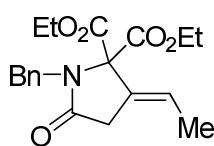
¹H-NMR (400 MHz, CDCl₃): 7.44-7.42 (*m*, 2H, H_{ar}), 7.34-7.31 (*m*, 6H, H_{ar}), 7.28-7.23 (*m*, 2H, H_{ar}), 6.80 (*t*, 1H, *J* = 2.5 Hz, H_{olef}), 4.24 (*dq*, 2H, *J* = 10.7, 7.1 Hz, OCHH), 4.29 (*dq*, 2H, *J* = 10.7, 7.1 Hz, OCHH), 3.93 (*s*, 2H, CH₂Ph), 2.93 (*t*, 2H, *J* = 6.6 Hz, CH₂N), 2.83 (*dt*, 2H, *J* = 6.1, 2.0 Hz, CH₂C=C), 1.33 (*t*, 6H, *J* = 7.1 Hz, CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.2 (2 × CO), 139.9 (C_{ar}), 139.4 (C_{ar}), 137.2 (C_{olef}), 128.6 (2 × CH_{ar}), 128.5 (2 × CH_{ar}), 128.3 (2 × CH_{ar}), 128.2 (2 × CH_{ar}), 126.98 (CH_{ar}), 126.94 (CH_{ar}), 126.0 (CH_{olef}), 78.8 (C(CO)₂), 61.5 (2 × OCH₂), 54.6 (CH₂Ph), 50.1 (CH₂N), 30.1 (CH₂), 14.3 (2 × CH₃). IR(film): 3061w, 3027w, 2980m, 2935w, 2834w, 1729s, 1494w, 1448m, 1368w, 1229s, 1139w, 1041m, 742w, 697m. MS (ESI+): 394 (100, [M+H]⁺). HRMS (ESI): calculated for C₂₄H₂₈NO₄ ([M+H]⁺) 394.2013, found 394.2011.

(E)-1-Benzyl 2,2-diethyl 3-pentylidenepyrrolidine-1,2,2-tricarboxylate 5h

 Diethyl 2-((benzyloxycarbonyl)(oct-3-ynyl)amino)malonate **4h** (104 mg, 0.25 mmol, 1.0 eq.) and ZnCl₂ (3 mg, 10 mol%) were dissolved in DCE (1.5 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 1:1) afforded (E)-1-benzyl 2,2-diethyl 3-pentylidenepyrrolidine-1,2,2-tricarboxylate **5h** (E/Z = >40:1, 83.3 mg, 0.20 mmol, 80%) as a colorless oil.

Mixture of rotamers (approx. 1:1): ¹H-NMR (400 MHz, CDCl₃): 7.40-7.27 (*m*, 5H, H_{ar}), 5.87/5.83 (*tt*, 1H, *J* = 7.4, 2.3 Hz, H_{olef}), 5.18/5.11 (*s*, 2H, CH₂Ph), 4.24-4.19/4.11/3.96 (*m*, 4H, 2 × CH₂O), 3.76-3.70 (*m*, 2H, NCH₂CH₂), 2.64 (*m*, 2H, NCH₂CH₂), 2.06-2.00 (*m*, 2H, CH₂CH₂CH₂CH₃), 1.39-1.22 (*m*, 4H, CH₂CH₂CH₂CH₃), 1.22/1.10 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃), 0.88/0.87 (*t*, 3H, *J* = 7.1 Hz, CH₂CH₂CH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 167.4 (2 × CO), 154.7/154.4 (CO), 137.1/136.9 (C_{olef}), 136.3/136.0 (C_{ar}), 128.5/128.5 (2 × CH_{ar}), 128.5/128.2 (2 × CH_{ar}), 128.1/128.0 (CH_{ar}), 127.7/127.7 (CH_{olef}), 73.8/72.8 (C), 67.3/67.3 (CH₂), 62.0/61.9 (2 × CH₂), 46.5/46.0 (CH₂), 31.1/31.0 (CH₂), 29.1 (CH₂), 27.6/26.7 (CH₂), 22.3 (CH₂), 14.1/14.0 (CH₃). IR (film): 2958m, 2932m, 2873w, 1174m, 1737s, 1715s, 1445w, 1410s, 1354m, 1232s, 1190w, 1135w, 1096w, 1060m, 1044w, 1009w, 863w, 771w, 739w, 698w. MS (ESI+): 418.26 (26, [M+H]⁺), 440.20 (100, [M+Na]⁺), 857.40 (77, [2M+Na]⁺). HRMS (ESI): calculated for C₂₃H₃₁NNaO₆ ([M+Na]⁺) 440.2044 found 440.2026.

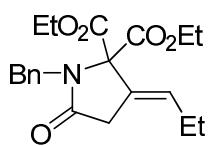
(E)-diethyl 1-benzyl-3-ethylidene-5-oxopyrrolidine-2,2-dicarboxylate 7a



Diethyl 2-(*N*-benzylpent-3-ynamido)malonate **6a** (173 mg, 0.5 mmol, 1.0 eq.) and ZnI₂ (16 mg, 10 mol%) were dissolved in DCE (3 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 2:3) afforded (E)-diethyl 1-benzyl-3-ethylidene-5-oxopyrrolidine-2,2-dicarboxylate **7a** (*E/Z* = >48:1, 137.7 mg, 0.40 mmol, 80%) as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.27-7.24 (*m*, 2H, H_{ar}), 7.20-7.15 (*m*, 3H, H_{ar}) 5.97 (*qt*, 1H, *J* = 6.9, 2.8 Hz, H_{olef}), 4.72 (*s*, 2H, CH₂Ph), 3.99-3.91 (*m*, 4H, 2xCH₂O), 3.23-3.20 (*m*, 2H, COCH₂), 1.73 (*dt*, 3H, *J* = 6.9, 1.7 Hz, C=CCH₃), 1.09 (*t*, 6H, *J* = 7.1 Hz, 2xCH₃). ¹³C-NMR (100 MHz, CDCl₃): 173.85 (CO), 167.13 (CO), 136.79 (C_{ar}), 128.16 (2xCH_{ar}), 127.21 (C_{olef}), 127.01 (2xCH_{ar}), 126.93 (CH_{ar}), 125.08 (CH_{olef}), 75.55 (C), 62.22 (2xCH₂), 45.82 (CH₂), 32.90 (CH₂), 15.13 (CH₃), 13.60 (2xCH₃). IR (film): 3063w, 3031w, 2982m, 2938w, 1737s, 1712s, 1496w, 1433w, 1389m, 1367w, 1351w, 1296w, 1244s, 1175m, 1051s, 700m. MS (ESI+): 317.25 (70), 346.18 (28, [M+H]⁺), 368.16 (100, [M+Na]⁺), 447.30 (41), 713.33 (12, [2M+Na]⁺). HRMS (ESI): calculated for C₁₉H₂₃NNaO₅ ([M+Na]⁺) 368.1468, found 368.1464. Cyclization of a closely related substrate under indium(III) catalysis was reported by Hatakeyama and co-workers.^[2]

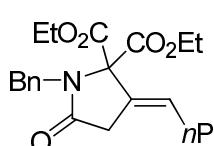
(E)-Diethyl 1-benzyl-5-oxo-3-propylidenepyrrolidine-2,2-dicarboxylate 7b



Diethyl 2-(*N*-benzylhex-3-ynamido)malonate **6b** (90 mg, 0.25 mmol, 1.0 eq.) and ZnCl₂ (3 mg, 10 mol%) were dissolved in DCE (1.5 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 6:1) afforded (E)-diethyl 1-benzyl-5-oxo-3-propylidenepyrrolidine-2,2-dicarboxylate **7b** (*E/Z* = 15:1, 45.0 mg, 0.127 mmol, 51%) as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.28-7.15 (*m*, 5H, H_{ar}), 5.88 (*tt*, 1H, *J* = 7.4, 2.8 Hz, H_{olef}), 4.72 (*s*, 2H, CH₂Ph), 3.97-3.83 (*m*, 4H, 2 × OCH₂), 3.21 (*td*, 2H, *J* = 2.8, 1.5 Hz, CH₂CO), 2.09 (*qnt*, 2H, *J* = 7.4, 1.4 Hz, C=CHCH₂CH₃), 1.10 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃), 1.02 (*t*, 3H, *J* = 7.4 Hz, C=CHCH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 173.9 (CO), 167.2 (2 × CO), 136.8 (C_{ar}), 132.0 (CH_{olef}), 128.2 (2 × CH_{ar}), 127.2 (2 × CH_{ar}), 127.0 (CH_{ar}), 125.9 (C_{olef}), 75.5 (C), 62.2 (2 × CH₂), 45.9 (CH₂), 32.8 (CH₂), 23.1 (CH₂), 13.6 (2 × CH₃), 13.0 (CH₃). IR (film): 2978m, 2936w, 2874w, 1740s, 1713s, 1497w, 1455w, 1387m, 1354w, 1246s, 1178m, 1116w, 1095w, 1049m, 977w, 867w, 763w, 702w. MS (ESI+): 360.23 (26, [M+H]⁺), 382.17 (100, [M+Na]⁺), 741.35 (75, [2M+Na]⁺). HRMS (ESI): calculated for C₂₀H₂₅NNaO₅ ([M+Na]⁺) 382.1625 found 382.1618.

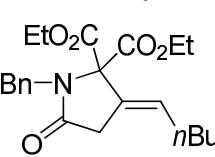
(E)-Diethyl 1-benzyl-3-butylidene-5-oxopyrrolidine-2,2-dicarboxylate 7c



Diethyl 2-(*N*-benzylhept-3-ynamido)malonate **6c** (93 mg, 0.25 mmol, 1.0 eq.) and ZnCl₂ (3 mg, 10 mol%) were dissolved in DCE (1.5 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 1:1) afforded (E)-diethyl 1-benzyl-3-butylidene-5-oxopyrrolidine-2,2-dicarboxylate **7c** (*E/Z* = >100:1, 48.3 mg, 0.129 mmol, 52%) as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.28-7.16 (*m*, 5H, H_{ar}), 5.88 (*tt*, 1H, *J* = 7.4, 2.7 Hz, H_{olef}), 4.72 (*s*, 2H, CH₂Ph), 3.96-3.83 (*m*, 4H, 2 × CH₂O), 3.22-3.21 (*m*, 2H, COCH₂), 2.06 (*qt*, 2H, *J* = 7.4, 1.3 Hz, C=CCH₂CH₂CH₃), 1.45 (*sext.*, 2H, *J* = 7.4 Hz, C=CCH₂CH₂CH₃), 1.10 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃), 0.91 (*t*, 3H, *J* = 7.4 Hz, C=CCH₂CH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 173.9 (CO), 167.2 (2 × CO), 136.8 (C_{ar}), 130.5 (CH_{olef}), 128.2 (2 × CH_{ar}), 127.3 (2 × CH_{ar}), 127.0 (CH_{ar}), 126.2 (C_{olef}), 75.6 (C), 62.2 (2 × CH₂), 45.9 (CH₂), 33.1 (CH₂), 31.6 (CH₂), 21.8 (CH₂), 13.6 (2 × CH₃), 13.5 (CH₃). IR (film): 2962m, 2934w, 2873w, 1740s, 1714s, 1497w, 1455w, 1431w, 1387m, 1367w, 1355w, 1297w, 1248s, 1177m, 1115w, 1095w, 1049s, 859w, 718m. MS (ESI+): 374.24 (41, [M+H]⁺), 396.20 (100, [M+Na]⁺), 769.43 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₂₁H₂₇NNaO₅ ([M+Na]⁺) 396.1781 found 396.1778. COSY, HMQC, HMBC were used for assignment.

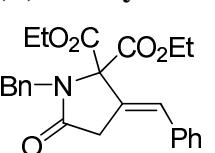
(E)-1-Benzyl 2,2-diethyl 3-pentylidenepyrrolidine-1,2,2-tricarboxylate 7d



Diethyl 2-(*N*-benzyl-*o*-3-ynamido)malonate **6d** (194 mg, 0.5 mmol, 1.0 eq.) and ZnCl₂ (7 mg, 10 mol%) were dissolved in DCE (3 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 3:2) afforded (*E*)-1-benzyl 2,2-diethyl 3-pentylidenepyrrolidine-1,2,2-tricarboxylate **7d** (*E/Z* = 42:1, 127.1 mg, 0.33 mmol, 66%) as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.28-7.16 (*m*, 5H, H_{ar}), 5.88 (*tt*, 1H, *J* = 7.5, 2.7 Hz, H_{olef}), 4.72 (*s*, 2H, CH₂Ph), 3.96-3.83 (*m*, 4H, 2 × CH₂O), 3.22-3.20 (*m*, 2H, CH₂CO), 2.08 (*qt*, 2H, *J* = 7.2, 1.4 Hz, CH₂Pr), 1.45-1.20 (*m*, 4H, CH₂CH₂CH₃), 1.10 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃), 0.90 (*t*, 3H, *J* = 7.2 Hz, CH₂CH₂CH₃). ¹³C-NMR (100 MHz, CDCl₃): 173.9 (2 × CO), 167.2 (CO), 136.8 (C_{ar}), 130.7 (CH_{olef}), 128.2 (2 × CH_{ar}), 127.3 (2 × CH_{ar}), 127.0 (CH_{ar}), 126.4 (C_{olef}), 75.6 (C), 62.2 (2 × CH₂), 45.8 (CH₂), 33.0 (CH₂), 30.7 (CH₂), 29.3 (CH₂), 22.1 (CH₂), 13.9 (CH₃), 13.6 (2 × CH₃). IR (film): 2959m, 2931m, 2872w, 1740s, 1714s, 1497w, 1455w, 1387m, 1254w, 1297w, 1247m, 1178m, 1095wm 1049m, 861w, 764w, 701w. MS (ESI+): 388.18 (75, [M+H]⁺). HRMS (ESI): calculated for C₂₂H₂₉NNaO₅ ([M+Na]⁺) 410.1938 found 410.1937. COSY, HMQC, HMBC and NOE were used for assignment.

(E)-Diethyl 1-benzyl-3-benzylidene-5-oxopyrrolidine-2,2-dicarboxylate 7e



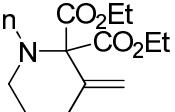
Diethyl 2-(*N*-benzyl-4-phenylbut-3-ynamido)malonate **6e** (64 mg, 0.157 mmol, 1.0 eq.) and ZnCl₂ (2 mg, 10 mol%) were dissolved in DCE (1.0 mL) and heated to 100 °C in a sealed tube for 15 h. The cooled reaction mixture was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 1:1) afforded (*E*)-diethyl 1-benzyl-3-benzylidene-5-oxopyrrolidine-2,2-dicarboxylate **7e** (approx. 95% pure, 16.2 mg, *E/Z* = >70:1, 0.0398 mmol, 25%) as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.42-7.20 (*m*, 10H, H_{ar}), 6.84 (*t*, 1H, *J* = 2.7 Hz, H_{olef}), 4.77 (*s*, 2H, CH₂Ph), 4.03-4.97 (*m*, 4H, 2 × CH₂O), 3.57 (*d*, 2H, *J* = 2.7 Hz, CH₂CO), 1.13 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 173.7 (CO), 167.0 (2 × CO), 136.6 (C_{ar}), 135.7 (C_{olef}), 135.6 (C_{ar}), 129.2 (CH_{olef}), 128.69 (2 × CH_{ar}), 128.66 (2 × CH_{ar}), 128.3 (2 × CH_{ar}), 128.1 (CH_{ar}), 127.4 (2 × CH_{ar}), 127.1 (CH_{ar}), 75.4 (C), 62.5 (2 × CH₂), 45.9 (CH₂), 35.1 (CH₂), 13.7 (2 × CH₃). IR (film): 3062w, 3029w, 2983m, 2938w, 1739s, 1713s, 1496w, 1449w, 1288m, 1356w, 1246s, 1181m,

1095w, 1047m, 920w, 857w, 761w, 697m, 656w. MS (ESI+): 408.23 (32, $[M+H]^+$), 430.18 (100, $[M+Na]^+$), 837.40 (49, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{24}H_{25}NNaO_5$ ($[M+Na]^+$) 430.1625 found 430.1620. COSY, HMQC, HMBC and NOE were used for assignment.

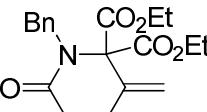
2. 2. 6- and 7-exo cyclizations

Diethyl 1-benzyl-3-methylenepiperidine-2,2-dicarboxylate 9

 Diethyl 2-(benzyl(pent-4-ynyl)amino)malonate **8** (194 mg, 0.59 mmol, 1.0 eq.) and $ZnCl_2$ (8 mg, 0.06 mmol, 10 mol%) were dissolved in DCE (3 mL) and heated in a sealed tube to 100 °C for 15 h. Then the reaction mixture was filtered through a plug of silica (eluent: Et_2O) and the solvent was removed. Purification by FC (PE/ Et_2O 5:1) afforded diethyl 1-benzyl-3-methylenepiperidine-2,2-dicarboxylate **9** (174.2 mg, 0.526 mmol, 90%) as a clear oil.

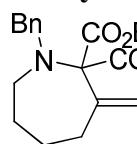
1H -NMR (400 MHz, $CDCl_3$): 7.50-7.48 (m, 2H, H_{ar}), 7.33-7.29 (m, 2H, H_{ar}), 7.25-7.21 (m, 1H, H_{ar}), 5.07 (s, 1H, H_{olef}), 4.76 (m, 1H, H_{olef}), 4.31 (q, 4H, $J = 7.1$ Hz, 2 × CH_2O), 3.90 (s, 2H, CH_2Ph), 2.61-2.58 (m, 2H, CH_2N), 2.35 (t, 2H, $J = 6.3$ Hz, $CH_2C=C$), 1.64-1.56 (m, 2H, $CH_2CH_2CH_2$), 1.31 (t, 6H, $J = 7.1$ Hz, 2 × CH_3). ^{13}C -NMR (100 MHz, $CDCl_3$): 170.0 (2 × CO), 143.5 (C_{olef}), 140.3 (C_{ar}), 128.3 (2 × CH_{ar}), 128.1 (2 × CH_{ar}), 126.8 (CH_{ar}), 112.0 (CH_{2olef}), 79.7 (C), 61.5 (2 × CH_2), 58.5 (CH_2), 46.8 (CH_2), 32.3 (CH_2), 26.0 (CH_2), 14.2 (2 × CH_3). IR (film): 2981m, 2941m, 2854m, 1730s, 1650m, 1494w, 1449m, 1365w, 1290s, 1247s, 1221m, 1150m, 1131w, 1050m, 1029m, 976w, 905w, 858wm 737w, 697w. MS (ESI+): 332.17 (100, $[M+H]^+$), 354.15 (100, $[M+Na]^+$), 685.31 (100, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{19}H_{26}NO_4$ ($[M+H]^+$) 332.1856 found 332.1857. Cyclization of a closely related substrate under indium(III) catalysis was reported by Hatakeyama and co-workers.^[2]

Diethyl 1-benzyl-3-methylene-6-oxopiperidine-2,2-dicarboxylate 11

 Diethyl 2-(*N*-benzylpent-4-ynamido)malonate **10** (0.32 mmol, 1.0 eq.) and 10 mg ZnI_2 (110 mg, 0.03 mmol, 10 mol%) were dissolved in 2 mL DCE and heated in a sealed tube to 100 °C for 15 h. Then the reaction mixture was filtered through a plug of silica (eluent: Et_2O) and the solvent was removed. Purification by FC (PE/ Et_2O 1:1) afforded diethyl 1-benzyl-3-methylene-6-oxopiperidine-2,2-dicarboxylate **11** (94.5 mg, 0.274 mmol, 86%) as a clear oil.

1H -NMR (400 MHz, $CDCl_3$): 7.27-7.23 (m, 2H, H_{ar}), 7.23-7.13 (m, 3H, H_{ar}), 5.26 (s, 1H, H_{olef}), 5.24 (t, 1H, $J = 1.2$ Hz, CH_{olef}), 4.62 (s, 2H, CH_2Ph), 4.08-4.00 (m, 2H, CH_2O), 3.90-3.81 (m, 2H, CH_2O), 2.69-2.59 (m, 4H, CH_2CH_2), 1.11 (t, 6H, $J = 7.1$ Hz, 2 × CH_3). ^{13}C -NMR (100 MHz, $CDCl_3$): 171.8 (2 × CO), 167.0 (CO), 139.4 (C_{olef}), 137.3 (C_{ar}), 128.0 (2 × CH_{ar}), 127.1 (2 × CH_{ar}), 126.7 (CH_{ar}), 114.8 (CH_{2olef}), 75.5 (C), 62.4 (2 × CH_2), 50.0 (CH_2), 32.6 (CH_2), 29.4 (CH_2), 13.6 (2 × CH_3). IR (film): 2982m, 2937w, 1735s, 1669s. MS (ESI+): 346.2 (38, $[M+H]^+$), 713.2 (100, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{19}H_{23}NNaO_5$ ($[M+Na]^+$) 368.1468 found 368.1470.

Diethyl 1-benzyl-3-methyleneazepane-2,2-dicarboxylate 13

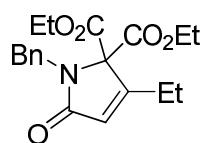


Diethyl 2-(*N*-benzyl(hex-5-yn-1-yl)amino)malonate **12** (173 mg, 0.5 mmol, 1.0 eq.) and zinc chloride (68 mg, 0.5 mmol, 1.0 eq.) were suspended in DCE (3 mL) and heated in a sealed tube to 120 °C for 15 h over night. The cooled reaction was filtered through a plug of silica (eluent: Et₂O) and the solvent was removed. After purification by FC (PE/Et₂O) diethyl 1-benzyl-3-methyleneazepane-2,2-dicarboxylate **13** (95.3 mg, 17.0 : 1.0 product/starting material, 0.26 mmol, 52%) was obtained as a colorless oil.

