

Supporting Information for

Enzymatic C(*sp*³)—H amination: P450-catalyzed conversion of carbonazidates into oxazolidinones

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Table S1. Amino acid mutations in the P450_{BM3} variants investigated in this study.

P450_{BM3} variants	Amino acid mutations compared to wild-type P450_{BM3}
P450 _{BM3}	-
FL#62	V78A, F81S, A82V, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
FL#62(T268A)	V78A, F81S, A82V, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, T268A, A290V, L353V
I-A1	V78A, F81T, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
I-B1	V78A, F81R, A82F, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
I-B3	V78F, F81R, F87V, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
I-G1	V78A, A82T, P142S, T175I, A180T, A184H, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
IV-F8	F81T, F87T, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
V-D11	V78Y, F81P, A82A, F87A, P142S, T175I, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, A328V, L353V
V-H2	V78S, F81I, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V

Figure S1. A) Chemical structures of the five probes used for high-throughput fingerprinting of the engineered CYP102A1 libraries.¹⁻² Probe **P1** and **P2** activity were used as predictor for C—H amination activity on carbonazidates **23** and **24**, respectively. B) Fingerprint profiles for the FL#62-derived P450 variants described in Figure 1. Fingerprints are normalized to the probe activity of reference enzyme P450_{BM3}(F87A). Standard deviation for normalized activity values are <15%.

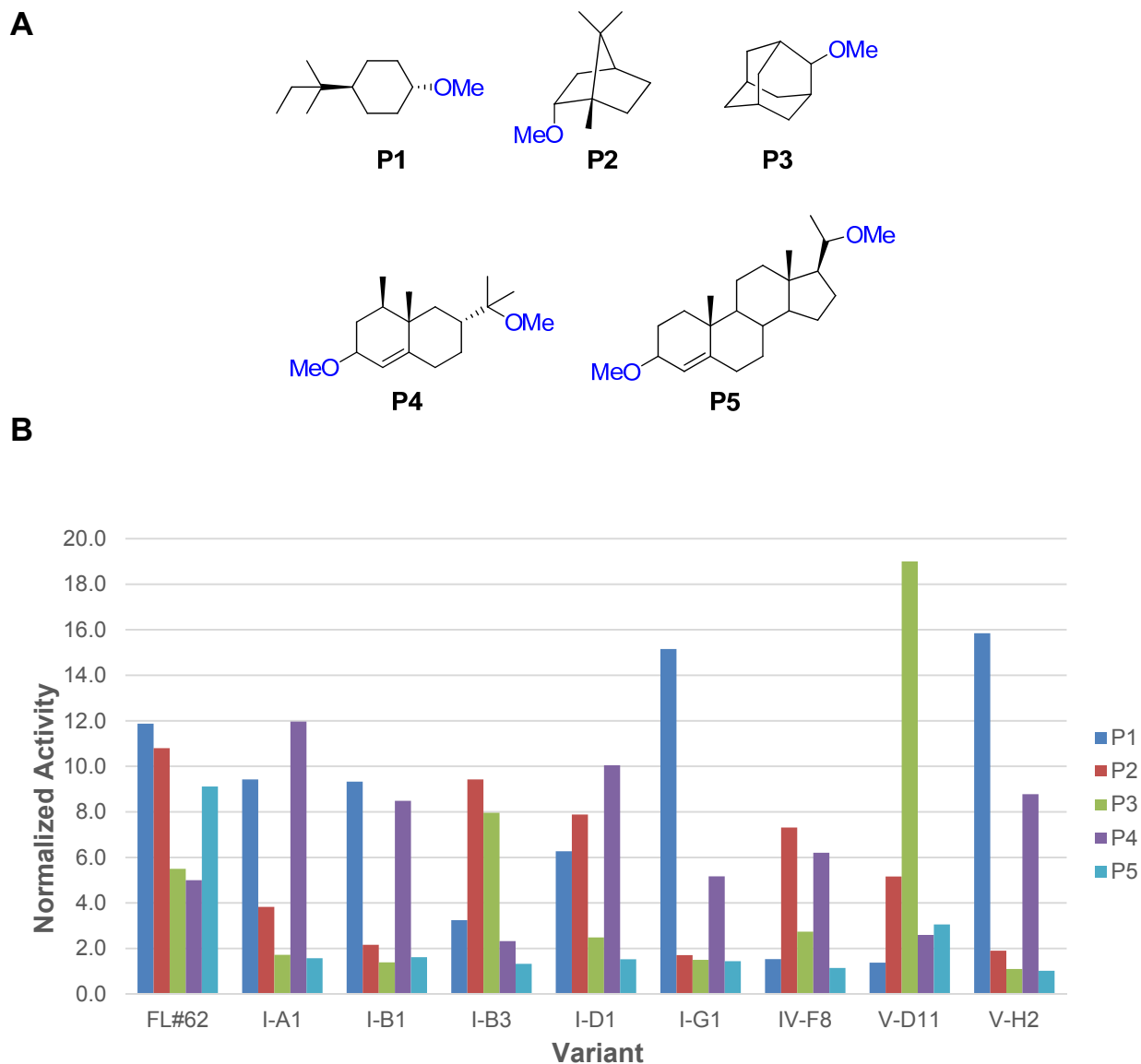


Figure S2. Representative HPLC traces for analysis of the C—H amination reactions. Overlay plot of the HPLC chromatogram corresponding to the reaction with FL#62 and carbonazidate **4** (blue), control reaction with no enzyme (red), and authentic oxazolidinone **5** standard prepared synthetically (see Synthetic Procedures). Carbamate and alcohol products elute at 13-14 min.

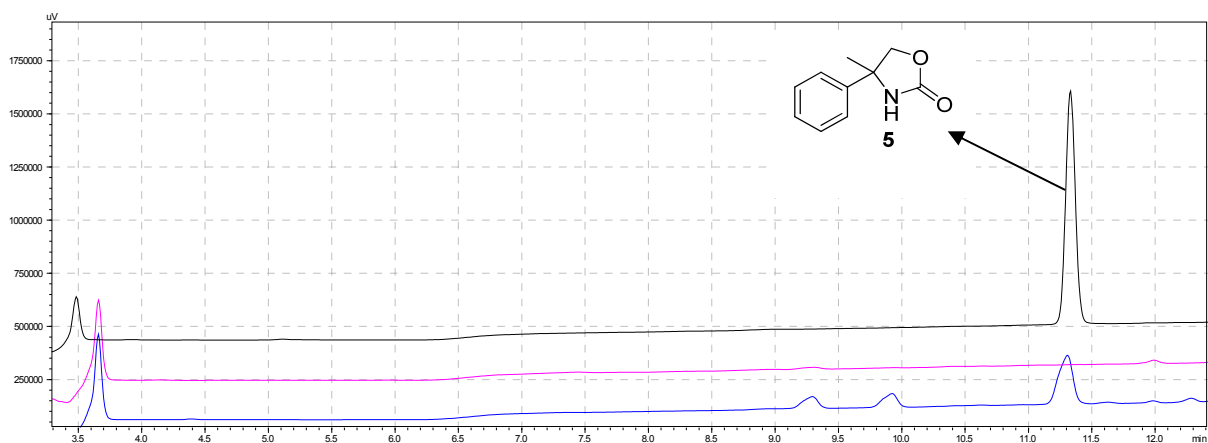
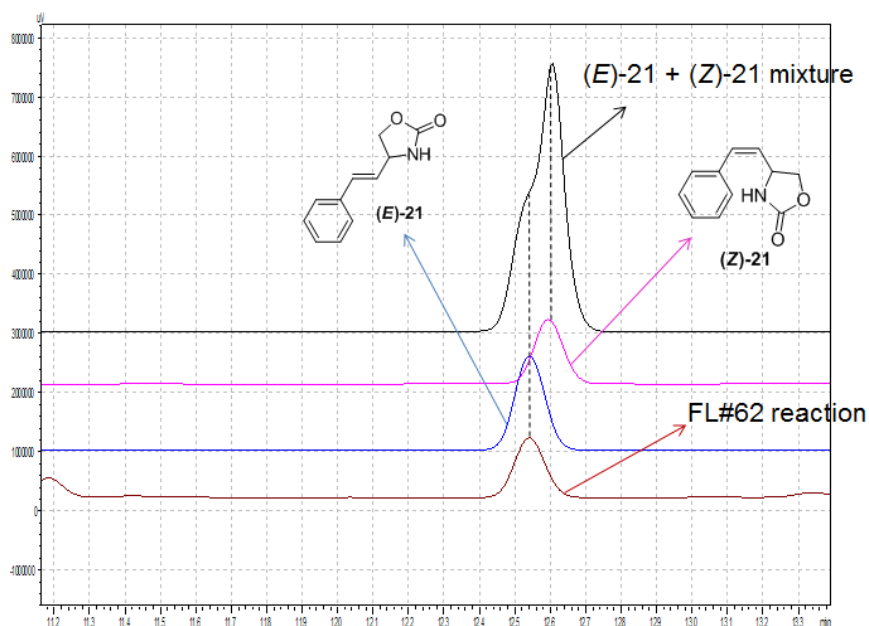


Figure S3. *Cis/trans* rearrangement. A) Overlay plot of HPLC traces corresponding to the *cis* and *trans* oxazolidinones (**Z**)-21 and (**E**)-21 injected alone (blue and red, respectively) and as a 1:2 mixture (black) and the trace corresponding to the reaction of FL#62 with (**Z**)-12 (brown). B) GC traces corresponding to the 1:2 mixture of authentic (**Z**)-21 and (**E**)-21 products (*top panel*) and to the reaction of FL#62 with (**Z**)-12 (*bottom panel*).

A)



B)

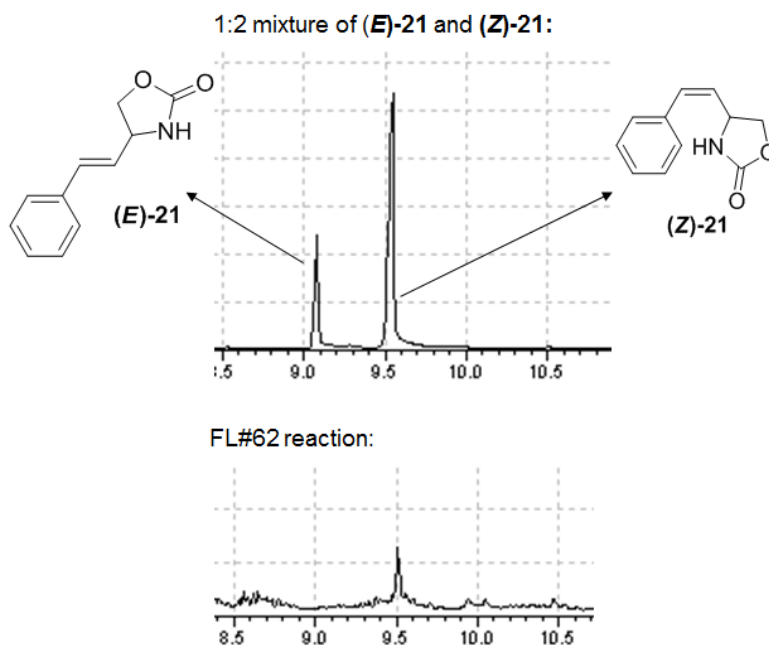
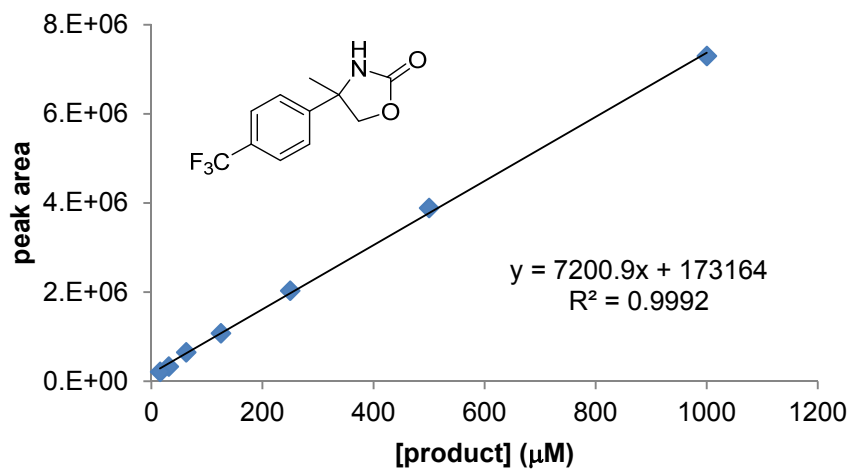
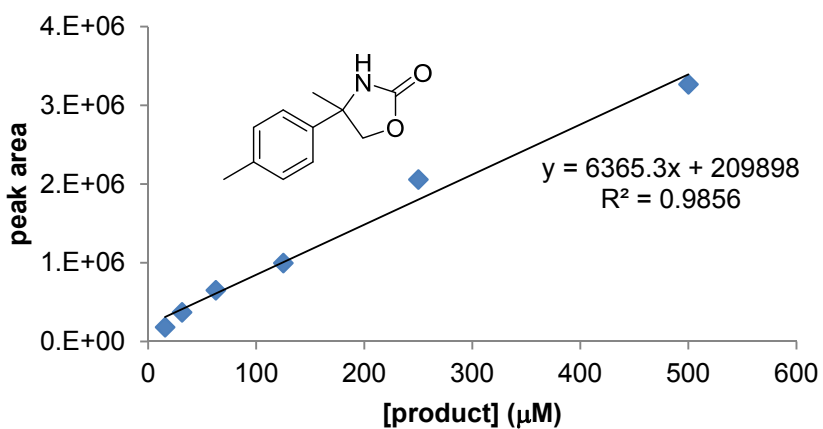
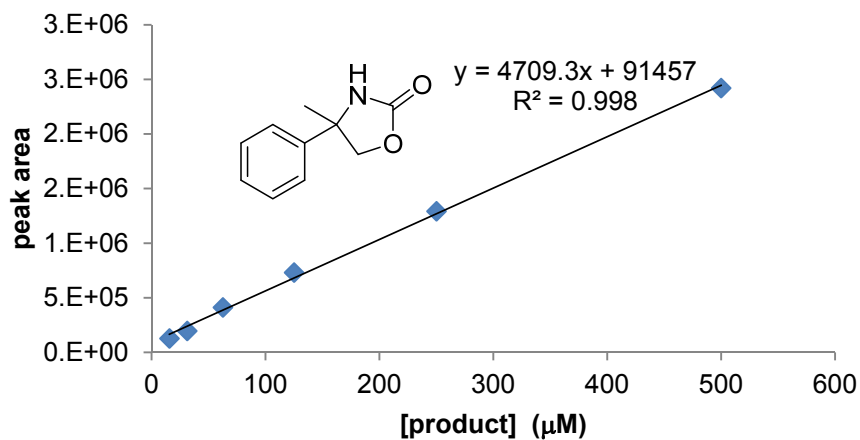
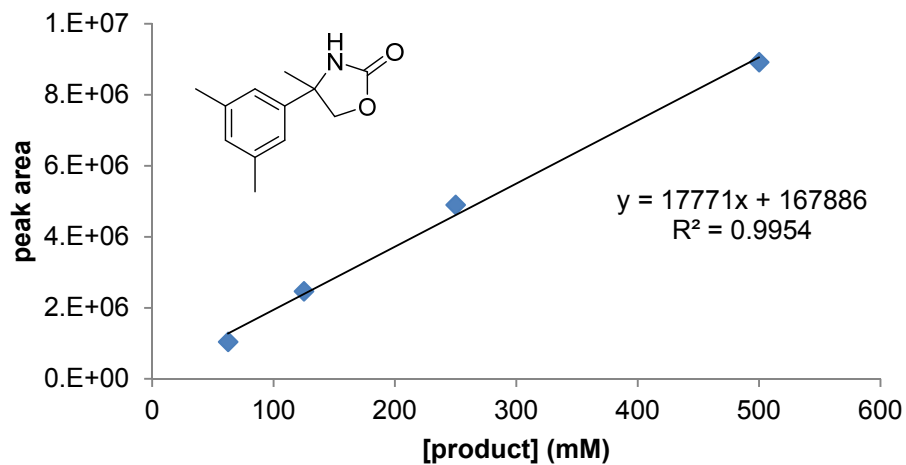
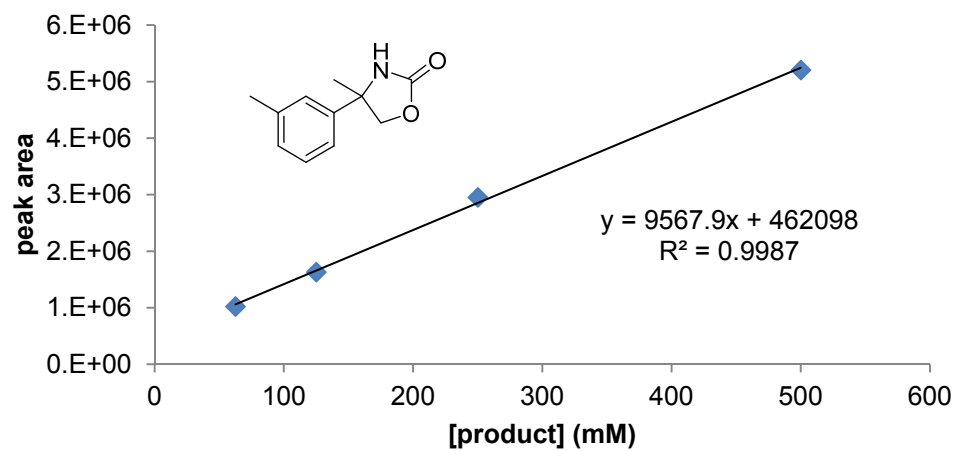
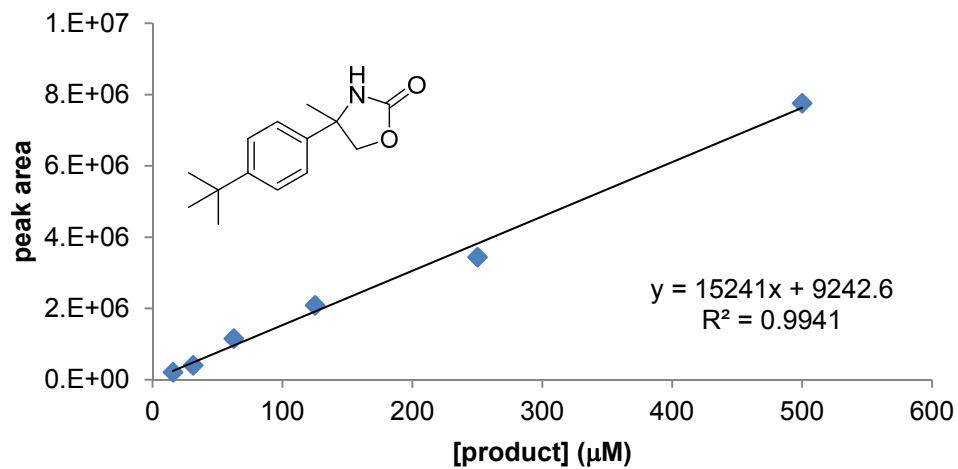


Figure S4. Calibration curves used for the quantification of the oxazolidinone products by HPLC. The graphs report the HPLC peak areas corresponding to the oxazolidinone product plotted against the oxazolidinone concentration.





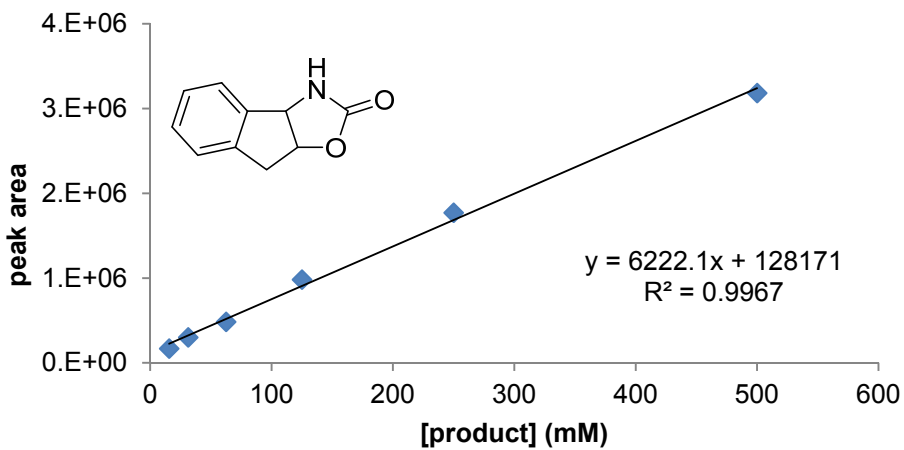
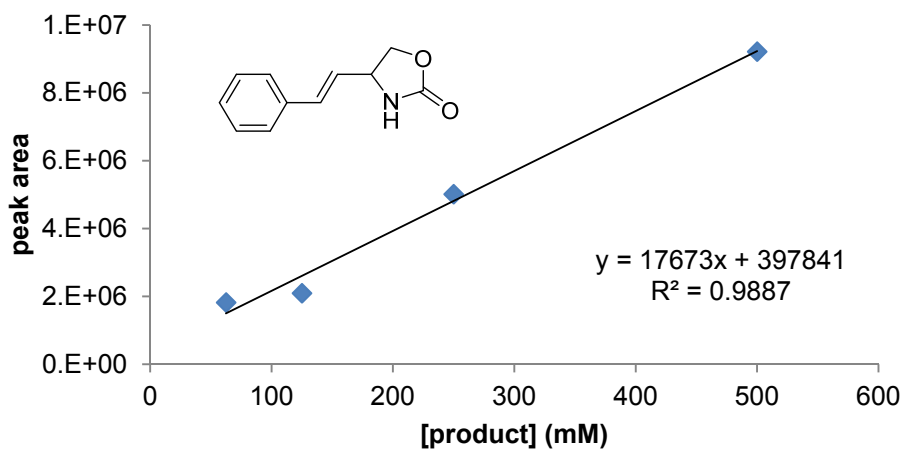
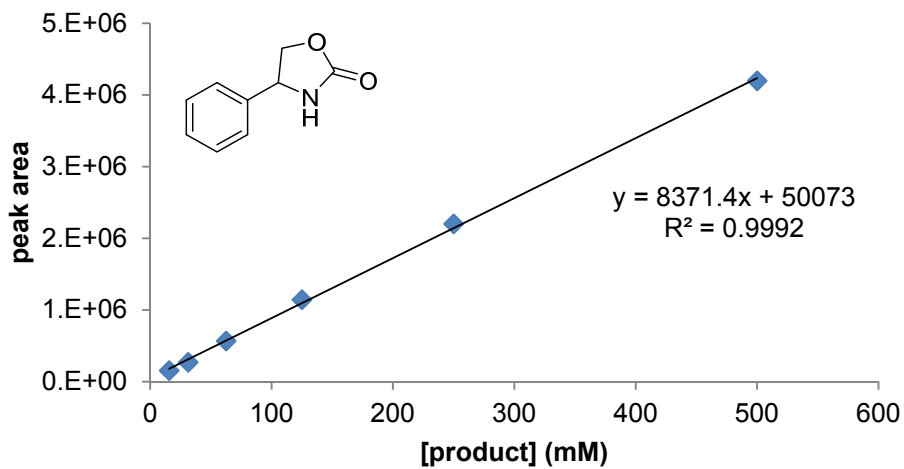
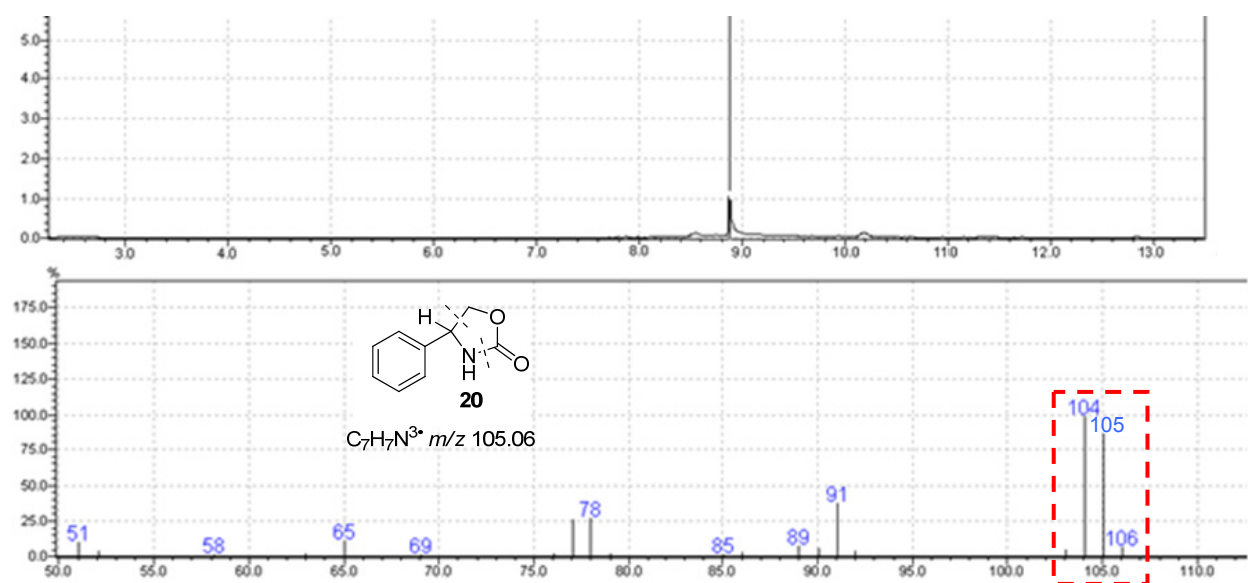
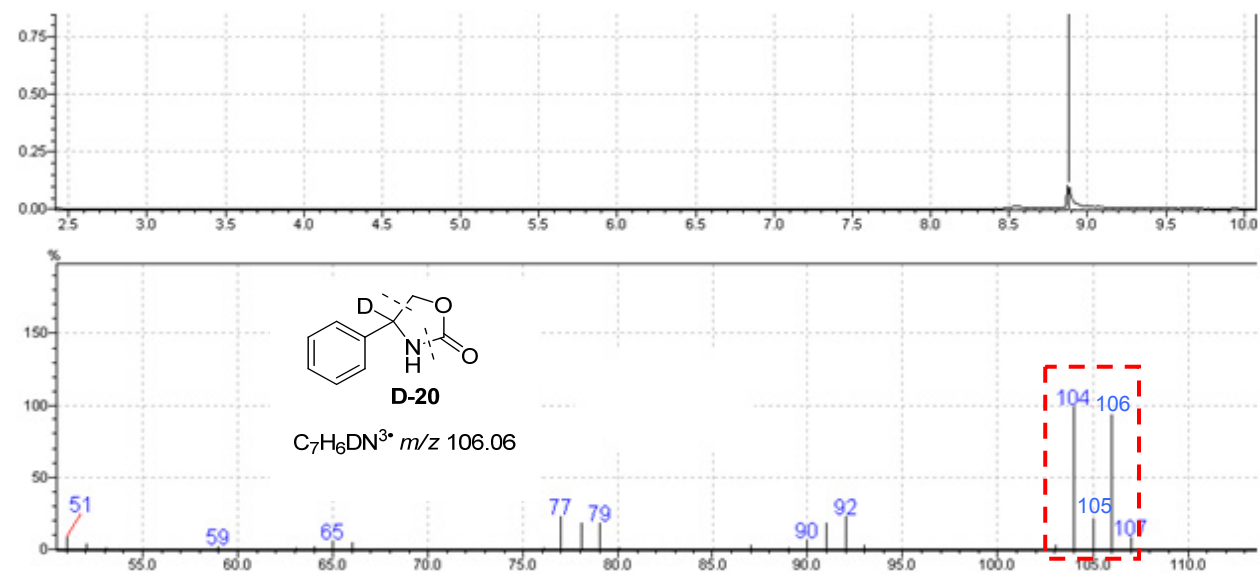


Figure S5. GC-MS traces for oxazolidinone products **20** and **D-20** as obtained for the authentic standards (a, b) and from the inter- and intermolecular H/D competition experiments. KIE values were obtained from integration of the MS signals corresponding to the characteristic fragmentation products with m/z of 105 (for **20**) and 106 (for **D-20**).

