

Supporting Information for

Chemo- and Diastereoselective Synthesis of *N*-Propargyl Oxazolidines through a Copper-Catalyzed Domino A³ Reaction

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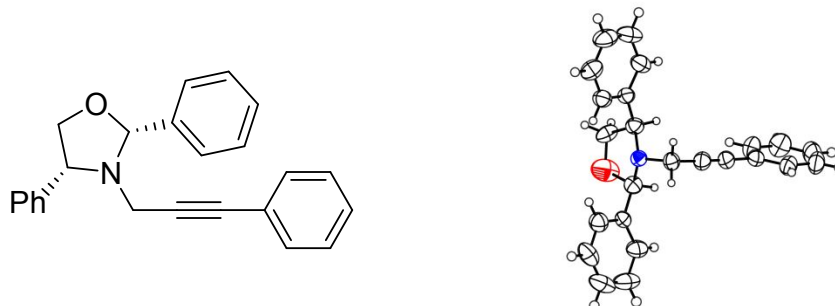
[†]These authors contributed equally

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Structure Determination, Crystal data and ORTEP drawing of compound **5a**
(ellipsoids show 50% probability levels, CCDC: 1886402)

ORTEP drawing:



Crystal data:

Empirical formula	C ₂₄ H ₂₁ NO
Formula weight	339.42
Temperature/K	293
Crystal system	triclinic
Space group	P-1
a/Å	9.5434(15)
b/Å	10.2429(15)
c/Å	10.6535(15)
α/°	71.312(4)
β/°	76.320(4)
γ/°	87.190(4)
Volume/Å ³	958.1(2)
Z	2
ρ _{calc} /g/cm ³	1.177
μ/mm ⁻¹	0.071
F(000)	360.0
Crystal size/mm ³	0.190 × 0.160 × 0.100
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	4.394 to 60.122
Index ranges	-12 ≤ h ≤ 13, -14 ≤ k ≤ 14, -15 ≤ l ≤ 13
Reflections collected	9067
Independent reflections	5507 [R _{int} = 0.0265, R _{sigma} = 0.0629]
Data/restraints/parameters	5507/0/236
Goodness-of-fit on F ²	1.049
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0901, wR ₂ = 0.1928
Final R indexes [all data]	R ₁ = 0.1697, wR ₂ = 0.2250
Largest diff. peak/hole / e Å ⁻³	0.20/-0.20

Experimental

Single crystals of $C_{24}H_{21}NO$ were grown from petroleum ether (bp 40-60 °C) and DCM at - 15 °C (refrigerator). A suitable crystal was selected and diffraction data were collected on a 'Bruker APEX-II CCD' diffractometer. The crystal was kept at 293 K during data collection. Using Olex2^[1], the structure was solved with the ShelXT^[2] structure solution program using intrinsic phasing and refined with the ShelXL^[3] refinement package using least squares minimisation.

[1] Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

[2] Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

[3] Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of 5a

Crystal Data for $C_{24}H_{21}NO$ ($M=339.42$ g/mol): triclinic, space group P-1 (no. 2), $a = 9.5434(15)$ Å, $b = 10.2429(15)$ Å, $c = 10.6535(15)$ Å, $\alpha = 71.312(4)$, $\beta = 76.320(4)$, $\gamma = 87.190(4)$, $V = 958.1(2)$ Å³, $Z = 2$, $T = 293$ K, $\mu(\text{MoK}\alpha) = 0.071$ mm⁻¹, $D_{\text{calc}} = 1.177$ g/cm³, 9067 reflections measured ($4.394^\circ \leq 2\theta \leq 60.122^\circ$), 5507 unique ($R_{\text{int}} = 0.0265$, $R_{\text{sigma}} = 0.0629$) which were used in all calculations. The final R_1 was 0.0901 ($I > 2\sigma(I)$) and wR_2 was 0.2250 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:

1. Fixed Uiso

At 1.2 times of:

All C(H) groups, All C(H,H) groups

2. Shared sites

{O15, C14A}

{C14, O15A}

3. Uiso/Uanis restraints and constraints

Uanis(O15) = Uanis(C14A)

Uanis(C14) = Uanis(O15A)

4. Others

Sof(O15A)=Sof(H7B)=Sof(H8B)=Sof(C14A)=Sof(H14C)=Sof(H14D)=1-FVAR(1)

Sof(O15)=Sof(H7A)=Sof(H8A)=Sof(C14)=Sof(H14A)=Sof(H14B)=FVAR(1)

5.a Ternary CH refined with riding coordinates:

C7(H7A), C7(H7B), C8(H8A), C8(H8B)

5.b Secondary CH2 refined with riding coordinates:

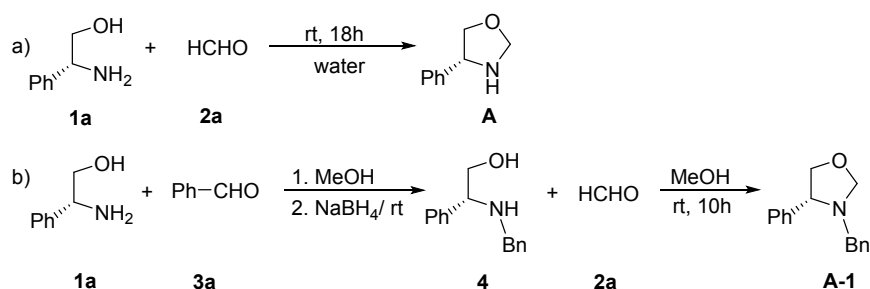
C6(H6A,H6B), C14(H14A,H14B), C14A(H14C,H14D)

5.c Aromatic/amide H refined with riding coordinates:

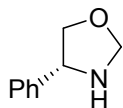
C9(H9), C11(H11), C12(H12), C13(H13), C16(H16), C17(H17), C18(H18),
C19(H19), C20(H20), C21(H21), C22(H22), C23(H23), C24(H24), C25(H25),
C26(H26)

This report has been created with Olex2, compiled on 2018.05.29 svn.r3508 for
OlexSys. Please [let us know](#) if there are any errors or if you would like to have
additional features.

General Procedure for the Synthesis of Oxazolidines A-1 and A



To a round flask equipped with a magnetically stirred chip was added chiral hydroxylamine **1a** (2g, 14.6 mmol), formaldehyde solution **2a** (1.2mL, 14.6 mmol) in water (50 mL). After stirring at room temperature for 18 hours, the targeted compound **A** was filtered and obtained as a white powder.