¹H-NMR (400 MHz, CDCl₃): 7.57 (*d*, 2H, *J* = 7.2 Hz, H_{ar}), 7.32 (*t*, 2H, *J* = 7.4 Hz, H_{ar}), 7.24 (*t*, 1H, *J* = 7.3 Hz, H_{ar}), 5.26 (*s*, 1H, H_{olef}), 5.17 (*s*, 1H, H_{olef}), 4.33-4.26 (*m*, 4H, 2 × CH₂O), 3.76 (*s*, 2H, CH₂Ph), 2.76-2.74 (*m*, 2H, CH₂N), 2.43-2.40 (*m*, 2H, CH₂C=C), 1.56-1.52 (*m*, 2H, NCH₂CH₂CH₂CH₂), 1.36-1.26 (*m*, 2H, NCH₂CH₂CH₂CH₂), 1.31 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.6 (2 × CO), 147.3 (C_{olef}), 140.5 (C_{ar}), 129.0 (2 × CH_{ar}), 127.9 (2 × CH_{ar}), 126.8 (CH_{ar}), 118.0 (CH_{2olef}), 80.7 (C), 61.2 (2 × CH₂), 58.3 (CH₂), 50.3 (CH₂), 34.0 (CH₂), 30.8 (CH₂), 30.7 (CH₂), 14.2 (2 × CH₃). IR (film): 2981m, 2936m, 2856w, 1745s, 1726s, 1644w, 1495w, 1453m, 1367w, 1241s, 1151m, 1129m, 1095w, 1046s, 943w, 903w, 866w, 743m, 700m. MS (ESI+): 346.23 (88, [M+H]⁺), 368.19 (100, [M+Na]⁺), 713.38 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₂₀H₂₈NO₄ ([M+H]⁺) 346.2013 found 346.2008.

2. 3. 5-endo Cyclizations of Propargyl Amino Malonates

Diethyl 1-benzyl-3-ethyl-5-oxo-1*H*-pyrrole-2,2(5*H*)-dicarboxylate 15a

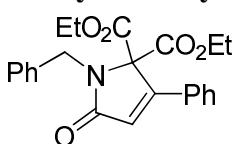


Diethyl 2-(*N*-benzylpent-2-ynamido)malonate **14a** (173 mg, 0.5 mmol, 1.0 eq.) were dissolved in 3 mL DCE and 16 mg zinc iodide (0.05 mmol, 10 mol%) were added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et₂O) and the solvent was removed.

Purification by FC (PE/Et₂O 1:1) afforded 160.0 mg diethyl 1-benzyl-3-ethyl-5-oxo-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (0.46 mmol, 93%) as a clear oil.

¹H-NMR (400 MHz, C₆D₆): 7.36-7.34 (*m* 2H, H_{ar}), 7.16-7.12 (*m*, 2H, H_{ar}), 7.09-7.05 (*m*, 1H, H_{ar}), 6.12 (*t*, 1H, *J* = 1.9 Hz, H_{olef}), 5.09 (*s*, 2H, CH₂Ph), 3.80-3.66 (*m*, 4H, 2 × CH₂O), 2.47 (*qd*, 1H, *J* = 7.3, 1.9 Hz, C=CHCH₂), 0.99 (*t*, 3H, *J* = 7.3 Hz, CH₃), 0.82 (*t*, 6H, *J* = 7.1 Hz, 2 × OCH₂CH₃). ¹H-NMR (400 MHz, CDCl₃): 7.30-7.28 (*m* 2H, H_{ar}), 7.04-7.00 (*m*, 2H, H_{ar}), 6.96-6.93 (*m*, 1H, H_{ar}), 6.00 (*t*, 1H, *J* = 1.9 Hz, H_{olef}), 5.05 (*s*, 2H, CH₂Ph), 3.65-3.52 (*m*, 4H, 2 × CH₂O), 2.36 (*qd*, 1H, *J* = 7.3, 1.9 Hz, C=CHCH₂), 0.83 (*t*, 3H, *J* = 7.3 Hz, CH₃), 0.66 (*t*, 6H, *J* = 7.1 Hz, 2 × OCH₂CH₃). ¹³C-NMR (100 MHz, C₆D₆): 171.2 (CO), 165.6 (2 × CO), 159.9 (C_{olef}), 138.7 (C_{ar}), 128.3 (2 × CH_{ar}), 127.6 (2 × CH_{ar}), 127.0 (CH_{ar}), 123.9 (CH_{olef}), 78.0 (C), 62.4 (2 × CH₂), 45.3 (CH₂), 21.6 (CH₂), 13.5 (2 × CH₂), 11.4 (CH₃). IR (film): 2980s, 2940w, 1740s, 1708s, 1497w, 1455w, 1428w, 1383m, 1320w, 1298w, 1244s, 1184w, 1047w, 860s, 720w, 698w, 678w. MS (ESI+): 346.18 (62, [M+H]⁺), 368.13 (100, [M+Na]⁺), 691.35 (33, [2M+H]⁺), 713.25 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₁₉H₂₃NNaO₅ ([M+Na]⁺) 368.1468 found 368.1460.

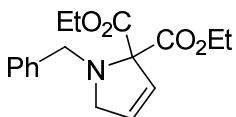
Diethyl 1-benzyl-5-oxo-3-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15b**



Diethyl 2-(*N*-benzyl-3-phenylpropiolamido)malonate **14b** (197 mg, 0.5 mmol, 1.0 eq.) were dissolved in DCE (3 mL) and zinc iodide (16 mg, 0.05 mmol, 10 mol%) was added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 1:1) afforded diethyl 1-benzyl-5-oxo-3-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15b** (172.8 mg, 0.44 mmol, 88%) as a clear oil.

¹H-NMR (400 MHz, C₆D₆): 7.56-7.52 (m, 4H, H_{ar}), 7.16-7.06 (m, 6H, H_{ar}), 6.64 (s, 1H, H_{olef}), 5.14 (s, 2H, CH₂Ph), 3.74-3.59 (m, 4H, 2 × CH₂O), 0.68 (t, 6H, J = 7.1 Hz, 2 × CH₃). ¹H-NMR (400 MHz, CDCl₃): 7.46-7.40 (m, 4H, H_{ar}), 7.06-6.94 (m, 6H, H_{ar}), 6.50 (s, 1H, H_{olef}), 5.05 (s, 2H, CH₂Ph), 3.61-3.46 (m, 4H, 2 × CH₂O), 0.55 (t, 6H, J = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, C₆D₆): 170.7 (CO), 165.6 (2 × CO), 154.5 (C_{olef}), 138.1 (C_{ar}), 131.3 (C_{ar}), 130.0 (CH_{ar}), 128.6 (2 × CH_{ar}), 128.4 (2 × CH_{ar}), 128.4 (4xCH_{ar}), 127.3 (CH_{ar}), 124.6 (CH_{olef}), 77.2 (C), 62.4 (2 × CH₂), 45.5 (CH₂), 13.3 (2 × CH₃). IR (film): 2982w, 2935w, 1739s, 1704s, 1497w, 1446w, 1382w, 1297w, 1239s, 1178w, 1050m, 863w, 775w, 723w, 700w. MS (ESI+): 394.17 (90, [M+H]⁺), 416.13 (100, [M+Na]⁺), 787.35 (81, [2M+H]⁺), 809.26 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₂₃H₂₃NNaO₅ ([M+Na]⁺) 416.1468 found 416.1470.

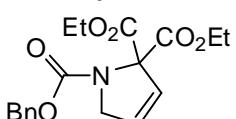
Diethyl 1-benzyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15c**



Diethyl 2-(benzyl(prop-2-ynyl)amino)malonate **14c** (152 mg, 0.5 mmol, 1.0 eq.) and ZnCl₂ (7 mg, 0.05 mmol, 10 mol%) were dissolved in DCE (3 mL) and heated in a sealed tube to 100 °C for 15 h. Then the reaction mixture was filtered through a plug of silica (Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 7:1) afforded diethyl 1-benzyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15c** (approx. 95% pure, 133 mg, 0.41 mmol, 83%) as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.41-7.39 (m, 2H, H_{ar}), 7.33-7.30 (m, 2H, H_{ar}), 7.27-7.22 (m, 1H, H_{ar}), 6.11 (dt, 1H, J = 6.1, 2.0 Hz, H_{olef}), 5.94 (dt, 1H, J = 6.1, 2.0 Hz, H_{olef}), 4.28 (q, 4H, J = 7.1 Hz, 2 × CH₂O), 4.14 (s, 2H, CH₂Ph), 3.59 (t, 2H, J = 2.0 Hz, CH₂N), 1.31 (t, 6H, J = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.7 (2 × CO), 139.8 (C_{olef}), 132.5 (C_{ar}), 128.3 (2 × CH_{ar}), 128.3 (CH_{ar}), 127.73 (CH_{ar}), 126.9 (CH_{olef}), 81.3 (C), 61.4 (2 × CH₂), 58.8 (CH₂), 54.2 (CH₂), 14.2 (2 × CH₃). IR (film): 2981m, 2944w, 2799w, 1732s, 1453w, 1369w, 1247m, 1150w, 1103w, 1075m, 703m. MS (ESI+): 304.16 (54, [M+H]⁺), 326.13 (100, [M+Na]⁺), 629.30 (18, [2M+Na]⁺). HRMS (ESI): calculated for C₁₇H₂₁NNaO₄ ([M+Na]⁺) 326.1363 found 326.1362. HMQC was used for assignment

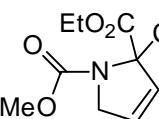
1-Benzyl 2,2-diethyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate **15d**



Diethyl 2-(*N*-(benzyloxycarbonyl)propiolamido)malonate **14d** (174 mg, 0.5 mmol, 1.0 eq.) were dissolved in DCE (3 mL) and zinc chloride (7 mg, 0.05 mmol, 10 mol%) was added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 2:1) afforded 1-benzyl 2,2-diethyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate **15d** (127.0 mg, 0.365 mmol, 73%) as a clear oil.

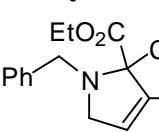
Mixture of rotamers: $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.40-7.27 (*m*, 5H, H_{ar}), 6.10/6.06 (*dt*, 1H, $J = 6.2, 2.1$ Hz, H_{olef}), 5.89/5.83 (*dt*, 1H, $J = 6.1, 2.1$ Hz, H_{olef}), 5.20/5.15 (*s*, 2H, CH_2Ph), 4.41/4.36 (*t*, 2H, $J = 2.1$ Hz, CH_2N), 4.30-4.23 (*m*, 2H, 2 \times CH_2O) and 4.06 (*q*, 2H, $J = 7.1$ Hz, 2 \times CH_2O), 1.27/1.13 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 167.2/167.1 (2 \times CO), 154.01/153.96 (CO), 136.5/136.0 (C_{ar}), 129.9/129.8 (CH_{olef}), 128.4/128.3 (2 \times CH_{ar}), 128.1/128.0 (2 \times CH_{ar}), 127.9 (CH_{ar}), 127.0/126.7 (CH_{olef}), 78.3, 77.7 (C), 67.5/67.3 (CH_2), 62.2/62.1 (2 \times CH_2), 54.8/54.2 (CH_2), 14.0/13.8 (2 \times CH_3). IR (film): 2982m, 2873w, 1752s, 1715s, 1499w, 1446w, 1411s, 1352m, 1309m, 1281m, 1237s, 1213s, 1151w, 1112w, 1095w, 1049s, 1027w, 861w, 822w, 743w, 698m. MS (ESI $+$): 348.17 (40, $[\text{M}+\text{H}]^+$), 370.12 (100, $[\text{M}+\text{Na}]^+$), 717.25 (77, $[2\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{18}\text{H}_{22}\text{NO}_6$ ($[\text{M}+\text{H}]^+$) 348.1442 found 348.1440.

2,2-diethyl 1-methyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate 15e

 Diethyl 2-((methoxycarbonyl)(prop-2-yn-1-yl)amino)malonate (136 mg, 0.5 mmol, 1.0 eq.) were dissolved in DCE (3 mL) and zinc iodide (16 mg, 0.05 mmol, 10 mol%) was added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et_2O) and the solvent was removed. Purification by FC (PE/ Et_2O 1:1) afforded 2,2-diethyl 1-methyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate (108.3 mg, 0.399 mmol, 80%) as a clear oil.

Mixture of rotamers: $^1\text{H-NMR}$ (400 MHz, CDCl_3): 6.10/6.06 (*dt*, 1H, $J = 6.1, 1.9$ Hz, H_{olef}), 5.88/5.83 (*dt*, 1H, $J = 6.1, 2.2$ Hz, H_{olef}), 4.38/4.31 (*t*, 2H, $J = 2.1$ Hz, CH_2N), 4.38-4.18 (*m*, 4H, 2 \times CH_2O), 3.76/3.69 (*s*, 3H, CH_3O), 1.29 (*q*, 6H, $J = 7.0$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 167.2/167.1 (2 \times CO), 154.6 (CO), 129.9/129.8 (CH_{olef}), 126.8/126.6 (CH_{olef}), 78.2/77.7 (C), 62.1/62.0 (2 \times CH_2), 54.7/54.1 (CH_2), 52.8/52.6 (CH_3), 14.0/13.9 (2 \times CH_3). IR (film): 2982m, 2873m, 1753s, 1715s, 1146w, 1411s, 1352m, 1309w, 1281w, 1237s, 1213s, 1151w, 1112w, 1049m, 861w, 822w, 743w, 698m. MS (ESI $+$): 272.13 (61, $[\text{M}+\text{H}]^+$), 294.10 (100, $[\text{M}+\text{Na}]^+$), 565.22 (81, $[2\text{M}+\text{Na}]^+$). HRMS (ESI): calculated for $\text{C}_{12}\text{H}_{17}\text{NNaO}_6$ ($[\text{M}+\text{Na}]^+$) 294.0948 found 294.0947.

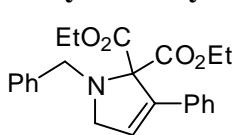
Diethyl 1-benzyl-3-ethyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate 15f

 Diethyl 2-(benzyl(pent-2-ynyl)amino)malonate **14f** (166 mg, 0.5 mmol, 1.0 eq.) were dissolved in DCE (3 mL) and zinc iodide (16 mg, 0.05 mmol, 10 mol%) was added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et_2O) and the solvent was removed. Purification by FC (PE/ Et_2O 10:1) afforded diethyl 1-benzyl-3-ethyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15f** (147.0 mg, 0.44 mmol, 89%) as a clear oil.

$^1\text{H-NMR}$ (400 MHz, C_6D_6): 7.56-7.54 (*m*, 2H, H_{ar}), 7.33-7.29 (*m*, 2H, H_{ar}), 7.23-7.20 (*m*, 1H, H_{ar}), 5.58-5.56 (*m*, 1H, H_{olef}), 4.52 (*s*, 2H, CH_2Ph), 4.12 (*q*, 4H, $J = 7.1$ Hz, 2 \times CH_2O), 3.64 (*q*, 2H, $J = 2.2$ Hz, CH_2N), 2.54 (*qq*, 2H, $J = 7.4, 2.2$ Hz, $\text{C}=\text{CHCH}_2\text{CH}_3$), 1.15 (*t*, 3H, $J = 7.4$ Hz, $\text{C}=\text{CHCH}_2\text{CH}_3$), 1.04 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.49-7.47 (*m*, 2H, H_{ar}), 7.23-7.19 (*m*, 2H, H_{ar}), 7.13-7.10 (*m*, 1H, H_{ar}), 5.46-5.43 (*m*, 1H, H_{olef}), 4.47 (*s*, 2H, CH_2Ph), 4.01 (*q*, 4H, $J = 7.1$ Hz, 2 \times CH_2O), 3.56 (*q*, 2H, $J = 2.2$ Hz, CH_2N), 2.48 (*qq*, 2H, $J = 7.4, 2.2$ Hz, $\text{C}=\text{CHCH}_2\text{CH}_3$), 1.05 (*t*, 3H, $J = 7.4$ Hz, $\text{C}=\text{CHCH}_2\text{CH}_3$), 0.92 (*t*, 6H, $J = 7.1$ Hz, 2 \times CH_3). $^{13}\text{C-NMR}$ (100 MHz, C_6D_6): 169.4 (2 \times CO), 142.6 (C_{olef}), 140.7 (C_{ar}), 128.6

($2 \times$ CH_{ar}), 128.5 ($2 \times$ CH_{ar}), 127.1 (CH_{ar}), 125.7 (CH_{olef}), 83.4 (C), 61.0 ($2 \times$ CH₂), 58.1 (CH₂), 54.9 (CH₂), 21.4 (CH₂), 14.2 ($2 \times$ CH₃), 12.2 (CH₃). IR (film): 3063w, 3028w, 2979m, 2939w, 2879w, 2801w, 1732s, 11495w, 1454w, 1368w, 1246m, 1146m, 1095w, 1076w, 1053m, 1038m, 958w, 823w, 742w, 702w. MS (ESI+): 332.18 (97, [M+H]⁺), 354.15 (100, [M+Na]⁺), 384.18 (88), 685.33 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₁₉H₂₅NNaO₄ ([M+Na]⁺) 354.1676 found 354.1675. COSY, HMQC, HMBC were used for assignment.

Diethyl 1-benzyl-3-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate 15g

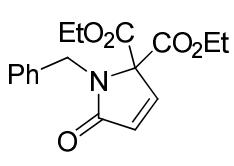
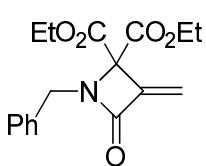


Diethyl 2-(benzyl(3-phenylprop-2-ynyl)amino)malonate **14g**

(190 mg, 0.5 mmol, 1.0 eq.) were dissolved in DCE (3 mL) and zinc iodide (16 mg, 0.05 mmol, 10 mol%) were added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled reaction was filtered through a plug of silica (Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 6:1) afforded **14g** diethyl 1-benzyl-3-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (130.5 mg, 0.344 mmol, 69%) as a clear oil.

¹H-NMR (400 MHz, CDCl₃): 7.43-7.39 (*m*, 4H, H_{ar}), 7.35-7.24 (*m*, 6H, H_{ar}), 6.34 (*t*, 1H, *J* = 2.1 Hz, H_{olef}), 4.31-4.19 (*m*, 4H, 2 × CH₂O), 4.10 (*s*, 2H, CH₂Ph), 3.70 (*d*, 2H, *J* = 2.1 Hz, CH₂N), 1.20 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 169.1 (CO), 140.4 (C_{ar}), 139.4 (C_{ar}), 134.3 (C_{olef}), 129.9 (CH_{olef}), 128.4 (4 × CH_{ar}), 127.9 (2 × CH_{ar}), 127.6 (CH_{ar}), 127.3 (2 × CH_{ar}), 127.1 (CH_{ar}), 82.2 (C), 61.4 (2 × CH₂), 57.9 (CH₂), 54.3 (CH₂), 14.1 (2 × CH₃). IR (film): 3062w, 2032w, 2983m, 2938w, 2906w, 1740s, 1704s, 1599w, 1515w, 1496m, 1447w, 1387w, 1368w, 1327w, 1297w, 1239s, 1176w, 1102w, 1052m, 862m, 775m, 700w. MS (ESI+): 380.23 (43, [M+H]⁺), 402.18 (97, [M+Na]⁺), 781.37 (100, [2M+Na]⁺). HRMS (ESI): calculated for C₂₃H₂₆NNaO₄ ([M+H]⁺) 380.1856 found 380.1855. COSY, HMQC, HMBC were used for assignment.

Diethyl 1-benzyl-3-methylene-4-oxoazetidine-2,2-dicarboxylate 16 and diethyl 1-benzyl-5-oxo-1*H*-pyrrole-2,2(5*H*)-dicarboxylate 15h



Diethyl 2-(N-benzylpropiolamido)-malonate **14h** (159 mg, 0.5 mmol, 1.0 eq.) was dissolved in DCE (3 mL) and zinc chloride (7 mg, 0.05 mmol, 10 mol%) was added. The reaction was heated in a sealed tube to 100 °C for 15 h. The cooled

reaction was filtered through a plug of silica (Et₂O) and the solvent was removed. Purification by FC (PE/Et₂O 1:1) afforded diethyl 1-benzyl-3-methylene-4-oxoazetidine-2,2-dicarboxylate **16** (105.5 mg, 0.33 mmol, 66%) and diethyl 1-benzyl-5-oxo-1*H*-pyrrole-2,2(5*H*)-dicarboxylate **15h** (44.7 mg, 0.14 mmol, 28%) as clear oils.

Diethyl 1-benzyl-3-methylene-4-oxoazetidine-2,2-dicarboxylate **16**:

¹H-NMR (400 MHz, CDCl₃): 7.32-7.25 (*m*, 5H, H_{ar}), 5.86 (*d*, 1H, *J* = 2.1 Hz, CH_{olef}), 5.51 (*d*, 1H, *J* = 2.1 Hz, CH_{olef}), 4.74 (*s*, 2H, CH₂Ph), 4.03 (*q*, 4H, *J* = 7.1 Hz, 2 × CH₂O), 1.15 (*t*, 6H, *J* = 7.1 Hz, 2 × CH₃). ¹³C-NMR (100 MHz, CDCl₃): 166.1 (2 × CO), 162.6 (CO), 145.3 (C_{olef}), 135.4 (C_{ar}), 128.6 (2 × CH_{ar}), 128.4 (2 × CH_{ar}), 127.7 (CH_{ar}), 112.0 (CH_{olef}), 70.6 (C), 62.4 (2 × CH₂), 45.6 (CH₂), 13.7 (2 × CH₃). IR (film): 2983w, 1775s, 1745s, 1347w, 1326w, 1237m, 1107w, 1078m, 667m. MS

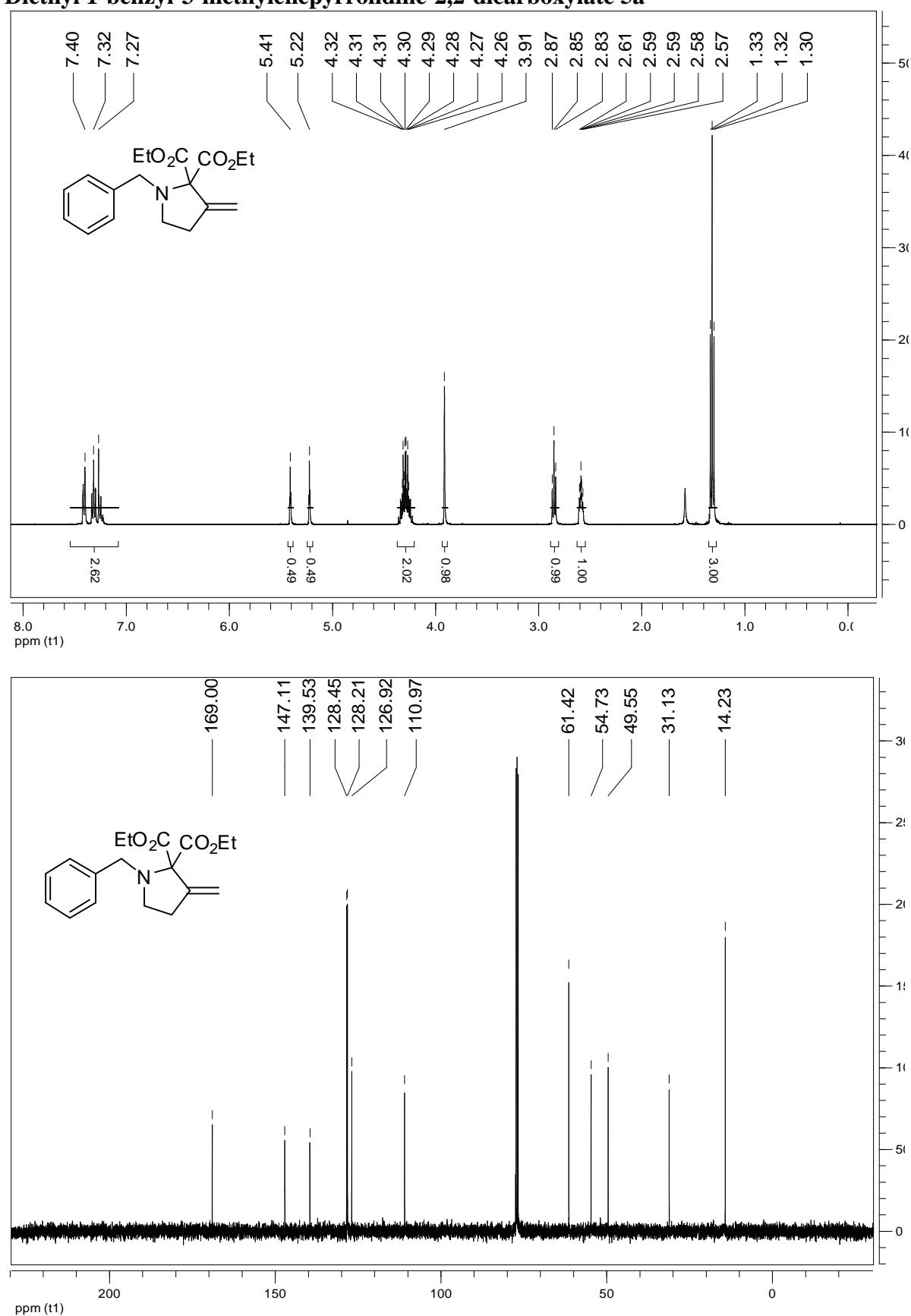
(ESI+): 340.11 (100, $[M+Na]^+$), 657.26 (67, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{17}H_{19}NaNO_5$ ($[M+Na]^+$) 340.1155 found 340.1158.