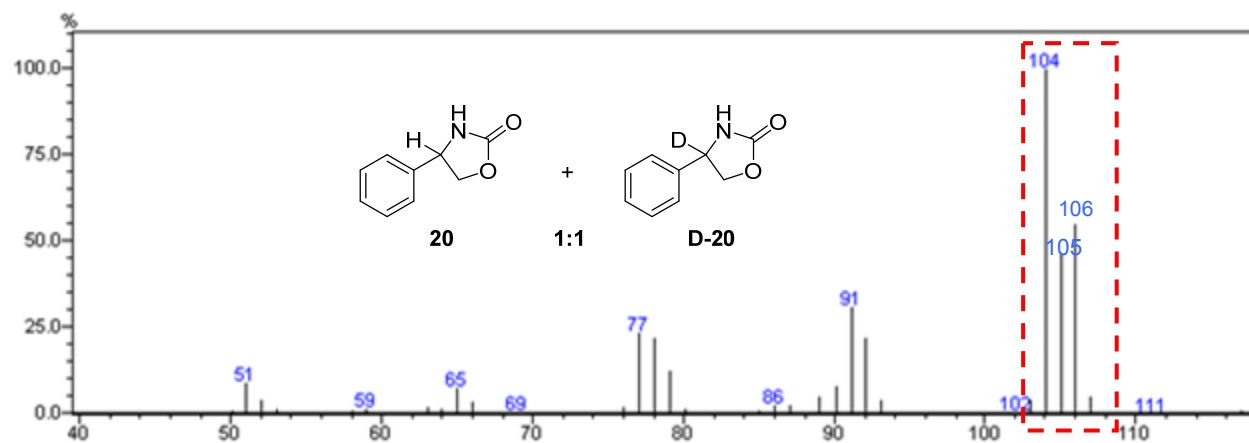
a) GC-MS trace and EI-MS spectrum for authentic standard **20**.



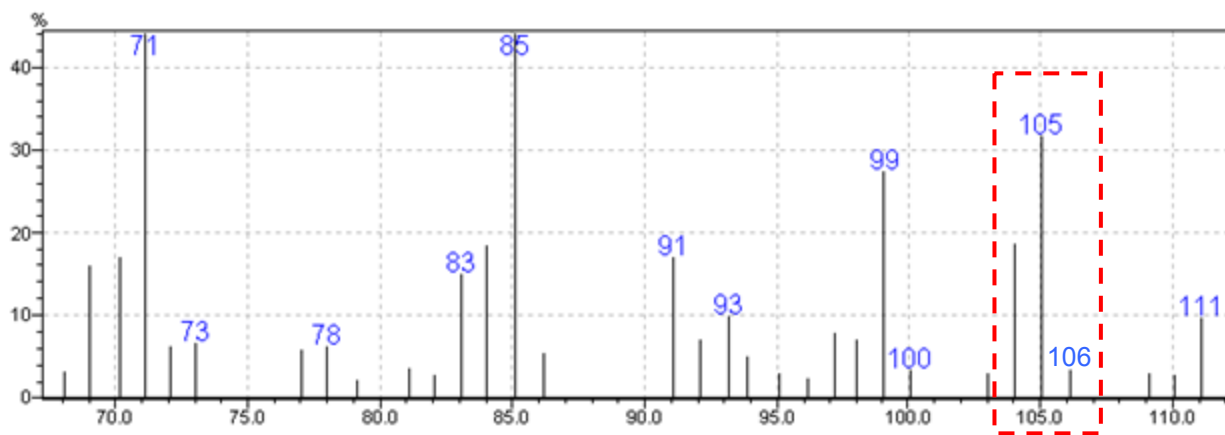
b) GC-MS trace and EI-MS spectrum for authentic standard **D-20**.



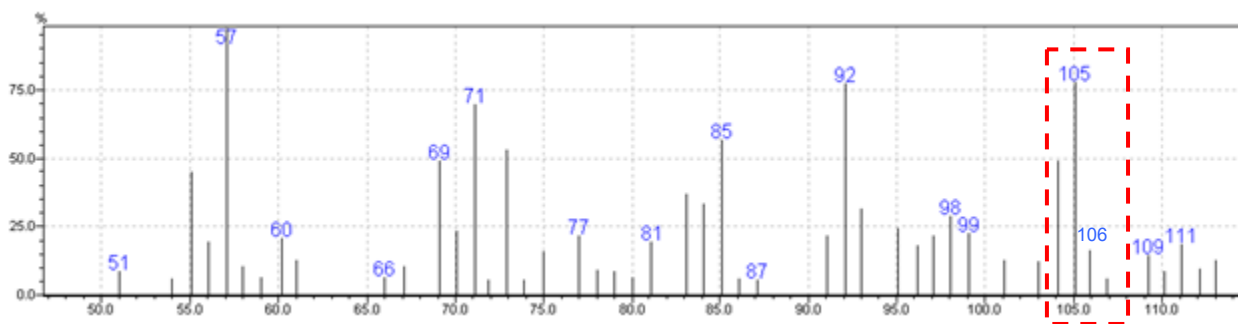
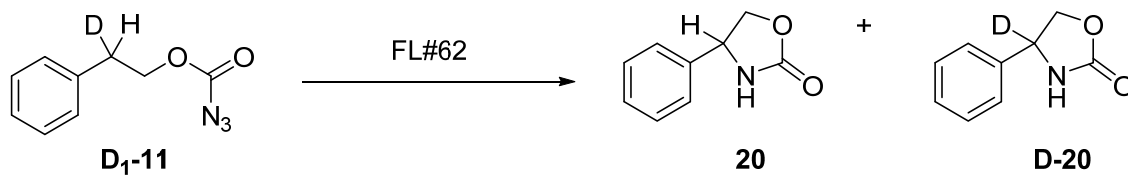
c) EI-MS spectrum for a 1:1 mixture of **20** and **D-20**.



d) EI-MS spectrum for oxazolidinone products obtained from intermolecular competition experiment.



e) EI-MS spectrum for oxazolidinone products obtained from intramolecular competition experiment.



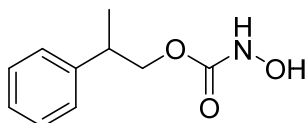
Synthetic Procedures

General information

All the chemicals and reagents were purchased from commercial suppliers (Sigma-Aldrich, AK Scientific, Acros) and used without any further purification, unless otherwise stated. All dry reactions were carried out under argon or nitrogen in oven-dried glassware with magnetic stirring using standard gas-light syringes, cannulae and septa. ^1H and ^{13}C NMR spectra were measured on Bruker DPX-400 (operating at 400 MHz for ^1H and 100 MHz for ^{13}C) or Bruker DPX-500 (operating at 500 MHz for ^1H and 125 MHz for ^{13}C). Tetramethylsilane (TMS) served as the internal standard (0 ppm) for ^1H NMR and CDCl_3 was used as the internal standard (77.0 ppm) for ^{13}C NMR. Silica gel chromatography purifications were carried out using AMD Silica Gel 60 230-400 mesh.

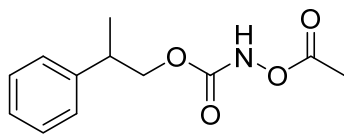
A. Synthesis of acyloxycarbamate substrates

2-phenylpropyl hydroxycarbamate (61)



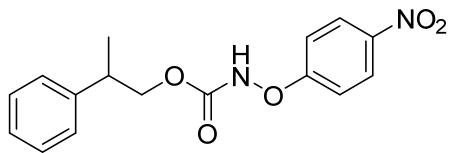
To flame dried 100 mL round bottom was added 2-phenylpropan-1-ol (1.03 mL, 7.3 mM), 1,1'-carbonyldiimidazole (1.31 g, 8.1 mM), and 15 mL dry CH_2Cl_2 . Reaction was allowed to stir under inert atmosphere until starting material was consumed (45 min). Reaction was washed twice with 15 mL of saturated NH_4Cl followed by once with 15 mL brine. Organics were dried over sodium sulfate and concentrated under reduced pressure. The resulting product was immediately carried on with addition of 24 mL of pyridine and hydroxylamine hydrochloride (1.52 g, 22 mM). After 3 h, 60 mL of CH_2Cl_2 was added and the organics were washed twice with 100 mL 10% aqueous sulfuric acid and once with 100 mL brine. The combined organic layers were dried over sodium sulfate, concentrated under reduced pressure, and the product was purified by column chromatography (30% EtOAc in hexane) to afford 2-phenylpropyl hydroxycarbamate **61** (0.63 g, 44%). ^1H NMR (500 MHz, CDCl_3): δ 1.30 (d, 3H, $J = 7.0$ Hz), 3.07-3.15 (m, 1H), 4.20-4.29 (m, 2H), 7.19-7.25 (m, 3 H), 7.31 (t, 2H, $J = 7.1$ Hz); ^{13}C NMR (125 MHz, CDCl_3): δ 17.9, 39.1, 70.9, 126.8, 127.3, 128.6, 142.8, 159.7. LC-MS (ESI) calculated for $\text{C}_{10}\text{H}_{13}\text{NO}_3$ $[\text{M}+\text{Na}]^+$ m/z : 218.1; found: 218.1

2-phenylpropyl acetoxycarbamate (1)



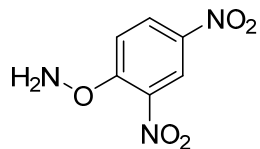
To a flame dried 10 mL round bottom flask at 0 °C under inert atmosphere was added 2-phenylpropyl hydroxycarbamate **61** (91 mg, 0.47 mM), acetyl chloride (30 μ L, 0.42 mM), 4-(dimethylamino) pyridine (11 mg, 0.10 mM), 2 mL dry CH_2Cl_2 , and 1 mL triethylamine. Reaction was stirred at 0 °C for five minutes before being allowed to warm to room temperature. After 12 h, 10 mL of saturated aqueous sodium bicarbonate was added and reaction was extracted three times with 10 mL of CH_2Cl_2 . Combined organics were washed with brine, dried over sodium sulfate, and the residue was purified by flash column chromatography (5-30% ethyl acetate in hexanes) to afford 2-phenylpropyl acetoxycarbamate (**1**) (42.3 mg, 38%). $\delta^1\text{H}$ NMR (500 MHz, CDCl_3): δ 1.31 (d, 3H, $J = 7.0$ Hz), 2.15 (s, 3H), 3.09-3.17 (m, 1H), 4.28 (d, 2H, $J = 7.0$ Hz), 7.20-7.28 (m, 3H), 7.32 (t, 2H, $J = 7.8$ Hz), 8.11 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 17.9, 18.3, 39.0, 71.3, 126.9, 127.3, 128.6, 142.6, 156.5, 169.8; LC-MS (ESI) calculated for $\text{C}_{12}\text{H}_{15}\text{NO}_4$ $[\text{M}+\text{Na}]^+$ m/z : 260.2; found: 260.2.

2-phenylpropyl (4-nitrophenoxy)carbamate (2)



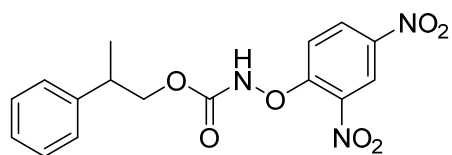
To a flame dried 10 mL round bottom flask at 0 °C under inert atmosphere was added 2-phenylpropyl hydroxycarbamate **61** (93.8 mg, 0.48 mM), 4-nitrochlorobenzene (76 mg, 0.48 mM), potassium carbonate (138 mg, 1 mM), and 5 mL dry dimethylformamide. Reaction was stirred for 5 minutes at 0 °C before being allowed to warm to room temperature for 12 h. Water (10 mL) was added and reaction was extracted three times with 10 mL CH_2Cl_2 . Combined organics were washed with brine, dried over sodium sulfate, and the residue was purified by flash column chromatography (5-30% EtOAc in hexane) to afford 2-phenylpropyl (4-nitrophenoxy)carbamate (**2**) (37 mg, 24%). ^1H NMR (500 MHz, CDCl_3): δ 1.28 (d, 3H, $J = 7.0$ Hz), 3.12 (q, 1H, $J = 6.9$ Hz), 4.28-4.38 (m, 2H), 7.12 (d, 2H, $J = 9.2$ Hz), 7.16 (d, 2H, $J = 7.3$ Hz), 7.21-7.31 (m, 3 H), 7.81 (bs, 1H), 8.18 (d, 2H, $J = 9.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3): δ 17.8, 39.0, 71.5, 113.5, 125.8, 126.9, 127.3, 128.6, 142.3, 143.2, 157.1, 164.3; LC-MS (ESI) calculated for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$ m/z : 317.2; found: 317.2.

O-(2,4-dinitrophenyl)hydroxylamine (28)



This compound was prepared following a reported procedure.³ ¹H NMR (500 MHz, CDCl₃): δ 6.39 (s, 2H), 8.06 (d, 1H, *J* = 9.5 Hz), 9.45 (dd, 1H, *J*₁ = 2.5, *J*₂ = 9.4 Hz), 8.82 (d, 1H, *J* = 2.6 Hz); ¹³C NMR (125 MHz, CDCl₃): 116.4, 122.0, 129.3, 136.5, 140.7, 159.6; LC-MS (ESI, Neg) calculated for C₁₆H₁₆ N₂O₅ [M-H]⁻ *m/z*: 198.2; found: 198.2.

2-phenylpropyl (2,4-dinitrophenoxy)carbamate (3)

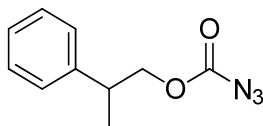


To a flame dried 10 mL round bottom flask at 0 °C under inert atmosphere was added 2-phenylpropan-1-ol (103 μL, 0.73 mM), 20% phosgene in toluene (912 μL, 2.64 mM), and 2 mL dry toluene. Reaction was stirred for five minutes at 0 °C before being allowed to warm to room temperature. After three hours starting material was consumed, reaction was opened, and argon purged through solution for twenty minutes to remove excess phosgene. Toluene was removed under reduced pressure and replaced with 3 mL of dry CH₂Cl₂. Solution was cooled to 0 °C before adding O-(2,4-dinitrophenyl)hydroxylamine (160 mg, 0.80 mM) and triethylamine (122 μL, 0.88 mM). Reaction was stirred at 0 °C for 5 mins before warming to room temperature for 12 h. 10 mL of saturated aqueous sodium bicarbonate was added and reaction was extracted three times with 10 mL of CH₂Cl₂. Combined organics were washed with brine, dried over sodium sulfate, and the residue was purified by flash column chromatography (5-30% EtOAc in hexane) to afford 2-phenylpropyl (2,4-dinitrophenoxy)carbamate (**3**) (31.0 mg, 12%). ¹H NMR (500 MHz, CDCl₃): δ 1.40 (d, 3H, *J* = 7.1 Hz), 3.20-3.28 (m, 1H), 4.35-4.47 (m, 2H), 7.24-7.29 (m, 3H), 7.35 (t, 2H, *J* = 7.3 Hz), 7.48 (d, 1H, *J* = 9.0 Hz), 8.51 (dd, 1H, *J*₁ = 2.2, *J*₂ = 8.9 Hz), 8.96 (d, 1H, *J* = 2.3 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 17.7, 38.9, 75.0, 121.9, 126.2, 127.1, 127.3, 128.7, 129.2, 141.3, 141.9, 145.2, 148.5, 151.3; MS analysis could not be performed due to decomposition upon ESI ionization conditions.

B. Synthesis of carbonazidate substrates.

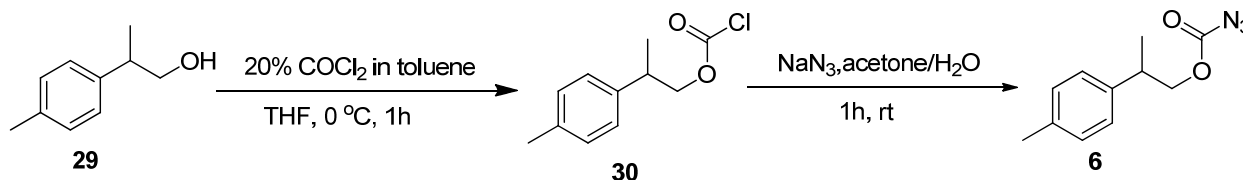
Carbonazidates **4**,⁴ **7**,⁵ **23**,⁶ and **24**⁷ were synthesized according to reported procedures. The corresponding spectral data were found to be in agreement with the reported ones.

2-phenylpropyl carbonazidate (**4**)



¹H NMR (400 MHz, CDCl₃): δ 7.39-7.27 (m, 5H), 4.40-4.36 (m, 1H), 4.32-4.27 (m, 1H), 3.22-3.17 (m, 1H), 1.38 (d, 3H, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 157.08, 141.9, 128.4, 127.0, 126.7, 72.9, 38.6, 17.4; LC-MS (ESI) calculated for C₁₀H₁₂N₃O₂[M+H]⁺ *m/z*: 206.2, Observed: 206.3.

Synthesis of 2-(p-tolyl)propyl carbonazidate (**6**)

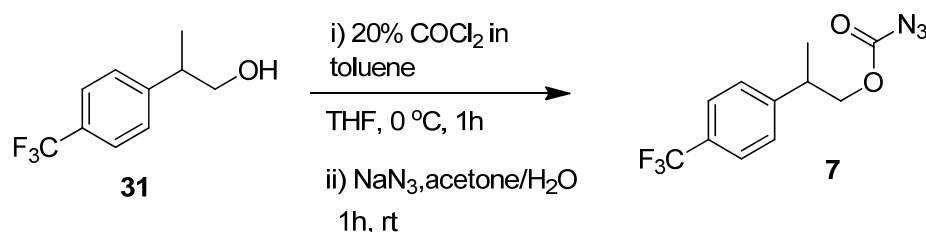


To a stirred solution of 2-(p-tolyl)propan-1-ol (**29**)⁶ (400 mg, 2.67 mmol) in dry THF (3.0 mL) at 0 °C, COCl₂ (20% in toluene, 3 mmol) was added slowly and stirred for 1-2 h at room temperature. After the completion of reaction (as observed from TLC), nitrogen was bubbled through the reaction for 1 h to remove excess phosgene. The reaction mixture was then concentrated and the obtained residue was flash chromatographed on a silica gel which furnished 2-(p-tolyl)propyl carbonochloridate (**30**) in 85% yield as a colorless oil. *R_f* = 0.82 (2% EtOAc in hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.23-7.18 (m, 4H), 4.49-4.45 (m, 1H), 4.40-4.36 (m, 1H), 3.25-3.21 (m, 1H), 2.41 (s, 3H), 1.41 (d, 3H, *J* = 7.3 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 150.5, 138.4, 136.6, 129.3, 127.0, 76.5, 38.2, 20.9, 17.5.

To a stirred solution of 2-(p-tolyl)propyl carbonochloridate (**30**) (300 mg, 1.41 mmol) in acetone/water (1:1) (5 mL) at 0 °C was added NaN₃ (135 mg, 1.5 mmol) and left stirred at room temperature. After the completion of reaction (as observed from TLC, in about 45 min), reaction mixture was concentrated under vacuum, followed by extraction with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure. The residue was flash chromatographed on silica gel which furnished 2-(p-tolyl)propyl carbonazidate (**6**) as a colorless oil in

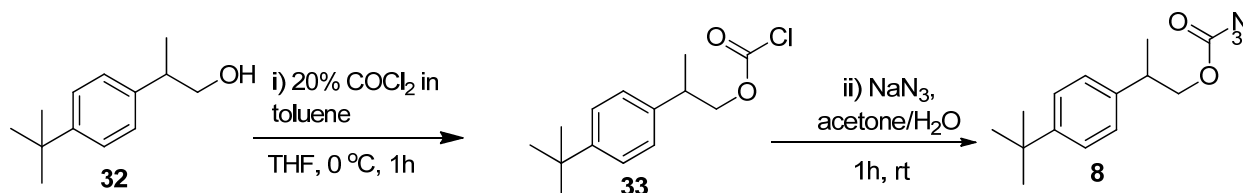
96% yield. $R_f = 0.78$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.22-7.20 (m, 4H), 4.42-4.38 (m, 1H), 4.33-4.29 (m, 1H), 3.23-3.18 (m, 1H), 2.42 (s, 3H), 1.41 (d, 3H, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.1, 138.8, 136.2, 129.0, 126.8, 72.9, 38.1, 20.7, 17.4; LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{14}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+ m/z$: 220.2, Observed: 220.3.

Synthesis of 2-(4-(trifluoromethyl)phenyl)propyl carbonazidate (7)



To a stirred solution of 2-(4-((difluoro-1,3-methyl)-1,2-fluoranyl)phenyl)propan-1-ol (**31**)⁸ (400 mg, 1.96 mmol) in dry THF (3.0 mL) at 0°C , COCl_2 (20% in toluene, 3 mmol) was added slowly and stirred for 1-2 h at room temperature. After the completion of reaction (as observed from TLC), nitrogen was bubbled through the reaction for 1 h to remove excess phosgene. The reaction mixture was then concentrated and the obtained residue was used directly in the next step which was converted into 2-(4-(trifluoromethyl)phenyl)propyl carbonazidate (7) by procedure as described above as given for 2-(p-tolyl)propyl carbonazidate (6) in 81% yield (after two steps) as a colorless oil. $R_f = 0.79$ (2% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.58 (d, 2H, $J = 7.6$ Hz), 7.34 (d, 2H, $J = 7.5$ Hz), 4.35-4.25 (m, 2H), 3.25-3.20 (m, 1H), 1.41 (d, 3H, $J = 7.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 146.3, 127.6, 126.2, 125.5, 125.4, 123.9, 72.4, 38.7, 17.4; LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{11}\text{F}_3\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+ m/z$: 274.2, Observed: 274.1.

Synthesis of 2-(4-(tert-butyl)phenyl)propyl carbonazidate (8)

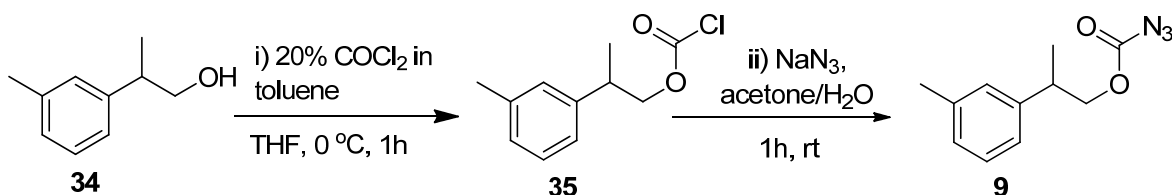


Compound 2-(4-(tert-butyl)phenyl)propan-1-ol (**32**)⁹ was converted into 2-(4-(tert-butyl)phenyl)propyl carbonochloridate (**33**) by following the same procedure as for 2-(p-tolyl)propyl carbonochloridate (**30**)

and isolated in 86% yield as colorless oil. $R_f = 0.83$ (5% EtOAc in hexane). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.41 (d, 2H, $J = 7.5$ Hz), 7.20 (d, 2H, $J = 7.6$ Hz), 4.49-4.33 (m, 2H), 3.22-3.19 (m, 1H), 1.40 (s, 9H), 1.38 (d, 3H, $J = 7.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.6, 149.9, 138.3, 126.9, 125.6, 76.6, 38.2, 34.4, 31.3, 17.6.

Compound 2-(4-(tert-butyl)phenyl)propyl carbonochloridate (**33**) was converted into 2-(4-(tert-butyl)phenyl)propyl carbonazidate (**8**) by the same procedure as described for 2-(p-tolyl)propyl carbonazidate (**7**) and isolated in 94% yield as colorless oil. $R_f = 0.80$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.38 (d, 2H, $J = 7.5$ Hz), 7.18 (d, 2H, $J = 7.4$ Hz), 4.35-4.25 (m, 2H), 3.17-3.15 (m, 1H), 1.34 (s, 9H), 1.34 (d, 3H, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 149.7, 138.9, 126.8, 125.4, 73.3, 38.2, 34.3, 31.3, 17.6. LC-MS (ESI) calculated for $\text{C}_{14}\text{H}_{20}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ m/z : 262.3, Observed: 262.3.

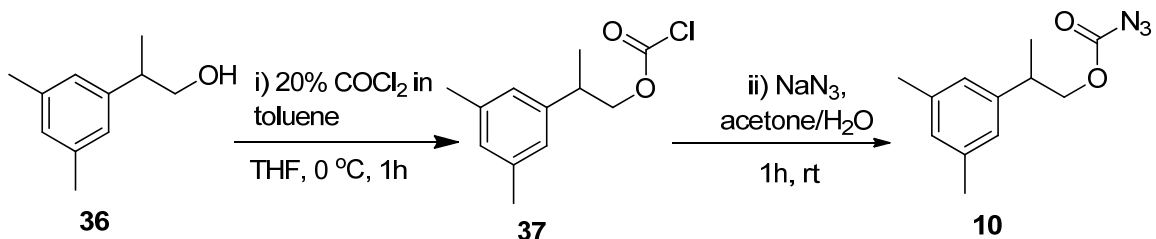
Synthesis of 2-(m-tolyl)propyl carbonazidate (**9**)



Compound 2-(m-tolyl)propan-1-ol (**34**)¹⁰ was converted into 2-(m-tolyl)propyl carbonochloridate (**35**) by following the same procedure as described for 2-(p-tolyl)propyl carbonochloridate (**30**) and isolated in 86% yield as colorless oil. $R_f = 0.85$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.33-7.29 (m, 1H), 7.17-7.10 (m, 3H), 4.51-4.37 (m, 2H), 3.26-3.21 (m, 1H), 2.44 (s, 3H), 1.41 (d, 3H, $J = 7.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.4, 141.3, 138.2, 128.5, 127.9, 127.8, 124.1, 76.4, 38.5, 21.3, 17.5.

Compound 2-(m-tolyl)propyl carbonochloridate (**35**) was converted into 2-(m-tolyl)propyl carbonazidate (**9**) by the same procedure as described for 2-(p-tolyl)propyl carbonazidate (**7**) and isolated in 93% yield as colorless oil. $R_f = 0.80$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.28-7.24 (m, 1H), 7.11-7.06 (m, 3H), 4.39-4.25 (m, 2H), 3.18-3.13 (m, 1H), 2.39 (s, 3H), 1.36 (d, 3H, $J = 7.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.2, 141.9, 138.0, 128.4, 127.9, 127.6, 124.1, 73.1, 38.6, 21.3, 17.6. LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{14}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ m/z : 220.2, Observed: 220.3.

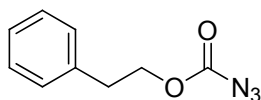
Synthesis of 2-(3,5-dimethylphenyl)propyl carbonazidate (10)



Compound 2-(3,5-dimethylphenyl)propan-1-ol (**36**)⁸ was converted into 2-(3,5-dimethylphenyl)propyl carbonochloridate (**37**) by following the same procedure as for 2-(p-tolyl)propyl carbonochloridate (**30**) and isolated in 84% yield as colorless oil. $R_f = 0.87$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.04 (s, 1H), 6.97 (s, 2H), 4.58-4.40 (m, 2H), 3.26-3.21 (m, 1H), 2.45 (s, 6H), 1.46 (d, 3H, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.4, 141.3, 138.0, 128.7, 124.9, 76.5, 38.5, 21.1, 17.5.

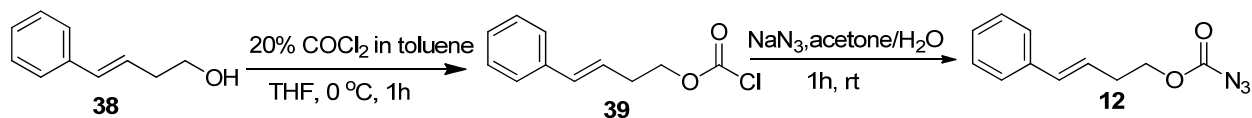
Compound 2-(3,5-dimethylphenyl)propyl carbonochloridate (**37**) was converted into 2-(3,5-dimethylphenyl)propyl carbonazidate (**10**) by using the same procedure as described for 2-(p-tolyl)propyl carbonazidate (**7**) and isolated in 95% yield as colorless oil. $R_f = 0.83$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.93 (s, 1H), 6.87 (s, 2H), 4.37-4.23 (m, 2H), 3.14-3.08 (m, 1H), 2.34 (s, 6H), 1.34 (d, 3H, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 141.9, 138.0, 128.5, 124.9, 72.2, 38.6, 21.2, 17.7. LC-MS (ESI) calculated for $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}$]⁺ m/z : 234.2, Observed: 234.2.