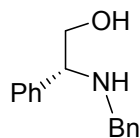


(R)-4-phenyloxazolidine (A) (1.7g, white solid, 81% yield, >20/1 dr) ^1H NMR (400 MHz, CDCl_3) δ 7.41 (d, $J = 7.3$ Hz, 2H), 7.33 (t, $J = 7.3$ Hz, 2H), 7.25 (d, $J = 7.1$ Hz, 1H), 4.83 (s, 1H), 4.66–4.55 (m, 1H), 4.19 (s, 2H), 3.87 (d, $J = 6.6$ Hz, 2H).

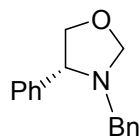
To a round flask equipped with a magnetically stirred chip was added chiral hydroxylamine **1a** (2g, 14.6 mmol), benzaldehyde **3a** (1.5g, 14.6 mmol) in dry MeOH (50 mL) and stirred at room temperature for 8 hours. The reaction was monitored by TLC. Then the mixture was carefully treated with sodium borohydride (0.7 g, 18.1 mmol) and kept stirring about 1 hour, before dilution by water and CH_2Cl_2 extraction (3x). Combined organic layers were washed with brine, dried over anhydrous NaSO_4 , filtered and concentrated to dryness. The crude product was purified by crystallization with 10% ethyl acetate in petroleum ether to afford the desired product **4** as the white solid.

To a test tube equipped with a magnetically stirred chip was added compound **4** (454mg, 2 mmol), formaldehyde solution **2a** (152mg, 2 mmol) in dry MeOH (10 mL). After stirring at room temperature for 10 hours, the resulting reaction suspension was concentrated and directly loaded onto a silicon gel column and

flushed about 10% ethyl acetate in petroleum ether to afford the desired product **A-1** as the light yellow oil.

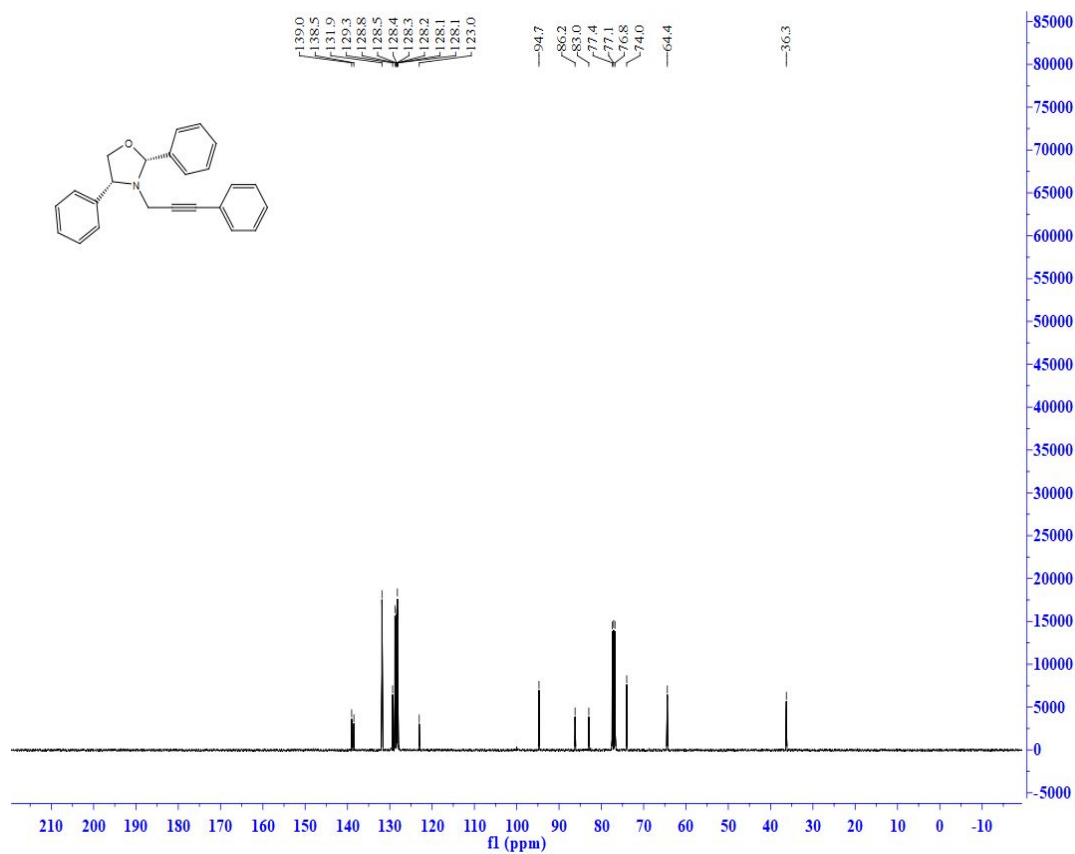
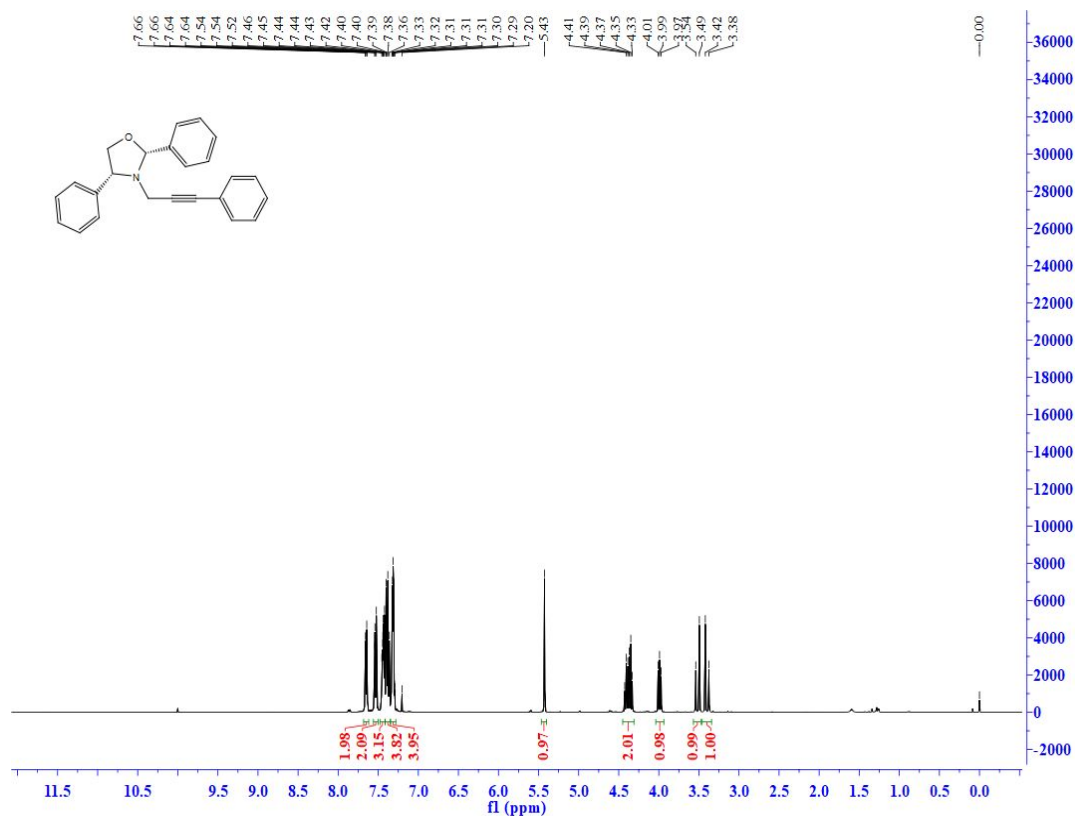