Diethyl 1-benzyl-5-oxo-1*H*-pyrrole-2,2(*H*)-dicarboxylate **15h**

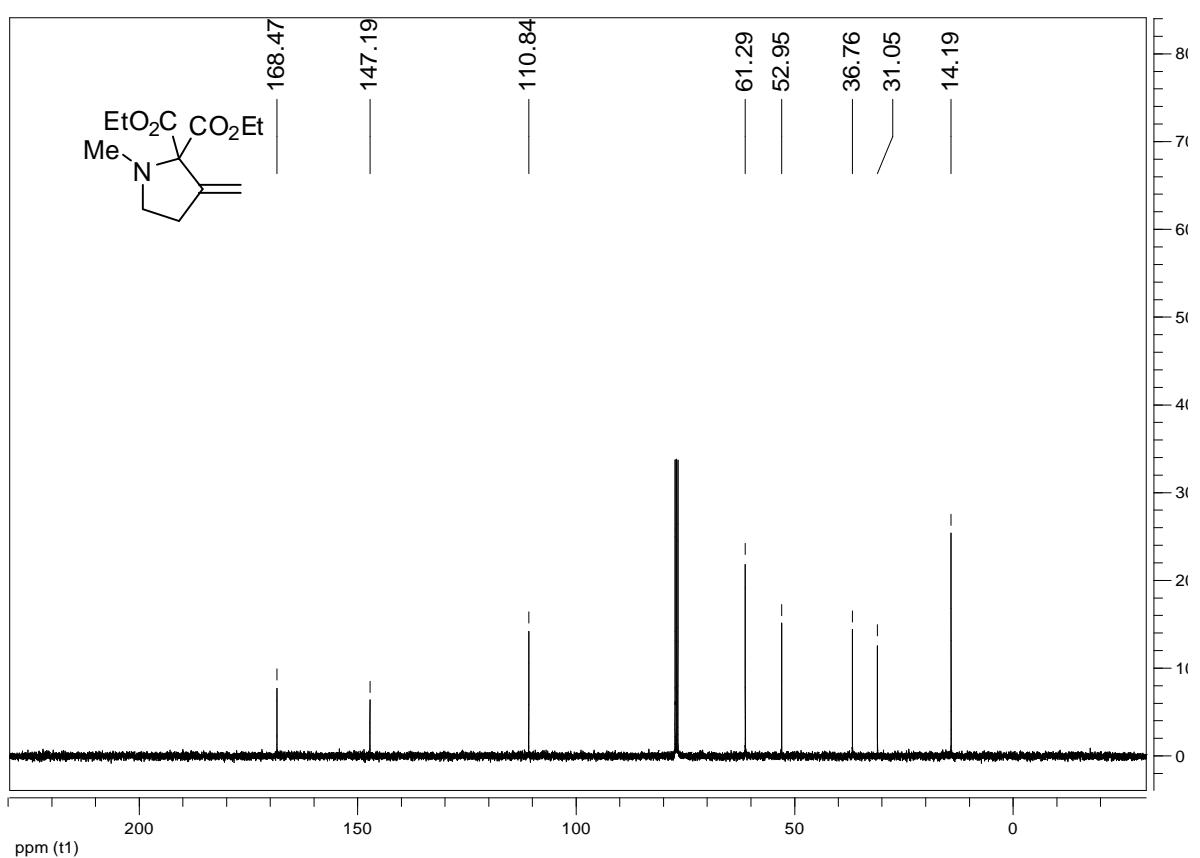
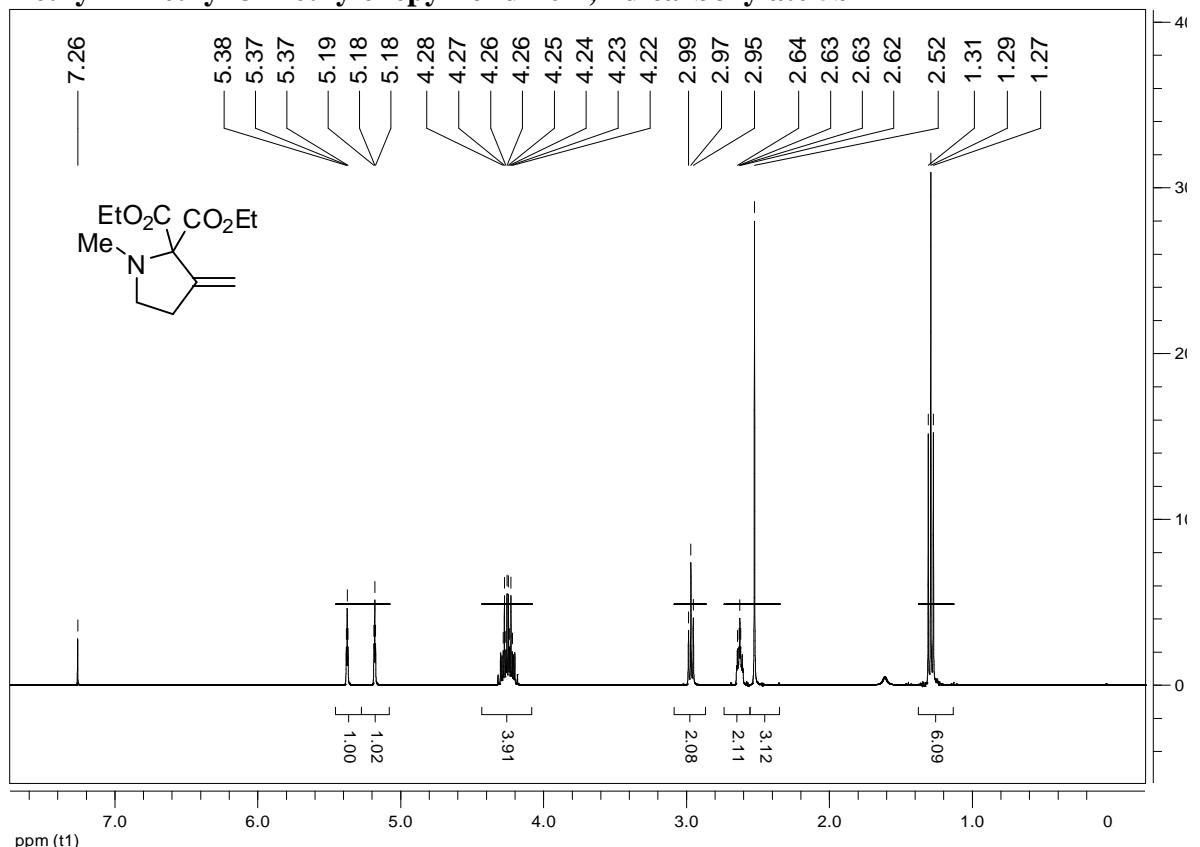
1H -NMR (400 MHz, $CDCl_3$): 7.29-7.25 (*m*, 2H, H_{ar}), 7.22-7.18 (*m*, 3H, H_{ar}), 7.13 (*d*, 1H, *J* = 5.9 Hz, $COCH_{olef}$), 6.39 (*d*, 1H, *J* = 5.9 Hz, $COCH=CH$), 4.89 (*s*, 2H, CH_2Ph), 3.94 (*q*, 4H, *J* = 7.1 Hz, 2 \times CH_2O), 1.12 (*t*, 6H, *J* = 7.1 Hz, 2 \times CH_3). ^{13}C -NMR (100 MHz, $CDCl_3$): 171.3 (CO), 165.0 (2 \times CO), 142.9 (CH_{olef}), 137.1 (C_{ar}), 128.9 (2 \times CH_{ar}), 128.2 (2 \times CH_{ar}), 127.5 (CH_{ar}), 127.1 (CH_{olef}), 76.0 (C), 62.8 (2 \times CH_2), 44.9 (CH_2), 13.7 (2 \times CH_3). IR (film): 3091w, 2982w, 2940w, 1742s, 1709s, 1467m, 1454w, 1430w, 1378w, 1369w, 1354w, 1339w, 1297m, 1264w, 1238w, 1216w, 1183w, 1097w, 1080w, 1044w, 852w, 737w. MS (ESI+): 340.11 (100, $[M+Na]^+$), 657.23 (80, $[2M+Na]^+$). HRMS (ESI): calculated for $C_{17}H_{19}NaNO_5$ ($[M+Na]^+$) 340.1155 found 340.1156. HMQC was used for assignment.

3. NMR spectra of the cyclization products

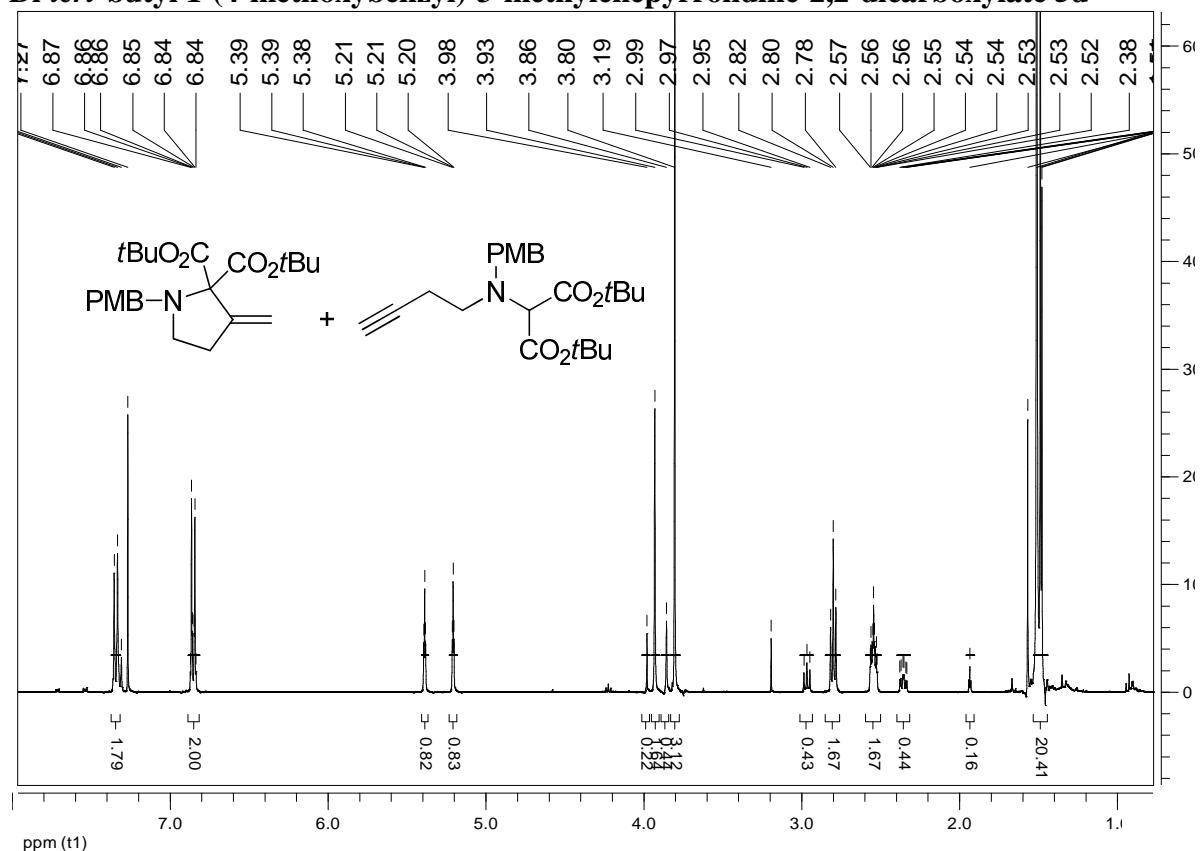
Diethyl 1-benzyl-3-methylenepyrrolidine-2,2-dicarboxylate 5a



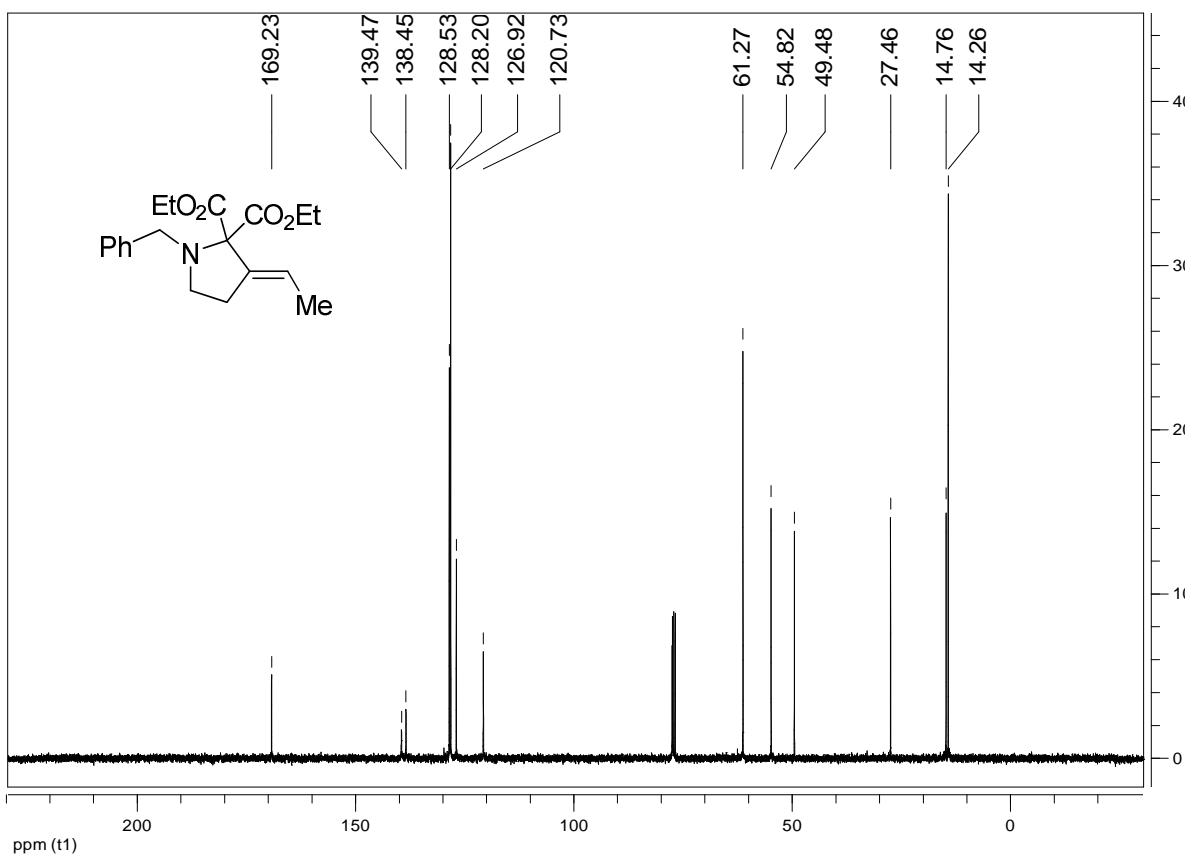
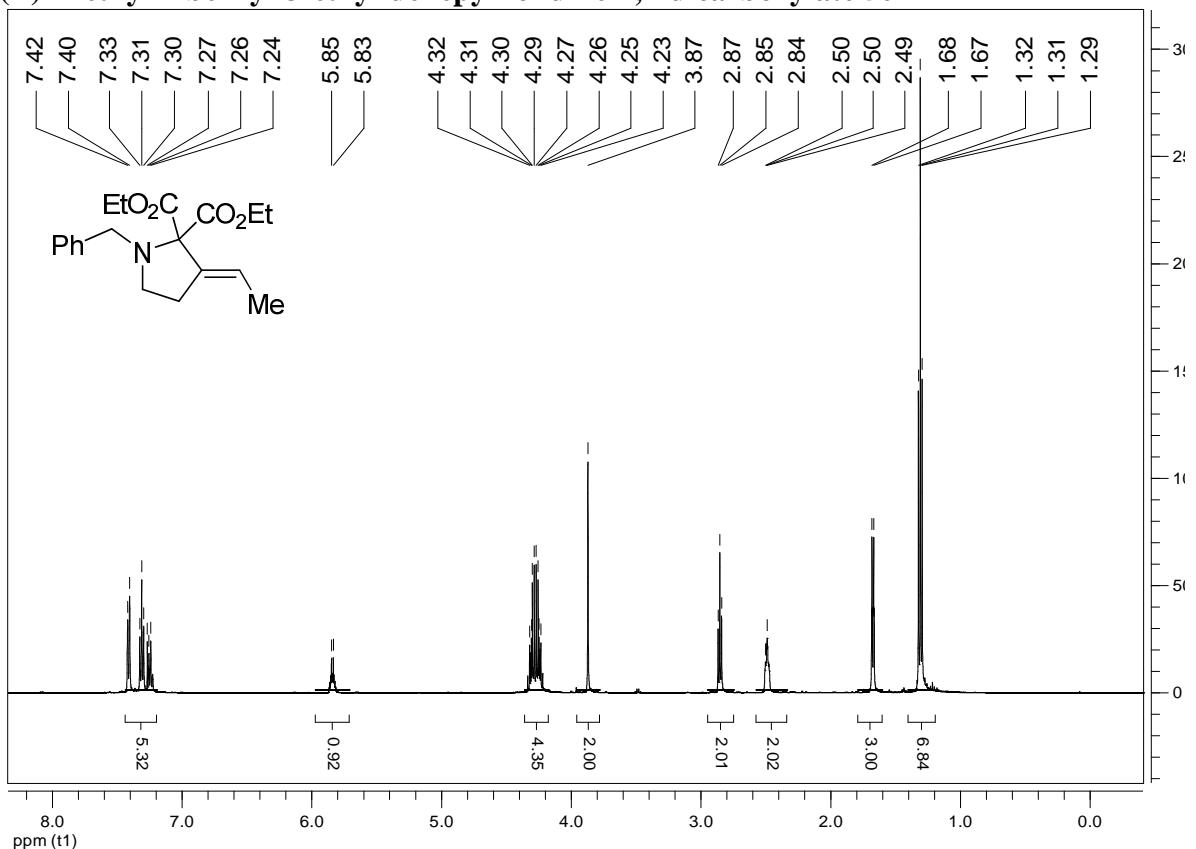
Diethyl 1-methyl-3-methylenepyrrolidine-2,2-dicarboxylate 5b