Phenethyl carbonazidate (11)



$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.35-7.22 (m, 5H), 4.43 (t, 2H, $J = 7.5$ Hz), 3.01 (t, 2H, $J = 7.4$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 136.7, 128.8, 128.6, 126.8, 68.8, 34.8; LC-MS (ESI) calculated for $\text{C}_9\text{H}_{10}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}$]⁺ m/z : 192.1, Observed: 192.1.

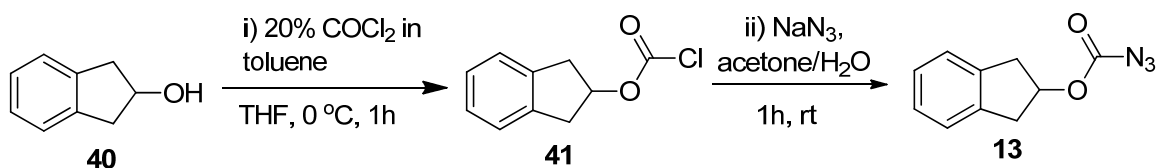
Synthesis of (*E*)-4-phenylbut-3-en-1-yl carbonazidate (**12**)



Compound (*E*)-4-phenylbut-3-en-1-ol (**38**)¹¹ was converted into (*E*)-4-phenylbut-3-en-1-yl carbonochloridate (**39**) by following the same procedure as for 2-(*p*-tolyl)propyl carbonochloridate (**30**) and isolated in 84% yield as colorless oil. $R_f = 0.74$ (5% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.27(m, 5H), 6.53 (d, 1H, $J = 14.4$ Hz), 6.19-6.12 (m, 1H), 4.43 (t, 2H, $J = 6.9$ Hz) 2.66-2.65 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 150.6, 136.8, 133.4, 128.3, 127.5, 126.1, 123.0, 71.0, 31.8.

Compound (*E*)-4-phenylbut-3-en-1-yl carbonochloridate (**39**) was converted into (*E*)-4-phenylbut-3-en-1-yl carbonazidate (**12**) by using the same procedure as described for 2-(*p*-tolyl)propyl carbonazidate (**7**) and isolated in 94% yield as colorless oil. $R_f = 0.72$ (5% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.19 (m, 5H), 6.51 (d, 1H, $J = 14.6$ Hz), 6.20-6.13 (m, 1H), 4.33 (t, 2H, $J = 7.2$ Hz) 2.64-2.59 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 157.3, 136.8, 132.9, 128.4, 127.3, 126.0, 124.2, 67.5, 32.0. LC-MS (ESI) calculated for C₁₁H₁₂N₃O₂[M+H]⁺ m/z : 218.2, Observed: 218.2.

Synthesis of 2,3-dihydro-1H-inden-2-yl carbonazidate (**13**)

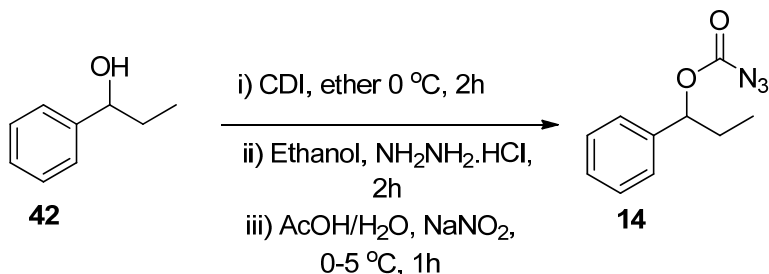


2-indanol (**40**) was converted into 2,3-dihydro-1H-inden-2-yl carbonochloridate (**41**) by following the same procedure as for 2-(*p*-tolyl)propyl carbonochloridate (**30**) and isolated in 82% yield as colorless oil. $R_f = 0.79$ (5% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.30-7.29 (m, 4H), 5.65 (m, 1H), 3.43-3.38 (m, 2H), 3.25-3.21 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 150.3, 139.1, 127.0, 124.6, 83.8, 39.1.

Compound 2,3-dihydro-1H-inden-2-yl carbonochloridate (**41**) was converted into 2,3-dihydro-1H-inden-2-yl carbonazidate (**13**) by using the same procedure as described for 2-(*p*-tolyl)propyl carbonazidate (**7**) and isolated in 94% yield as colorless oil. $R_f = 0.75$ (5% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.28-7.27 (m, 4H), 5.57 (m, 1H), 3.41-3.35 (m, 2H), 3.18-3.14 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ

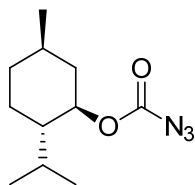
157.0, 139.4, 126.7, 124.3, 79.6, 38.9. LC-MS (ESI) calculated for $C_{10}H_{10}N_3O_2[M+H]^+$ m/z : 204.2, Observed: 204.3.

Synthesis of 1-phenylpropyl carbonazidate (**14**)



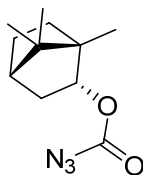
1-phenylpropan-1-ol (**42**) (3.5 mmol) was slowly added to a solution of 1,1'-carbonyldiimidazole (600 mg, 3.84 mmol) in THF (35 mL) at 0 °C and the resulting mixture was stirred at room temperature for 2 h. The mixture was washed with saturated aqueous NH₄Cl (15 mL) and brine (15 mL), then dried over Na₂SO₄. The solvent was removed under reduced pressure. The product obtained was dissolved in ethanol (35 mL), hydrazine hydrate (750 mg, 10 mmol) was added and the resulting mixture was stirred at room temperature for 2h. After the completion of reaction (as observed from TLC), the solvent was removed under reduced pressure, and the product obtained was used without any further purification in next step. The crude product hydrazinecarboxylate (6.5 mmol) was dissolved in a mixture of acetic acid (5 mL) and water (3 mL), and the solution was cooled to 0 °C, stirred and treated dropwise with NaNO₂ (462 mg, 6.7 mmol) while maintaining the temperature below 5 °C. After the addition, mixture was stirred for 15 min at below 5 °C and further for an hour at room temperature. After the completion of reaction, mixture was poured in water followed by extraction with ether (3 x 40 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure which furnished 1-phenylpropyl carbonazidate (**14**) as colorless oil in 72% yield. $R_f = 0.85$ (5% EtOAc in hexane), ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.31 (m, 5H), 5.63-5.59 (m, 1H), 2.06-1.97 (m, 1H), 1.93-1.84 (m, 1H), 0.94-0.91 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 157.0, 138.9, 128.5, 128.4, 126.5, 82.3, 29.0, 9.7. LC-MS (ESI) calculated for $C_{10}H_{12}N_3O_2[M+H]^+$ m/z : 206.2, Observed: 206.2.

(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl carbonazidate (23)



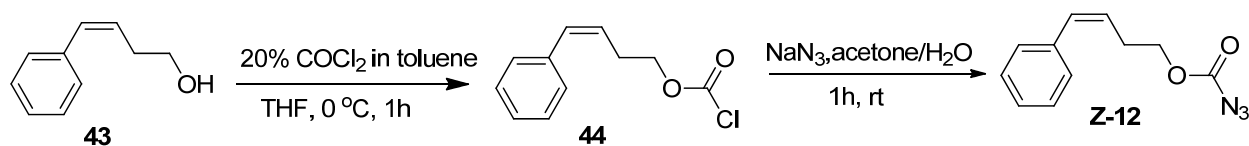
^1H NMR (400 MHz, CDCl_3): δ 4.65-4.63 (m, 1H), 2.07 (m, 1H), 1.90-1.89 (m, 1H), 1.68 (m, 2H), 1.46-1.40 (m, 2H), 1.08-1.02 (m, 2H), 0.92-0.89 (m, 7H), 0.80 (d, 3H, $J = 7.2$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ 157.1, 79.4, 46.8, 40.5, 33.9, 31.4, 26.2, 23.3, 21.9, 20.6, 16.3. LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{20}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ m/z : 226.2, Observed: 226.2.

(1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl carbonazidate (24)



^1H NMR (400 MHz, CDCl_3): δ 4.88-4.85 (m, 1H), 2.38-2.34 (m, 1H), 1.88-1.82 (m, 1H), 1.73-1.67 (m, 2H), 1.31-1.19 (m, 2H), 1.08-1.04 (m, 1H), 0.88 (s, 3H), 0.87 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 157.6, 84.7, 48.9, 47.9, 44.6, 36.2, 27.7, 26.7, 19.5, 18.7, 13.3. LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{18}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ m/z : 224.2, Observed: 224.3.

Synthesis of (Z)-4-phenylbut-3-en-1-yl carbonazidate (Z-12)

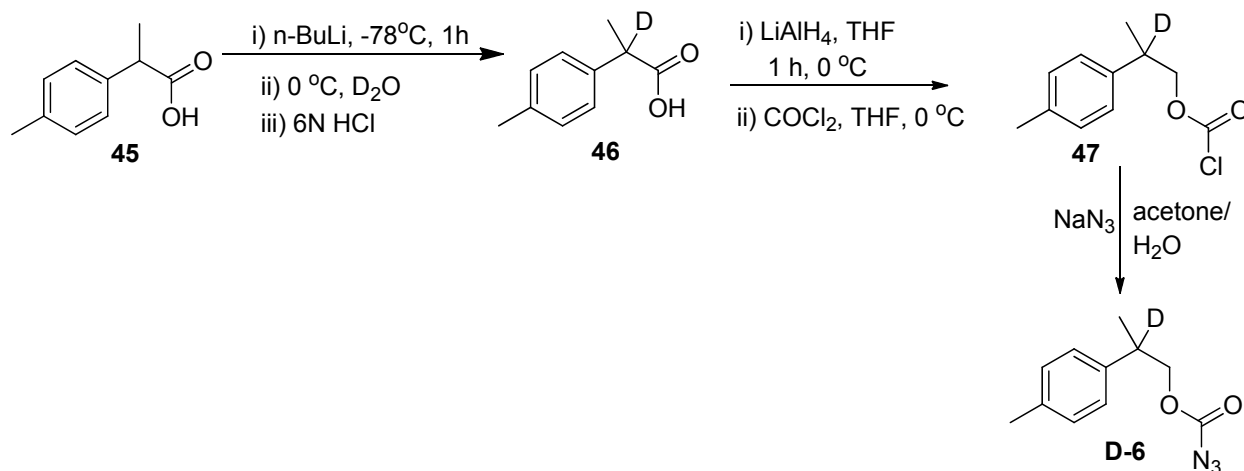


Compound (Z)-4-phenylbut-3-en-1-ol (**43**)¹² was converted into (Z)-4-phenylbut-3-en-1-yl carbonochloridate (**44**) by following the same procedure as for 2-(p-tolyl)propyl carbonochloridate (**30**) and isolated in 86% yield as colorless oil. $R_f = 0.75$ (5% EtOAc in hexane); ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.29 (m, 5H), 6.66 (d, 1H, $J = 7.4$ Hz), 5.70-5.63 (m, 1H), 4.41 (t, 2H, $J = 7.3$ Hz), 2.81-2.76 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.5, 136.6, 132.4, 128.5, 128.2, 127.0, 125.4, 71.2, 27.6.

Compound (*Z*)-4-phenylbut-3-en-1-yl carbonochloridate (**44**) was converted into (*Z*)-4-phenylbut-3-en-1-yl carbonazidate (**Z-12**) by using the same procedure as described for 2-(*p*-tolyl)propyl carbonazidate (**7**) in 92% yield as colorless oil. $R_f = 0.73$ (5% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36-7.25 (m, 5H), 6.58 (d, 1H, $J = 7.4$ Hz), 5.64-5.60 (m, 1H), 4.29 (t, 2H, $J = 7.3$ Hz), 2.75-2.70 (m, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.5, 136.8, 132.1, 128.6, 128.3, 127.0, 126.1, 67.8, 27.8. LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{12}\text{N}_3\text{O}_2[\text{M}+\text{H}]^+$ m/z : 218.2, Observed: 218.3.

C. Synthesis of deuterated carbonazidate substrates

Synthesis of 2-(*p*-tolyl)propyl-2-d carbonazidate (**D-6**)



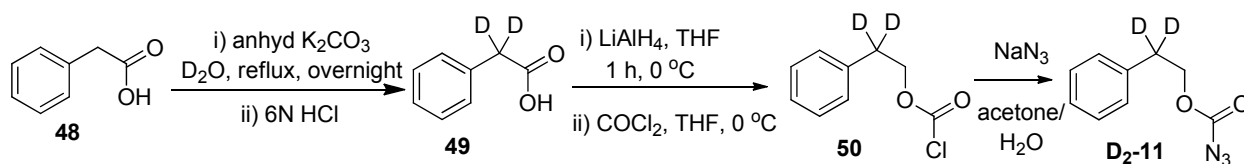
To a stirred solution of 2-(*p*-tolyl)propanoic acid (**45**) (492 mg, 3 mmol) in dry THF at -78°C was added $n\text{-BuLi}$ (2.05 mmol, 1.6 M in hexane) dropwise. The reaction mixture was left stirred for 1 h at -78°C , and was then gradually brought to 0°C , followed by quenching with D_2O . The reaction mixture was acidified with 6N HCl and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to give 2-(*p*-tolyl)propanoic-2-d acid (**46**) as a white solid in 91% yield and was used without any purification in the next step. $R_f = 0.39$ (5% MeOH in CH_2Cl_2). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 11.5 (s, br, 1H), 7.29-7.20 (m, 4H), 2.39 (s, 3H), 1.55 (s, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 181.2, 136.9, 136.6, 129.9, 127.4, 44.5, 20.9, 17.9.

Compound (*p*-tolyl)propanoic-2-d acid (**46**) was then reduced with LiAlH_4 to give the intermediate alcohol. The alcohol obtained was treated with COCl_2 via aforementioned procedure which furnished 2-(*p*-tolyl)propyl-2-d carbonochloridate (**47**) in 84% yield (over two steps) as colorless oil. $R_f = 0.78$ (5%

EtOAc in hexane). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.20-7.15 (m, 4H), 4.45-4.33 (m, 2H), 2.38 (s, 3H), 1.37 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.6, 138.4, 136.7, 129.4, 127.0, 76.5, 37.8, 20.9, 17.5.

Compound 2-(p-tolyl)propyl-2-d carbonochloridate (**47**) was then converted to 2-(p-tolyl)propyl-2-d carbonazidate (**D-6**) by procedure as described above for 2-(p-tolyl)propyl carbonazidate (**7**) in 93% yield as colorless oil. $R_f = 0.73$ (5% EtOAc in Hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.16-7.13 (m, 4H), 4.35-4.23 (m, 2H), 2.36 (s, 3H), 1.33 (s, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 138.9, 136.4, 129.2, 127.0, 73.1, 37.9, 20.9, 17.6. LC-MS (ESI) calculated for $\text{C}_{11}\text{H}_{13}\text{DN}_3\text{O}_2$ $[\text{M}+\text{H}]^+ m/z$: 221.2, Observed: 221.2.

Synthesis of 2-phenylethyl-2,2-d₂ carbonazidate (**D₂-11**)

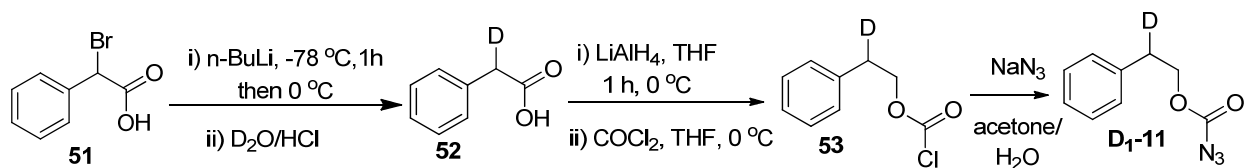


A mixture of phenylacetic acid (**48**) (2.50 g; 18.36 mmol), anhydrous potassium carbonate (10.30 g; 73.4 mmol) and deuterium oxide (15 mL) was refluxed overnight. After completion of reaction (as determined by GC-MS) the reaction mixture was cooled to about 0 °C, acidified to pH 2 with 6 N hydrochloric acid, and then extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure to give 2-phenylacetic-2,2-d₂ acid (**49**) as a white solid in 96% yield and was used without any purification in the next step. $R_f = 0.38$ (5% MeOH in CH₂Cl₂). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 10.9 (s, br, 1H), 7.37-7.29 (m, 5H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 178.2, 133.1, 129.3, 128.6, 127.3, 40.7.

To a stirred solution of 2-phenylacetic-2,2-d₂ acid (**49**) (1.0 g, 7.24 mmol) in dry THF (30 mL) at 0 °C was added LiAlH₄ (275 mg, 7.24 mmol) and left stirred at room temperature. After the completion of reaction (as observed from TLC, in about 45 min), reaction mixture was quenched with water at 0 °C, followed by extraction with ethyl acetate (3 x 40 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure which furnished the intermediate alcohol as colorless oil in 90% yield and was proceeded further in the next step without any purification. The obtained alcohol was then converted to 2-phenylethyl-2,2-d₂ carbonochloridate (**50**) as described above for 2-(p-tolyl)propyl carbonazidate (**30**) in 88% yield as colorless oil. $R_f = 0.75$ (5% EtOAc in Hexane). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.41-7.26 (m, 5H), 4.53 (s, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 150.4, 136.0, 128.8, 128.6, 126.9, 71.9, 33.8.

Compound 2-phenylethyl-2,2-d₂ carbonochloridate (**50**) was converted to 2-phenylethyl-2,2-d₂ carbonazidate (**D₂-11**) by procedure as described above for 2-(p-tolyl)propyl carbonazidate (**7**) in 95% as colorless oil. $R_f = 0.70$ (5% EtOAc in Hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.24 (m, 5H), 4.43 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 157.2, 136.5, 128.7, 128.4, 126.7, 68.5, 34.0. LC-MS (ESI) calculated for C₉H₇D₂N₃O₂ [M+H]⁺ m/z : 194.2, Observed: 194.2.

Synthesis of 2-phenylethyl-2-d carbonazidate (**D₁-11**)



To a stirred solution of 2-bromo-2-phenylacetic acid (**51**) (639 mg, 3 mmol) in dry THF at -78 °C was added n-BuLi (2 .05 mmol, 1.6 M in hexane) dropwise. The reaction mixture was left stirred for 1 h at -78 °C, and was then gradually brought to 0 °C, followed by quenching with D₂O. The reaction mixture was acidified with 6N HCl and with extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure to give 2-phenylacetic-2-d acid (**52**) as a white solid in 92% yield, which was used without any purification in the next step. $R_f = 0.34$ (5% MeOH in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 11.5 (s, br, 1H), 7.33-7.26 (m, 5H); 3.63 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 177.7, 133.2, 129.3, 128.6, 127.4, 40.7.

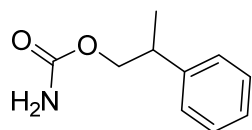
Compound 2-phenylacetic-2-d acid (**52**) was then reduced by LiAlH₄ followed by treatment with COCl₂ by following the aforementioned procedure which provided 2-phenylethyl-2-d carbonochloridate (**53**) in 82% yield (over two steps) as colorless oil. $R_f = 0.82$ (5% EtOAc in hexane). ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.21 (m, 5H), 4.5 (d, 2H, $J = 7.7$ Hz), 3.03-3.02 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 150.6, 136.1, 128.9, 128.7, 127.1, 72.1, 34.4.

Compound 2-phenylethyl-2-d carbonochloridate (**53**) was then converted to 2-phenylethyl-2-d carbonazidate (**D₁-11**) by using the same procedure as described above for 2-(p-tolyl)propyl carbonazidate (**7**) in 96% yield as colorless oil. $R_f = 0.70$ (5% EtOAc in Hexane). ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.24 (m, 5H), 4.43(d, 2H, $J = 7.4$ Hz). ¹³C NMR (100 MHz, CDCl₃): δ 157.2, 136.6, 128.9, 128.5, 126.7, 68.7, 34.4. LC-MS (ESI) calculated for C₉H₈DN₃O₂ [M+H]⁺ m/z : 193.2, Observed: 193.2.

D. Synthesis of carbamate standards

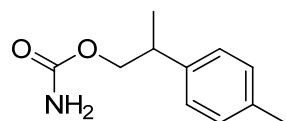
To a stirred solution of primary alcohol (5 mmol) and sodium isocyanate (10 mmol) in 10 mL of dry CH_2Cl_2 was added TFA (10.5 mmol) dissolved in 5 mL of dry CH_2Cl_2 at room temperature. After the completion of reaction (approx 5 h at room temperature), water (5 mL) was added, and extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to give the corresponding carbamate product which was then purified by flash column chromatography (85–91% yield). Spectral data for phenethyl carbamate and (1S,2S,5S)-2-isopropyl-5-methylcyclohexyl carbamate, 2,3-dihydro-1H-inden-2-yl carbamate matched the reported ones.¹³

2-phenylpropyl carbamate (54)



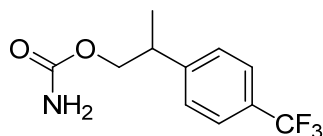
Yield (86%), $R_f = 0.38$ (20% EtOAc in hexane); ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.30 (m, 2H), 7.24-7.23 (m, 3H), 4.99 (br, s, 2H), 4.17-4.15 (m, 2H), 3.14-3.05 (m, 1H), 1.28 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 157.2, 143.2, 128.4, 127.2, 126.5, 69.7, 39.0, 17.9. GC-MS m/z (% relative intensity): 118(100), 105(39.4), 91(12.2).

2-(p-tolyl)propyl carbamate (55)



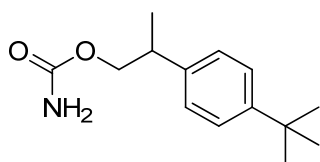
Yield (88%), $R_f = 0.40$ (30% EtOAc in hexane); ^1H NMR (400 MHz, CDCl_3): δ 7.16 (m, 4H), 5.10 (br, s, 2H), 4.18-4.16 (m, 2H), 3.11-3.07 (m, 1H), 2.36 (s, 3H), 1.31(d, 3H, $J = 4.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 157.1, 140.2, 136.1, 129.1, 127.1, 69.9, 38.7, 20.9, 18.1. GC-MS m/z (% relative intensity): 150(2.3), 132(100), 119(66.3), 91(31.4).

2-(4-(trifluoromethyl)phenyl)propyl carbamate (56)



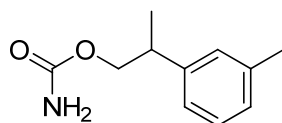
Yield (89%), R_f = 0.42 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.57-7.56 (m, 2H), 7.35-7.33 (m, 2H), 4.93 (br, s, 2H), 4.17-4.13 (m, 2H), 3.18-3.14 (m, 1H), 1.29 (d, 3H, J = 7.3 Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.0, 147.5, 128.8, 127.7, 125.4, 123.9, 69.3, 39.1, 17.8. GC-MS m/z (% relative intensity): 186(100), 73(11.1), 167(7.9), 159(12.6), 154(20.1), 153(13.4), 133(14.3), 117(25.7).

2-(4-(tert-butyl)phenyl)propyl carbamate(57)



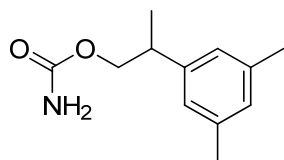
Yield (85%), R_f = 0.41 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36-7.34 (m, 2H), 7.19-7.17 (m, 2H), 5.01 (br, s, 2H), 4.17-4.15 (m, 2H), 3.11-3.06 (m, 1H), 1.34(s, 9H), 1.30 (d, 3H, J = 7.1 Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 149.2, 140.1, 126.8, 125.2, 69.9, 38.5, 34.3, 31.3, 17.9; GC-MS m/z (% relative intensity): 174(36.2), 159(100), 146(81.3), 131(15.1), 105(2.1), 91(3.9).

2-(m-tolyl)propyl carbamate (58)



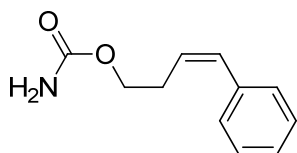
Yield (91%), R_f = 0.39 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.25-7.21 (m, 1H), 7.07-7.05 (m, 2H), 5.11 (br, s, 2H), 4.18-4.16 (m, 2H), 3.10-3.05 (m, 1H), 2.37 (s, 3H), 1.30 (d, 3H, J = 4.3 Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 157.3, 143.1, 137.8, 128.2, 127.9, 127.2, 124.1, 69.7, 38.9, 21.3, 18.0; GC-MS m/z (% relative intensity): 150(2.3), 132(100), 119(66.3), 91(31.4).

2-(3,5-dimethylphenyl)propyl carbamate (59)



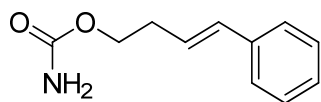
Yield (87%), $R_f = 0.36$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.87-6.83 (m, 3H), 4.63 (br, s, 2H), 4.14-4.13 (m, 2H), 3.03-2.98 (m, 1H), 2.29 (s, 6H), 1.26 (d, 3H, $J = 7.3$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 156.9, 143.2, 137.9, 128.3, 125.0, 70.0, 39.0, 21.3, 18.2; GC-MS m/z (% relative intensity): 147(13.2), 146(100), 133(38.9), 119(10.6), 117(10.4), 106(19.3), 91(15.7).

(Z)-3-phenylallyl carbamate (Z-27)



Yield (88%), $R_f = 0.45$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.35-7.21 (m, 5H), 6.53 (d, 2H, $J = 12.2$ Hz), 5.69-5.62 (m, 2H), 4.77 (s, 2H), 4.17-4.15 (m, 2H), 2.69-2.64 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 156.9, 137.1, 131.3, 128.6, 128.2, 127.4, 126.8, 64.5, 28.4; GC-MS m/z (% relative intensity): 130(100), 129(74.6), 155(39.2), 91(9.3).

(E)-4-phenylbut-3-en-1-yl carbamate (E-27)

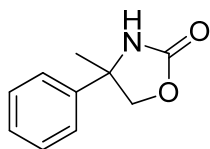


Yield (90%), $R_f = 0.45$ (20% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.35-7.33 (m, 5H), 6.47 (d, 2H, $J = 15.6$ Hz), 6.21-6.14 (m, 2H), 4.76 (s, 2H), 4.20-4.17 (m, 2H), 2.64-2.51 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 156.9, 137.3, 132.3, 128.5, 127.2, 126.0, 125.7, 64.3, 32.6; GC-MS m/z (% relative intensity): 130(100), 129(74.6), 155(39.2), 91(9.3).

E. Synthesis of oxazolidinone standards

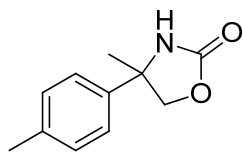
All the standard oxazolidinones, except **26** were synthesized by following a reported procedure¹³ as follows: To a stirred solution of carbamate (0.31 mmol) in 2 mL of CH₂Cl₂ were added successively MgO (29.25 mg, 0.72 mmol, 2.3 equiv), PhI(OAc)₂ (122 mg, 0.25 mmol, 1.4equiv) and Rh(II) catalyst (16 μmol, 0.05 equiv). The mixture was stirred vigorously and heated at 40 °C for 12 hrs. After cooling to 25 °C, the reaction was diluted with 10 mL of CH₂Cl₂ and filtered through a pad of Celite (30 x 20 mm). The filter cake was rinsed with 2 x 10 mL of CH₂Cl₂. The combined filtrates were evaporated under reduced pressure and the isolated residue purified by chromatography on silica gel. Spectral data of 4-phenyloxazolidin-2-one (**20**), 3,3a,8,8a-tetrahydro-2H-indeno[1,2-d]oxazol-2-one (**22**) and (E)-4-stryryloxazolidin-2-one (**21**) were found to be in good agreement with the reported ones.¹³⁻¹⁴

4-methyl-4-phenyloxazolidin-2-one (**5**)



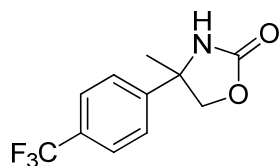
Yield (75%), $R_f = 0.41$ (30% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.38-7.30 (m, 5H), 6.73 (s, 1H), 4.38 (d, 1H, $J = 7.2$ Hz), 4.34 (d, 1H, $J = 7.2$ Hz), 1.74 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 159.4, 143.5, 128.9, 127.9, 124.5, 78.0, 60.5, 27.9; GC-MS m/z (% relative intensity): 177(1.2), 163(10.4), 162(100), 146(1.9), 119(28.2), 104(39.3), 91(46.1).