(R)-2-(benzylamino)-2-phenylethan-1-ol (4) (2.7g, white solid, 85% yield, >20/1 dr) ^1H NMR (400 MHz, CDCl_3) δ 7.47–7.24 (m, 10H), 3.88–3.83 (d, J = 8.7 Hz, 1H), 3.82–3.69 (m, 2H), 3.67–3.53 (m, 2H), 2.42 (s, 2H).

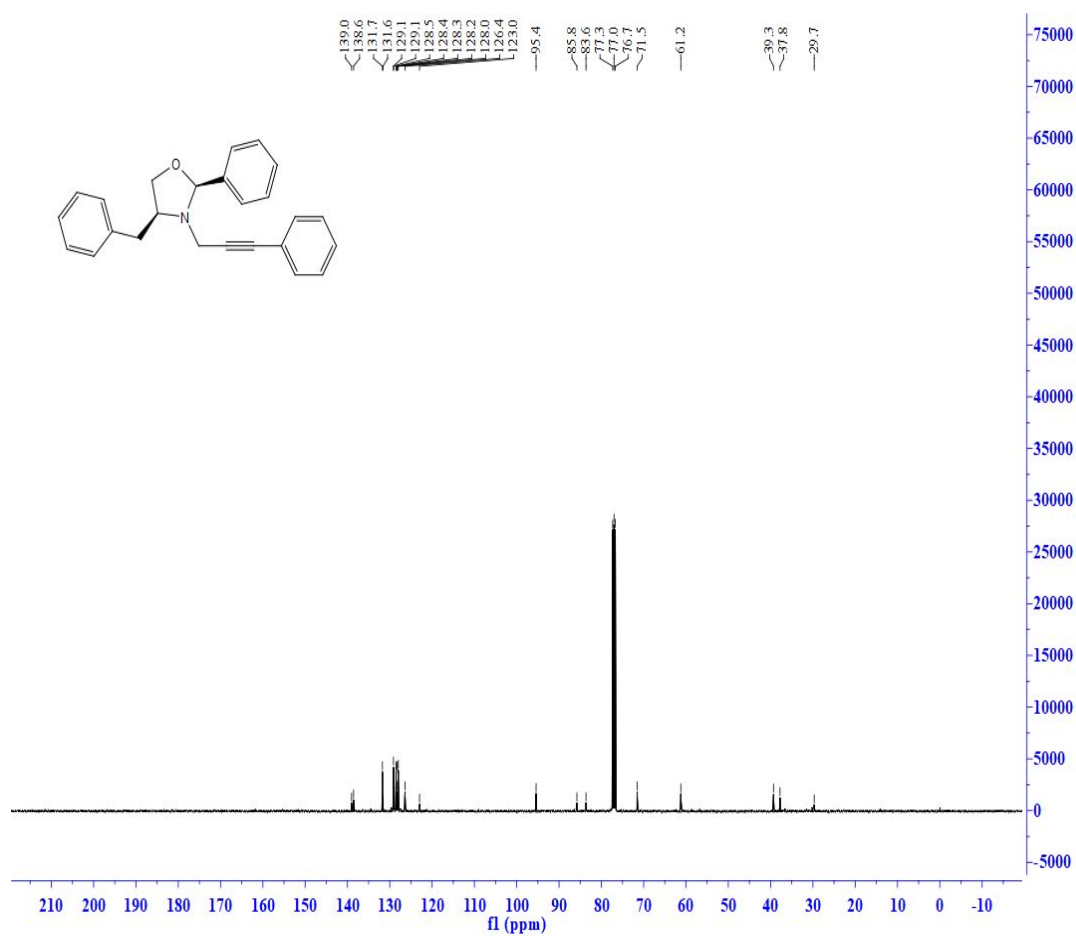
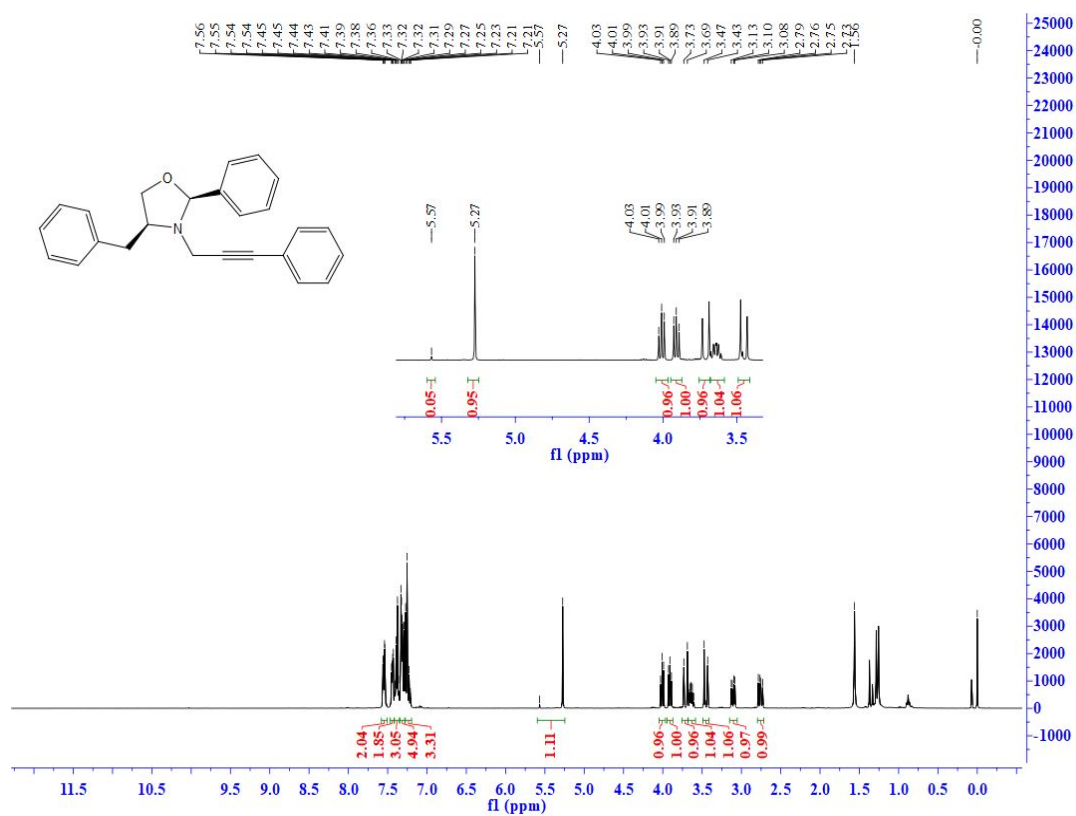