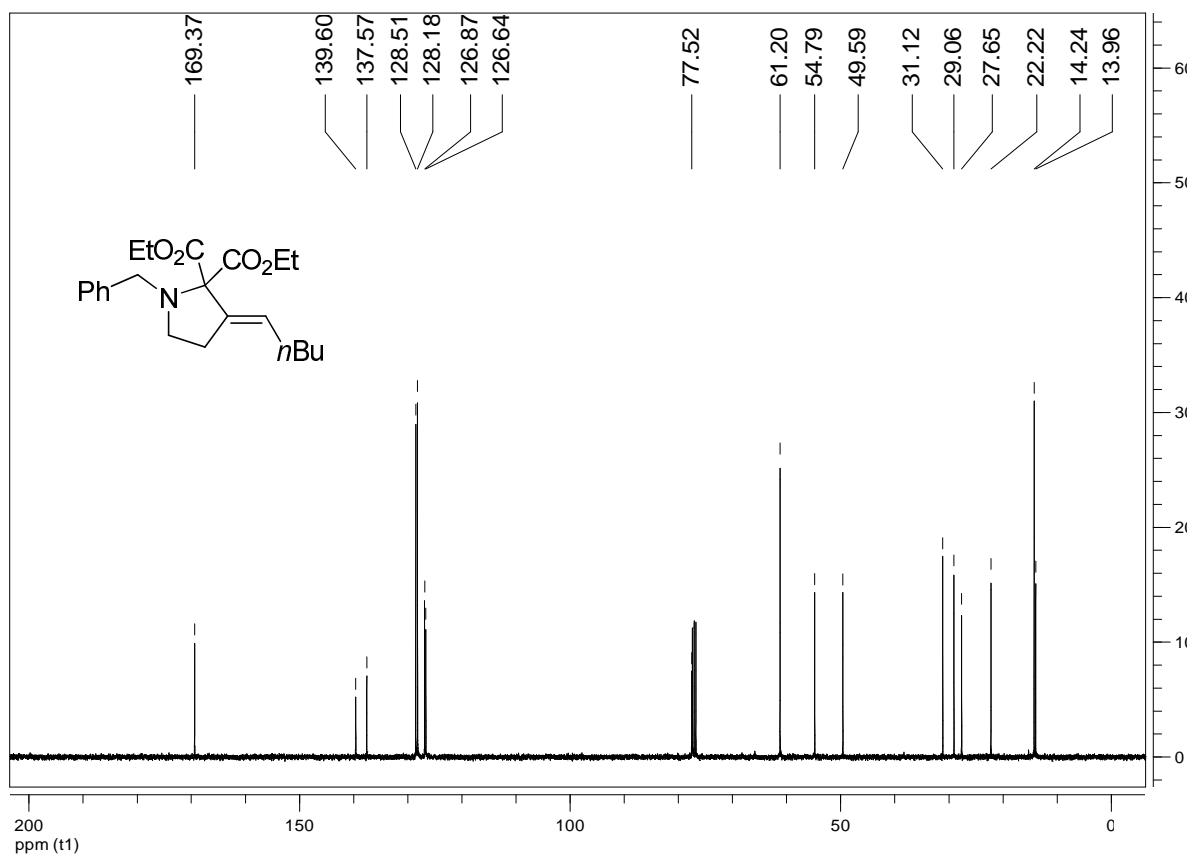
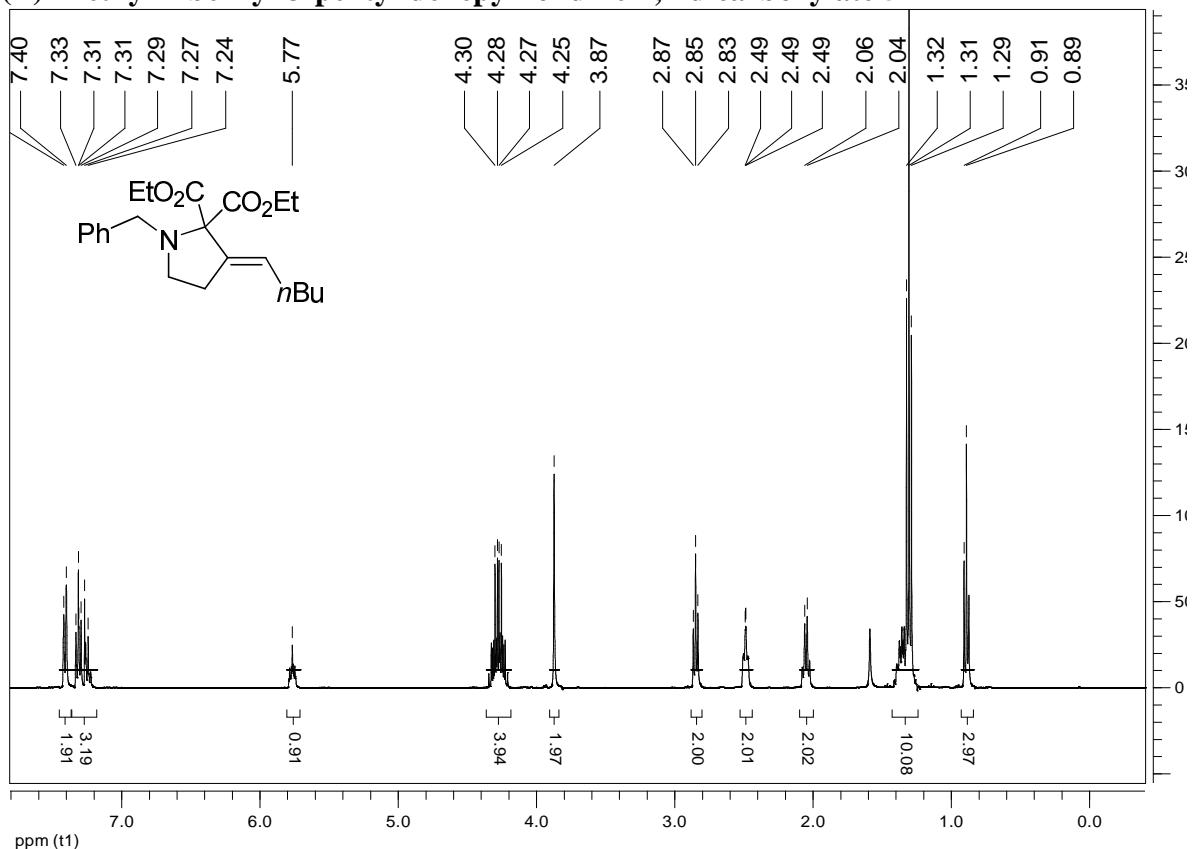
Di-*tert*-butyl 1-(4-methoxybenzyl)-3-methylenepyrrolidine-2,2-dicarboxylate 5d



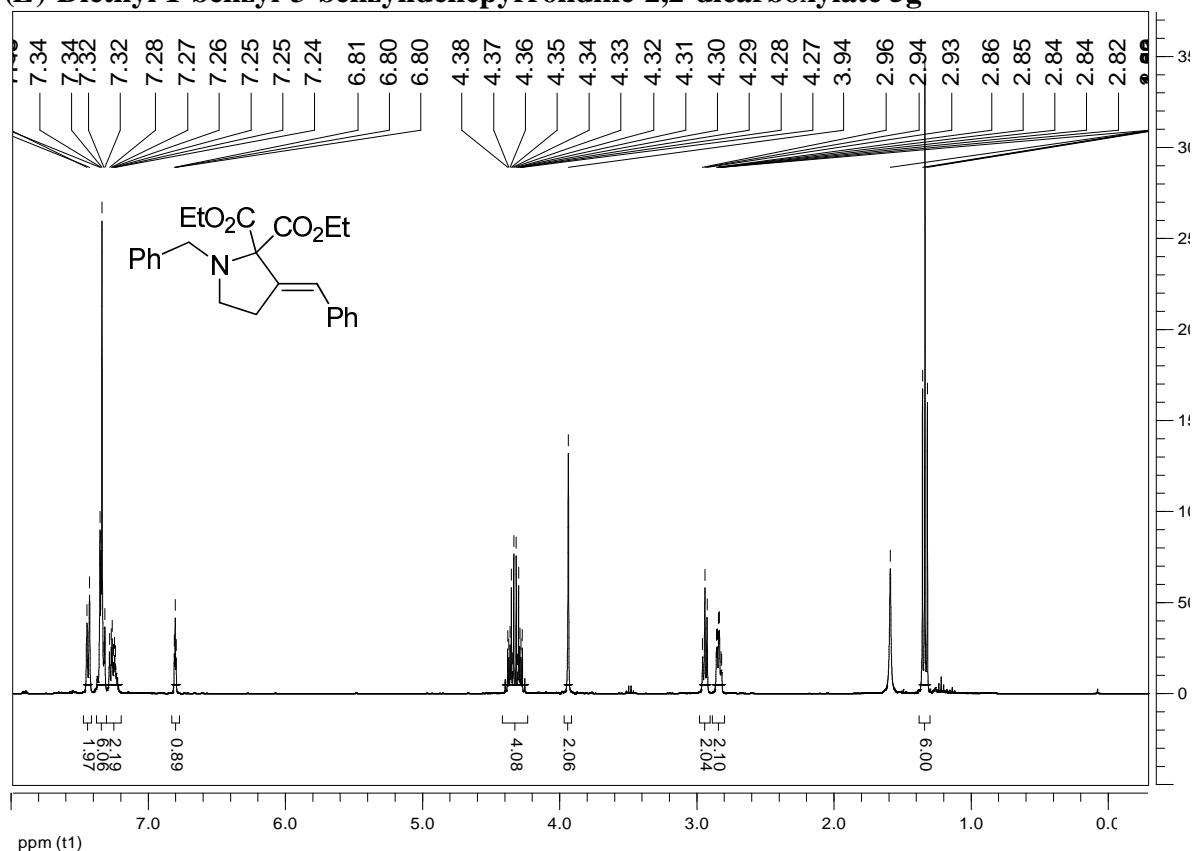
(E)-Diethyl 1-benzyl-3-ethylidenepyrrolidine-2,2-dicarboxylate 5e



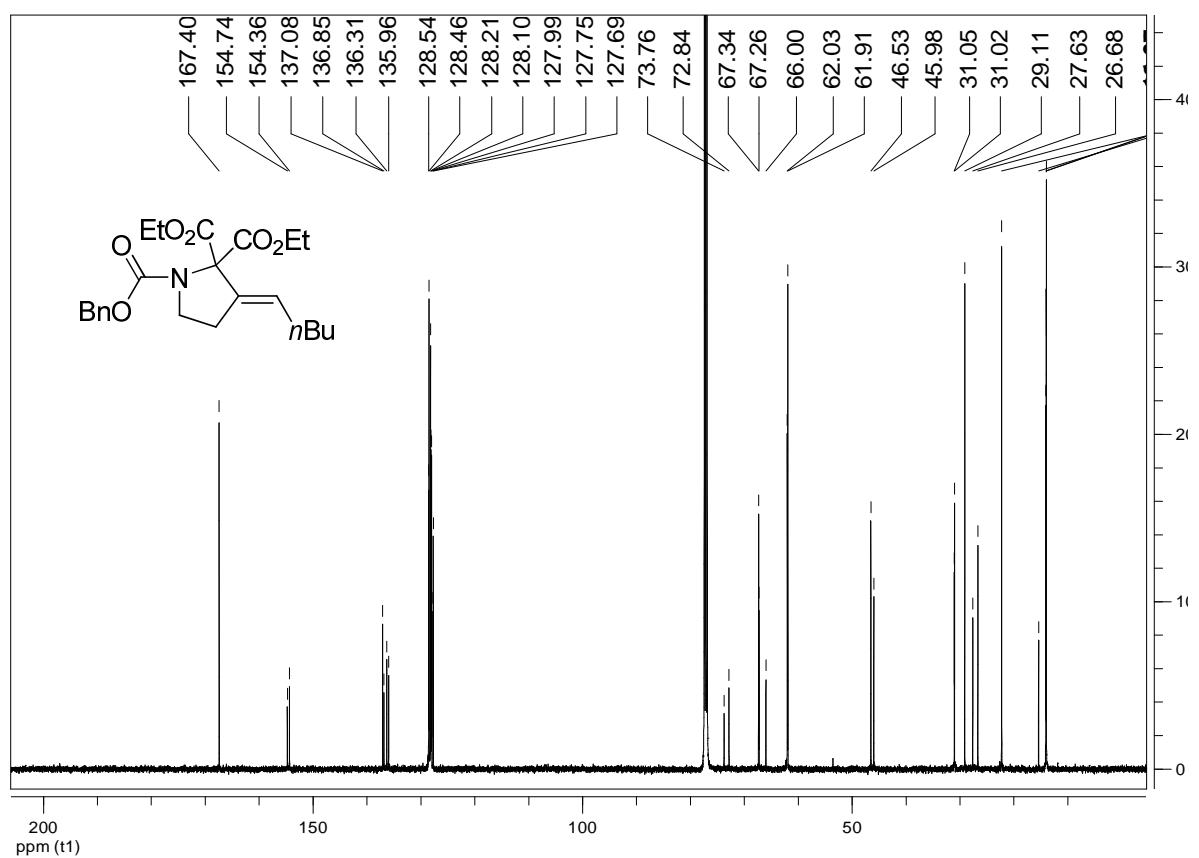
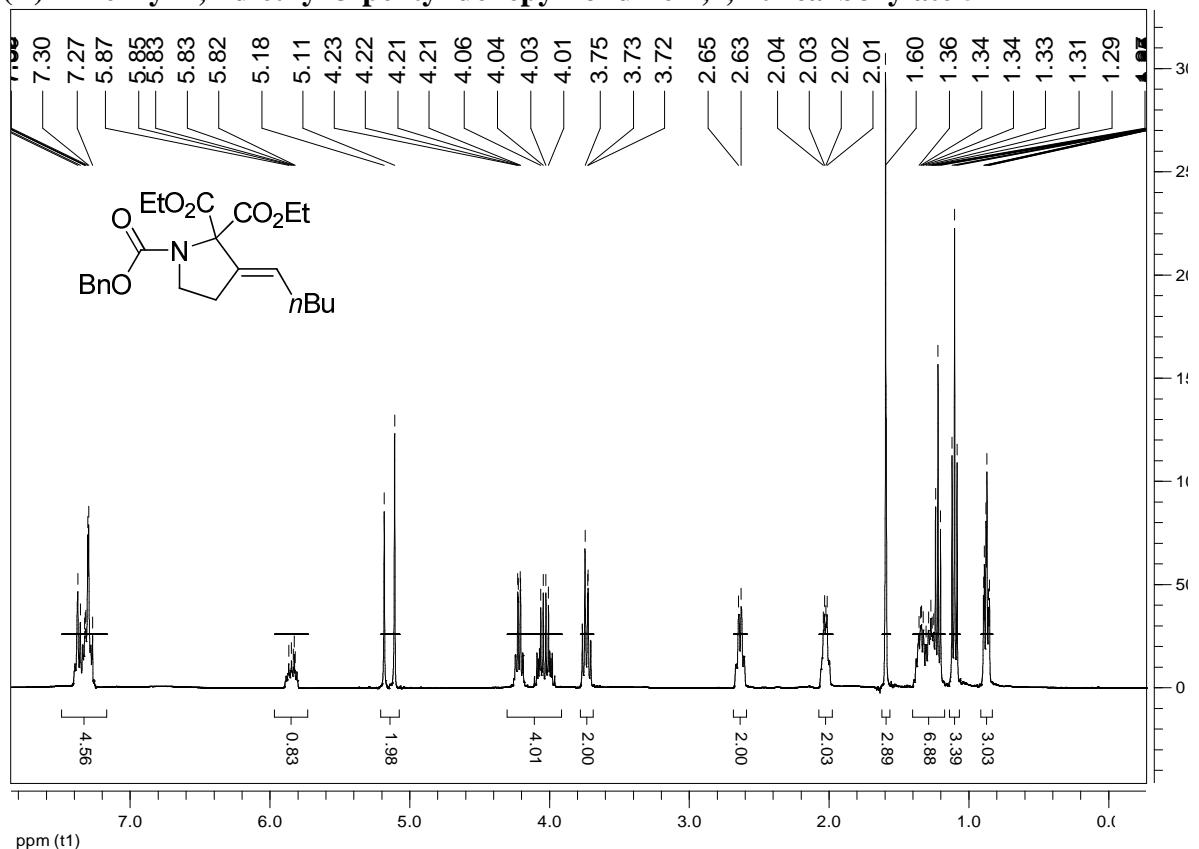
(E)-Diethyl 1-benzyl-3-pentylidenepyrrolidine-2,2-dicarboxylate 5f



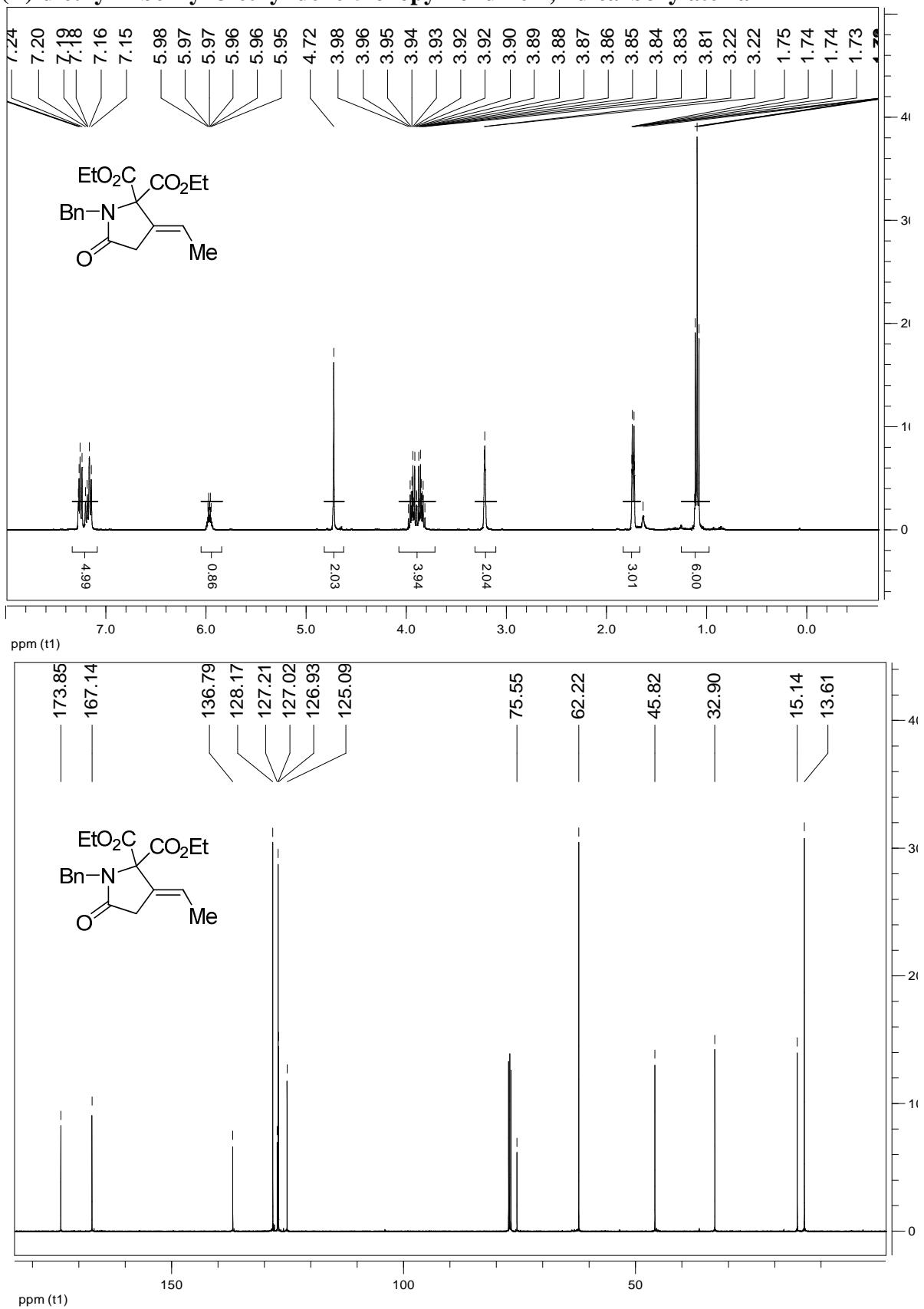
(E)-Diethyl 1-benzyl-3-benzylidenepyrrolidine-2,2-dicarboxylate 5g



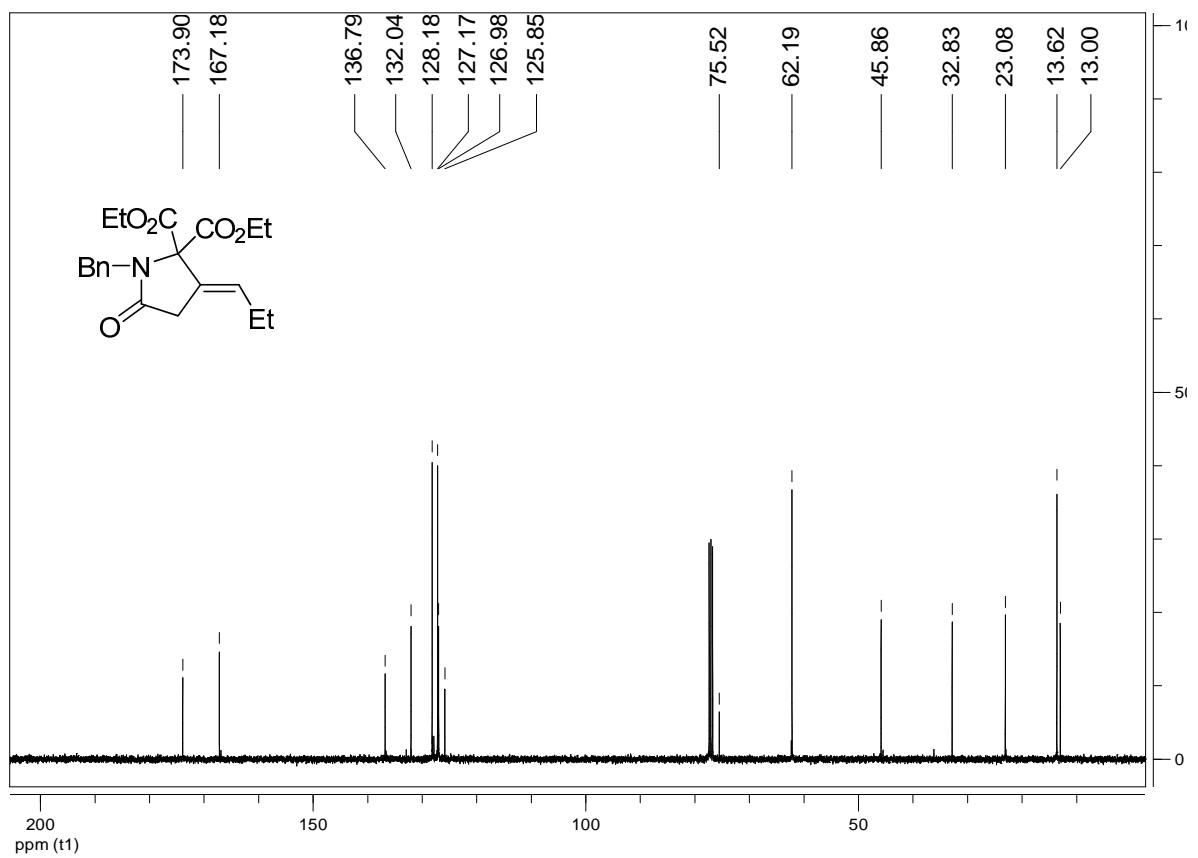
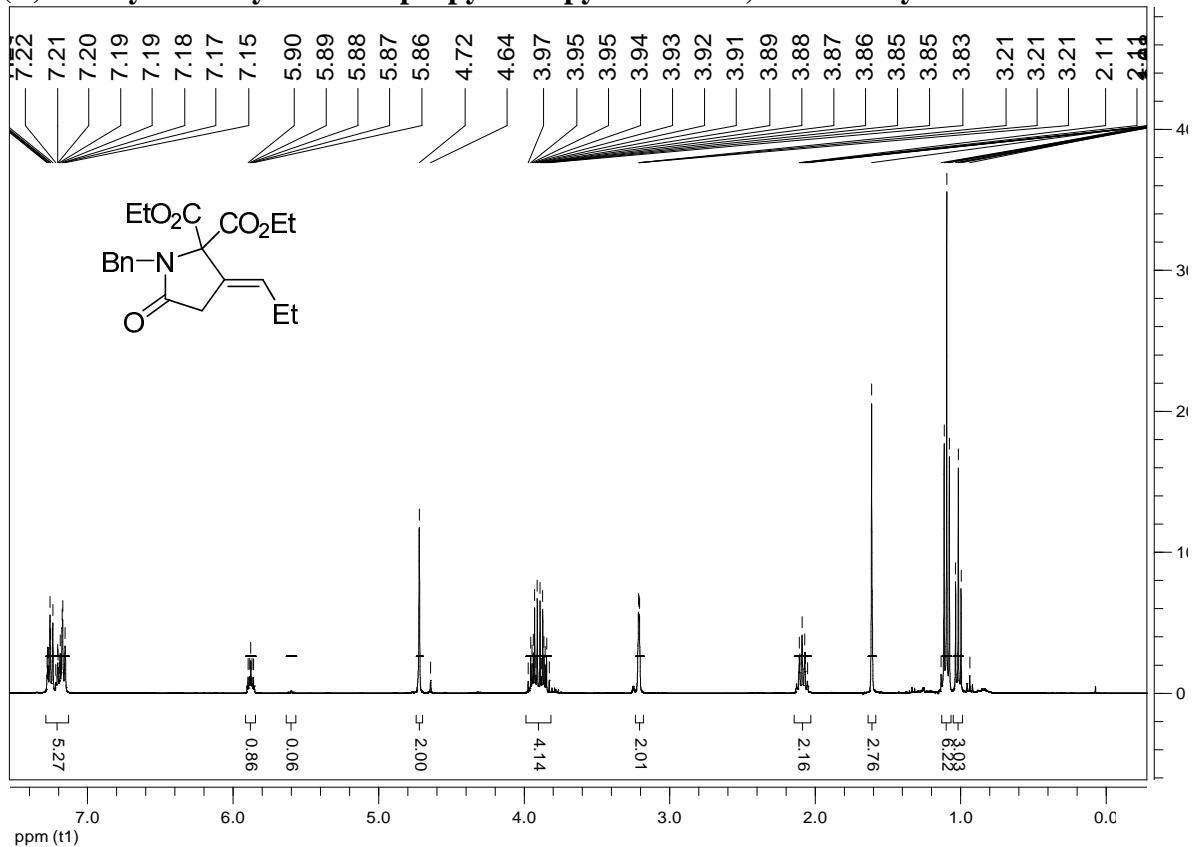
(E)-1-Benzyl 2,2-diethyl 3-pentylidene pyrrolidine-1,2,2-tricarboxylate 5h