4-methyl-4-(p-tolyl)oxazolidin-2-one (**15**)



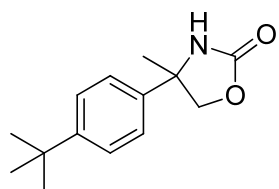
Yield (78%), $R_f = 0.37$ (30% EtOAc in hexane); ¹H NMR (400 MHz, CDCl₃): δ 7.26-7.19 (m, 4H), 6.76 (s, 1H), 4.36 (d, 1H, $J = 7.1$ Hz), 4.34 (d, 1H, $J = 7.1$ Hz), 2.35 (s, 3H), 1.73 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 159.5, 140.5, 137.6, 129.5, 124.5, 78.1, 60.3, 27.8, 20.9; GC-MS m/z (% relative intensity): 191(8.6), 176(100), 146(10), 133(43.4), 118(42.6), 105(49.7), 91(14.3).

4-methyl-4-(4-(trifluoromethyl)phenyl)oxazolidin-2-one (16)



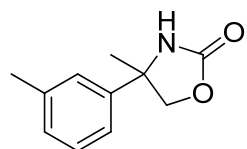
Yield (79%), $R_f = 0.32$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.66 (d, 1H, $J = 7.1$ Hz), 7.50 (d, 1H, $J = 7.2$ Hz), 7.16 (s, 1H), 4.43 (d, 1H, $J = 7.1$ Hz), 4.35 (d, 1H, $J = 7.1$ Hz), 1.77 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.4, 147.5, 130.1, 126.0(2C), 125.1, 124.2, 77.6, 60.5, 27.9; GC-MS m/z (% relative intensity): 231(11.4), 230(100), 226(3.5), 187(28.2), 172(54.8), 159(74.1), 145(14.2).

4-(4-(tert-butyl)phenyl)-4-methyloxazolidin-2-one (17)



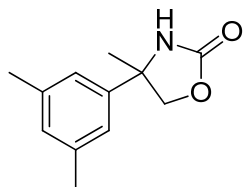
Yield (77%), $R_f = 0.30$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.40 (d, 1H, $J = 7.1$ Hz), 7.30 (d, 1H, $J = 7.2$ Hz), 6.22 (s, 1H), 4.34 (m, 2H), 1.74 (s, 3H), 1.31 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.2, 150.9, 140.3, 125.8, 124.4, 78.2, 60.1, 34.5, 31.2, 27.5; GC-MS m/z (% relative intensity): 233(5.2), 218(100), 203(4.9), 175(3.1), 160(20.6), 147(22.5), 133(20.8), 105(6.3), 91(5.4).

4-methyl-4-(m-tolyl)oxazolidin-2-one (18)



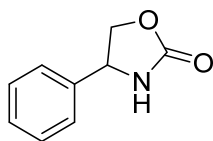
Yield (80%), $R_f = 0.36$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.27-7.24 (m, 1H), 7.15-7.09 (m, 3H), 7.02 (s, 1H), 4.36 (d, 1H, $J = 7.1$ Hz), 4.33 (d, 1H, $J = 7.1$ Hz), 2.35 (s, 3H), 1.71 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.6, 143.6, 138.6, 128.8, 128.5, 125.2, 121.5, 77.9, 60.5, 27.9, 21.5; GC-MS m/z (% relative intensity): 191(3.8), 176(100), 146(6.4), 133(31.7), 118(46.9), 105(88.3), 91(35.3), 77(9.7).

4-(3,5-dimethylphenyl)-4-methyloxazolidin-2-one (19)



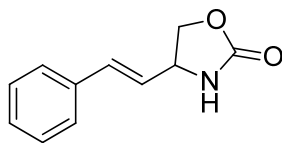
Yield (83%), R_f = 0.39 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.95-6.93 (m, 3H), 6.82 (s, 1H), 4.35(d, 1H, J = 7.1Hz), 4.32(d, 1H, J = 7.1Hz), 2.31(s, 6H), 1.70 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.5, 143.5, 138.5, 129.3, 122.3, 78.0, 60.4, 27.9, 21.4; GC-MS m/z (% relative intensity): 205(8.7), 190(100), 160(7.2), 147(38.4), 132(33), 119(84), 105(15.6), 91(27.8).

4-phenyloxazolidin-2-one (20)



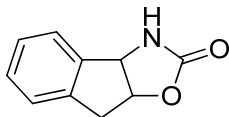
Yield (70%), R_f = 0.40 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.40-7.25 (m, 5H), 6.20 (s, 1H), 4.96-4.92 (t, 1H, J = 7.1 Hz), 4.18-4.14 (dd, 1H, J_1 = 7.2, J_2 = 8.4 Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.8, 139.5, 129.6, 128.7, 126.0, 72.5, 56.2; GC-MS m/z (% relative intensity): 163(50.4), 133(80.1), 105(85.2), 104(100), 91(26.5), 78(17.2).

(E)-4-styryloxazolidin-2-one (21)



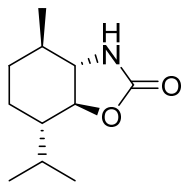
Yield (67%), R_f = 0.43 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36-7.26 (m, 5H), 6.60 (d, 1H, J = 14.1 Hz), 6.15-6.10 (m, 1H), 5.82 (s, 1H), 4.61-4.57 (m, 2H), 4.14 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.5, 135.3, 133.9, 128.7, 128.5, 126.6, 126.3, 70.2, 55.1; GC-MS m/z (% relative intensity): 190(3.3), 189(24.5), 159(3.2), 144(37.3), 130(100), 115(21.8), 104(20.6), 91(15).

3,3a,8,8a-tetrahydro-2H-indeno[1,2-d]oxazol-2-one (22)



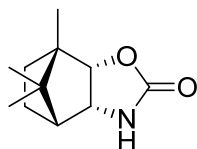
Yield (82%), $R_f = 0.42$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.28-7.22 (m, 5H), 6.91 (s, 1H), 5.41-5.38 (m, 1H), 5.16 (d, 1H, $J = 7.2$ Hz), 3.42-3.29 (m, 2 H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.7, 140.2, 139.7, 129.3, 127.9, 125.5, 124.8, 80.6, 61.2, 38.8; GC-MS m/z (% relative intensity): 175(100), 146(25.3), 131(95.6), 104(85.2), 78(24.7).

(3aS,4R,7S,7aS)-7-isopropyl-4-methylhexahydrobenzo[d]oxazol-2(3H)-one (25)



Yield (24%), $R_f = 0.26$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.31 (s, 1H), 3.80 (t, 1H, $J = 11.2$ Hz), 3.02 (t, 1H, $J = 11.1$ Hz), 1.88-1.69 (m, 4H), 1.59-1.22 (m, 1H), 0.99 (m, 11H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.9, 85.1, 66.7, 45.4, 35.5, 32.5, 28.9, 25.7, 19.6, 18.5, 18.4; GC-MS m/z (% relative intensity): 154(100), 140(137.4), 110(46.5), 93(24.2), 69(41.7), 55(12.4).

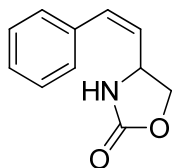
(3aR,4R,7S,7aS)-7,8,8-trimethylhexahydro-4,7-methanobenzo[d]oxazol-2(3H)-one (26) was synthesized by pyrolysis of carbonazidate **24** in tetrachloroethane at 130 °C for 1h followed by purification on flash column chromatography.⁷



Yield (31%), $R_f = 0.27$ (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.04 (s, 1H), 4.59 (d, 1H, $J = 7.2$ Hz), 4.18-4.14 (m, 1H), 1.87-1.85 (m, 1H), 1.73-1.68 (m, 1H), 1.61-1.55 (m, 2H), 1.35-1.29 (m, 1H), 0.94 (s, 6H), 0.90 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.6, 85.8, 54.9, 49.2, 48.5, 26.5, 20.1,

19.8, 17.9, 14.1; GC-MS m/z (% relative intensity): 195(5.1), 164(4.9), 134(7.4), 125(7.3), 119(8.5), 109(39.2), 95(100), 83(11.9).

(Z)-4-styryloxazolidin-2-one (Z-21)

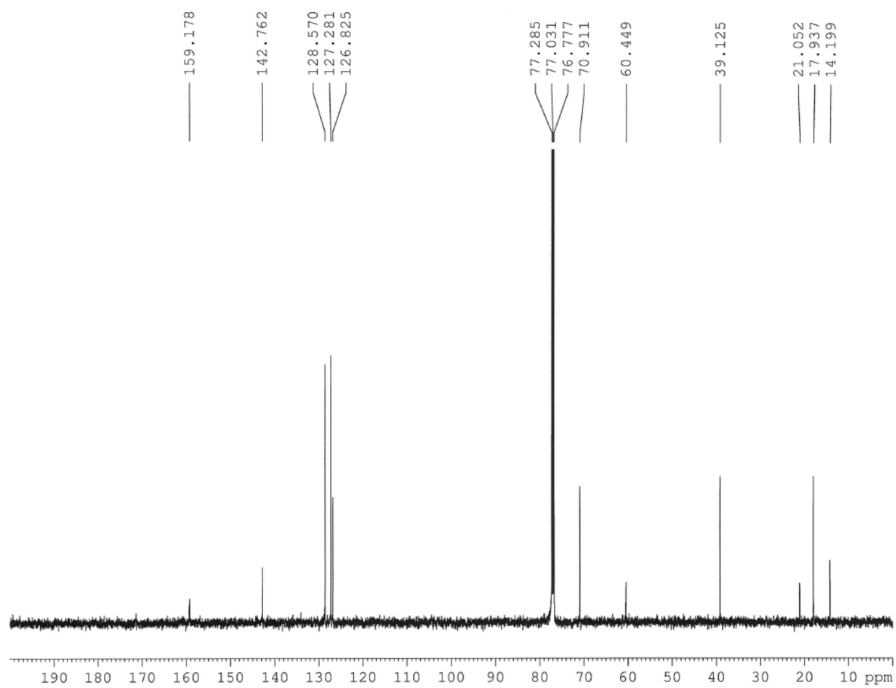
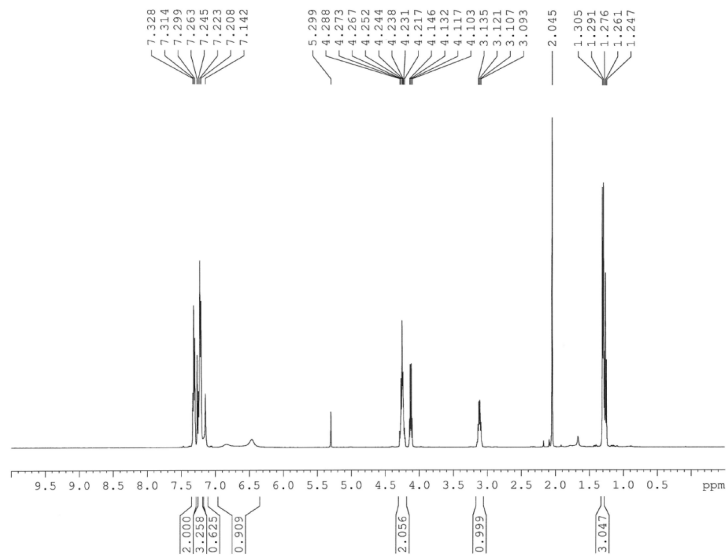


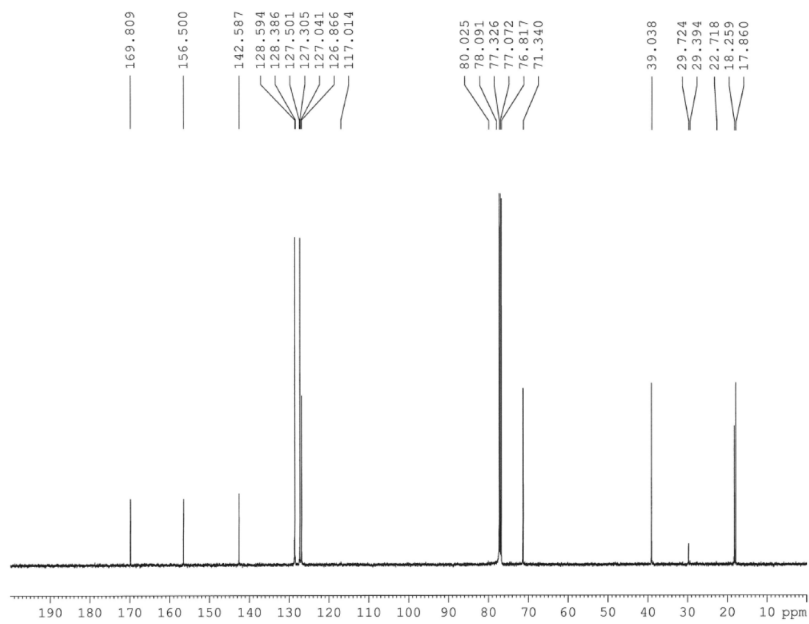
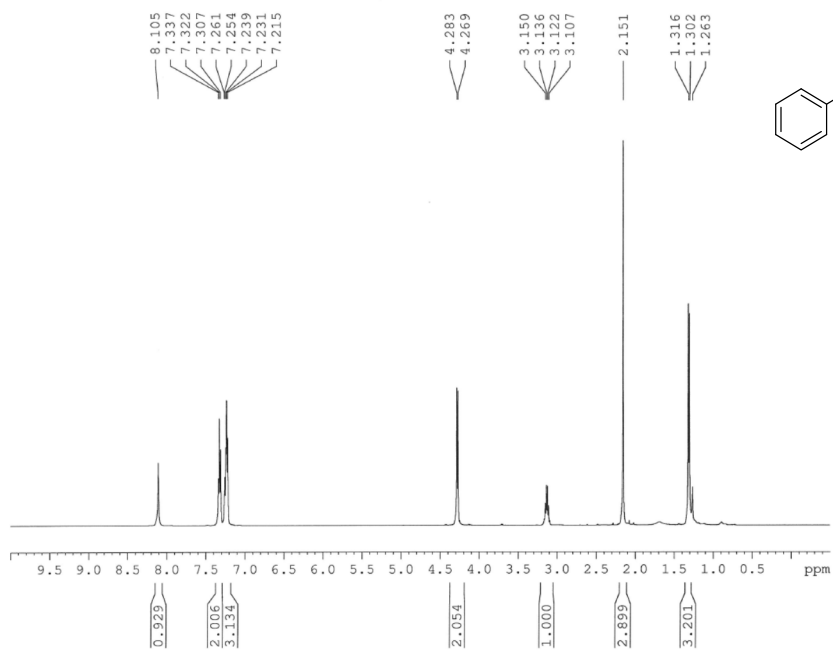
Yield (65%), R_f = 0.44 (30% EtOAc in hexane); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.37-7.11 (m, 5H), 6.72 (d, 1H, J = 12.1 Hz), 6.30 (s, 1H), 5.71-5.66 (m, 1H), 4.85-4.79 (m, 1H), 4.58-4.54 (m, 1H), 4.14-4.10 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 159.8, 135.3, 134.1, 129.3, 128.5, 128.3, 127.8, 70.3, 50.2; GC-MS m/z (% relative intensity): 190(3.3), 189(24.5), 159(3.2), 144(37.3), 130(100), 115(21.8), 104(20.6), 91(15).

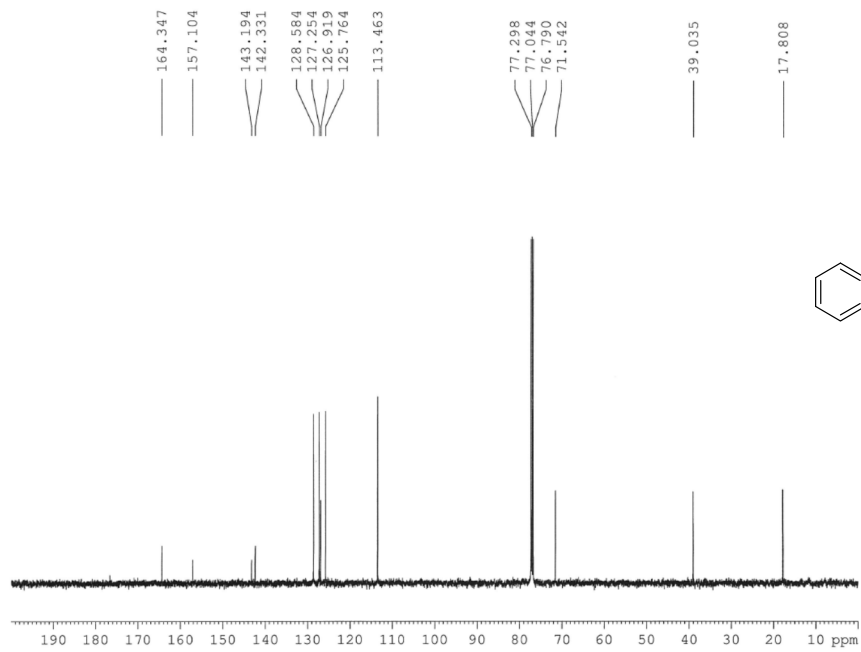
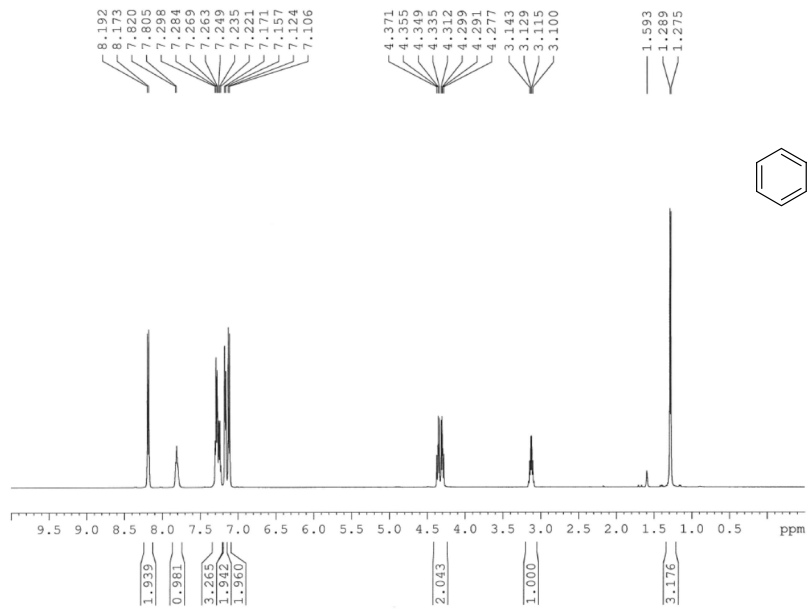
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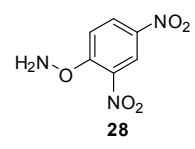
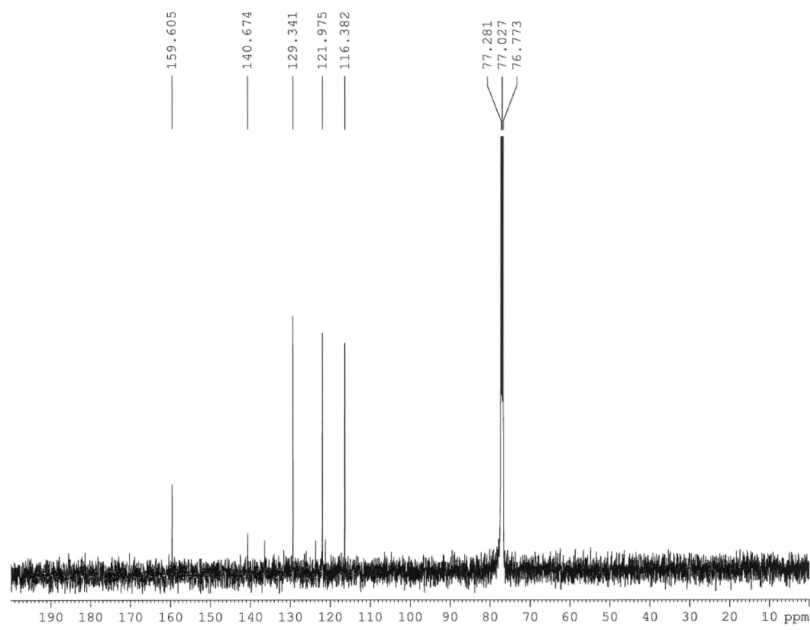
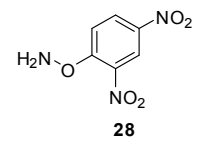
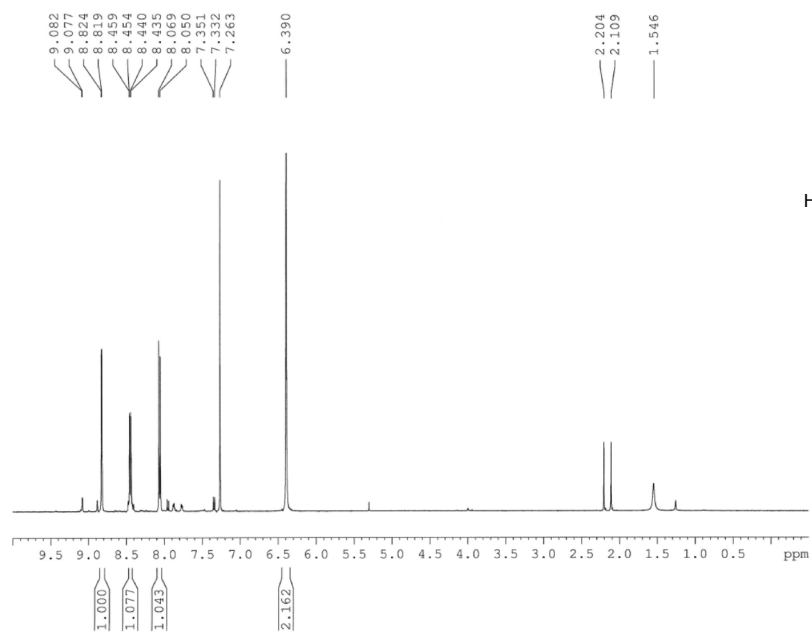
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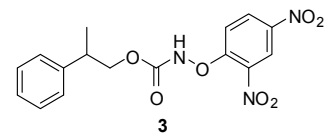
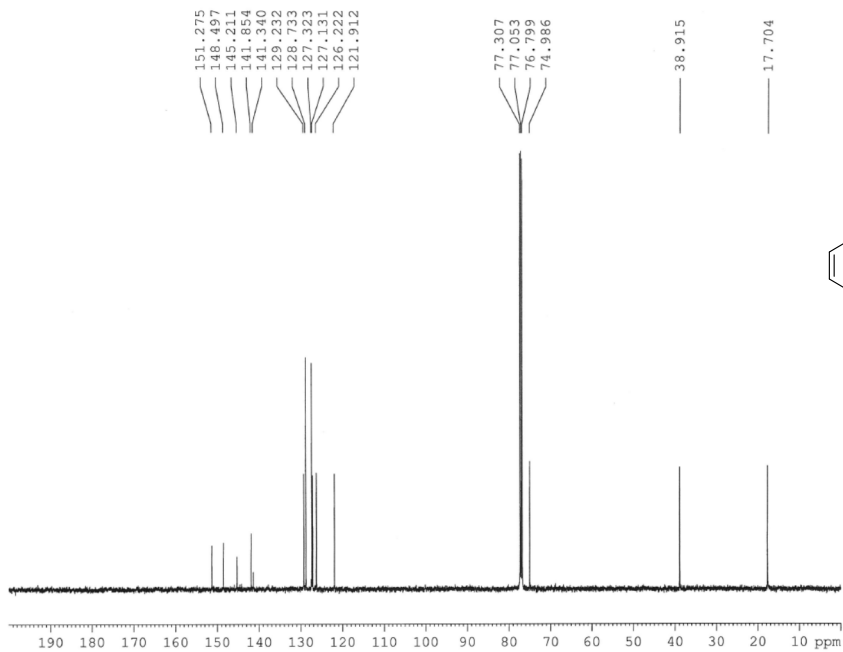
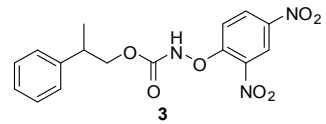
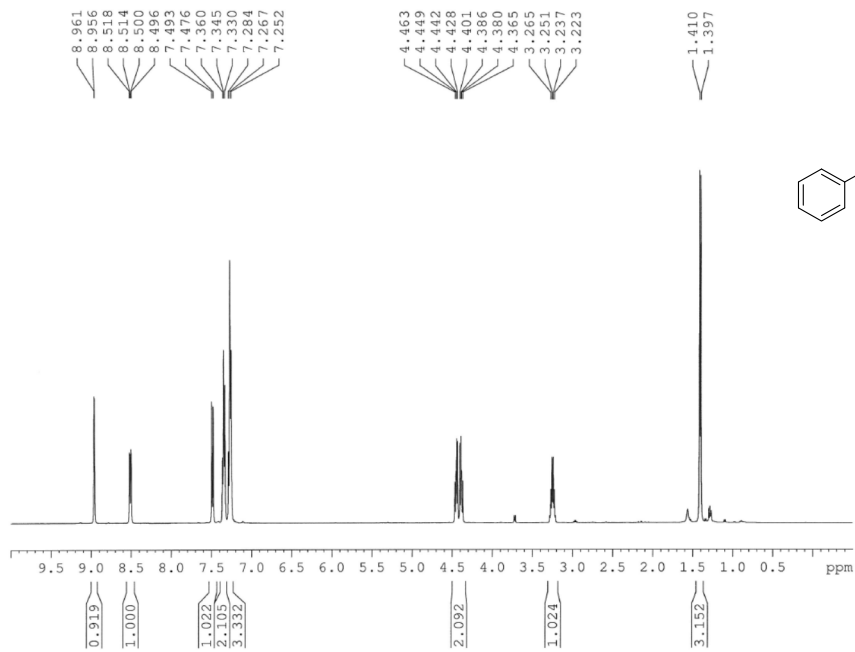
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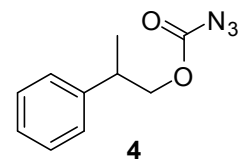
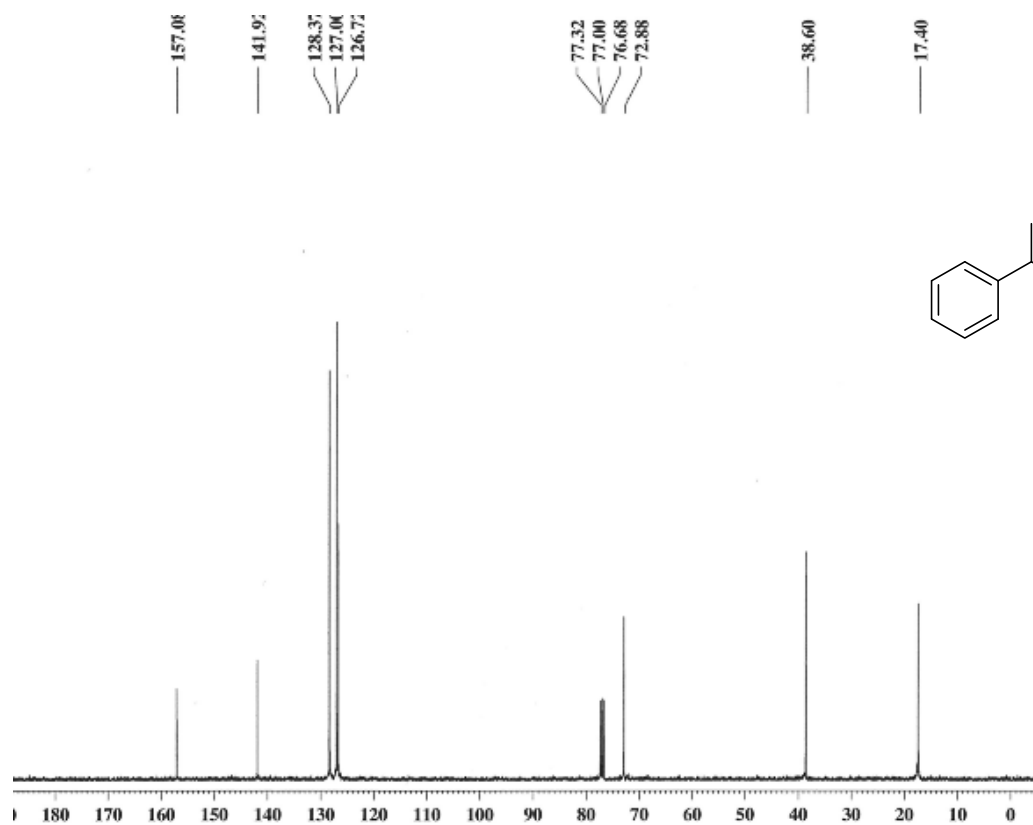
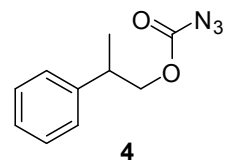
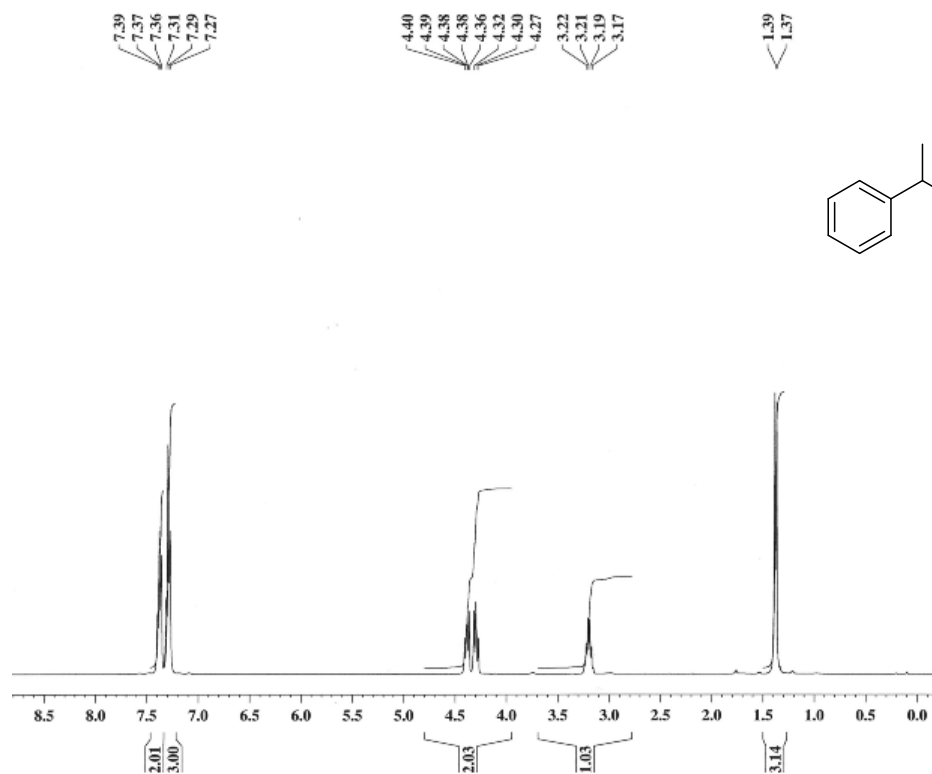