(R)-3-benzyl-4-phenyloxazolidine (A-1) (372 mg, light yellow oil, 78% yield, >20/1 dr) ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, J = 7.2 Hz, 2H), 7.45 (t, J = 7.3 Hz, 4H), 7.42–7.29 (m, 4H), 4.69 (d, J = 3.5 Hz, 1H), 4.39 (t, J = 7.5 Hz, 1H), 4.30 (d, J = 3.5 Hz, 1H), 4.06–3.94 (m, 2H), 3.83 (t, J = 7.8 Hz, 1H), 3.56 (d, J = 13.4 Hz, 1H).

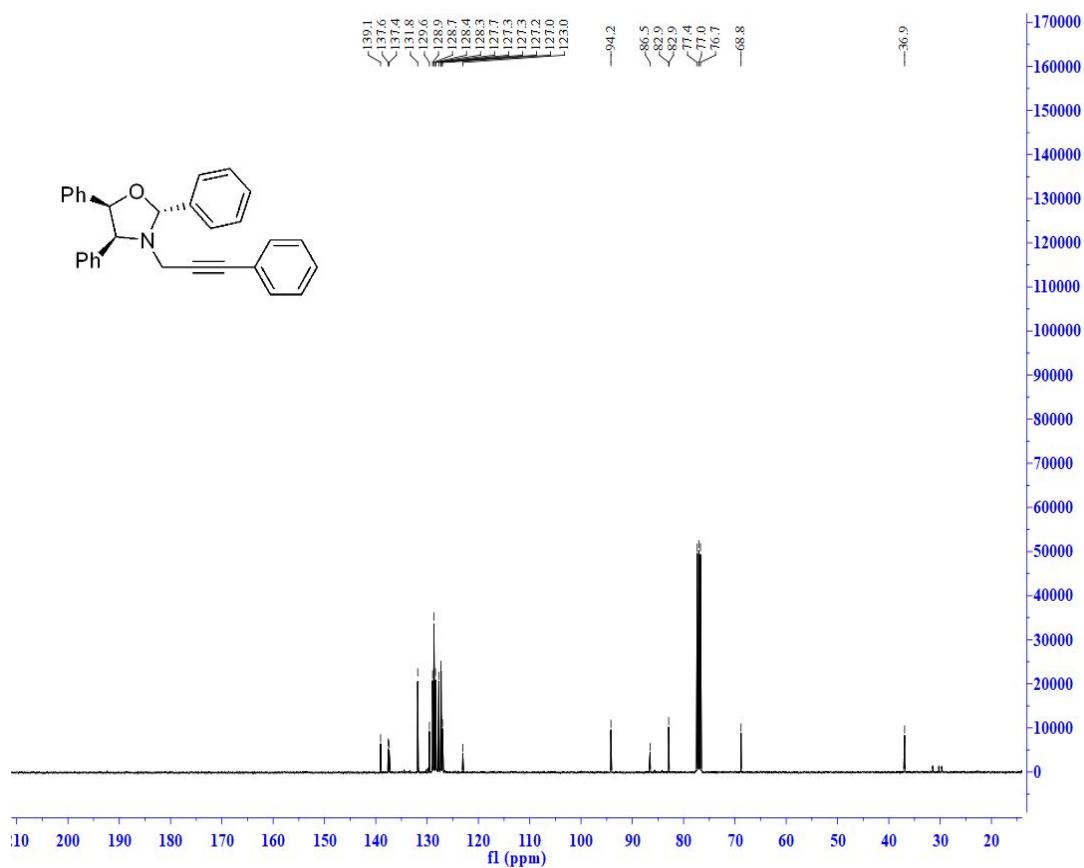
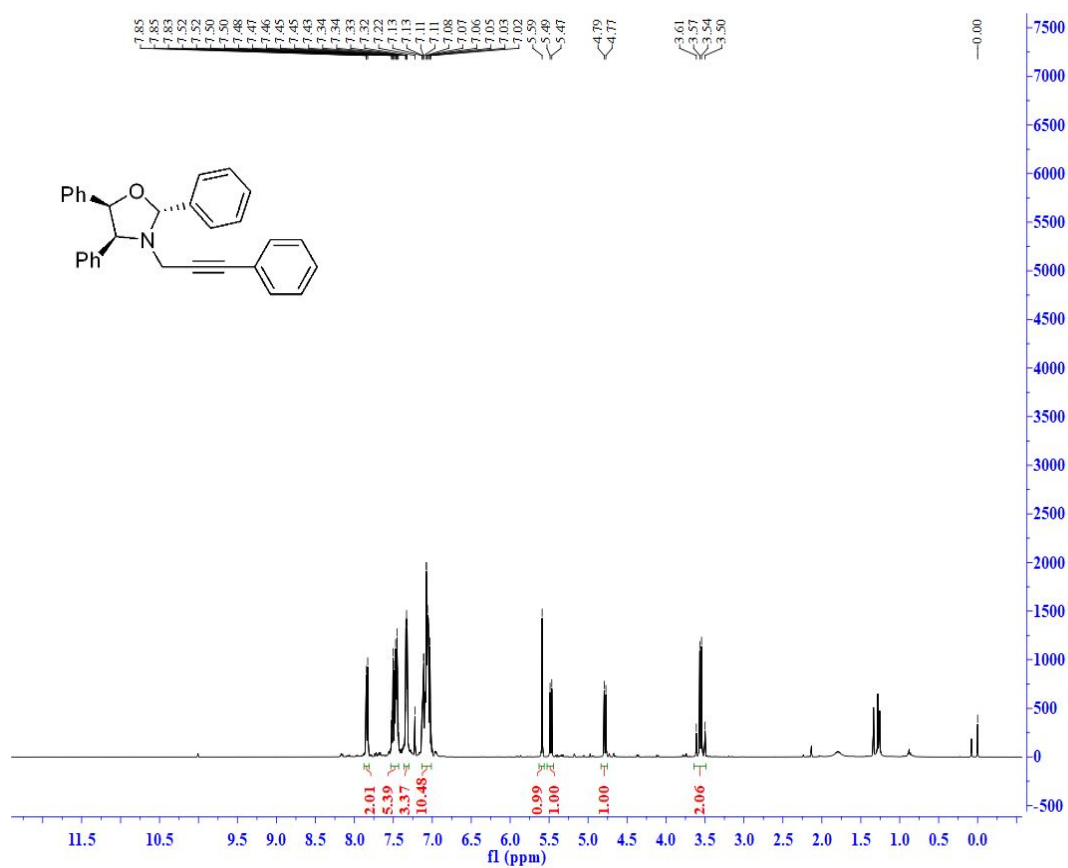
^1H NMR and ^{13}C NMR spectra of all compounds 5
(2*R*,4*R*)-2,4-diphenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5a)