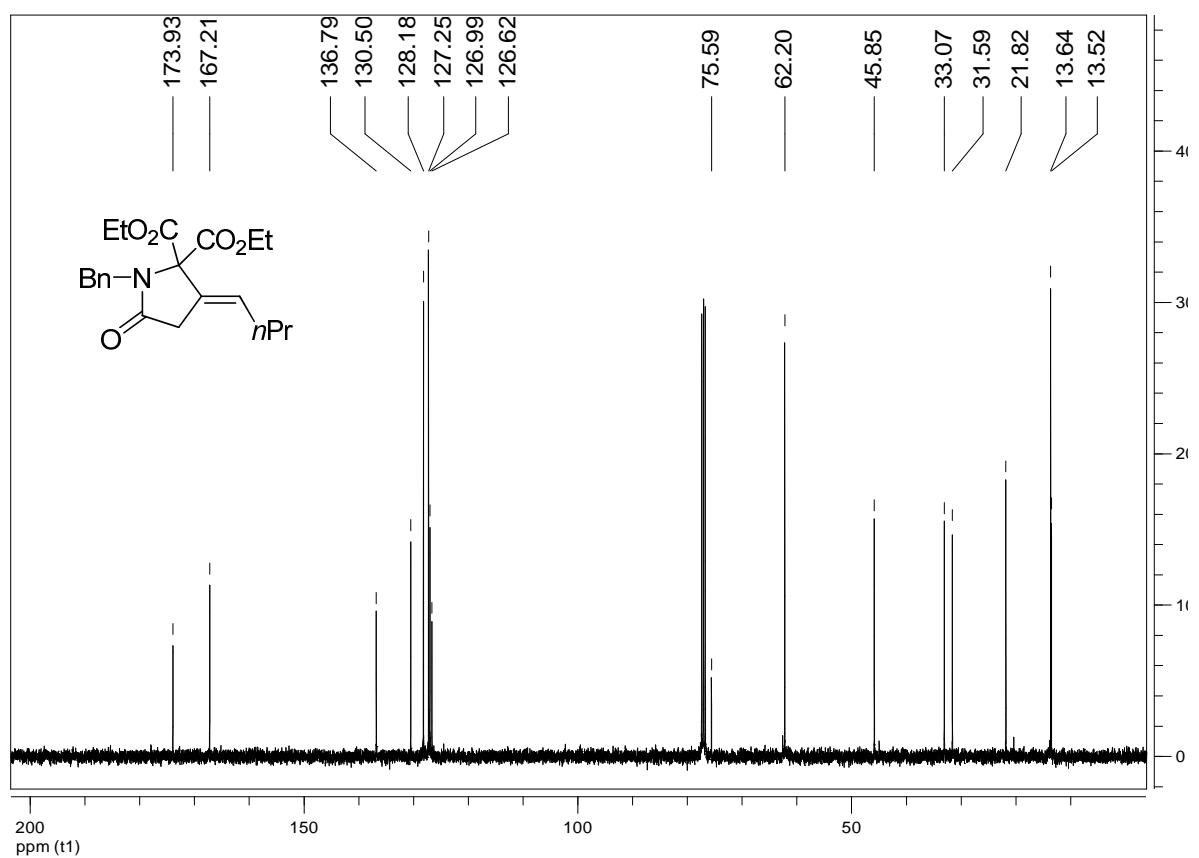
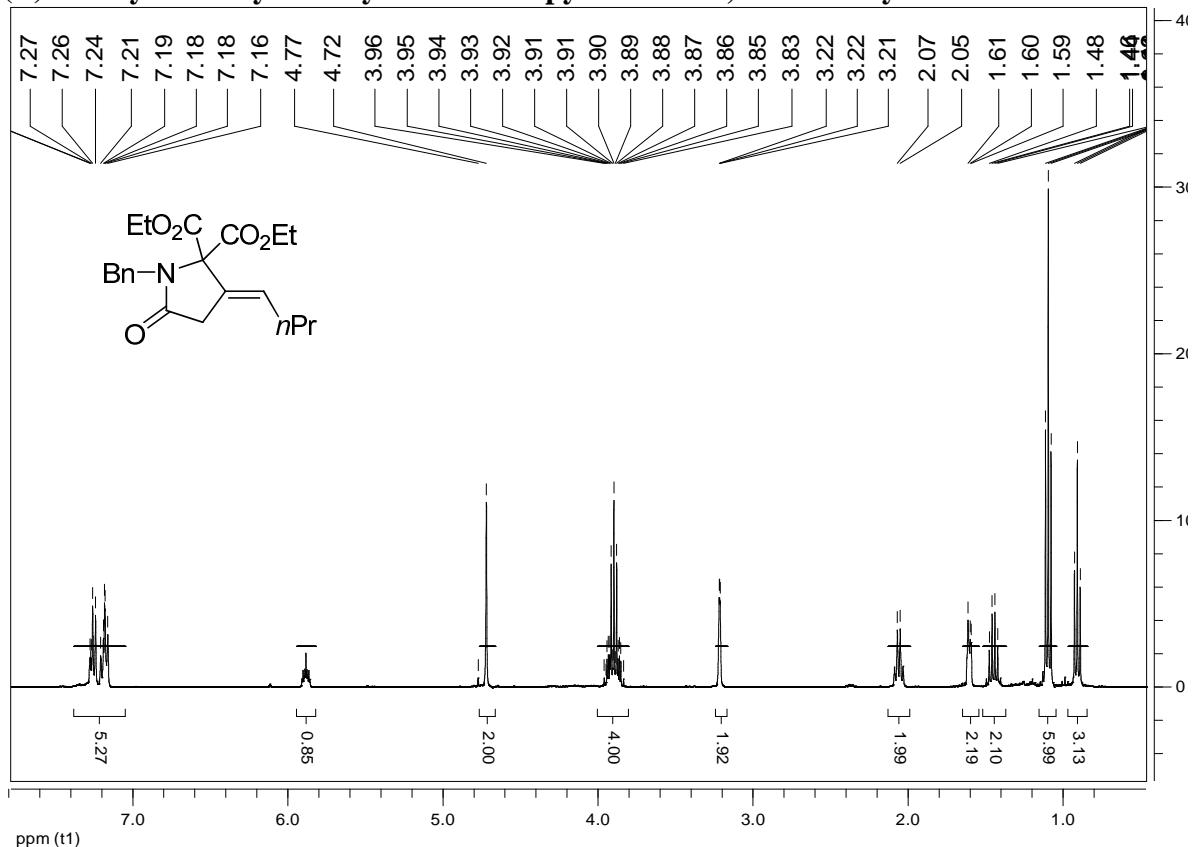
(E)-diethyl 1-benzyl-3-ethylidene-5-oxopyrrolidine-2,2-dicarboxylate 7a



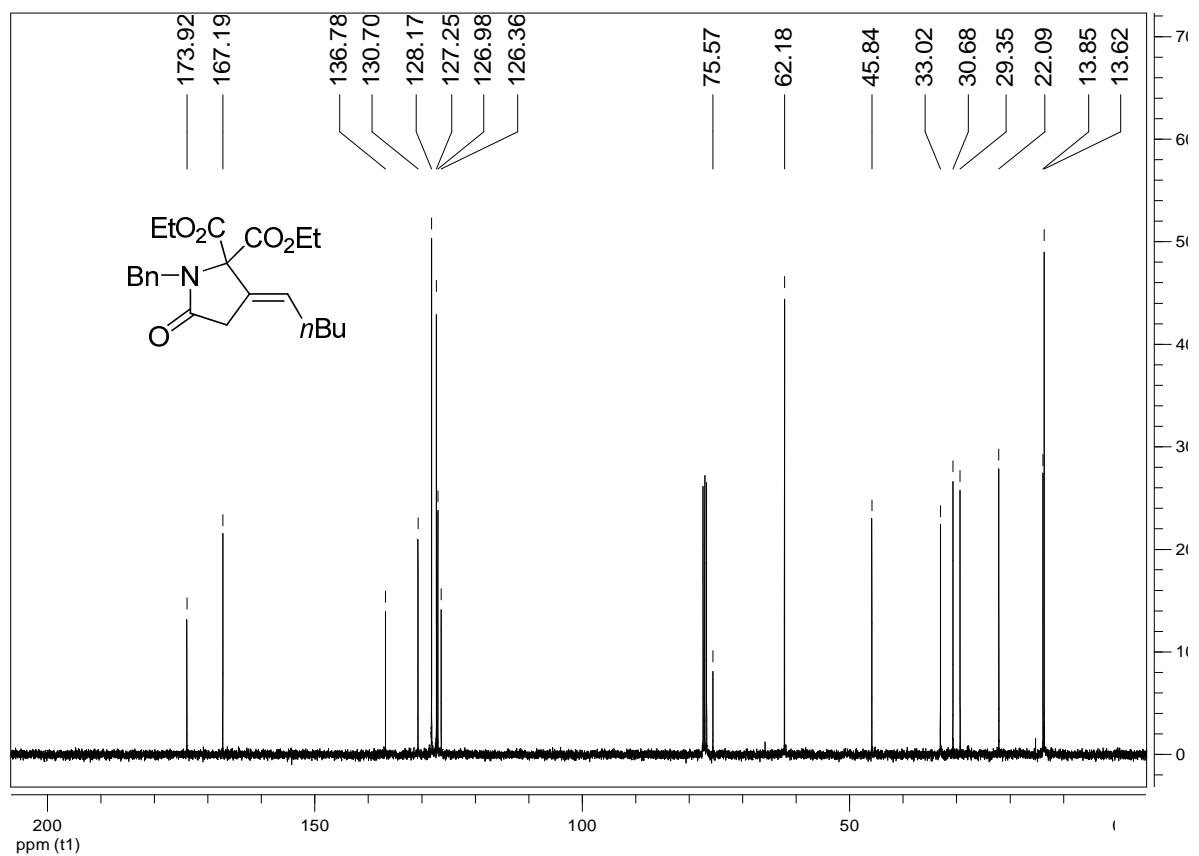
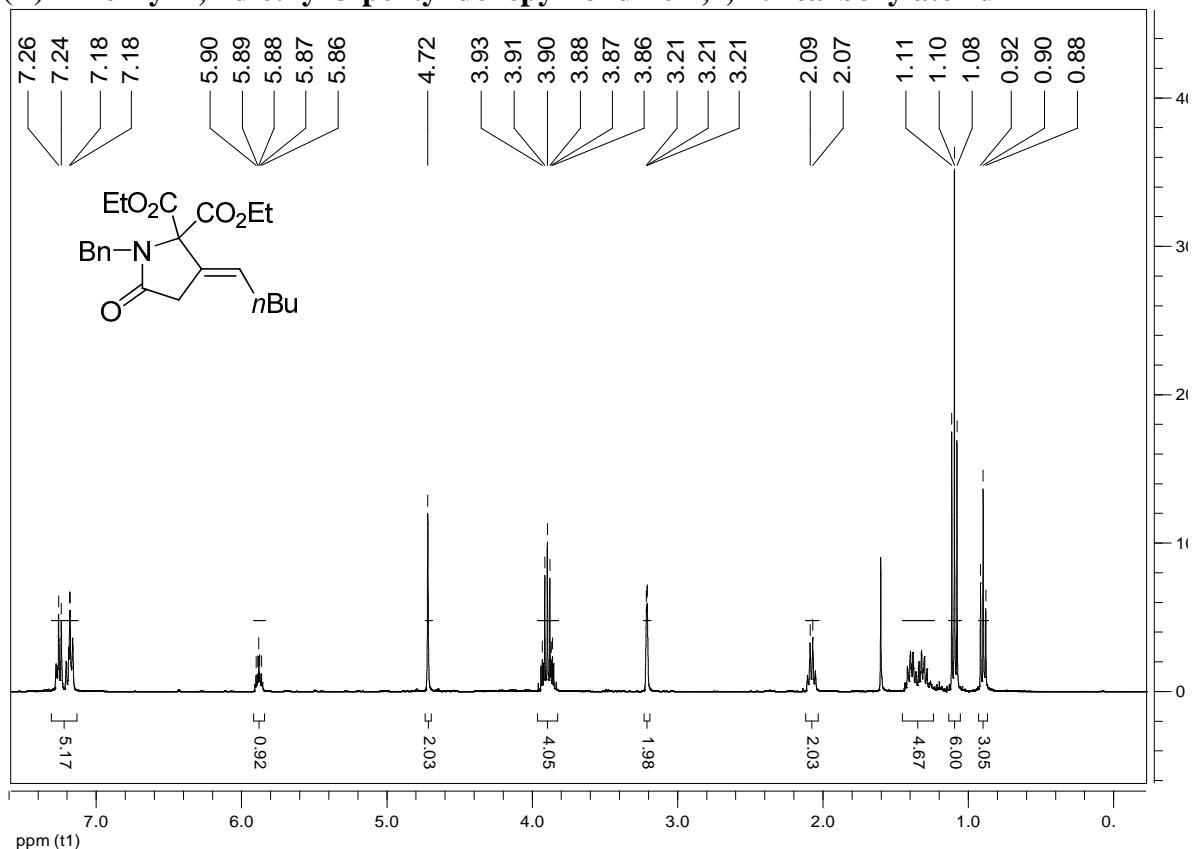
(E)-Diethyl 1-benzyl-5-oxo-3-propylidenepyrrolidine-2,2-dicarboxylate 7b



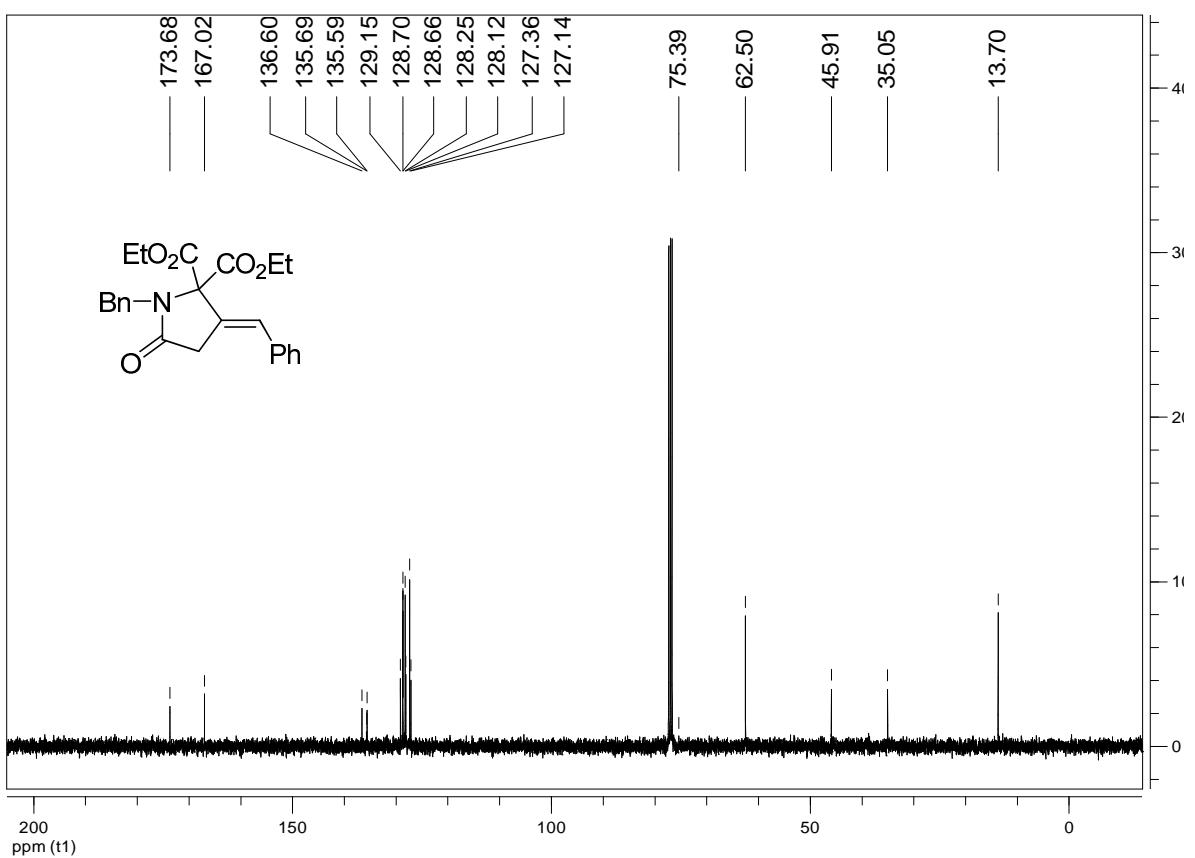
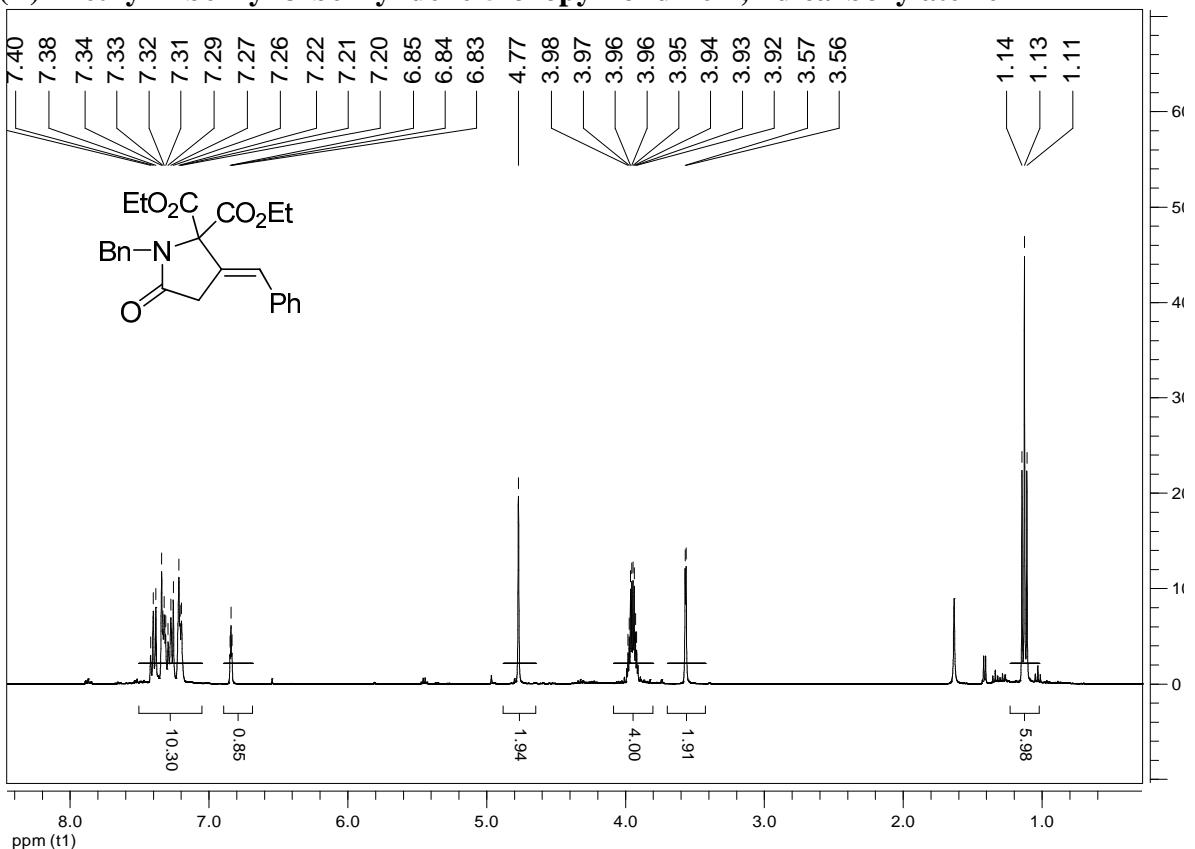
(E)-Diethyl 1-benzyl-3-butylidene-5-oxopyrrolidine-2,2-dicarboxylate 7c