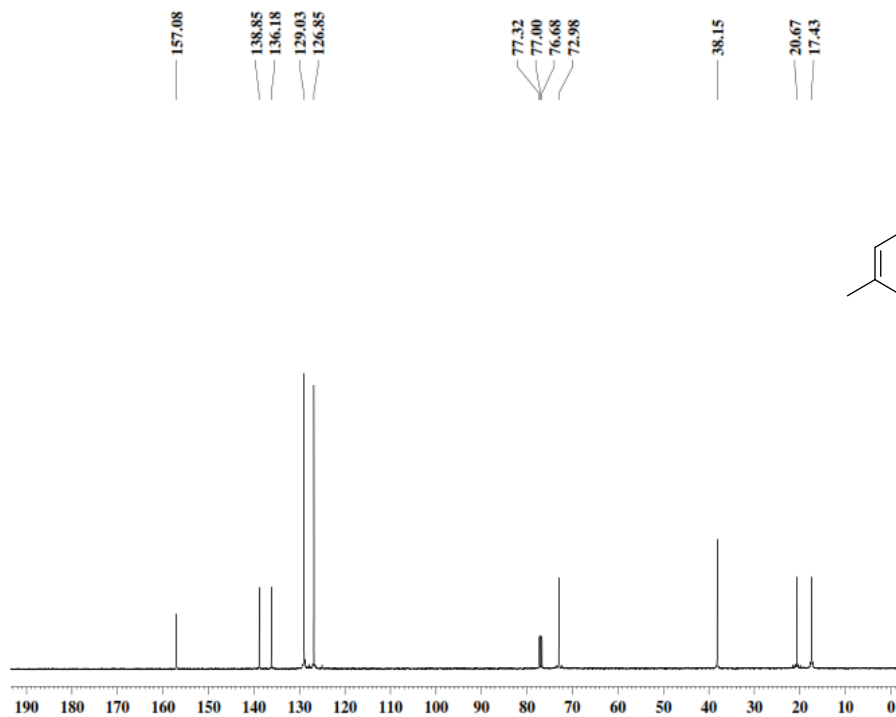
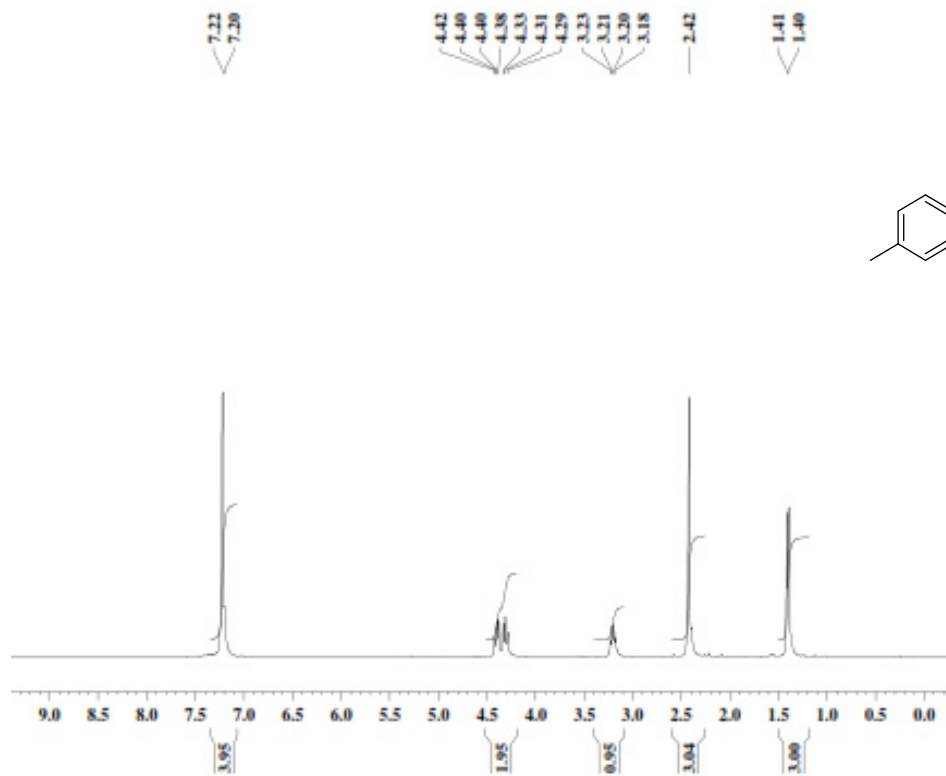


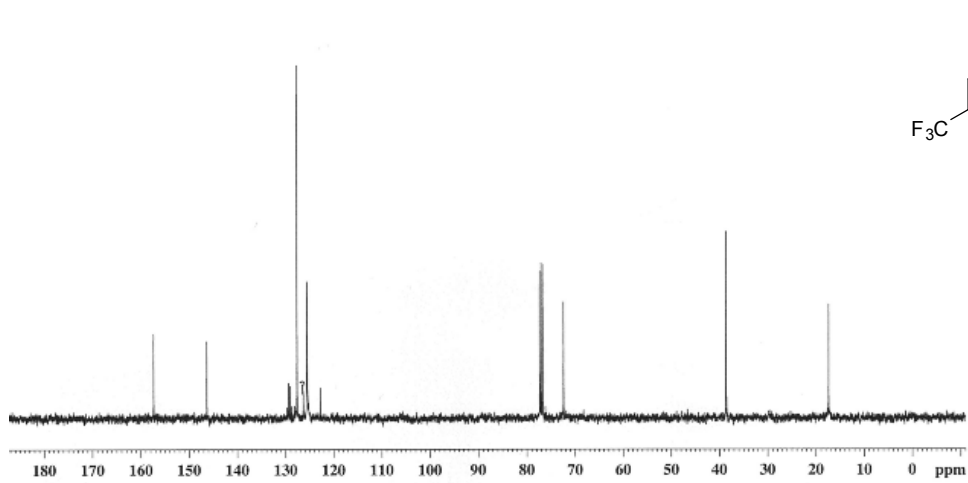
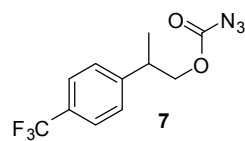
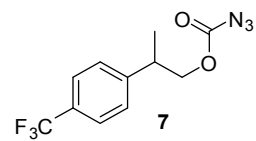
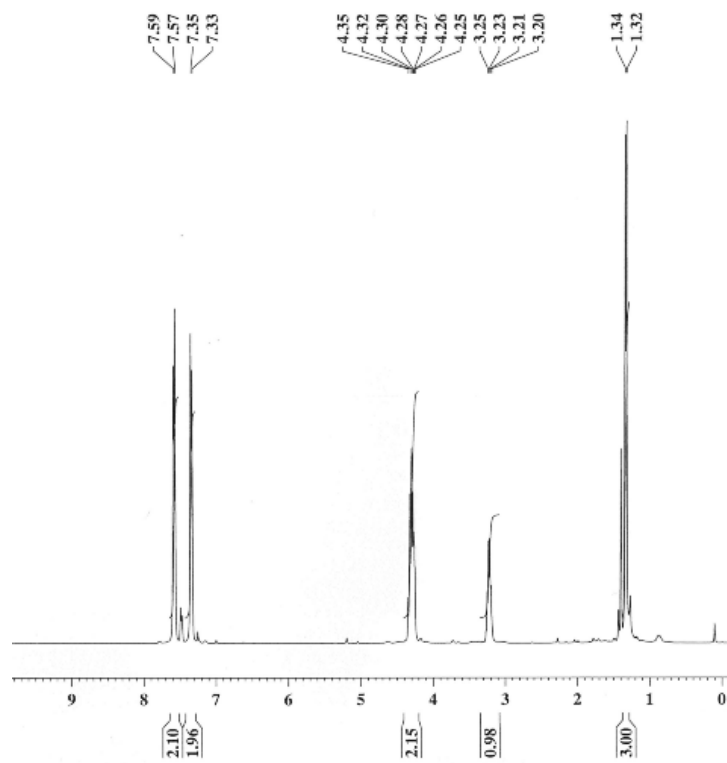


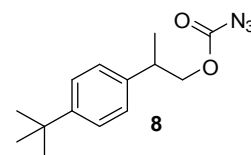
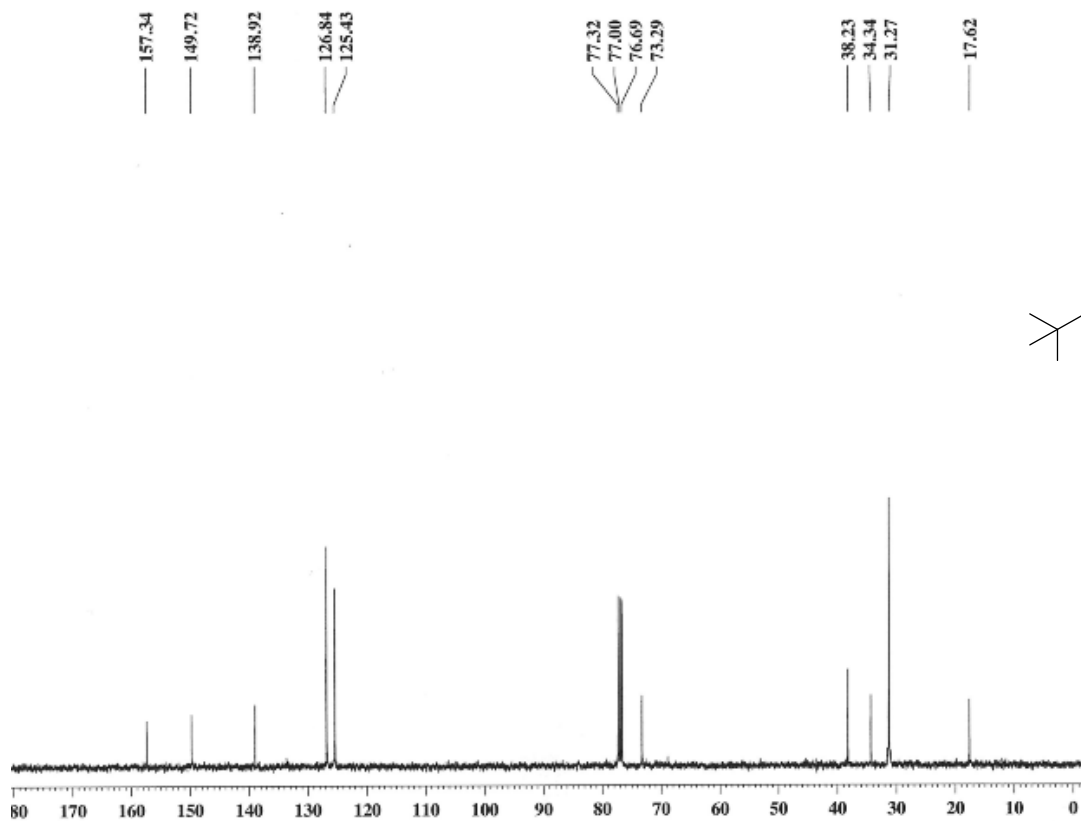
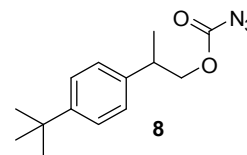
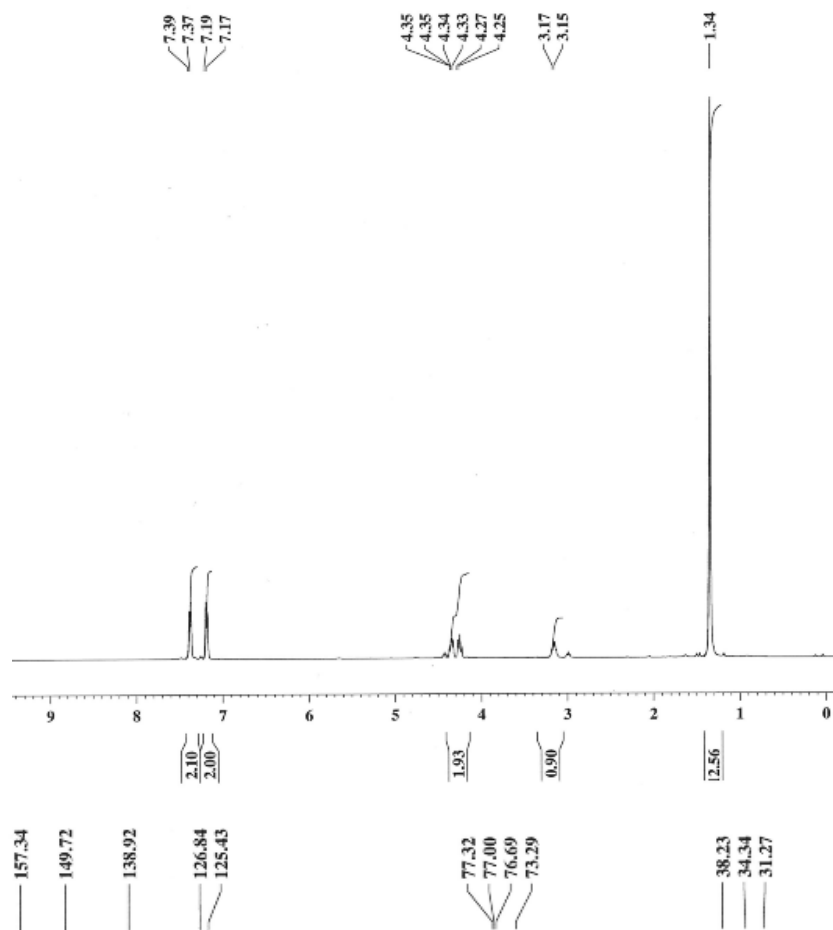


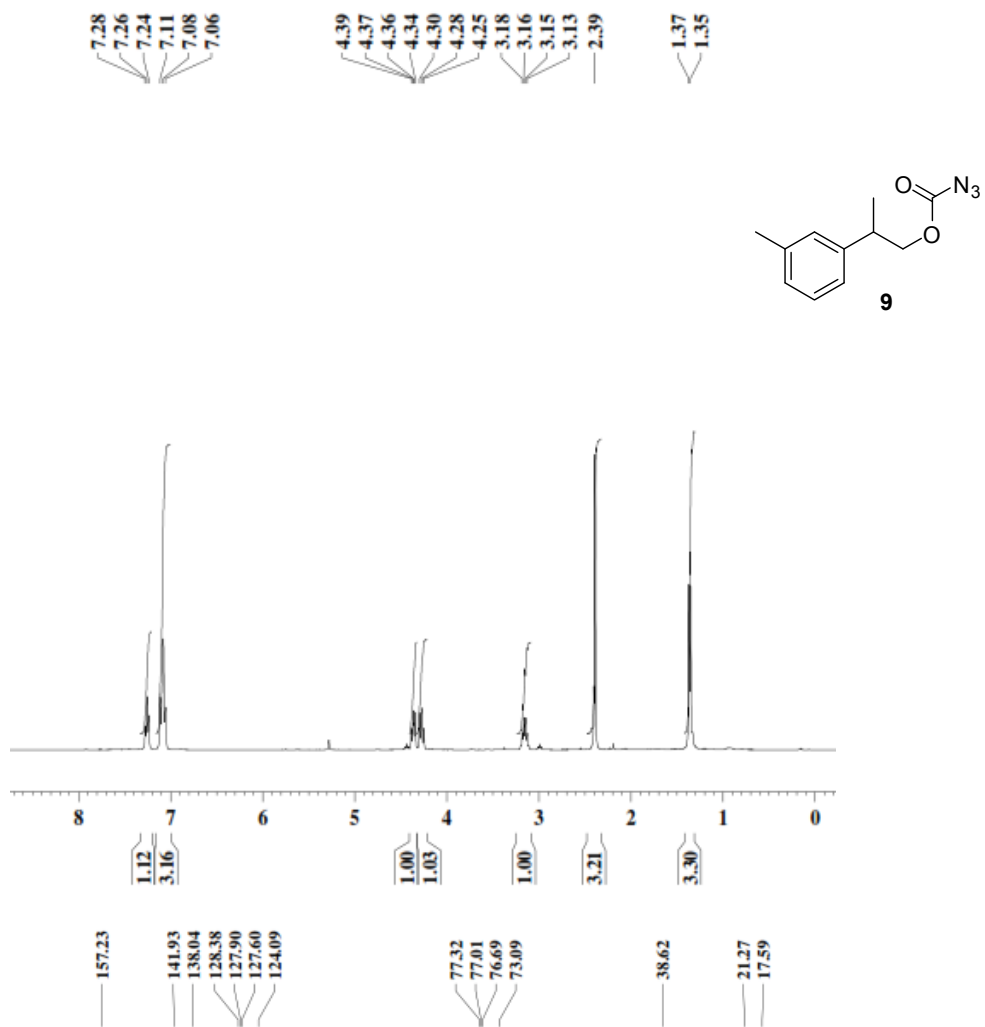


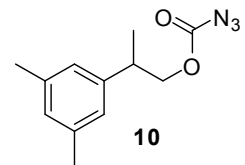
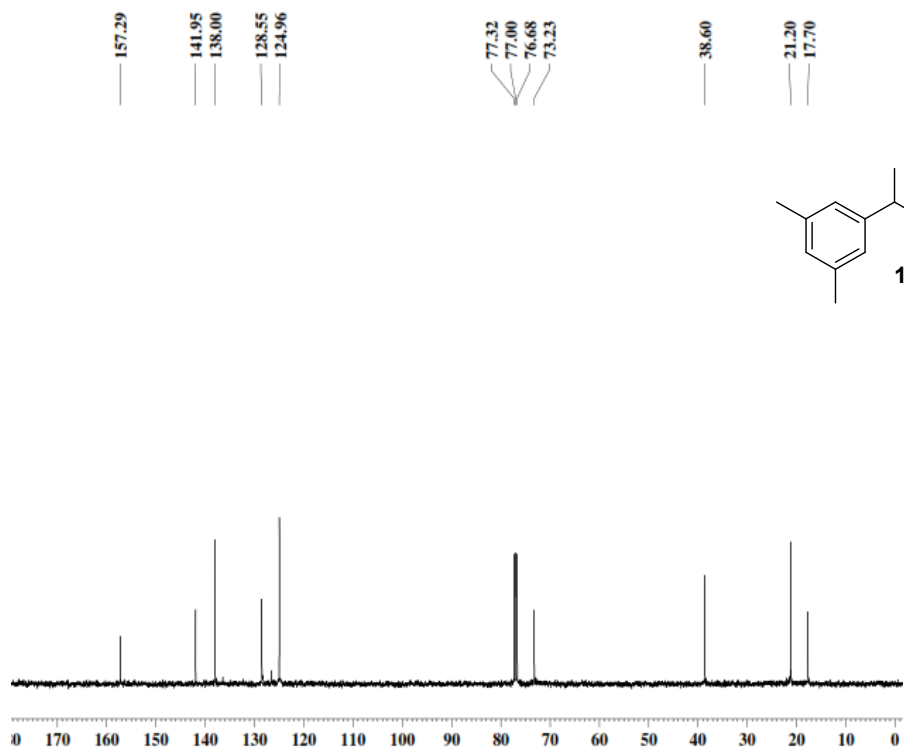
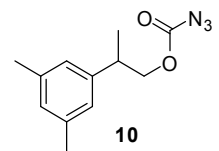
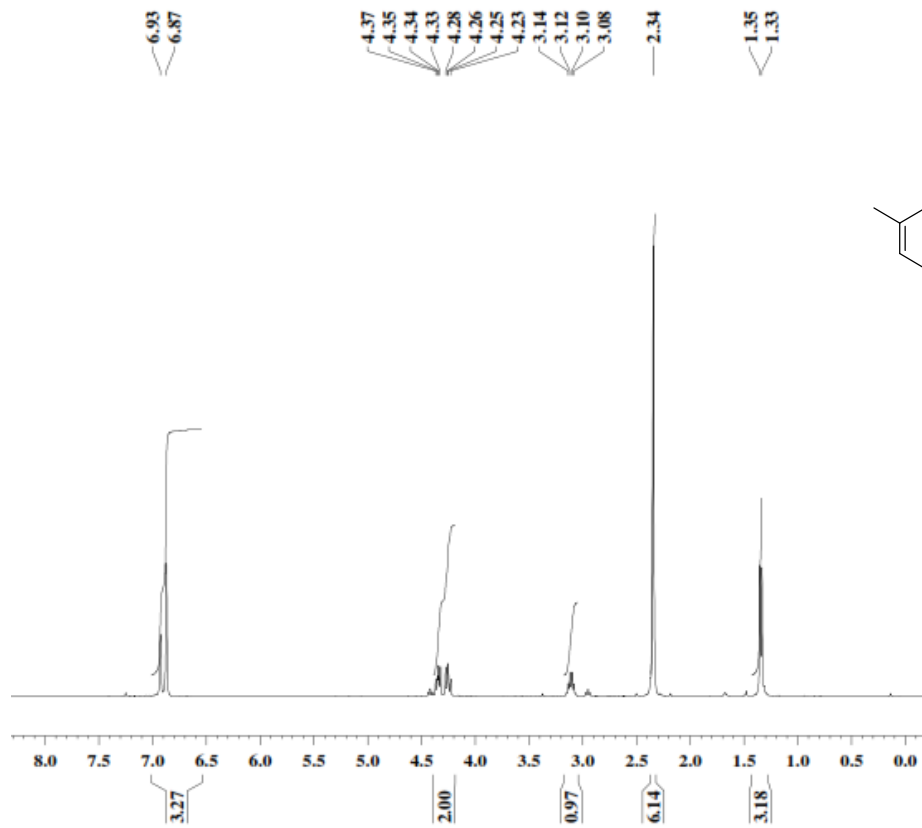








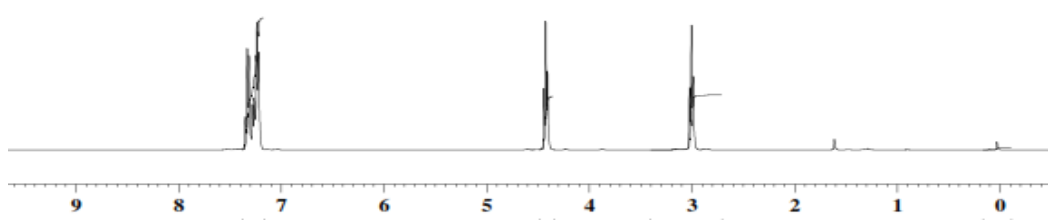
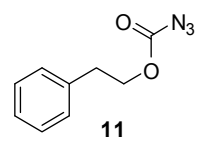




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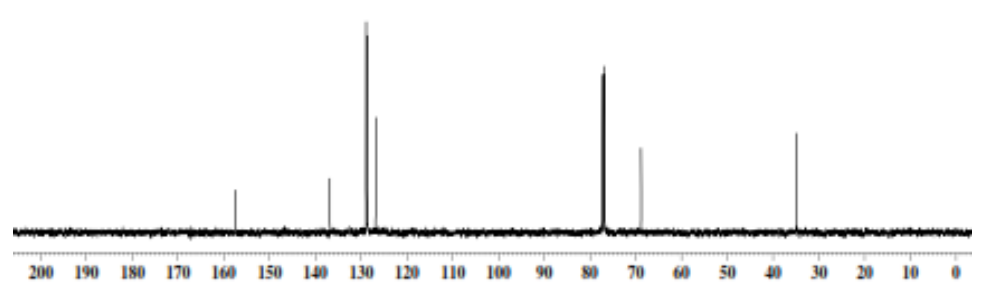
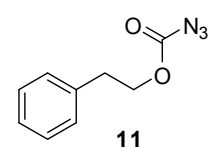