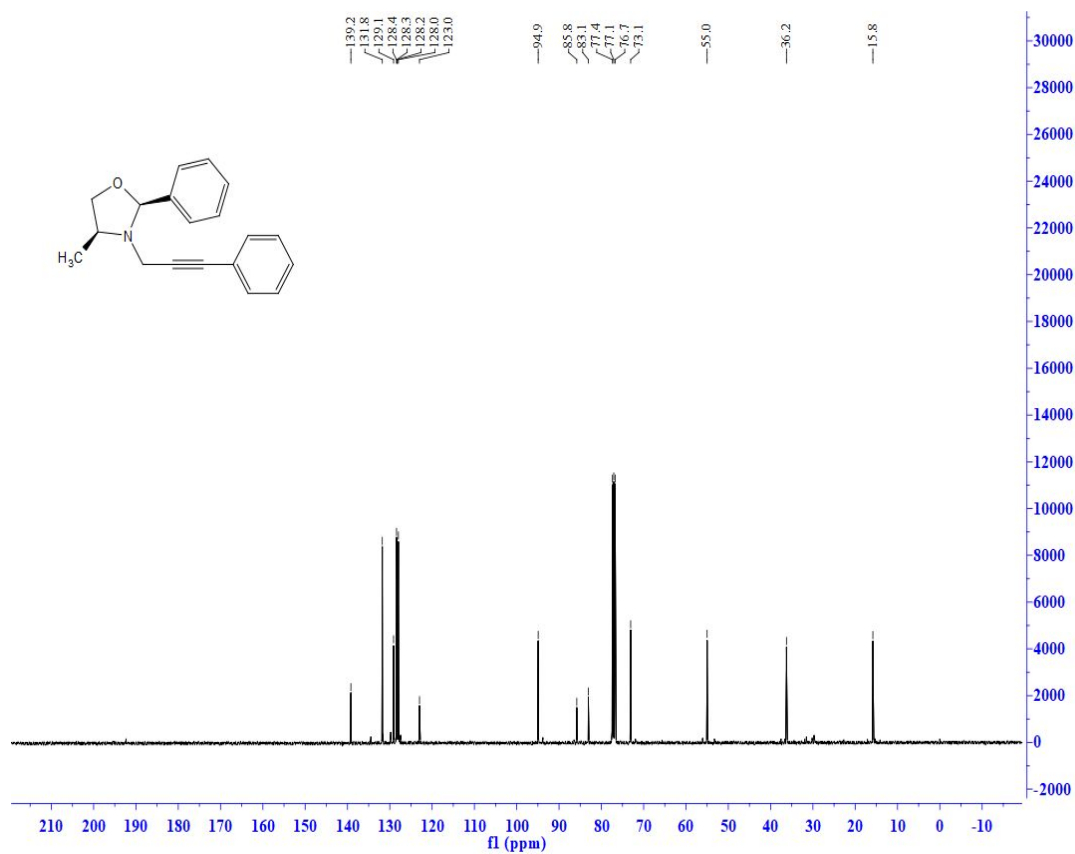
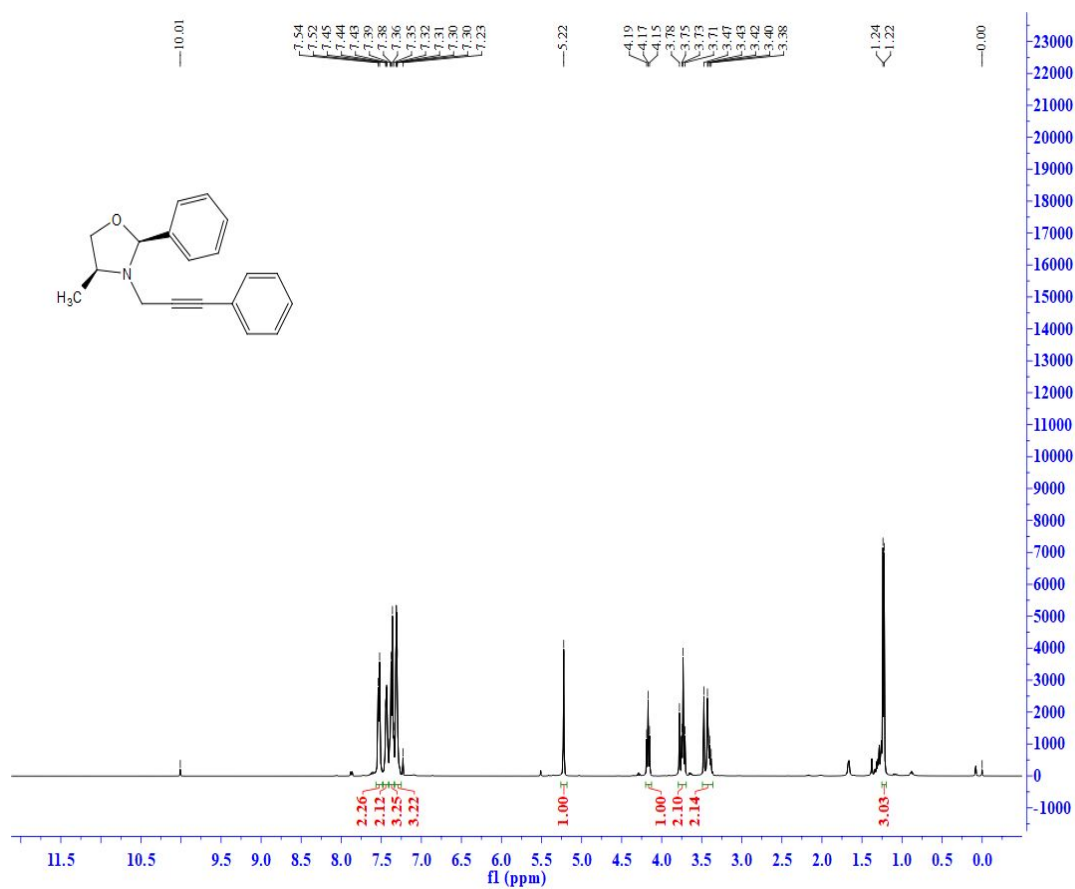
(2*S*,4*S*)-4-benzyl-2-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5b)