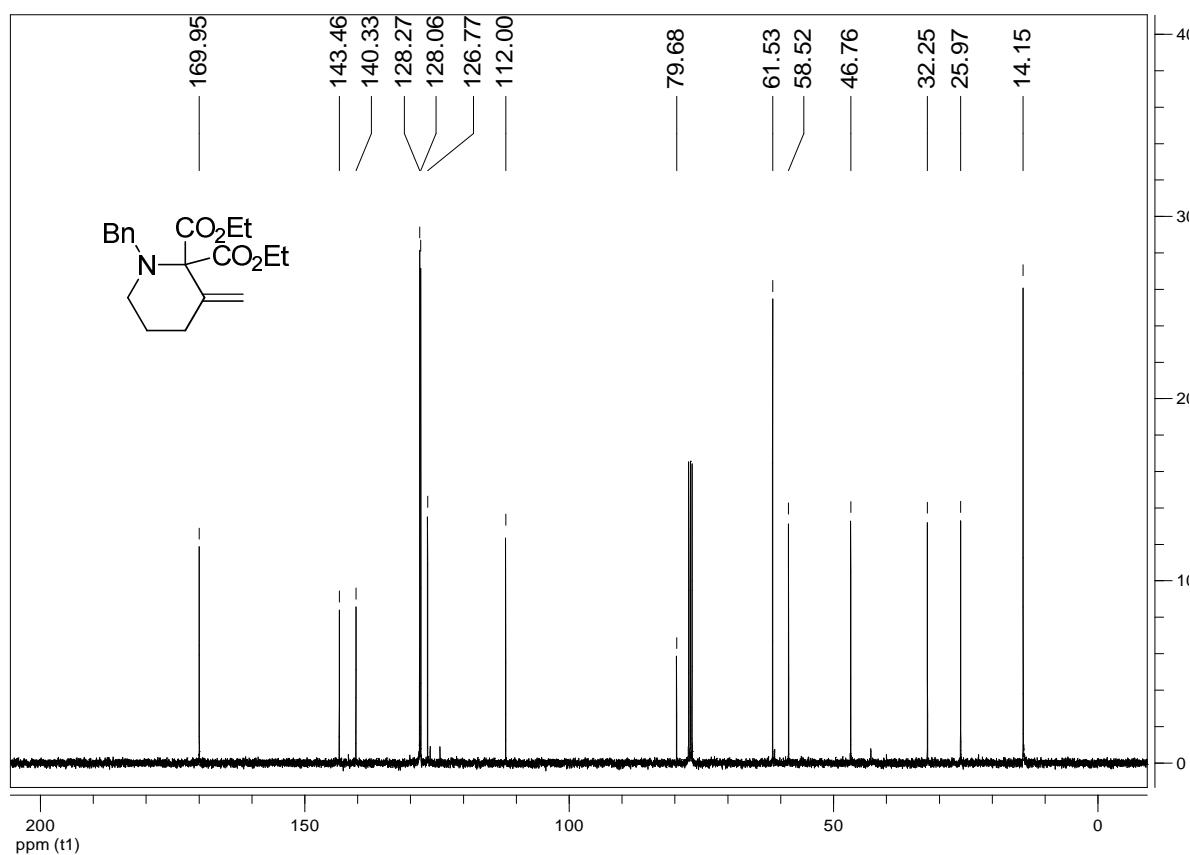
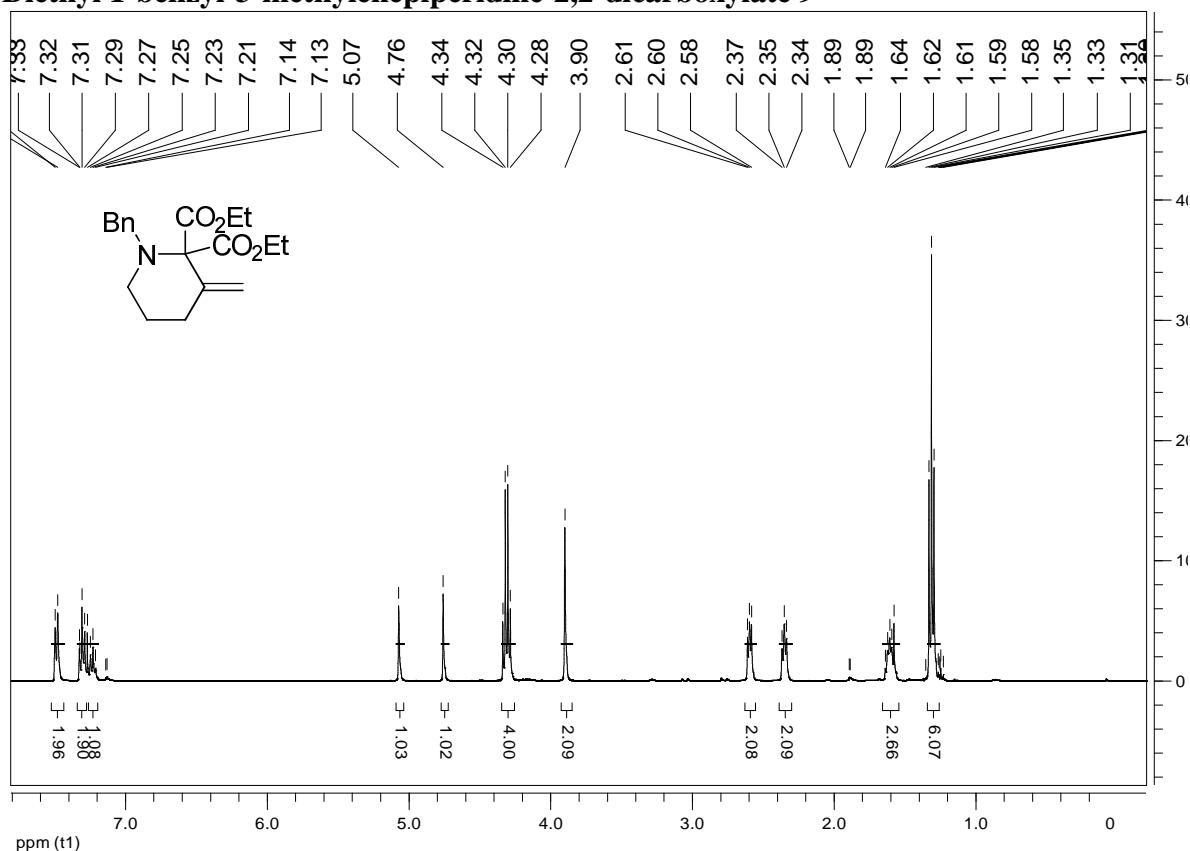
(E)-1-Benzyl 2,2-diethyl 3-pentylidenepyrrolidine-1,2,2-tricarboxylate 7d



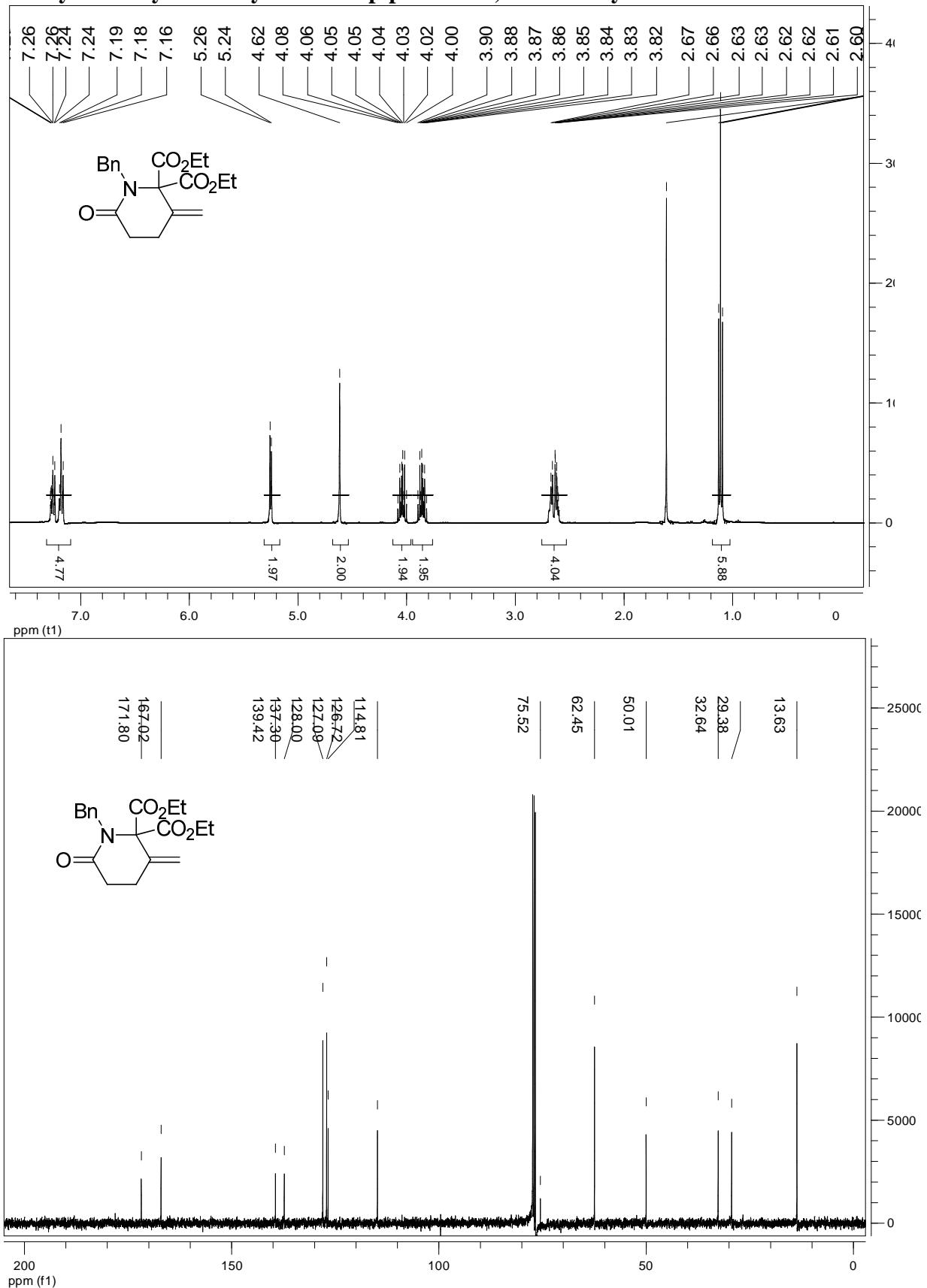
(E)-Diethyl 1-benzyl-3-benzylidene-5-oxopyrrolidine-2,2-dicarboxylate 7e



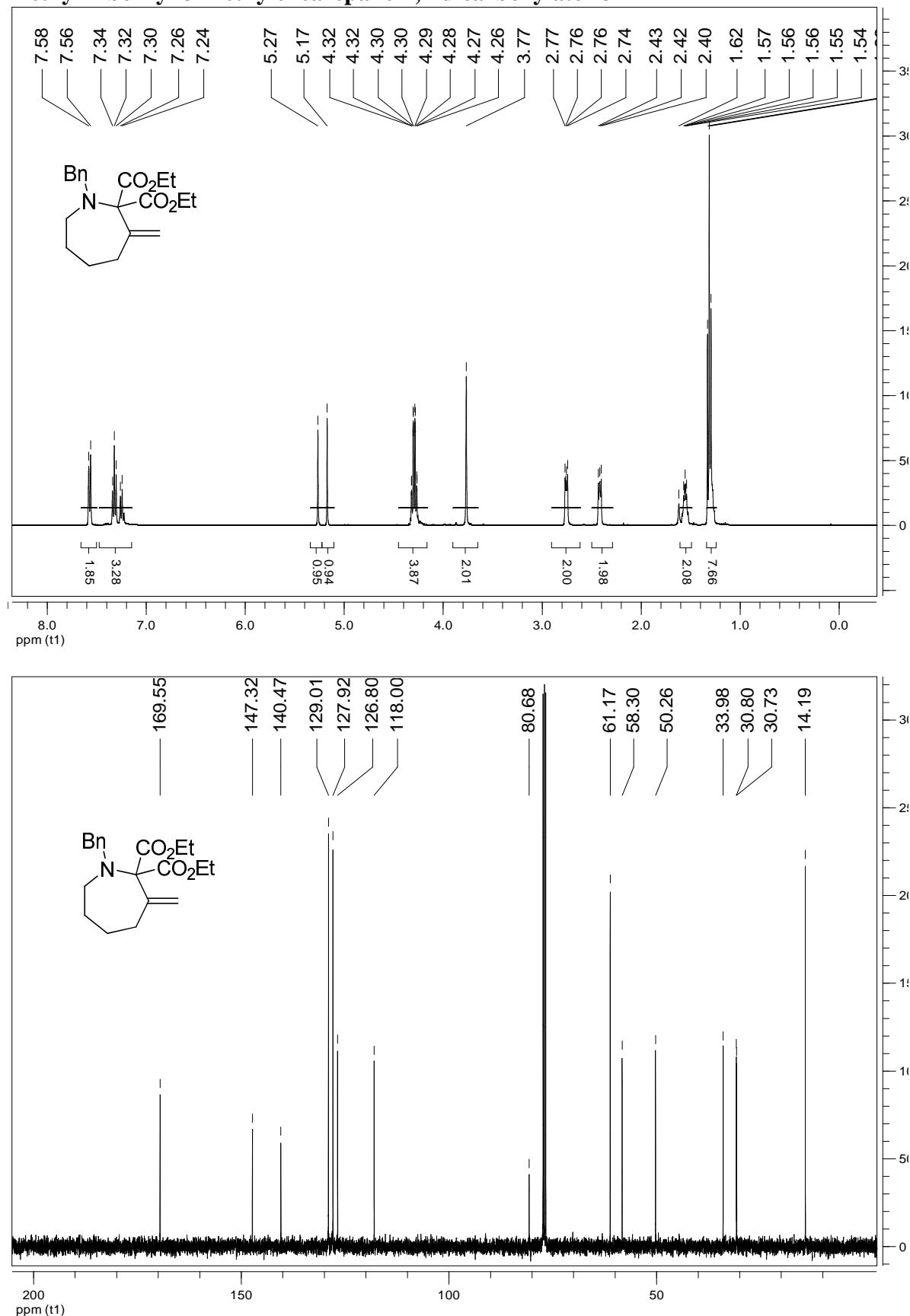
Diethyl 1-benzyl-3-methylenepiperidine-2,2-dicarboxylate 9



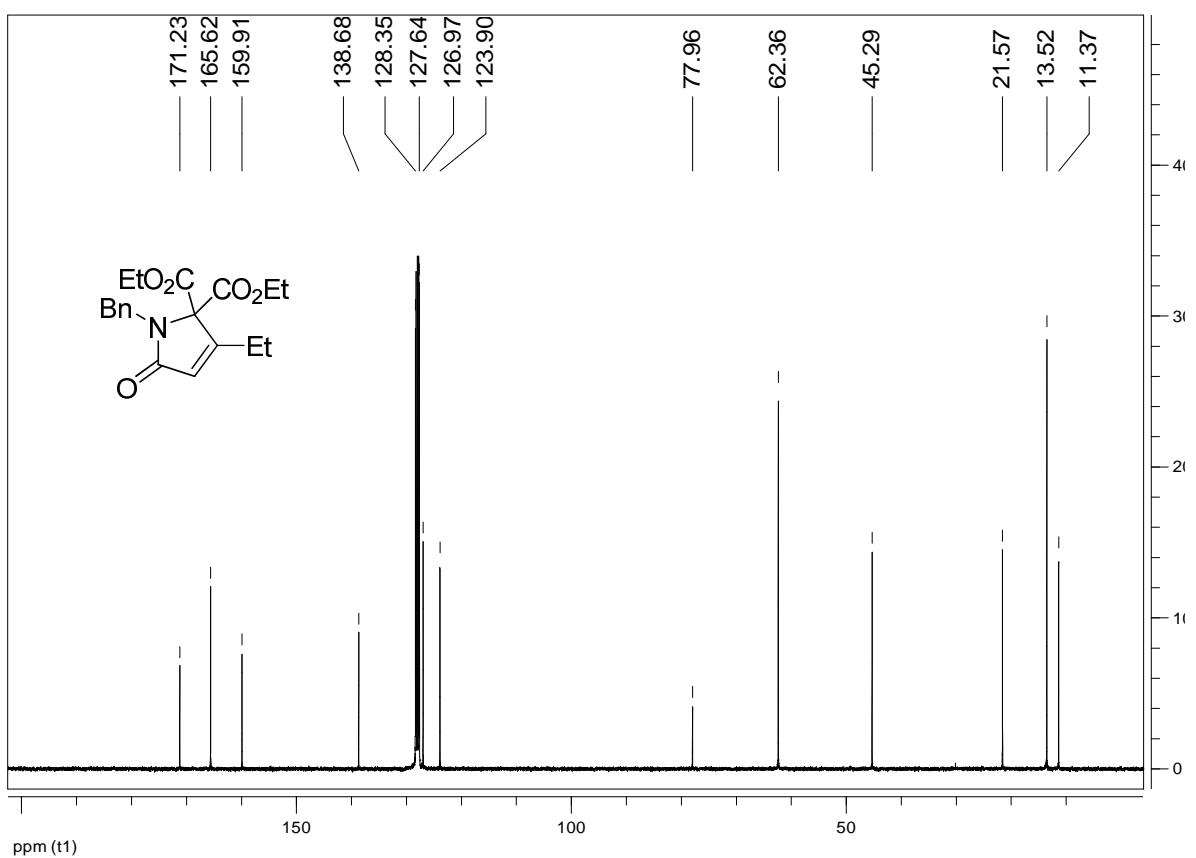
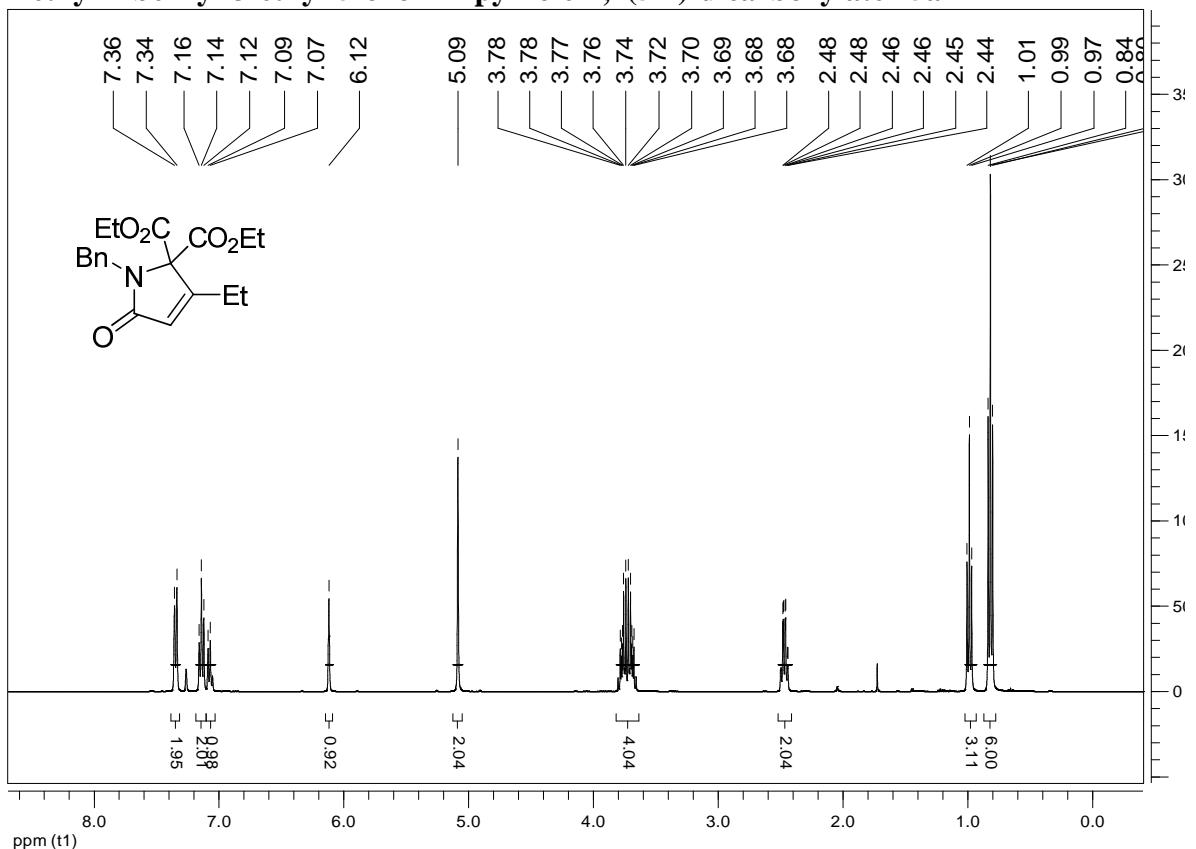
Diethyl 1-benzyl-3-methylene-6-oxopiperidine-2,2-dicarboxylate 11