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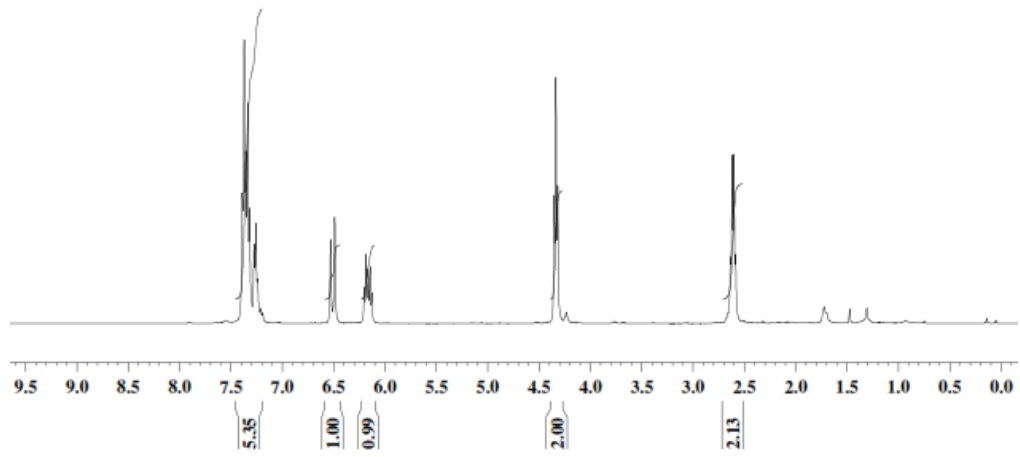
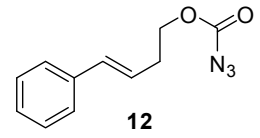
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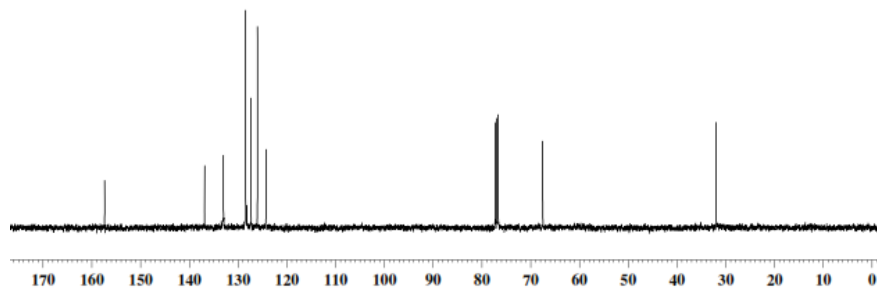
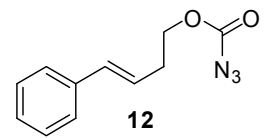
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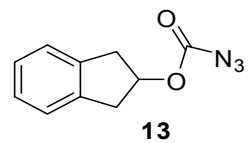
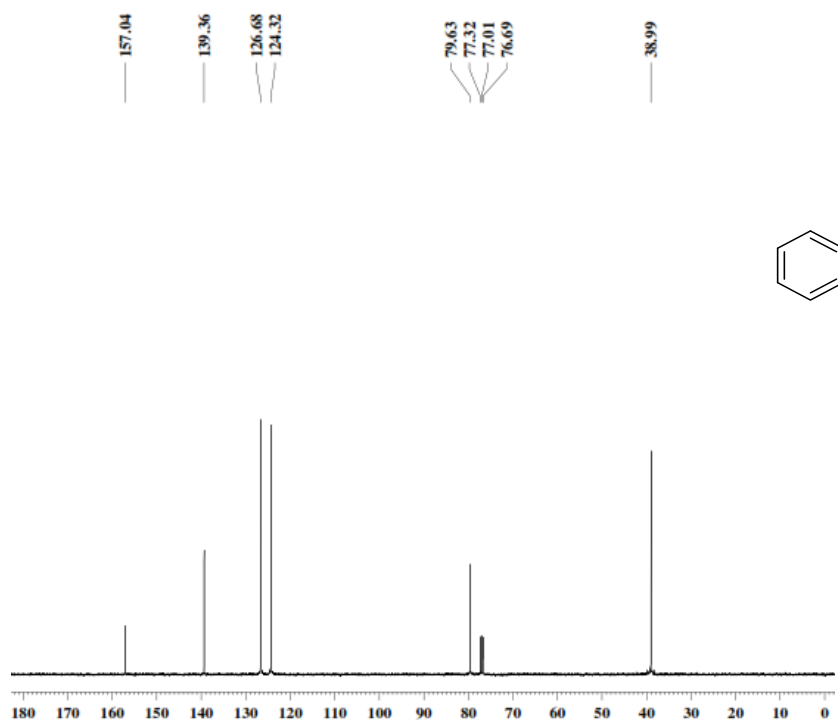
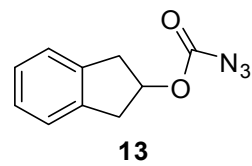
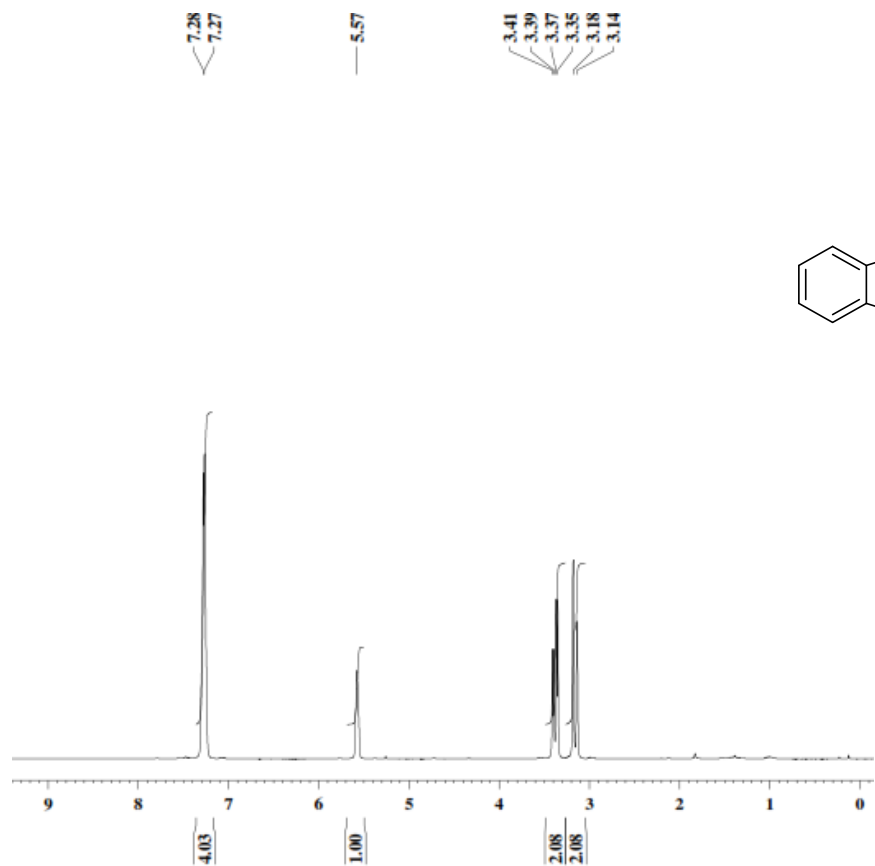


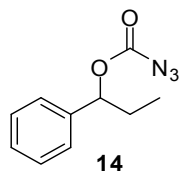
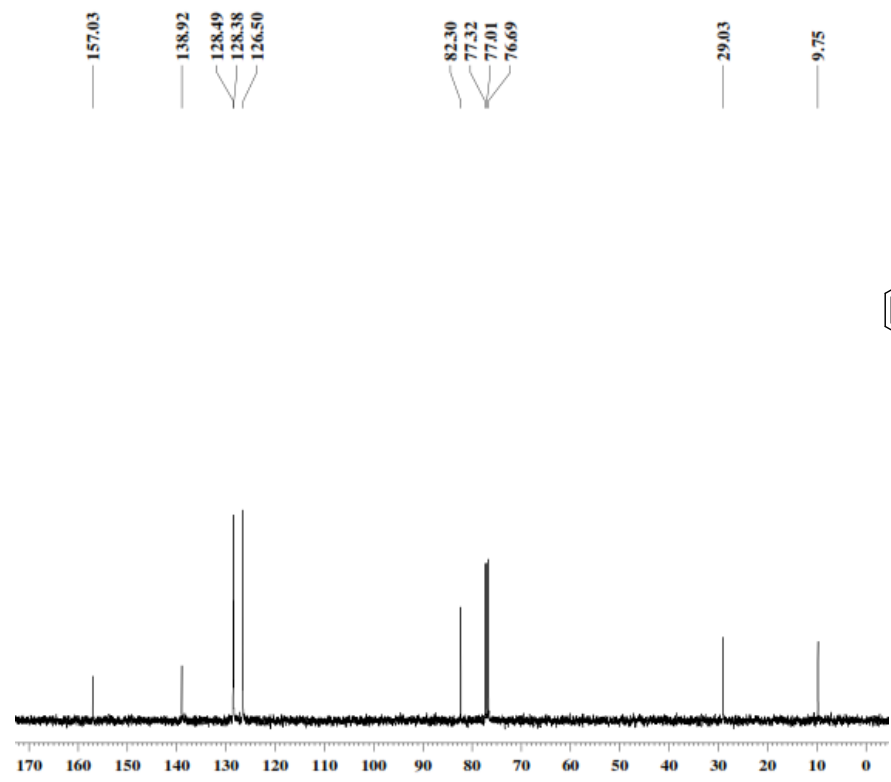
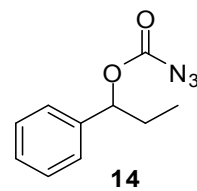
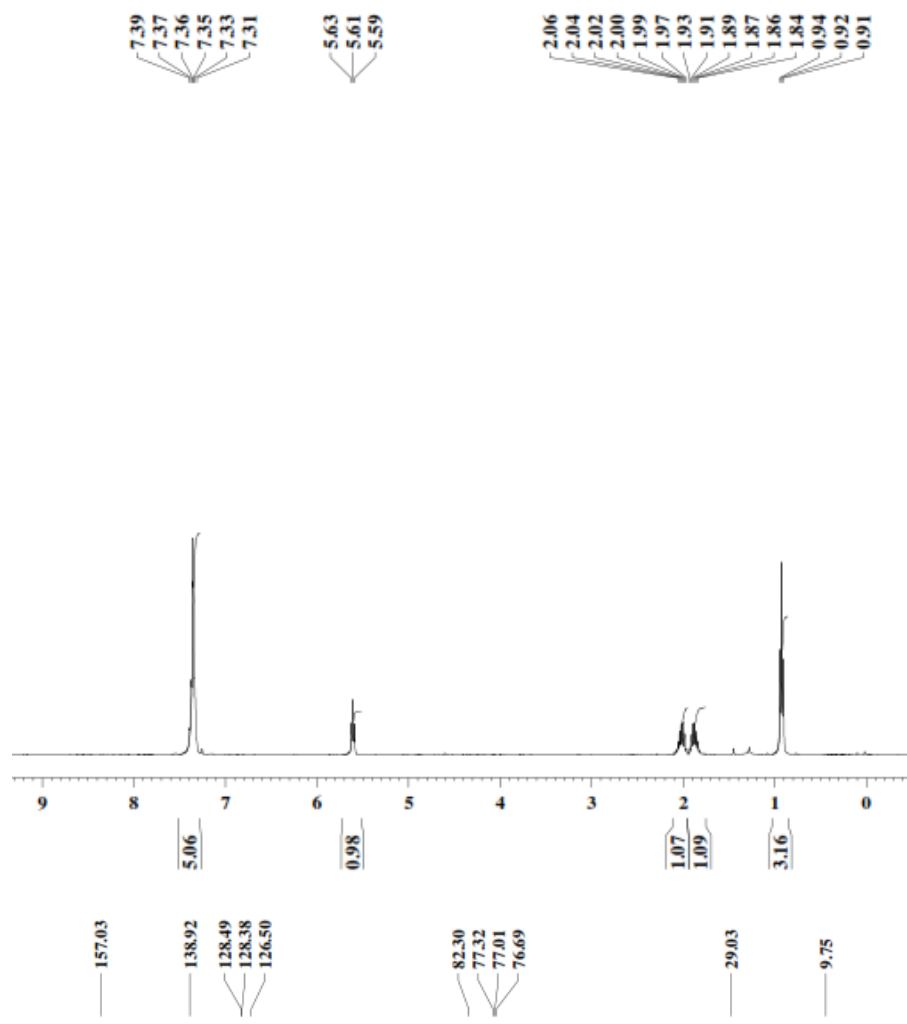
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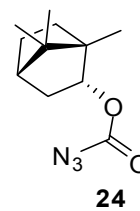
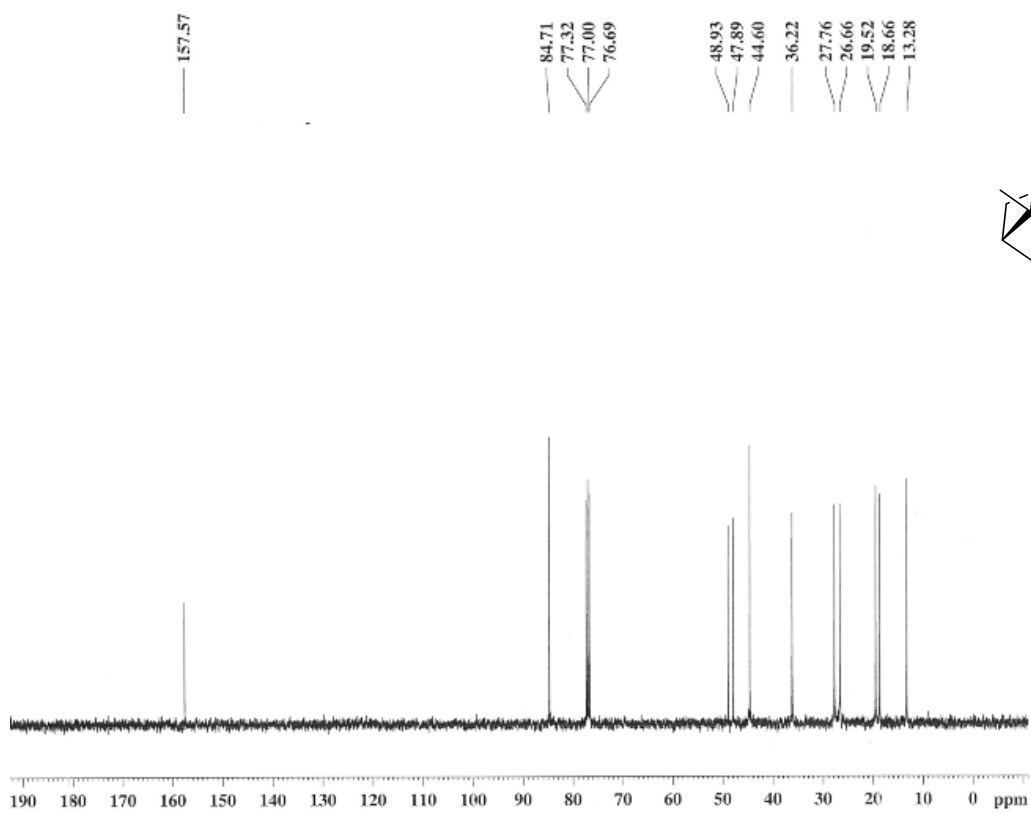
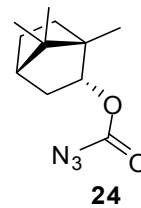
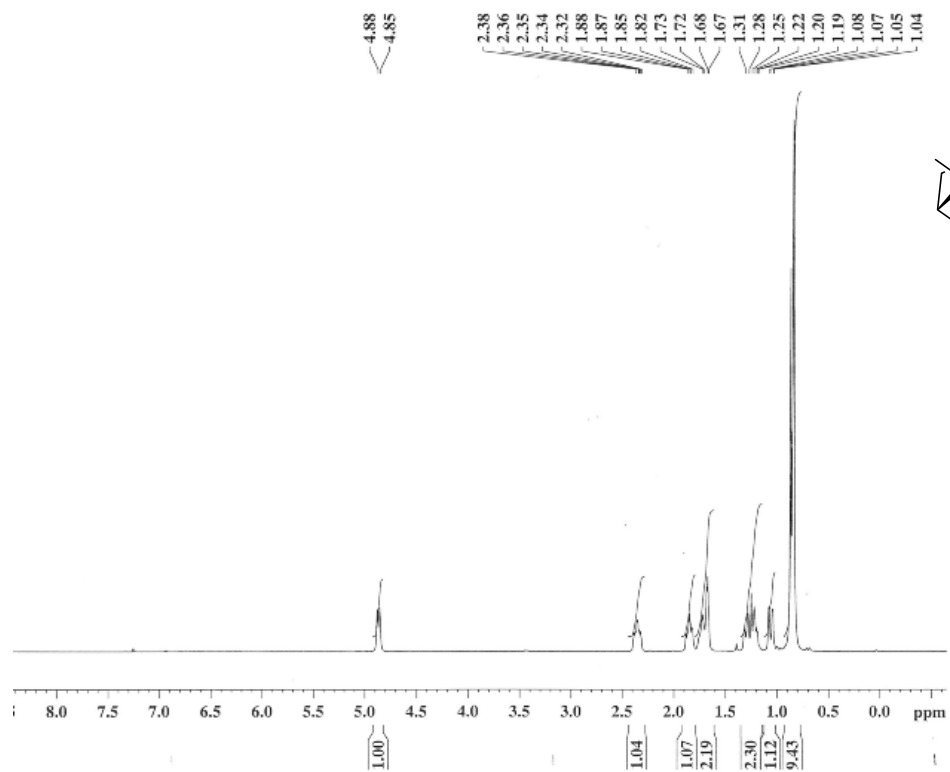


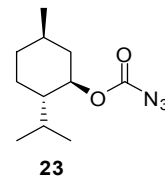
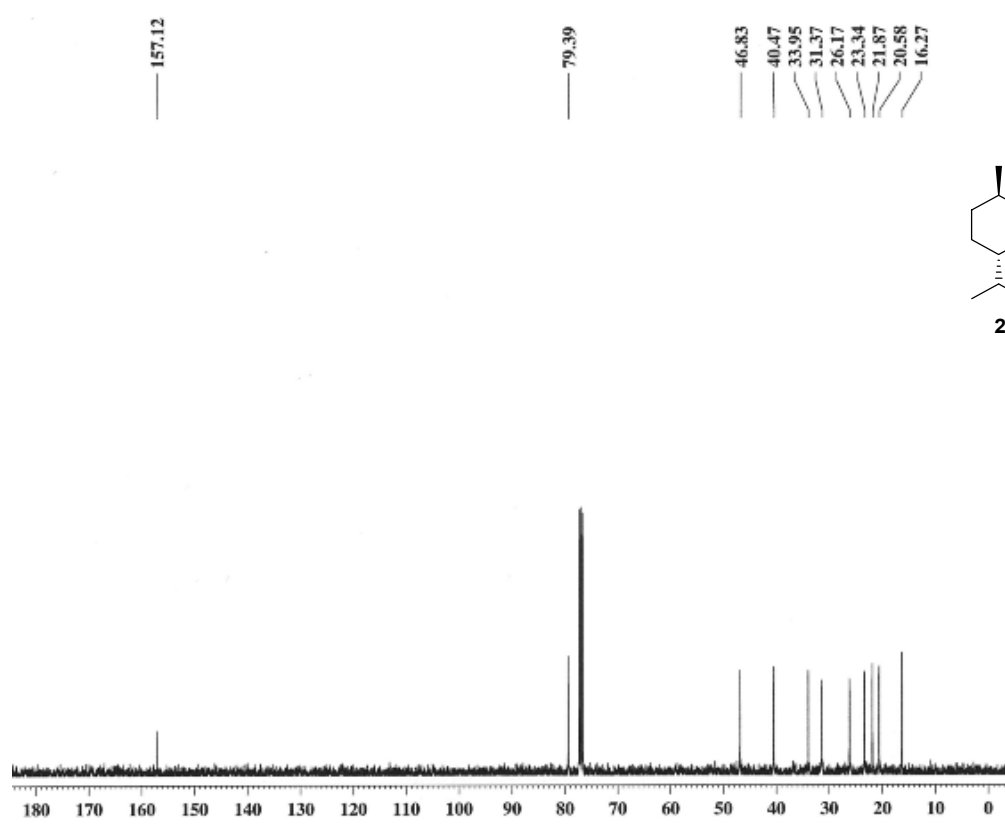
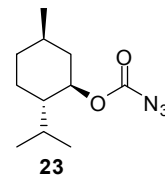
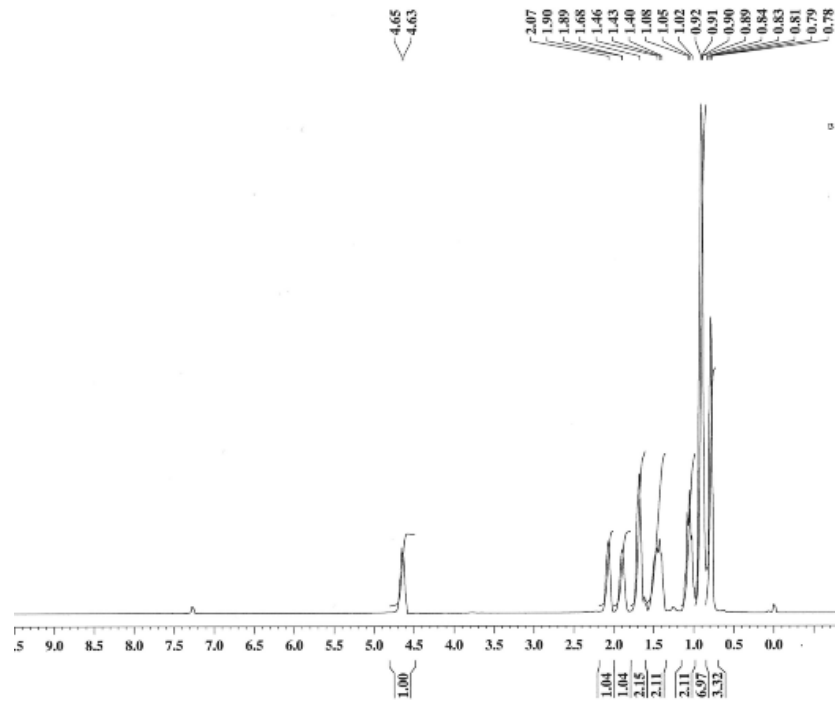
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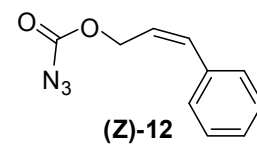
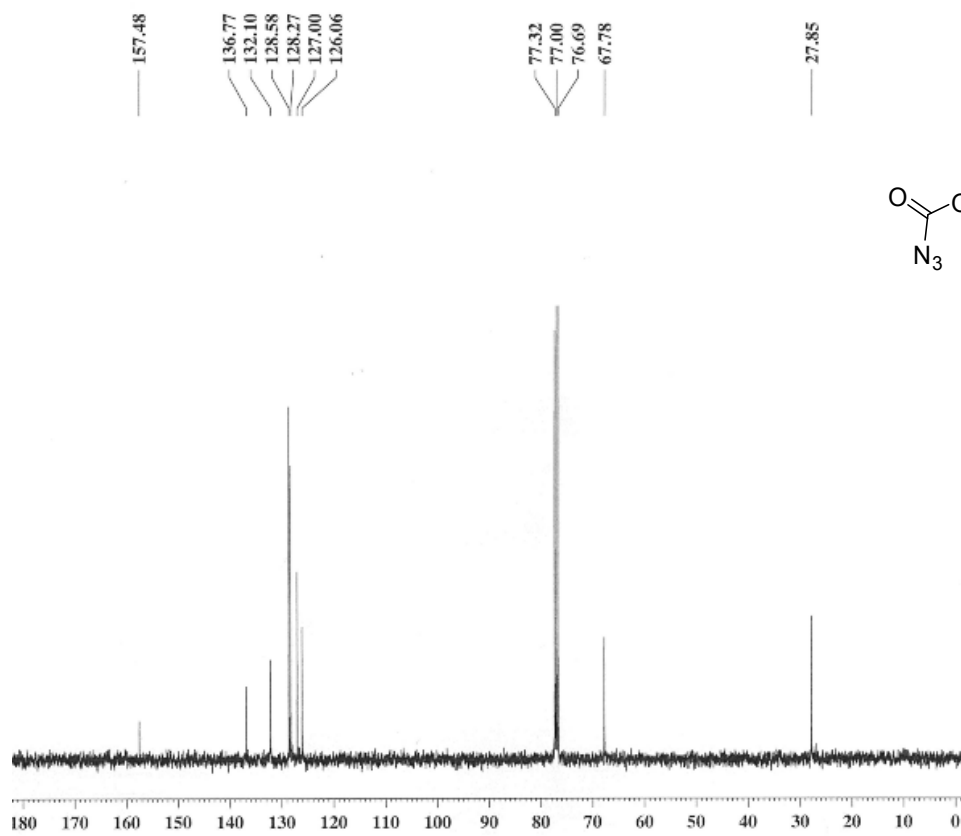
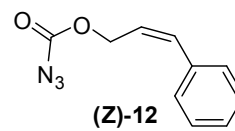
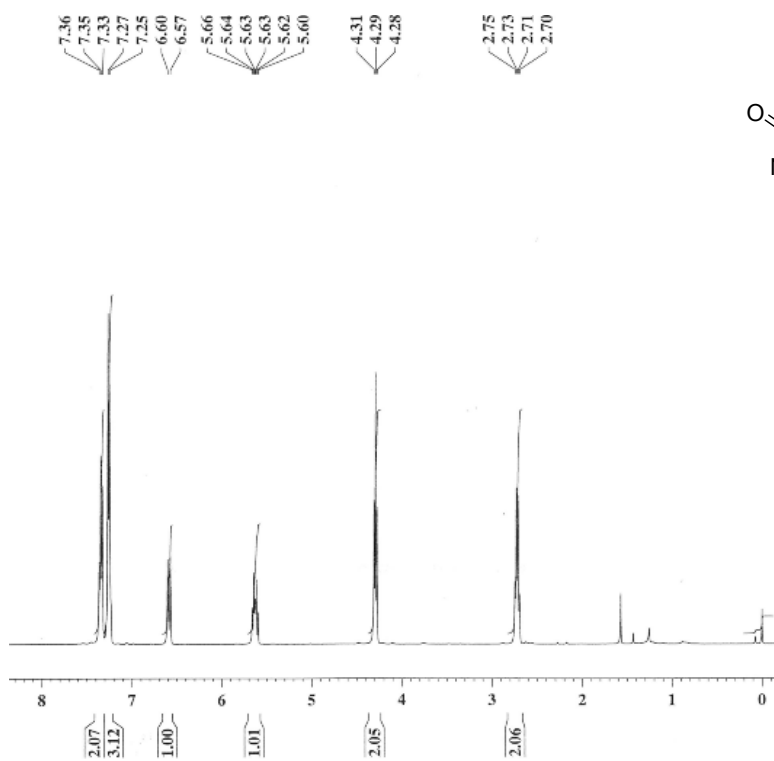


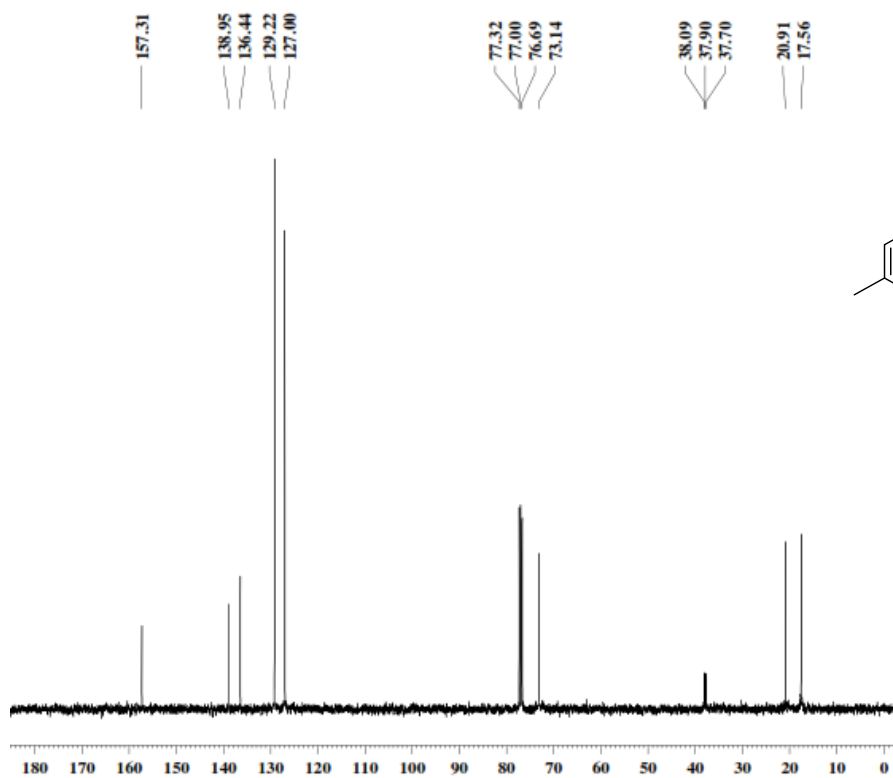
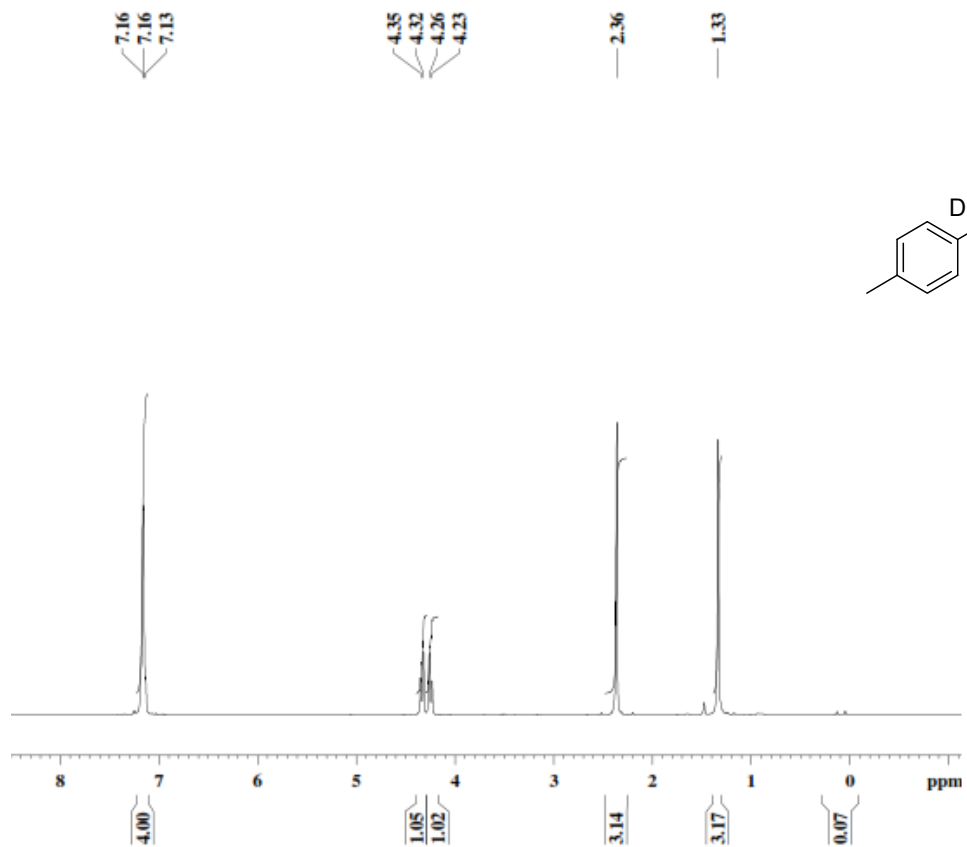