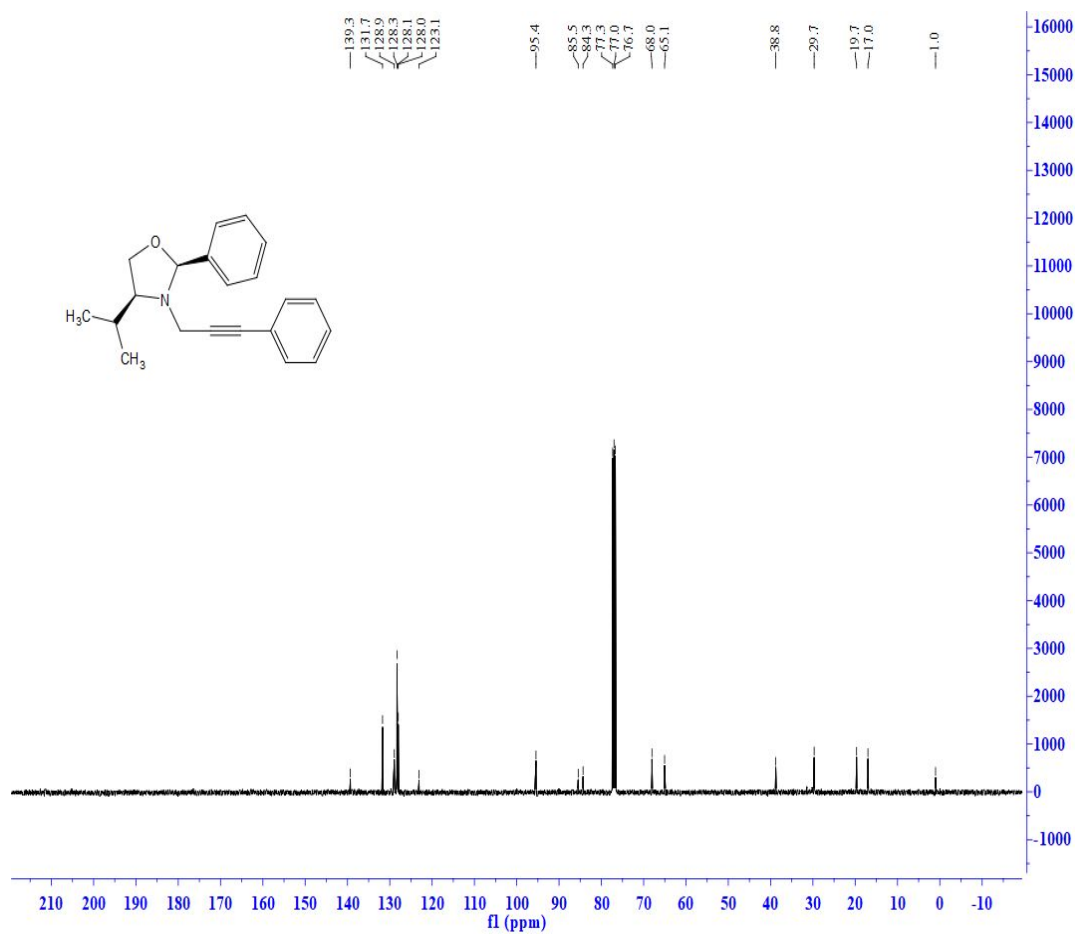
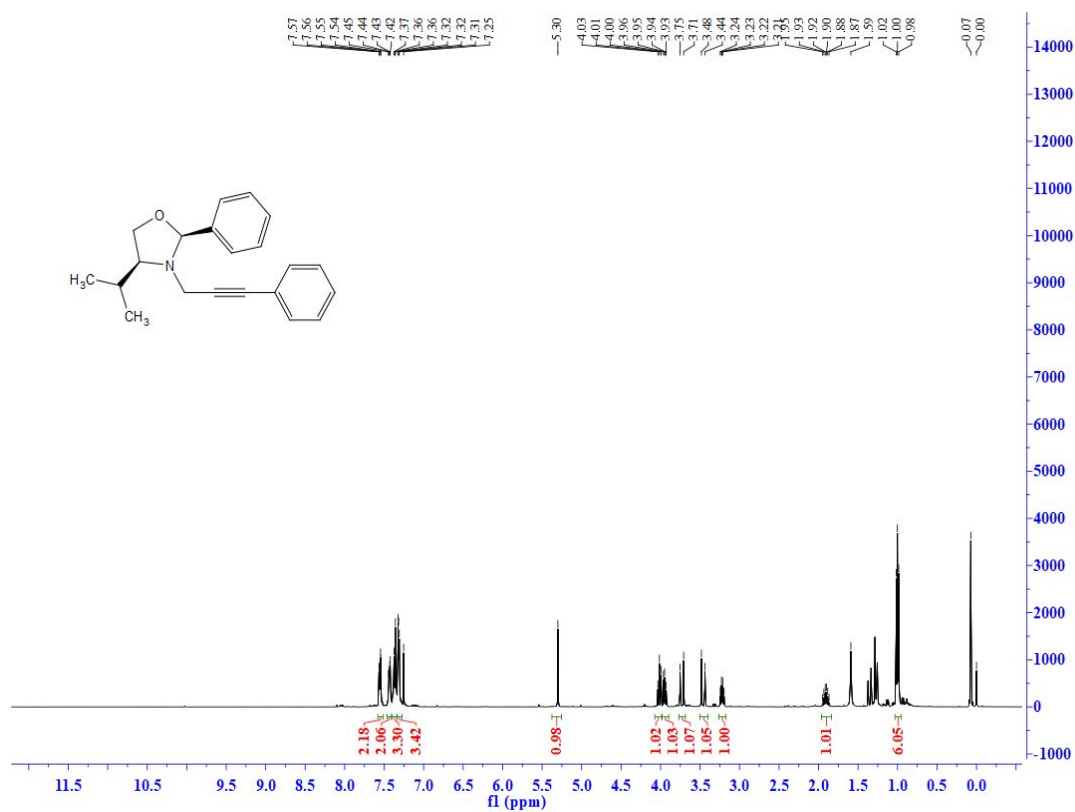
(2*S*,4*S*,5*S*)-2,4,5-triphenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5c)