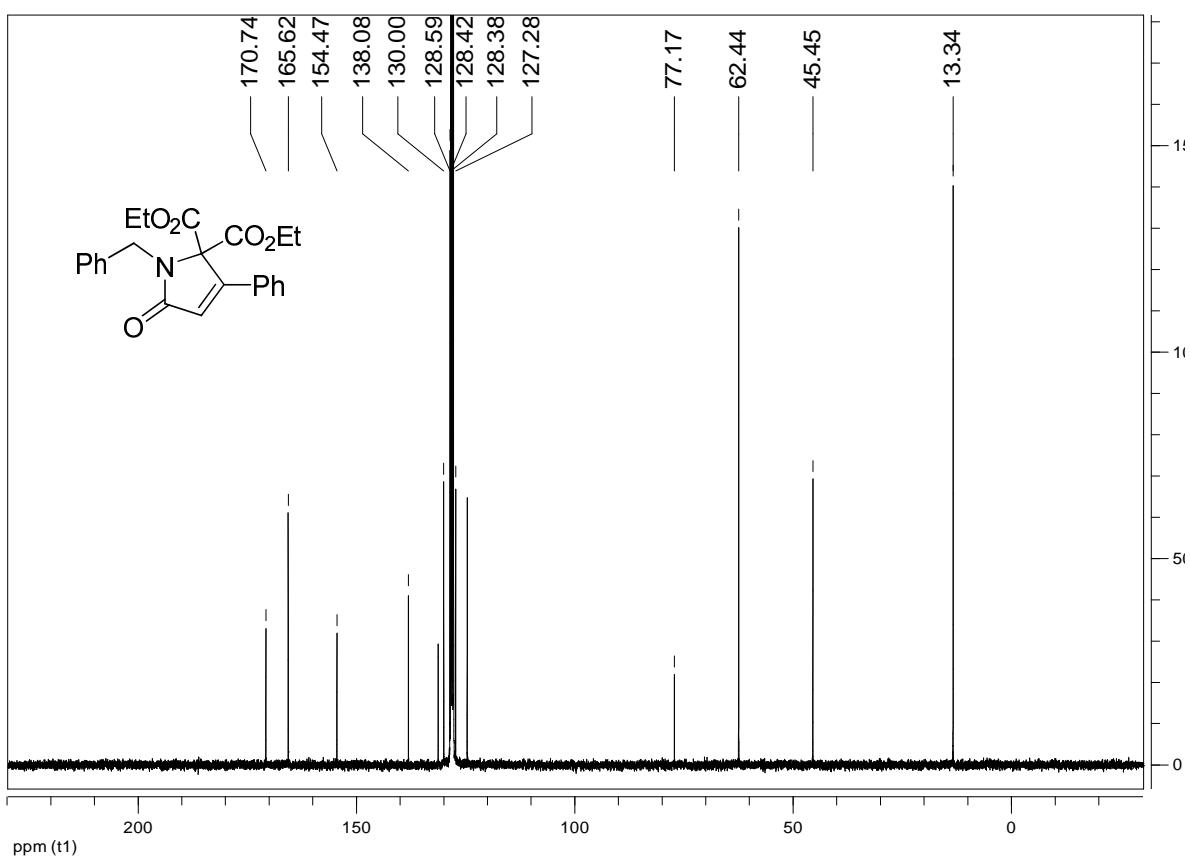
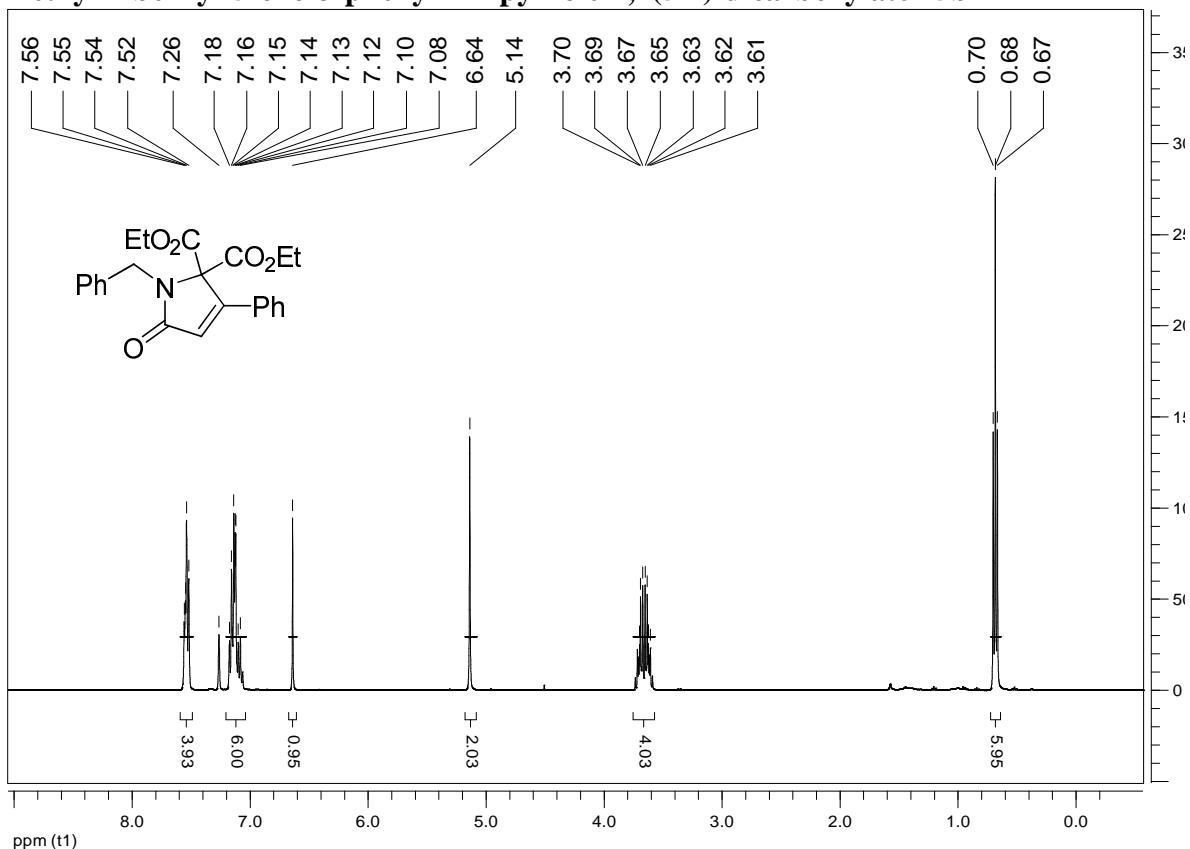
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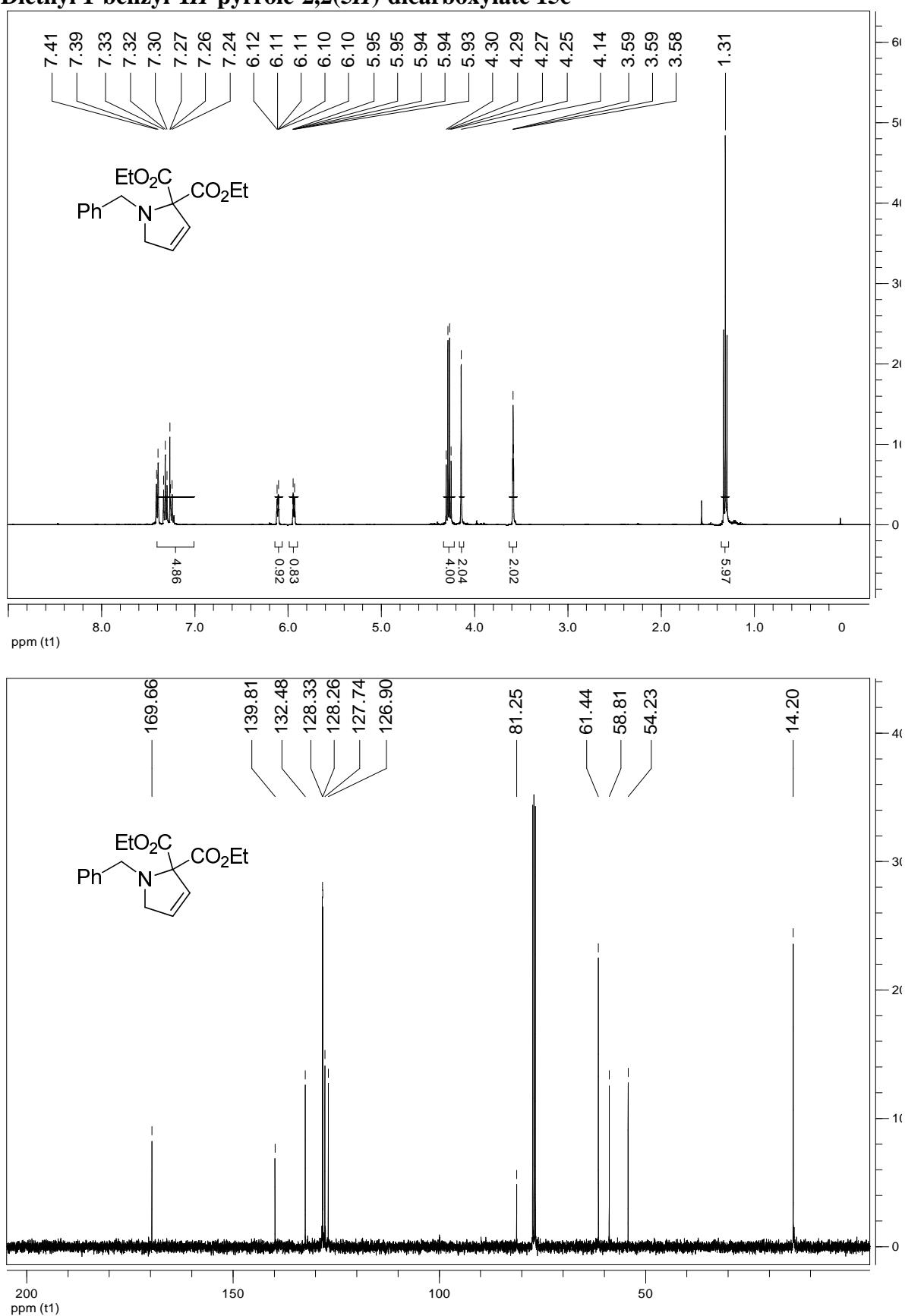
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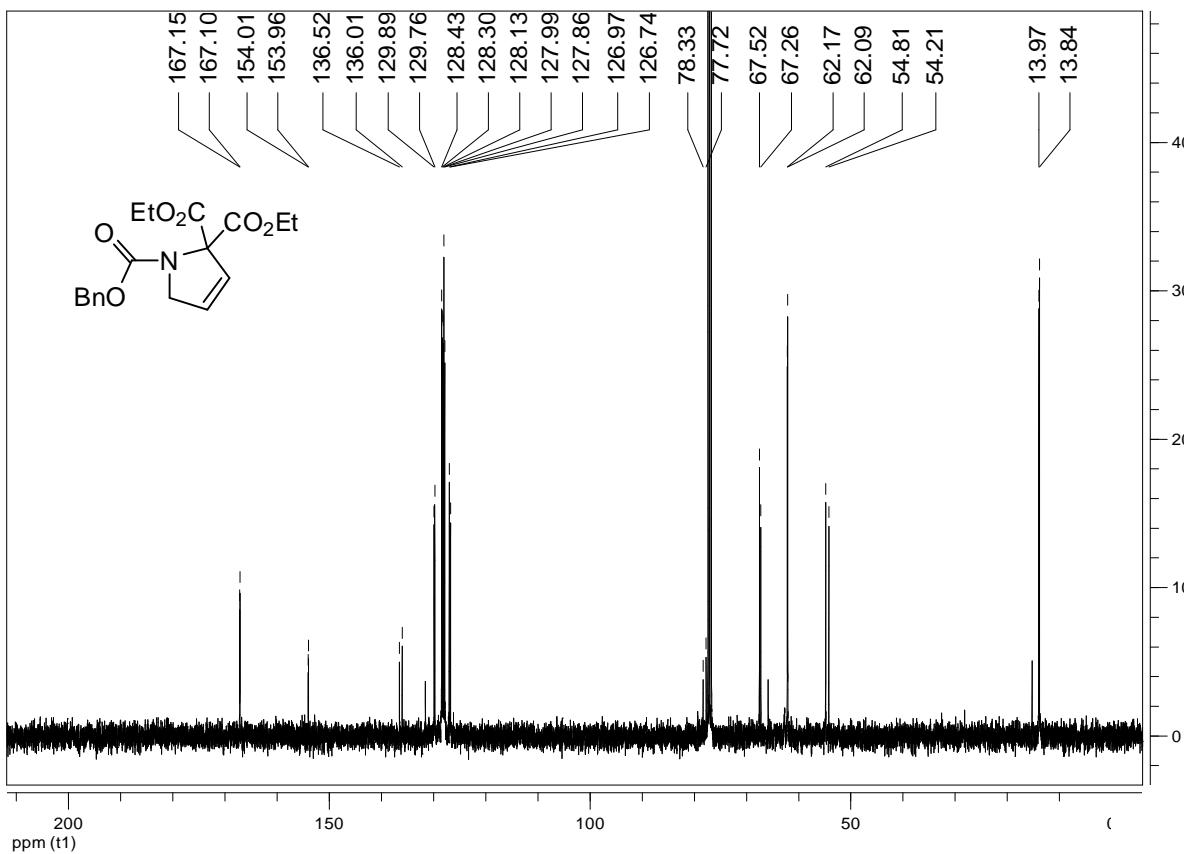
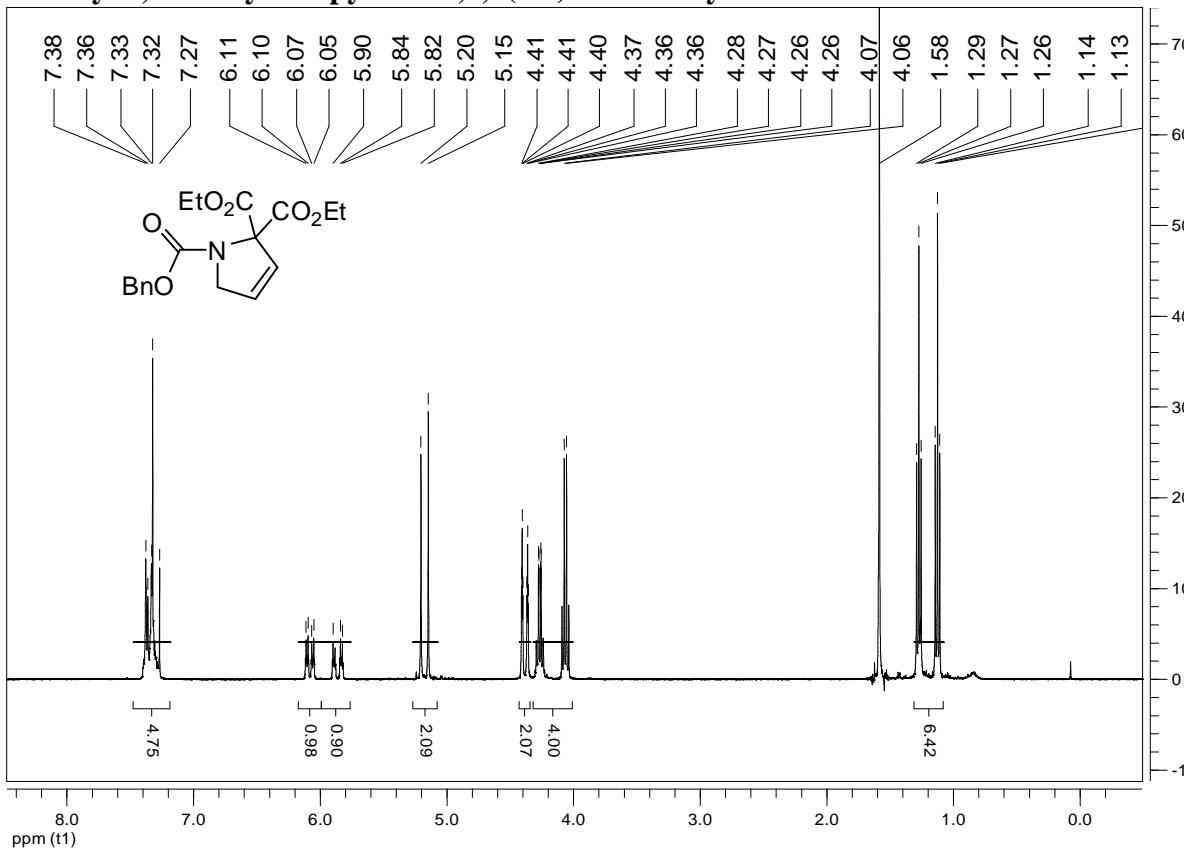
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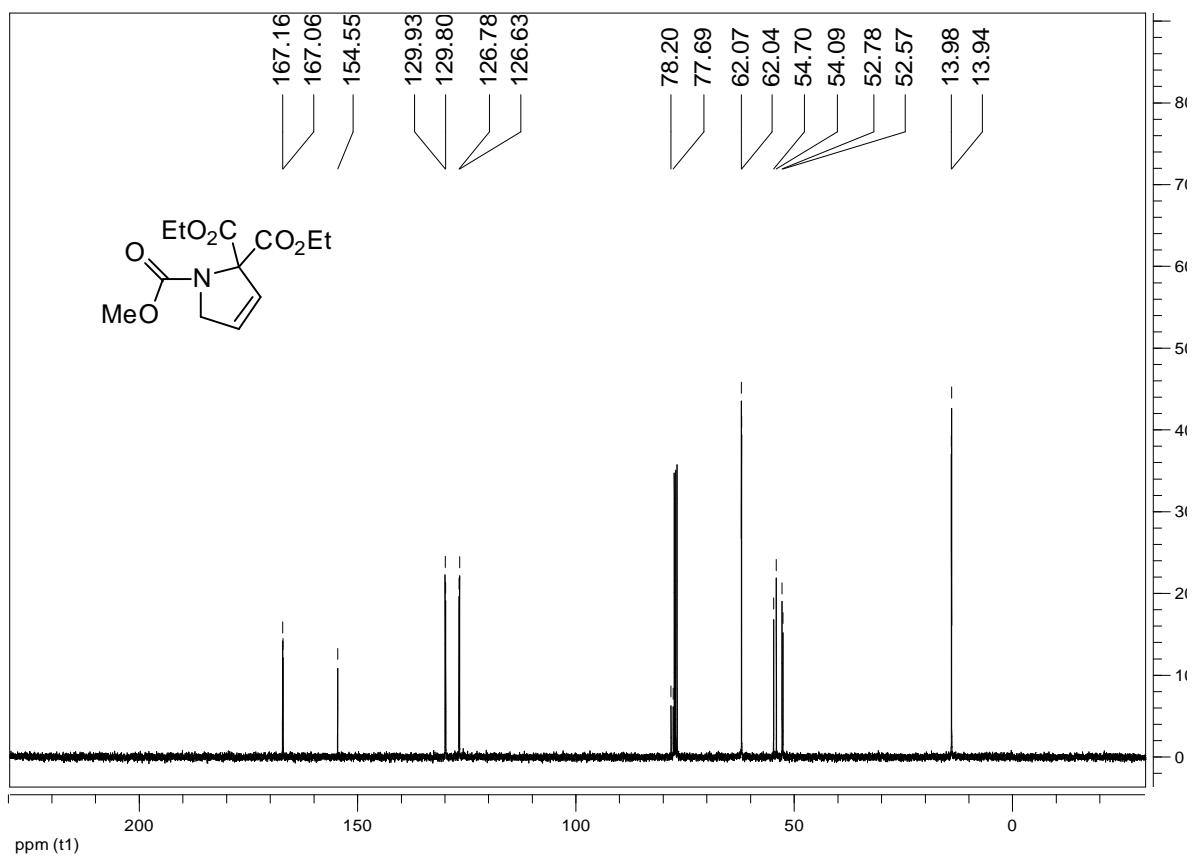
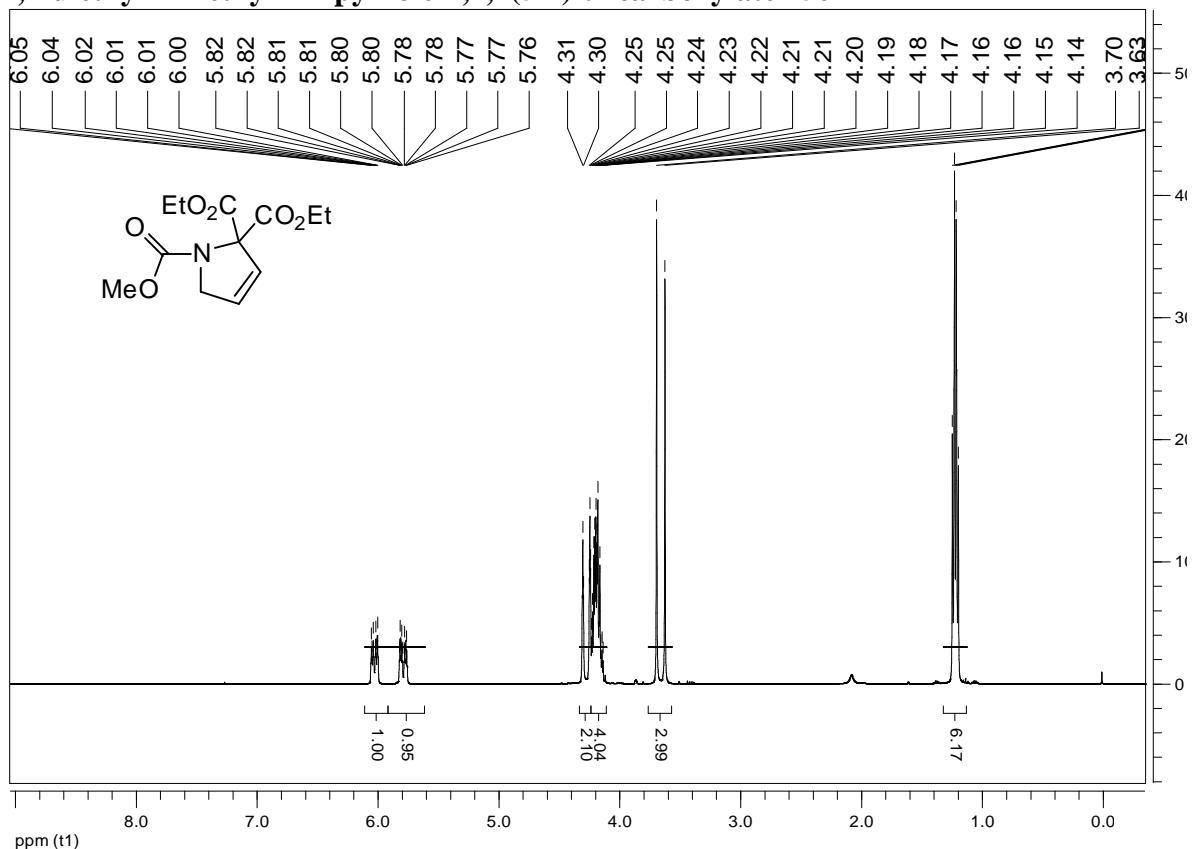
Diethyl 1-benzyl-1*H*-pyrrole-2,2(*5H*)-dicarboxylate 15c