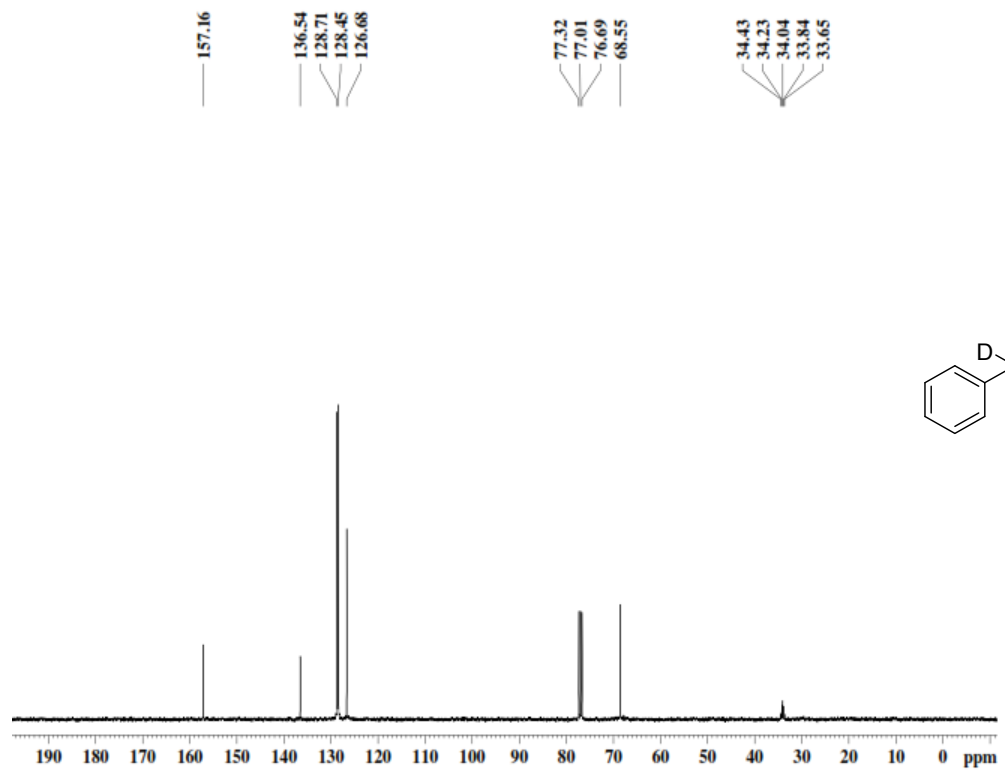
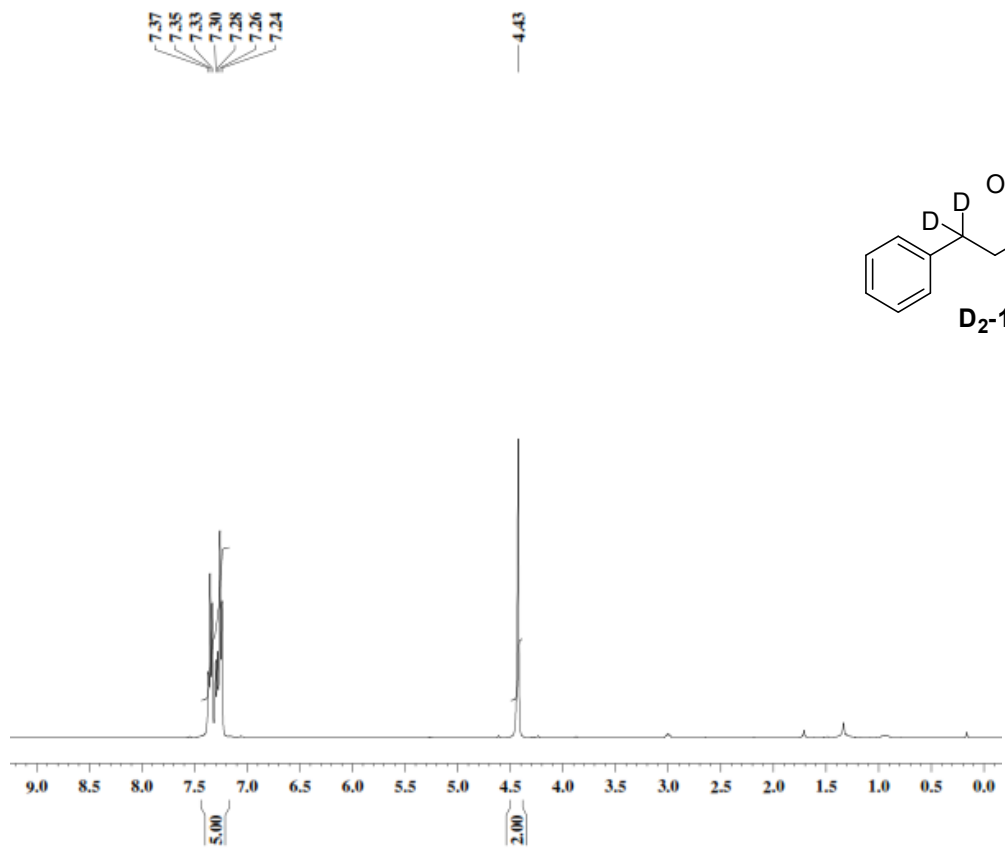








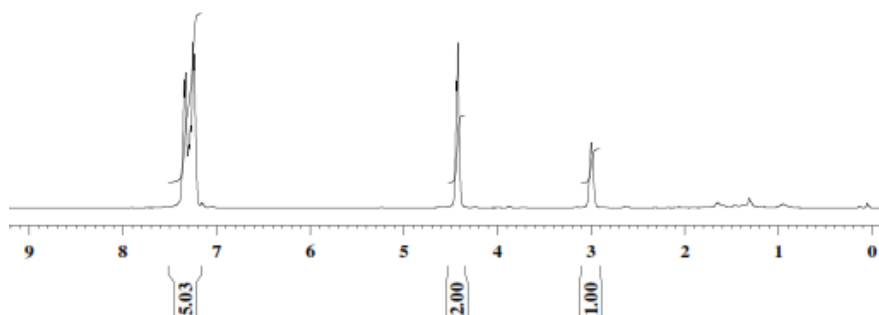
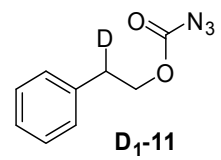




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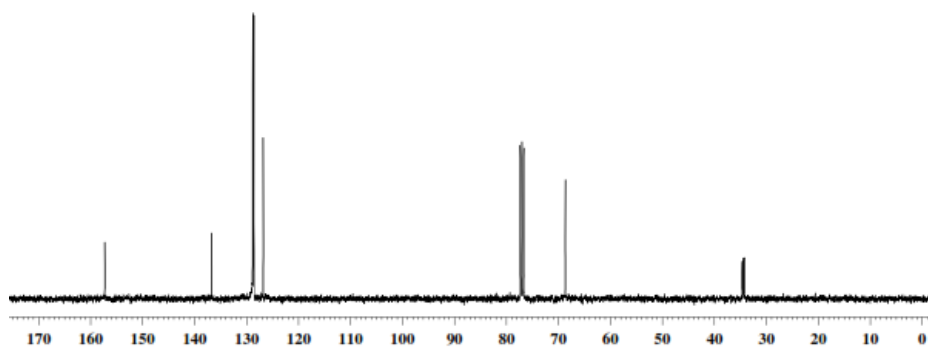
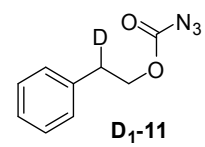


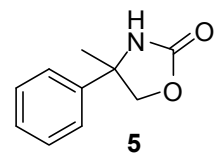
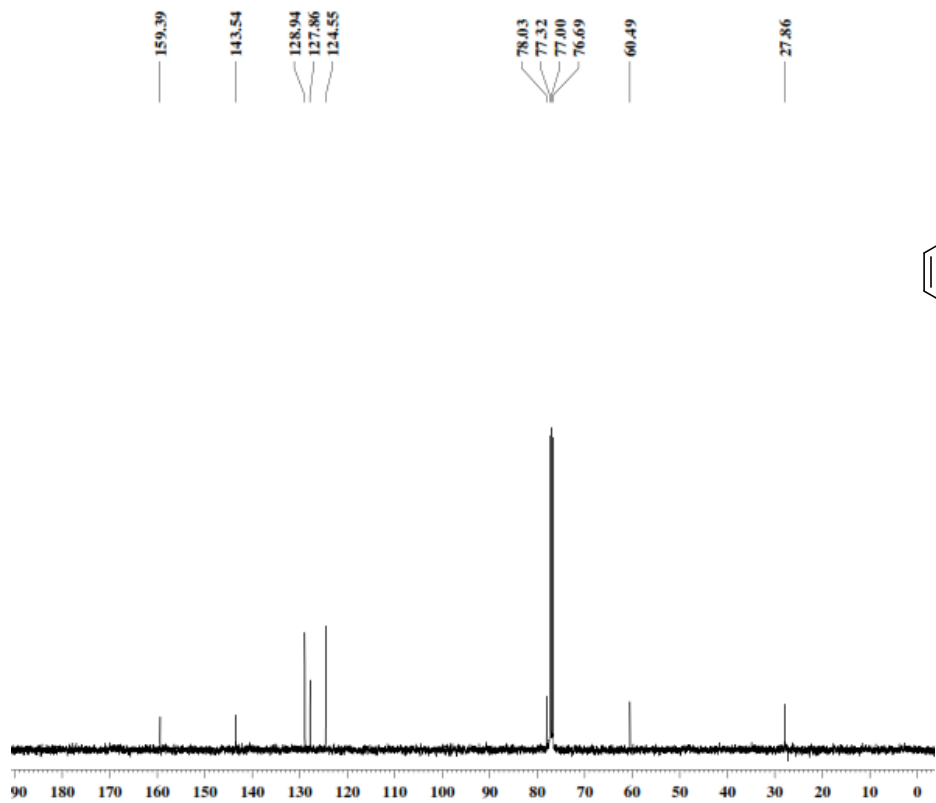
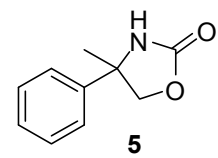
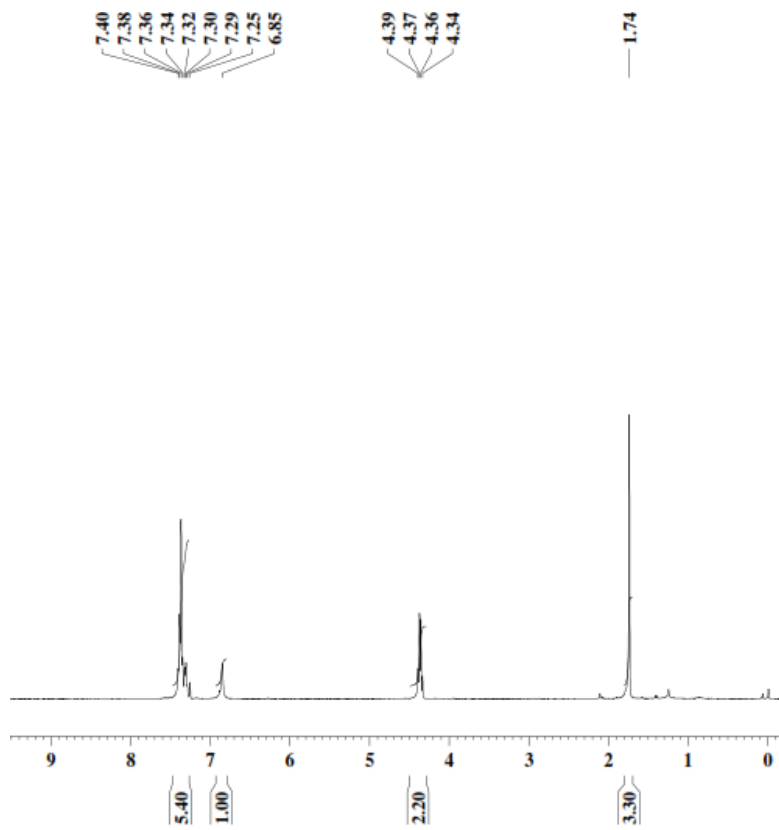
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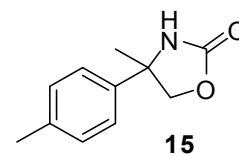
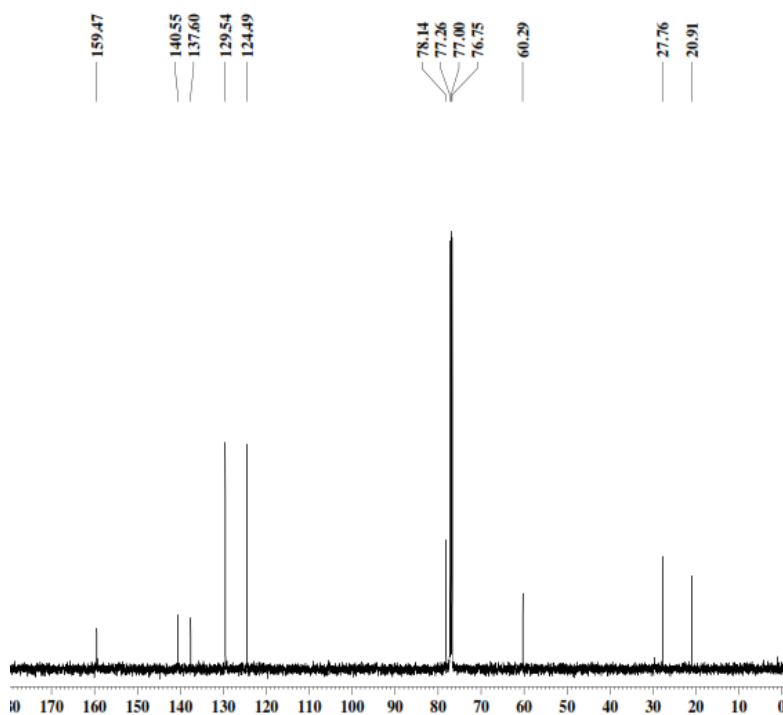
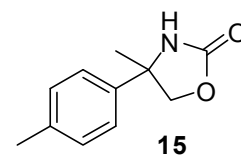
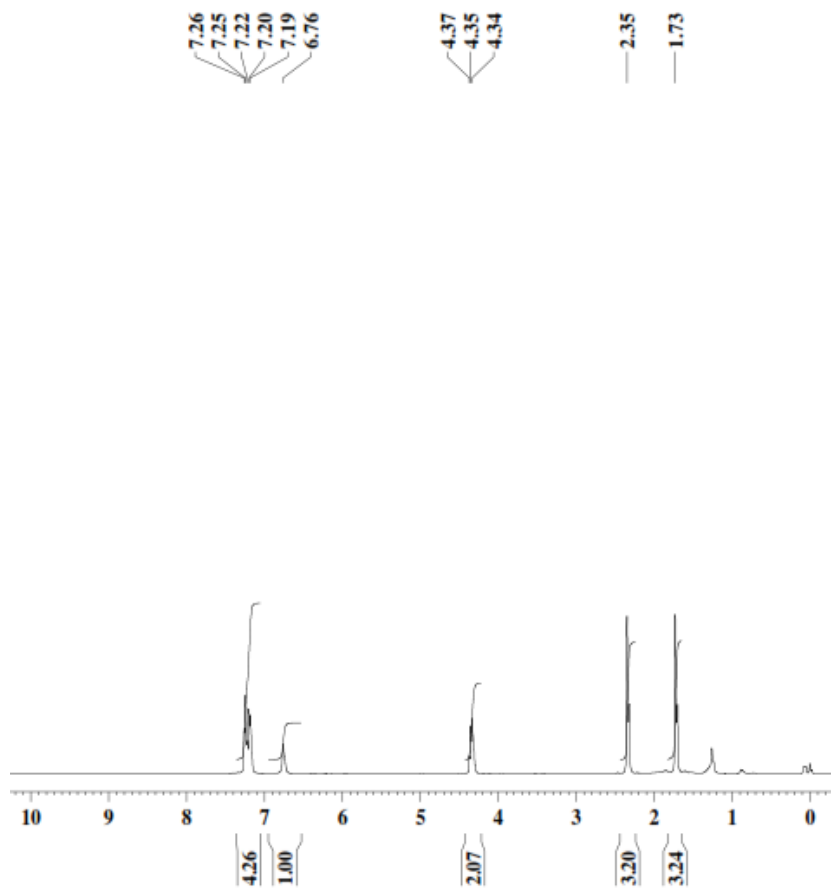
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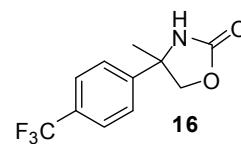
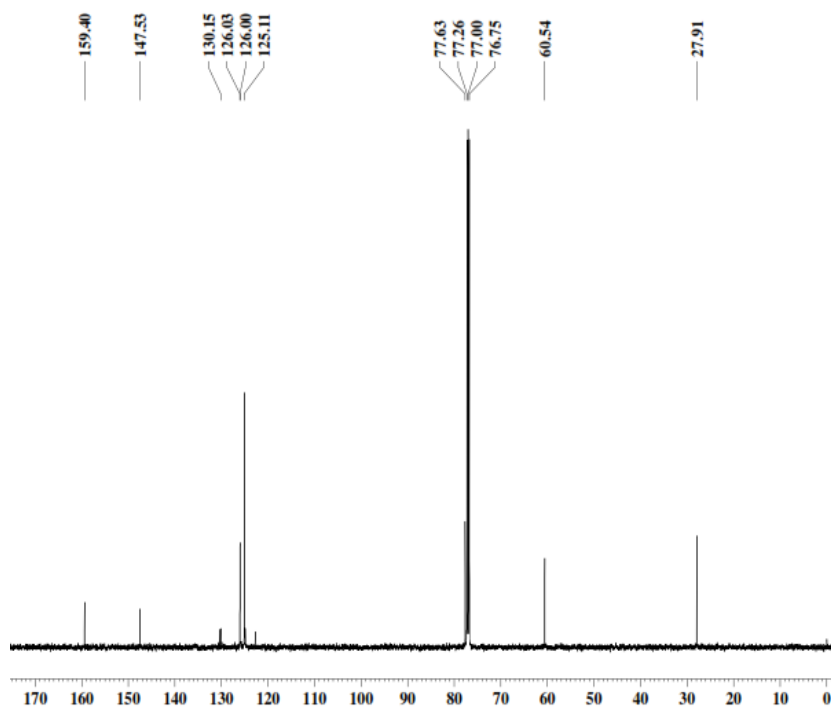
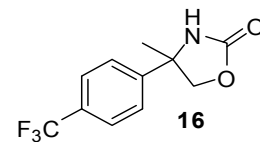
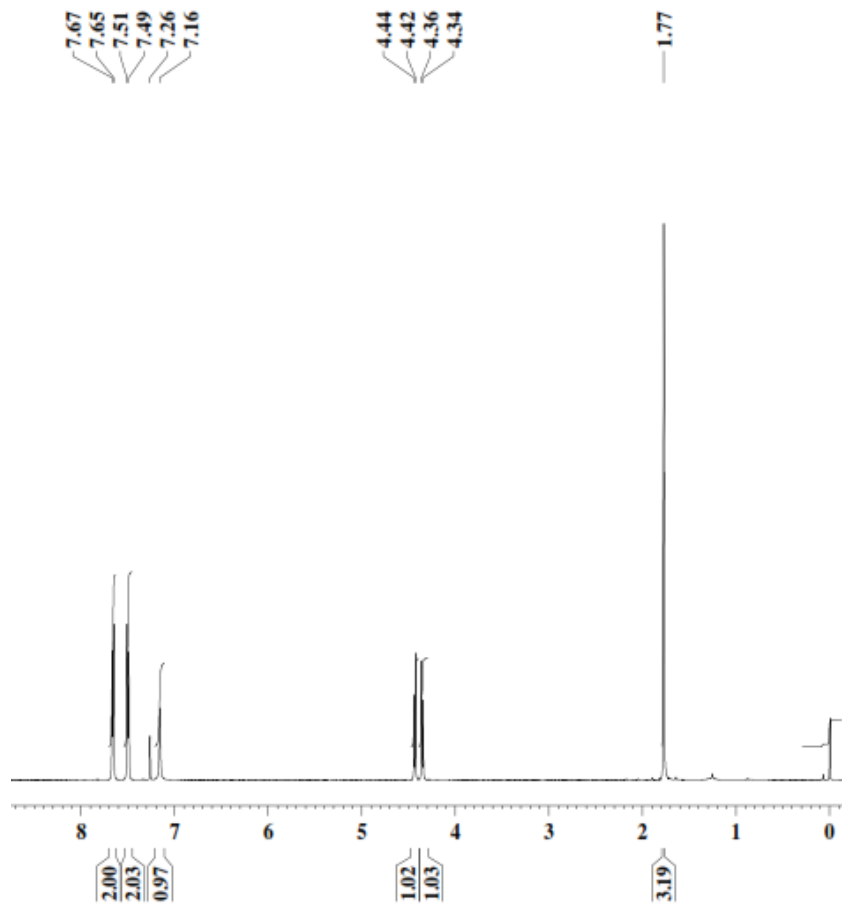
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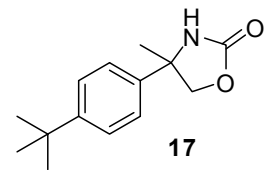
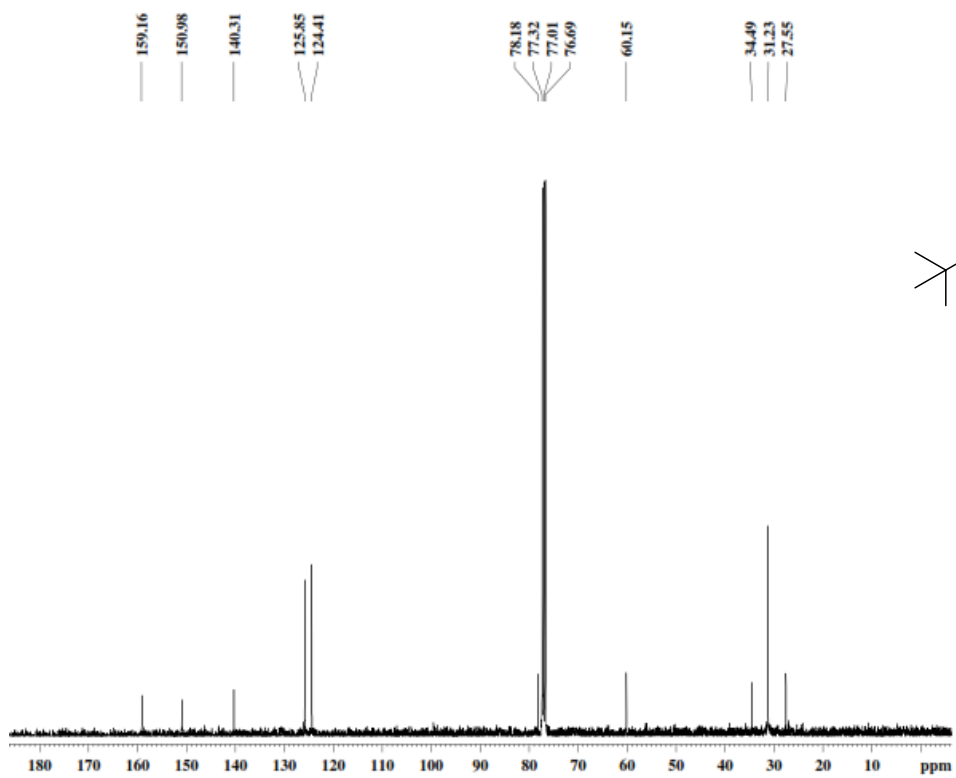
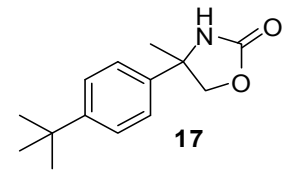
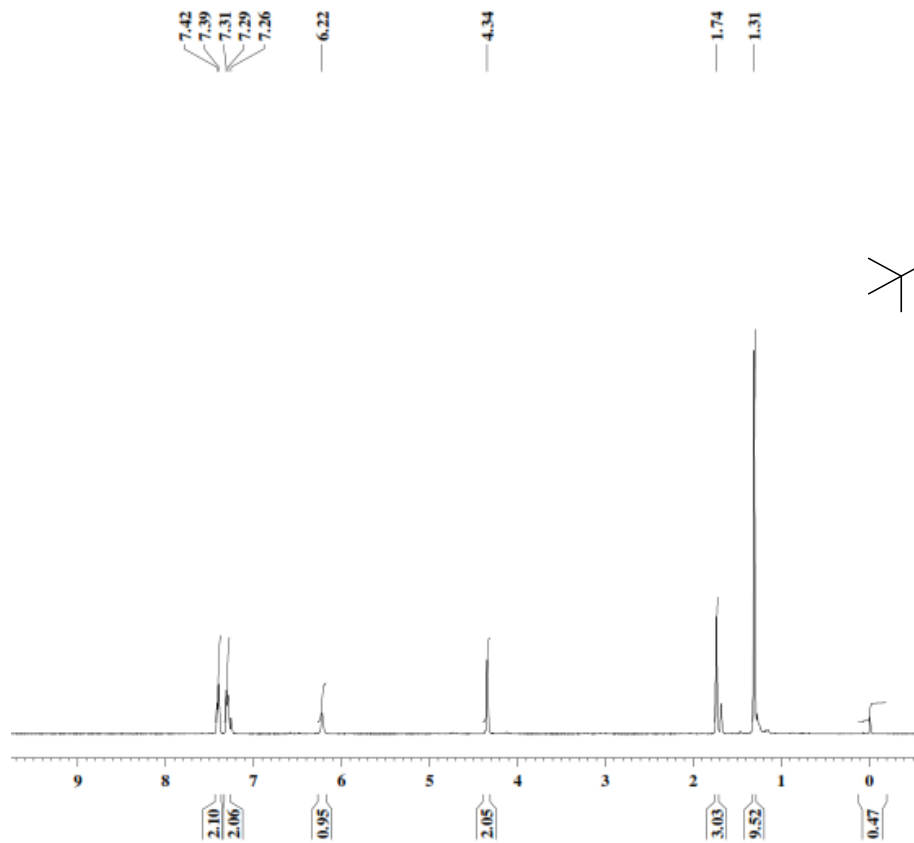
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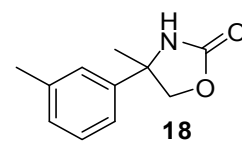
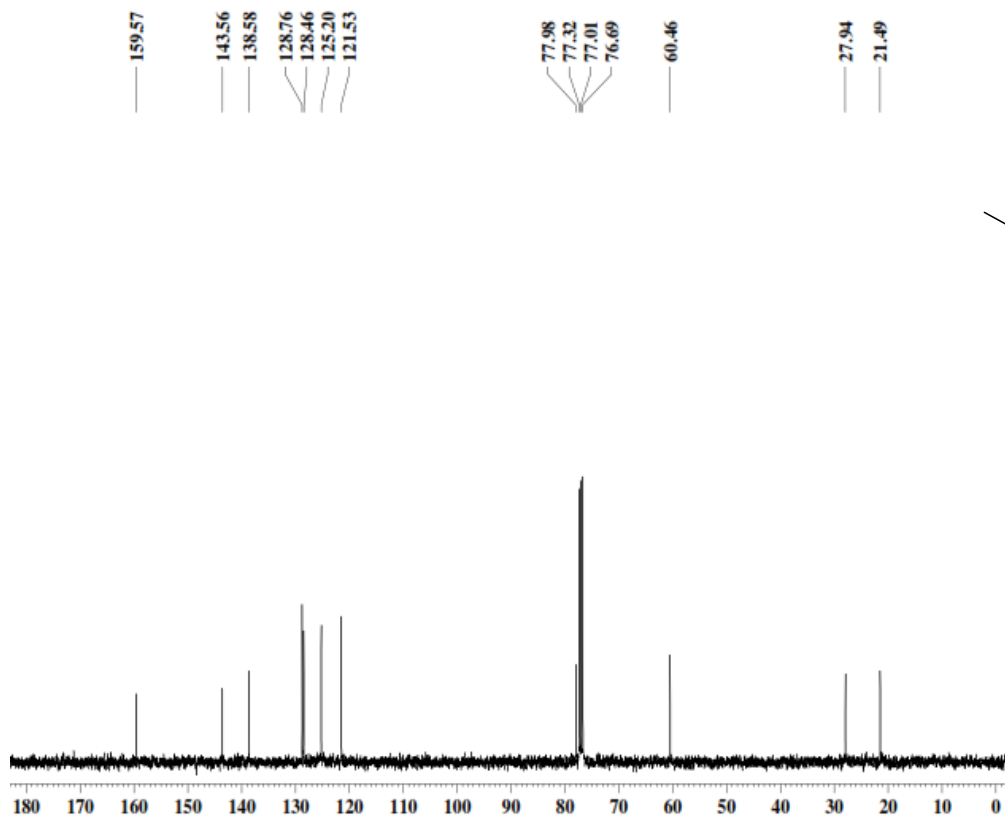
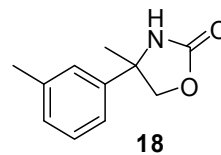
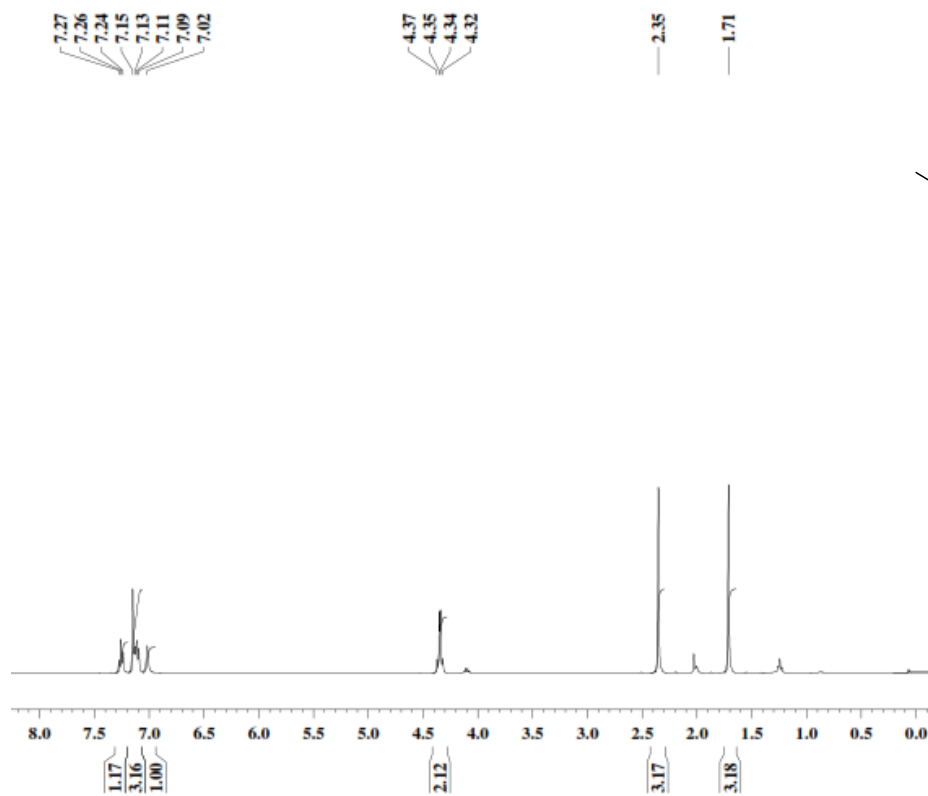