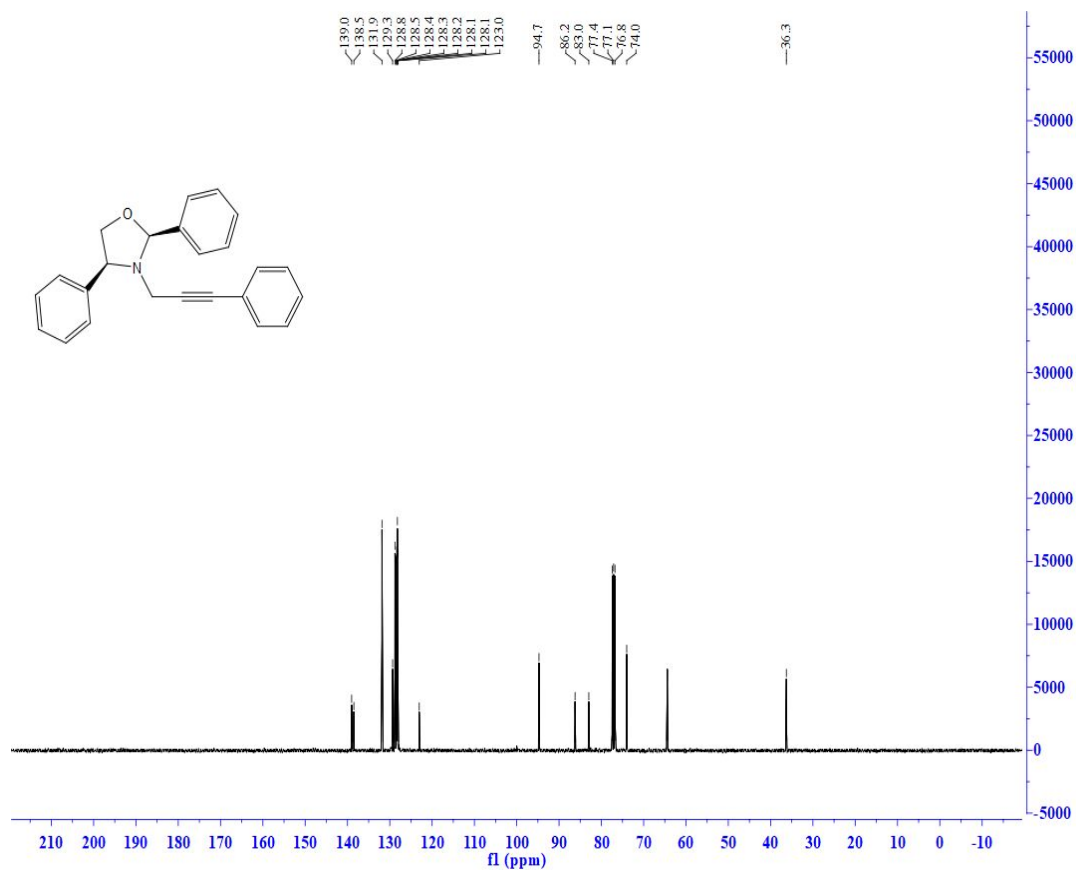
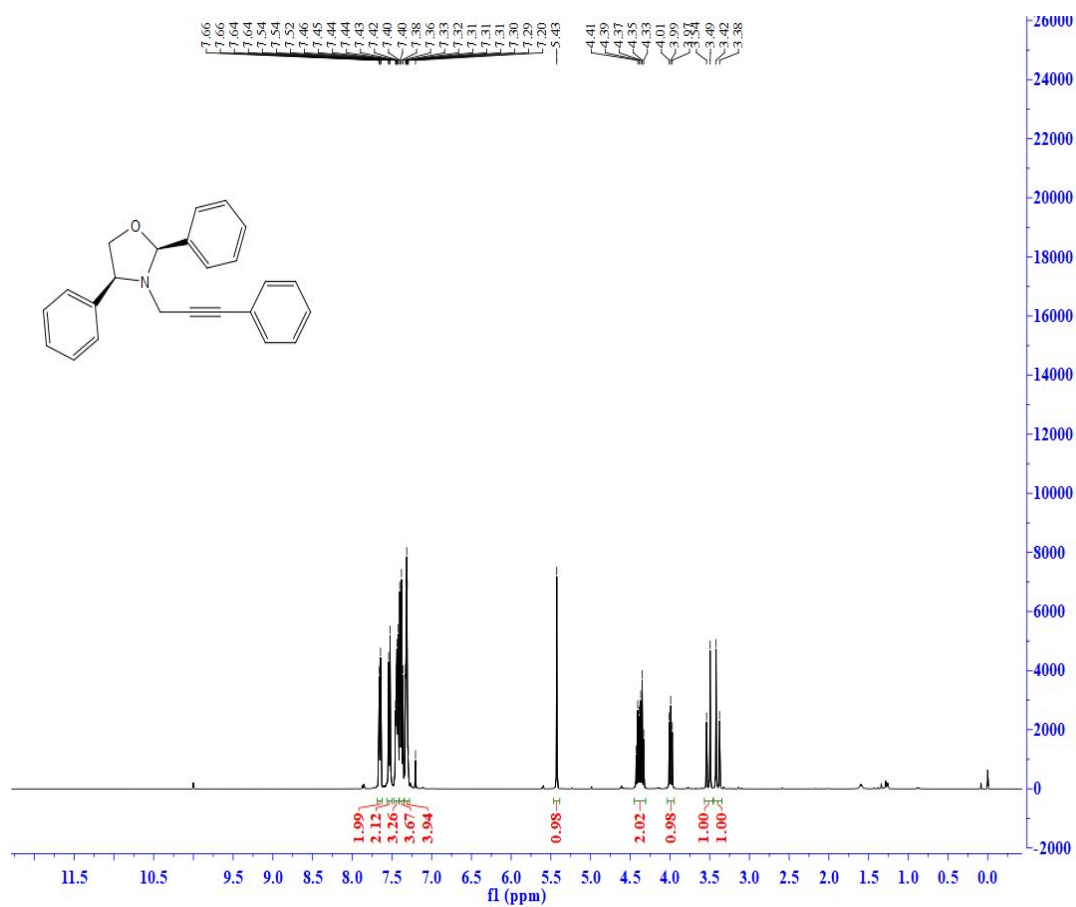
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