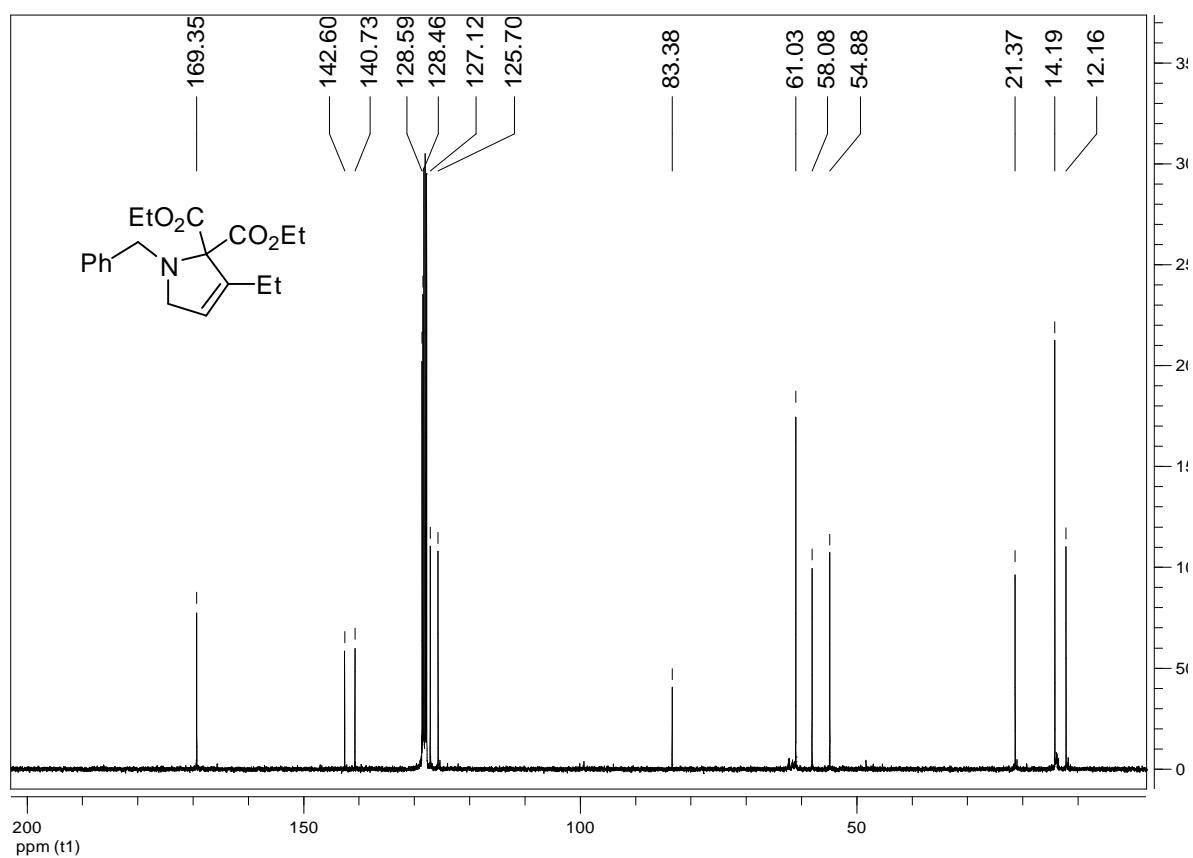
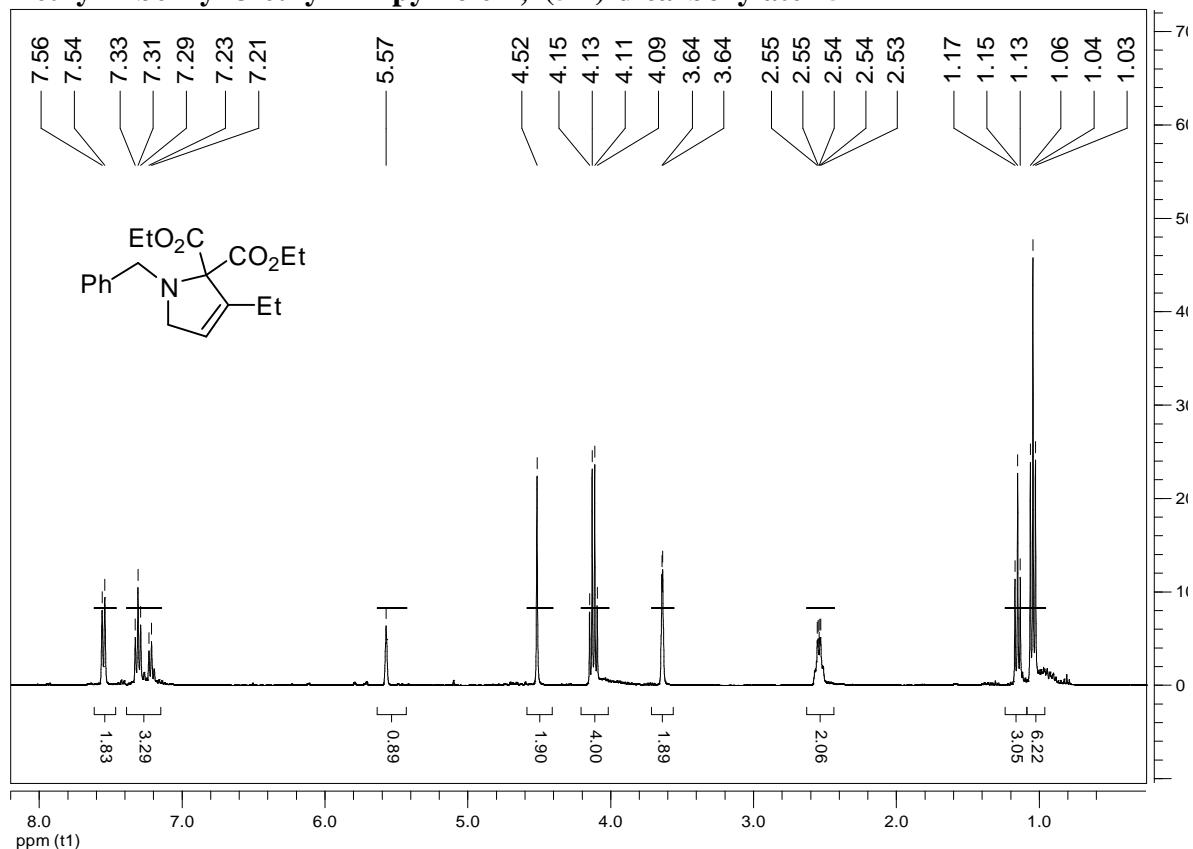
1-Benzyl 2,2-diethyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate 15d



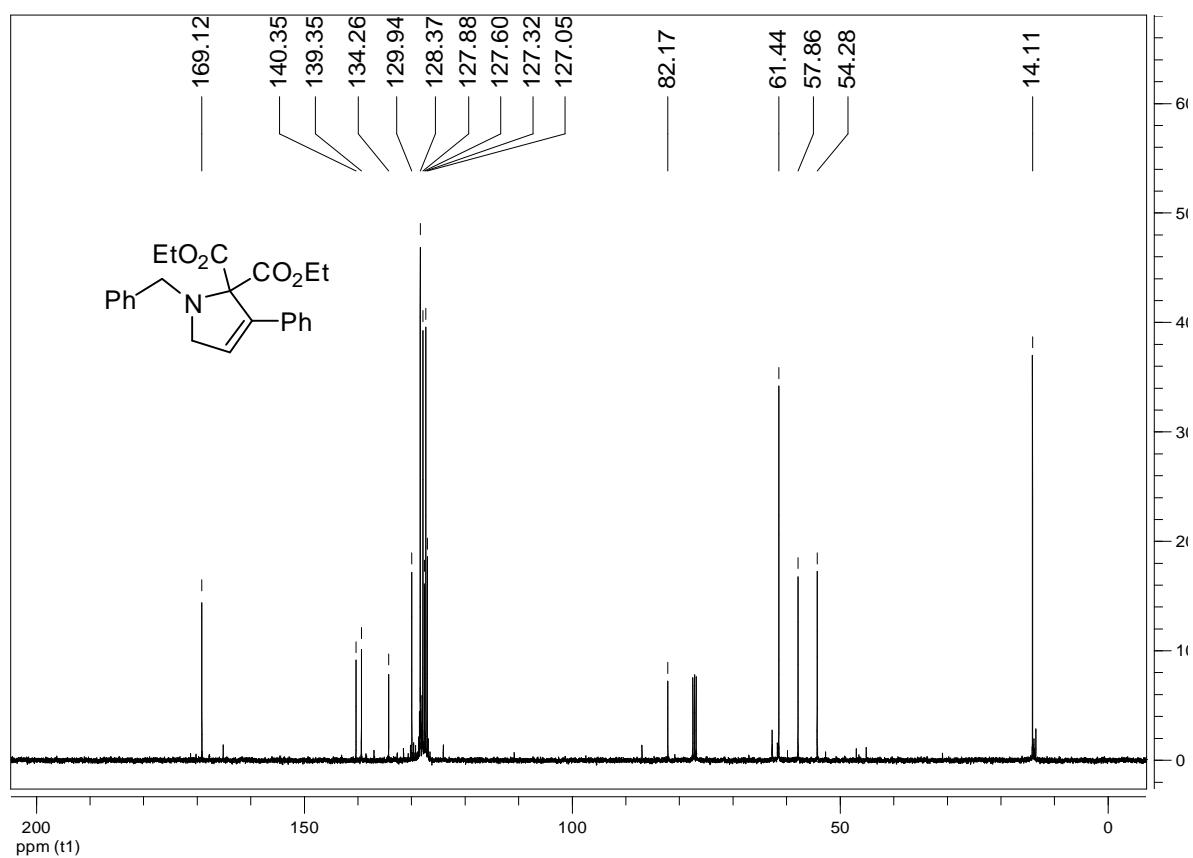
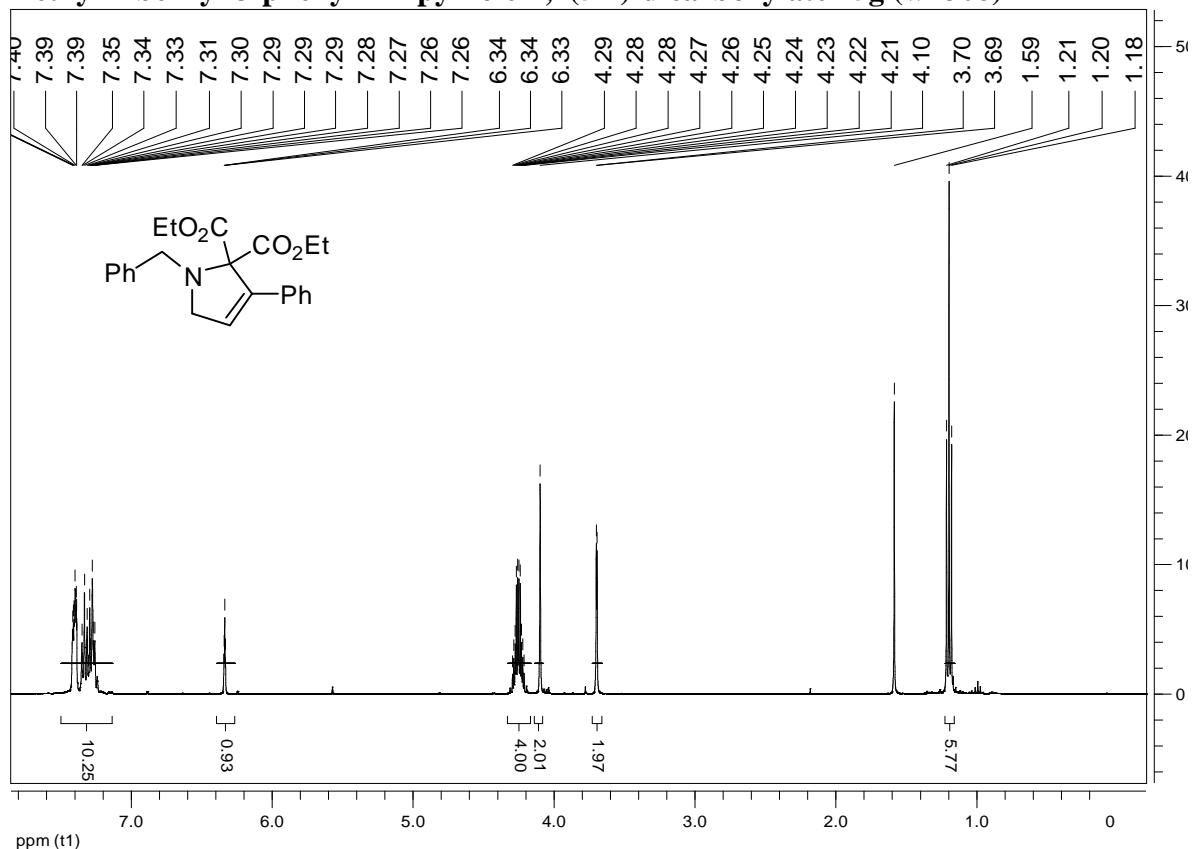
2,2-diethyl 1-methyl 1*H*-pyrrole-1,2,2(5*H*)-tricarboxylate 15e



Diethyl 1-benzyl-3-ethyl-1*H*-pyrrole-2,2(*5H*)-dicarboxylate 15f

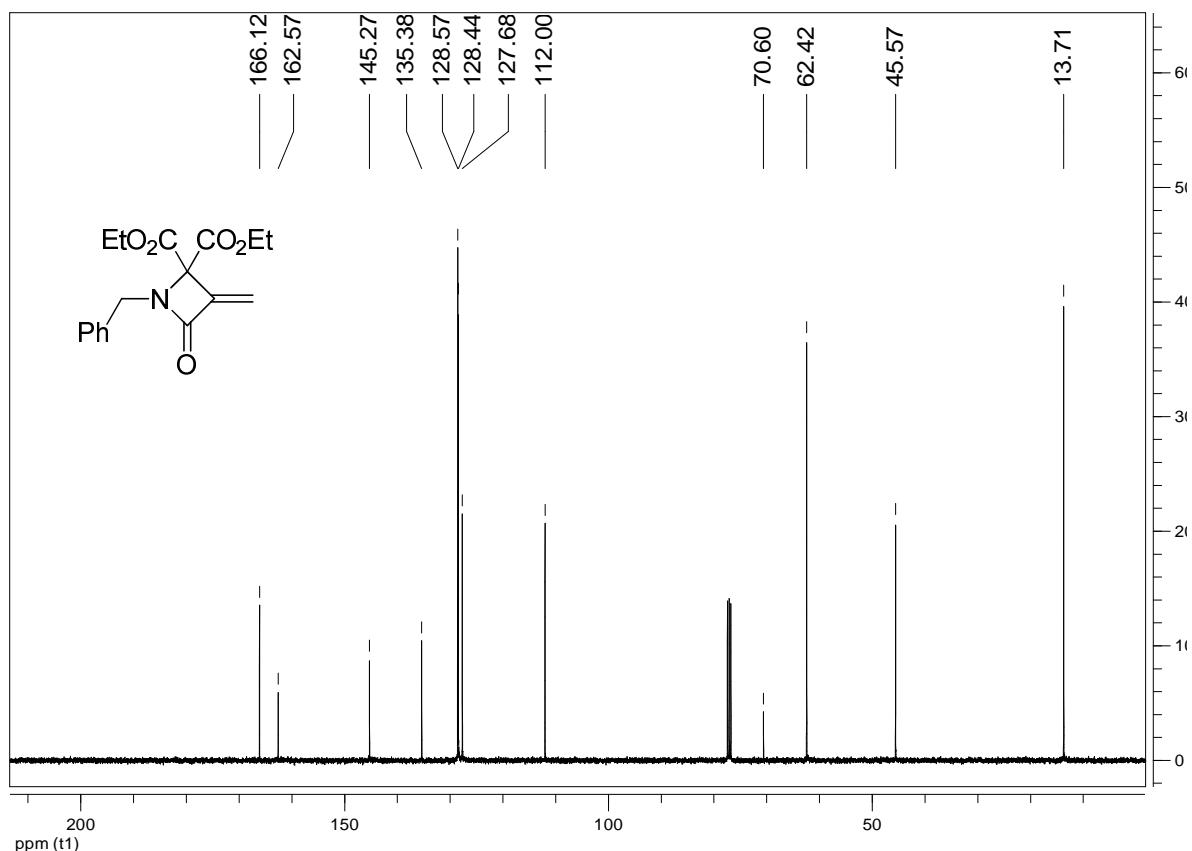
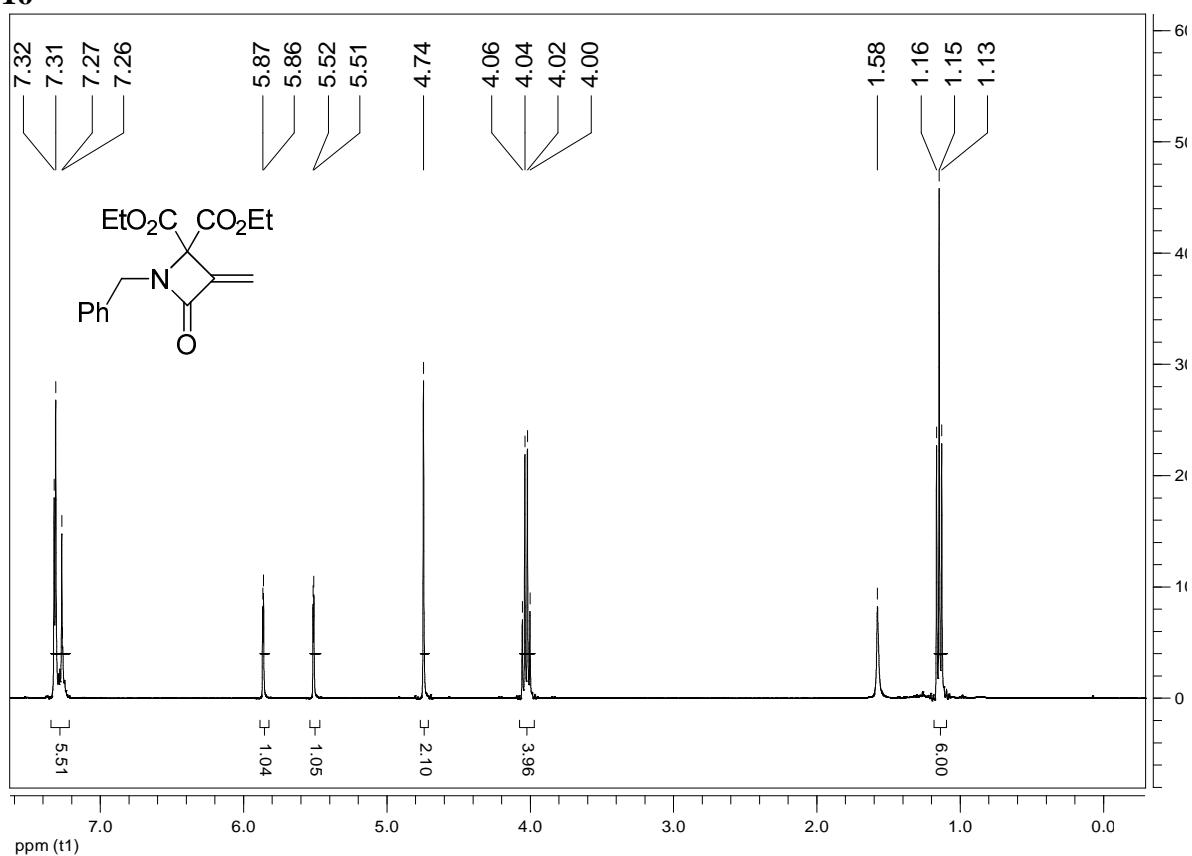


Diethyl 1-benzyl-3-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate 15g (wh308)

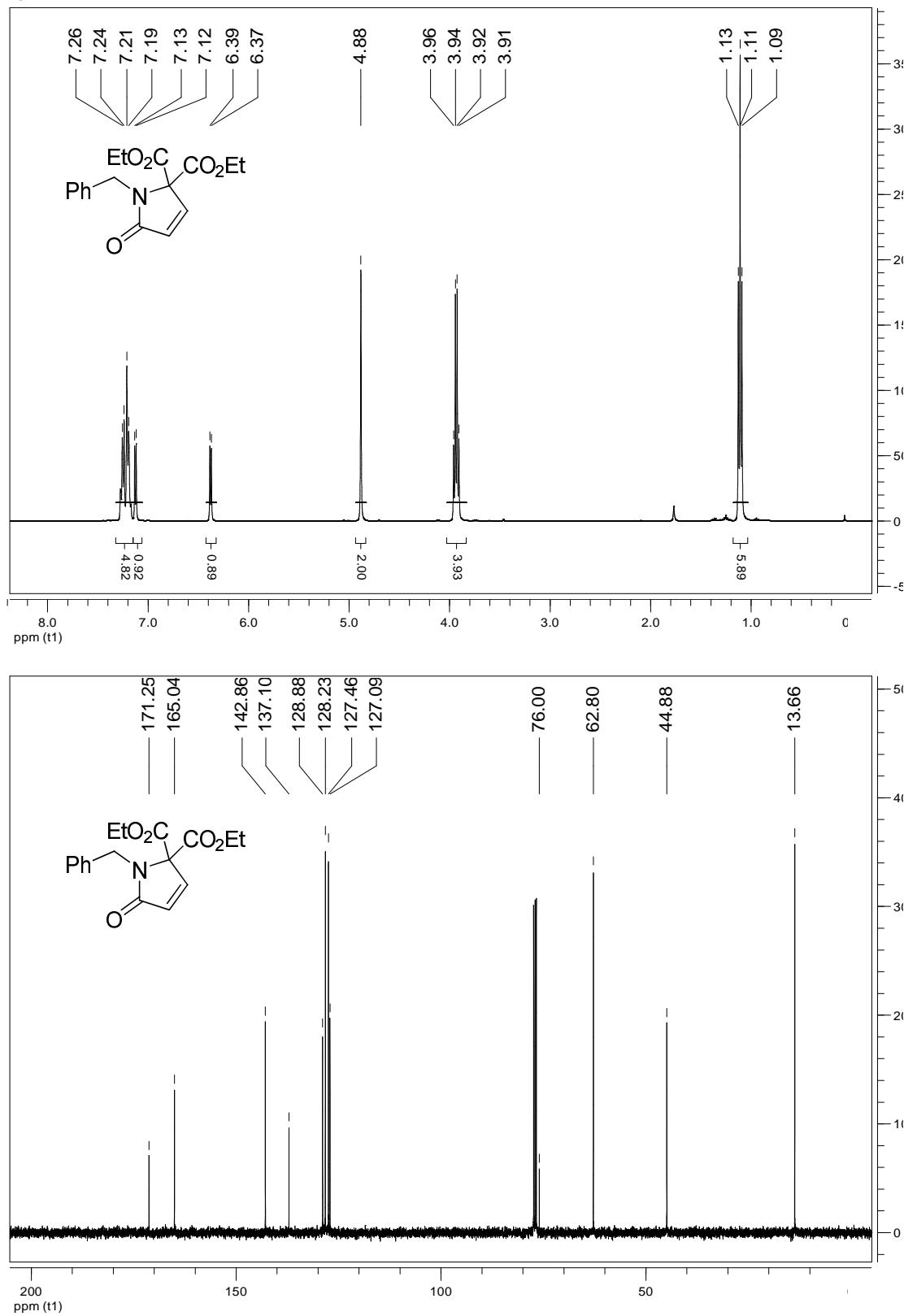


Diethyl 1-benzyl-3-methylene-4-oxoazetidine-2,2-dicarboxylate 16 and diethyl 1-benzyl-5-oxo-1*H*-pyrrole-2,2(*H*)-dicarboxylate 15h

16



15h



References

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