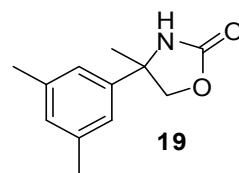
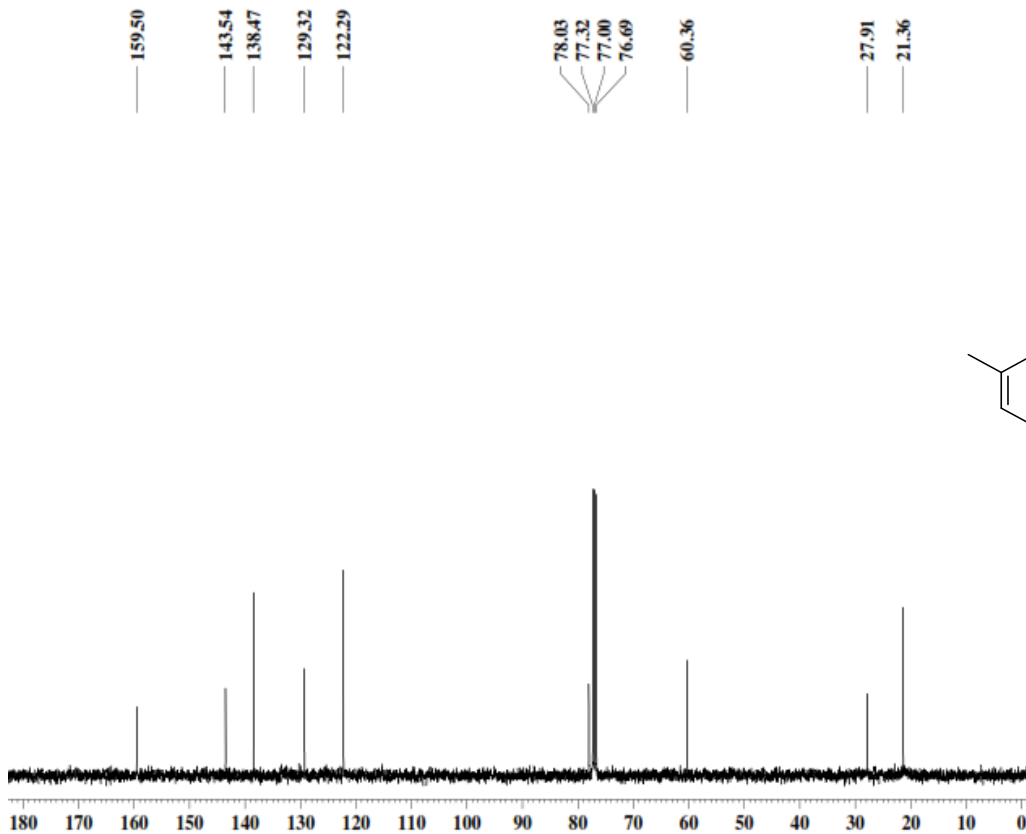
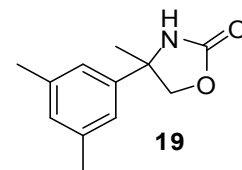
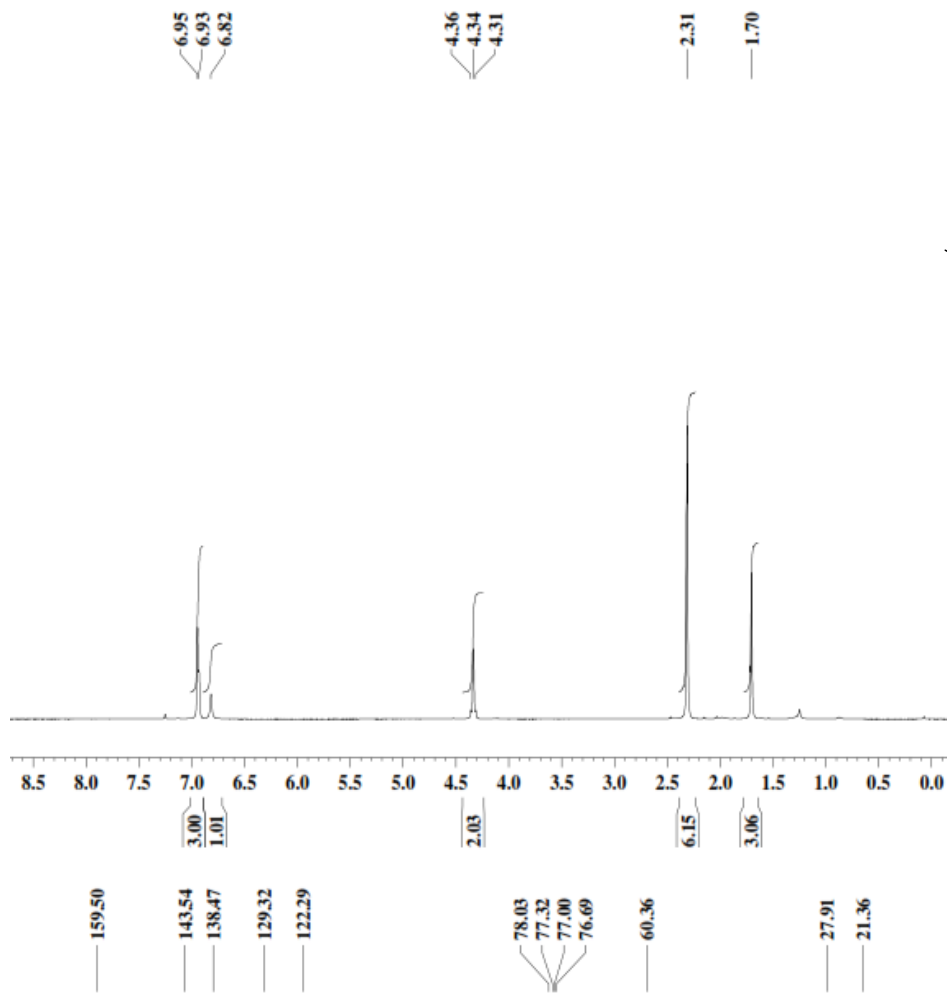




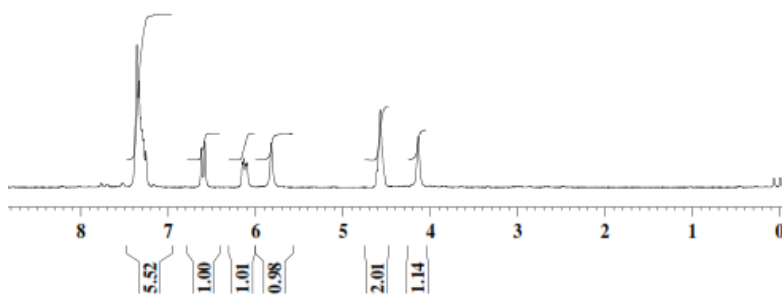
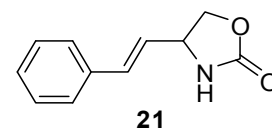




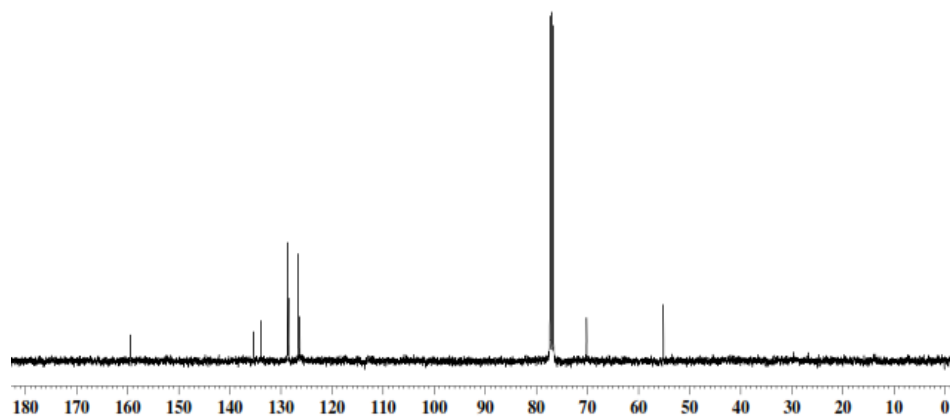
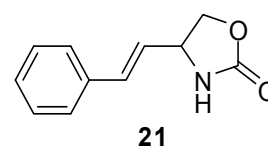




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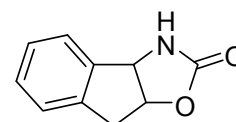
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126.33
77.32
77.00
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70.19
55.13



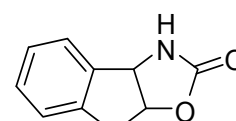
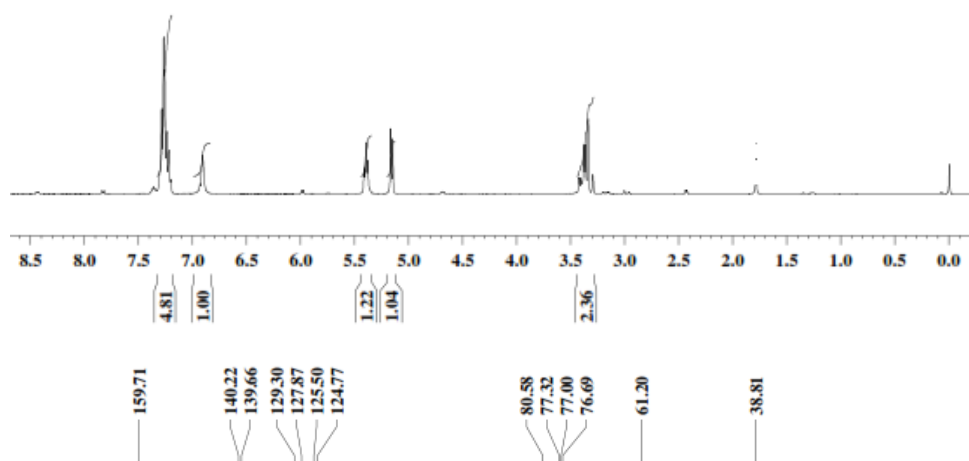
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6.91

5.41
5.39
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5.17
5.15

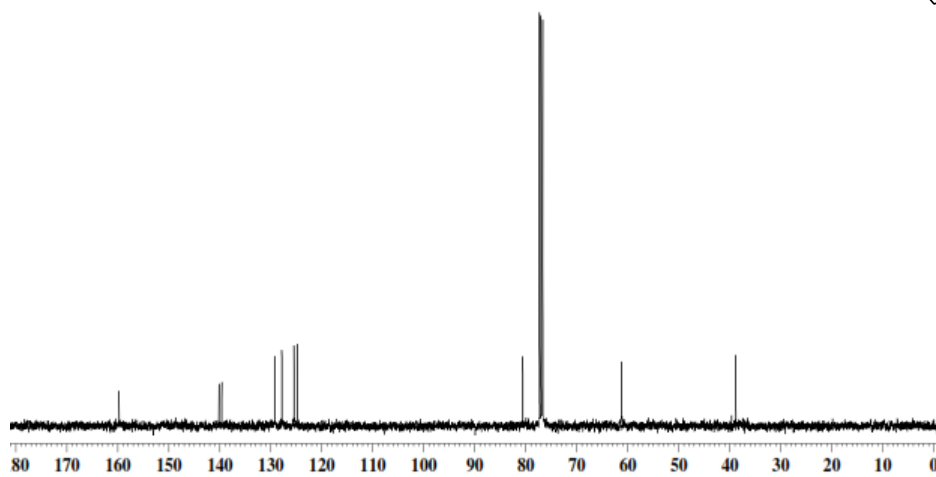
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3.29

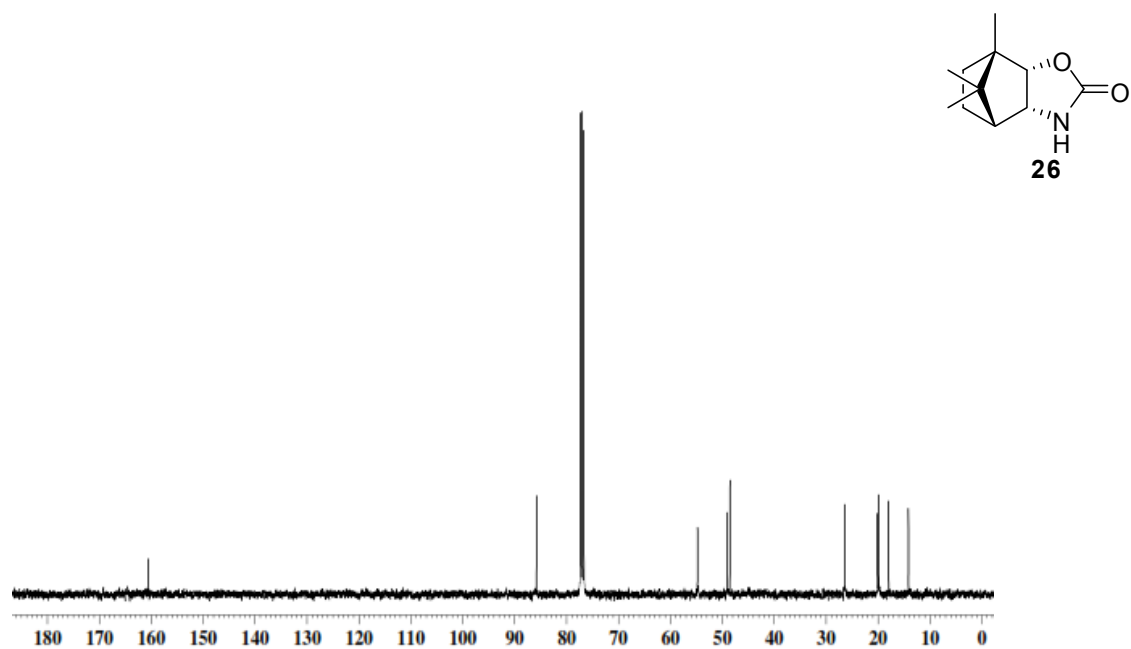
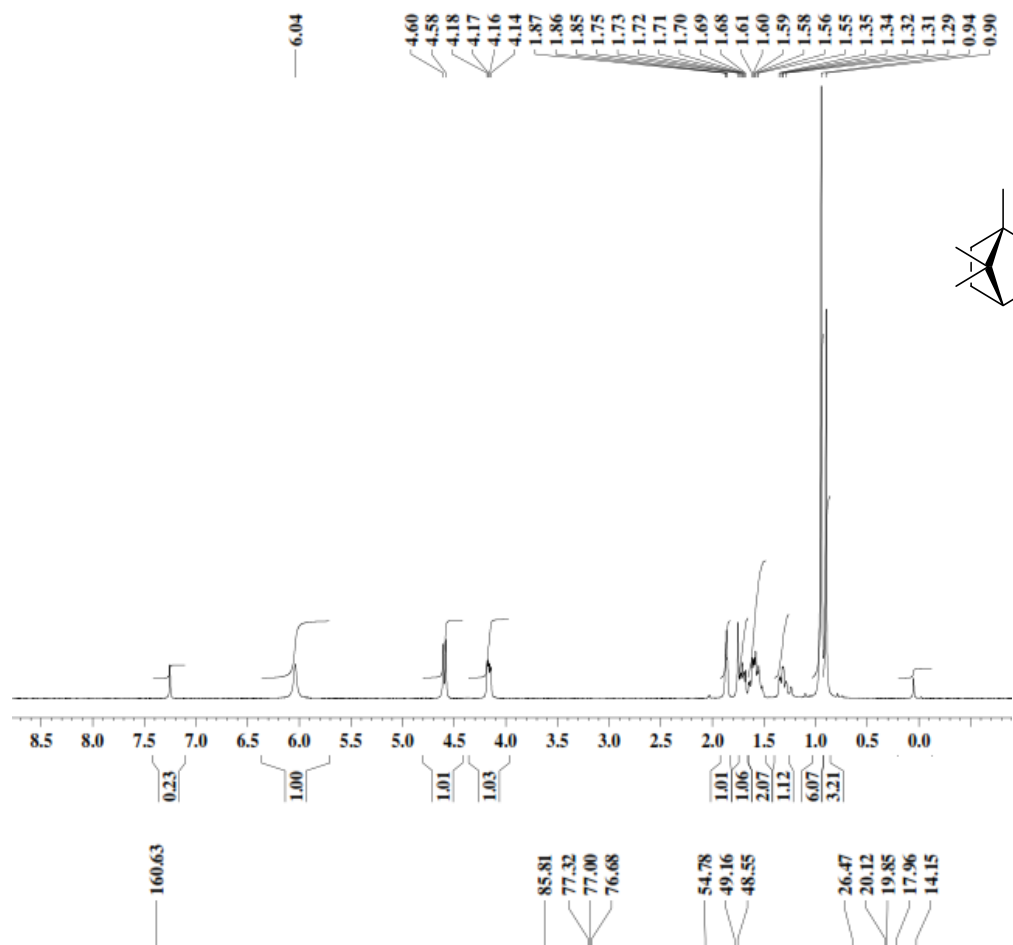


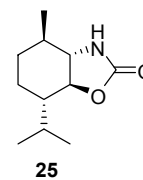
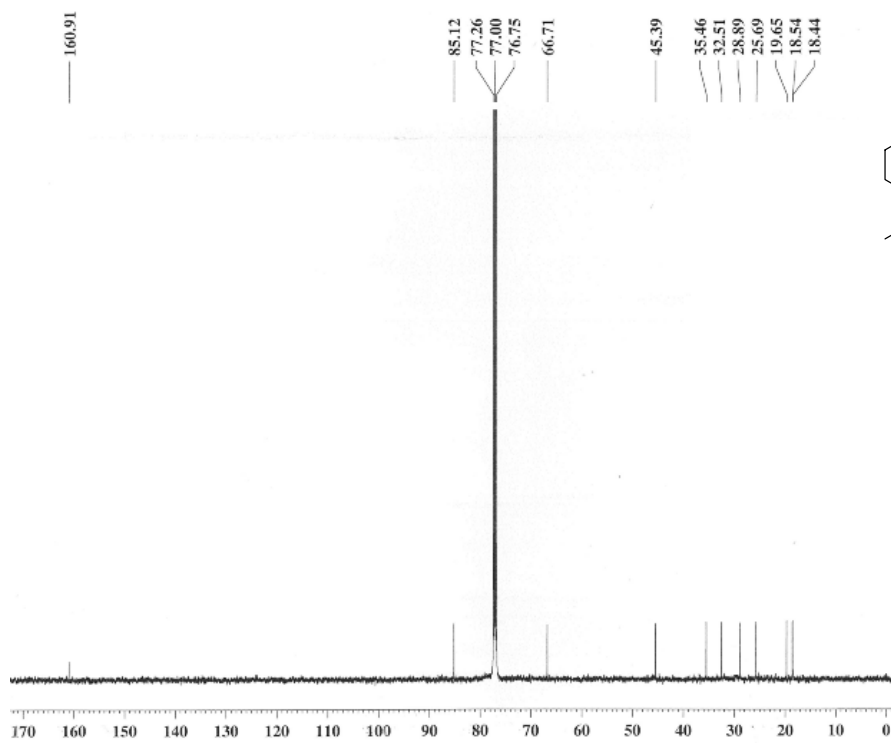
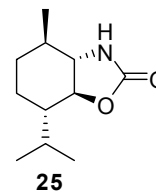
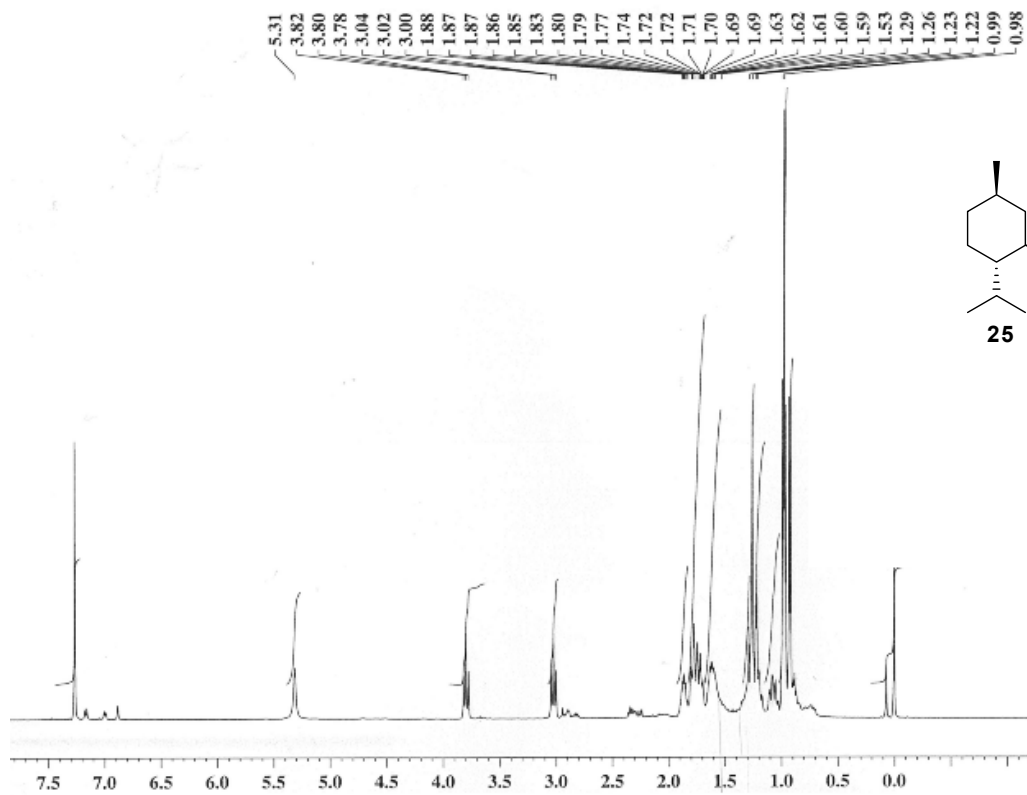
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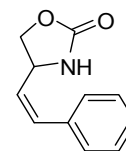
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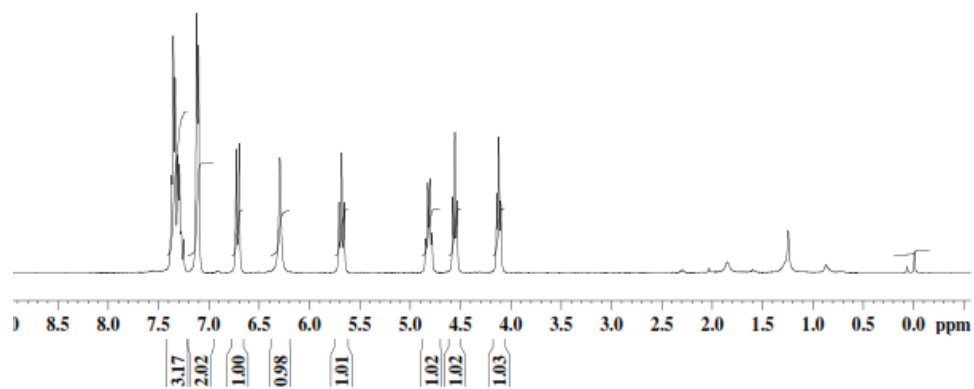




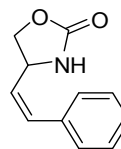
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6.70
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5.71
5.68
5.66
4.85
4.83
4.81
4.79
4.58
4.56
4.54
4.14
4.12
4.10



(Z)-21



159.81
135.33
134.11
129.29
128.52
128.32
127.85
77.32
77.00
76.69
70.30
50.18



(Z)-21