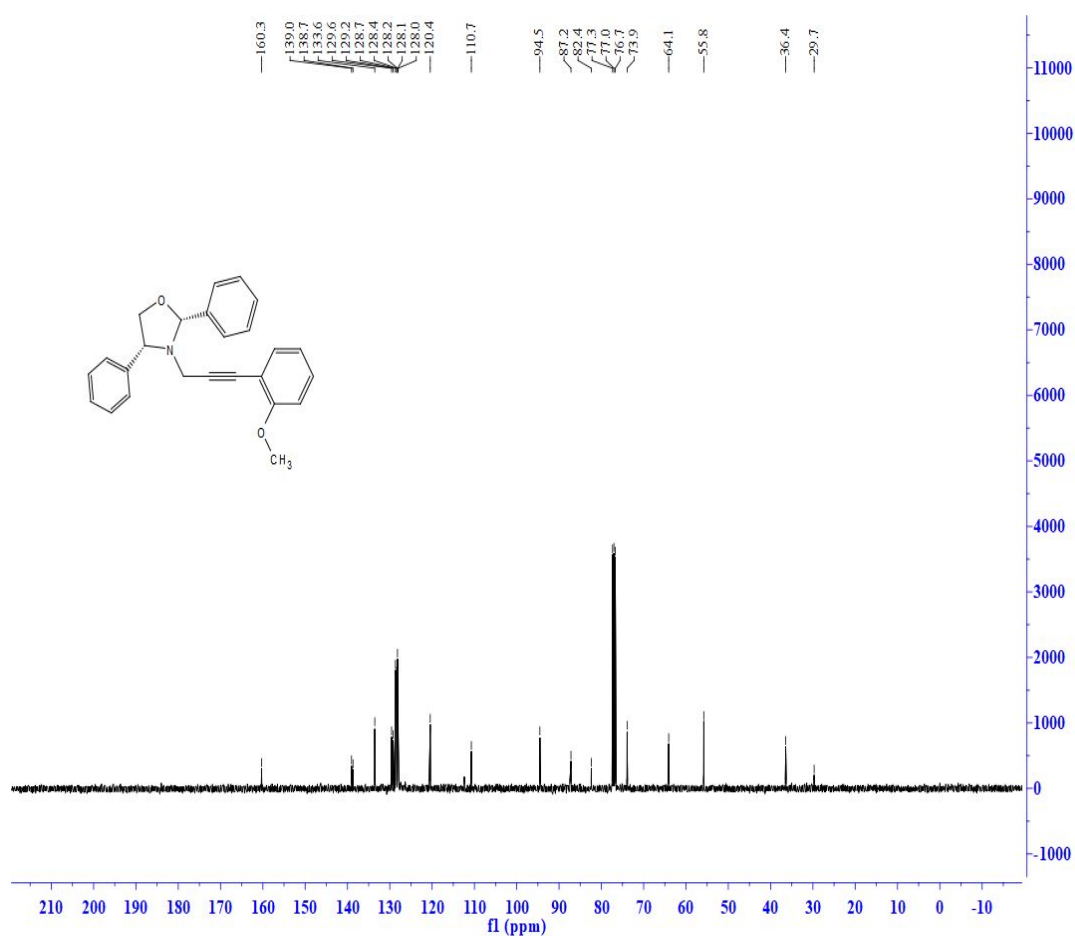
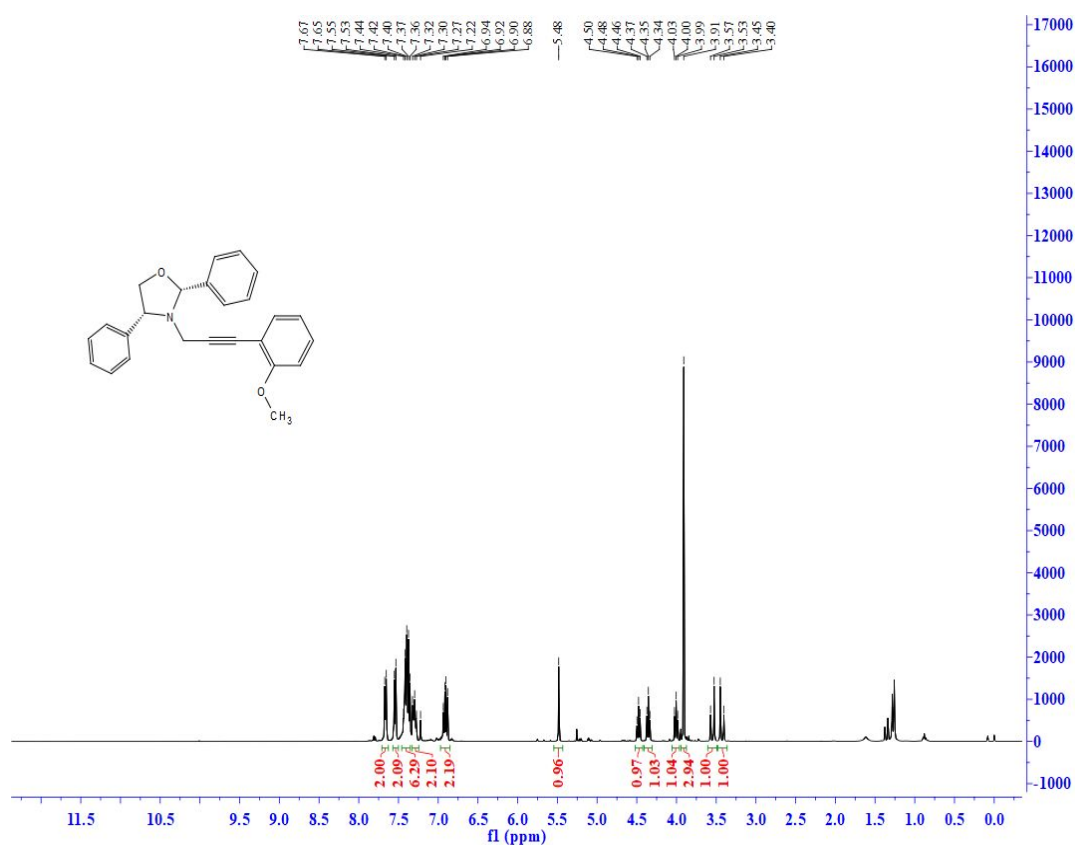
(2*S*,4*S*)-4-isopropyl-2-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5e)



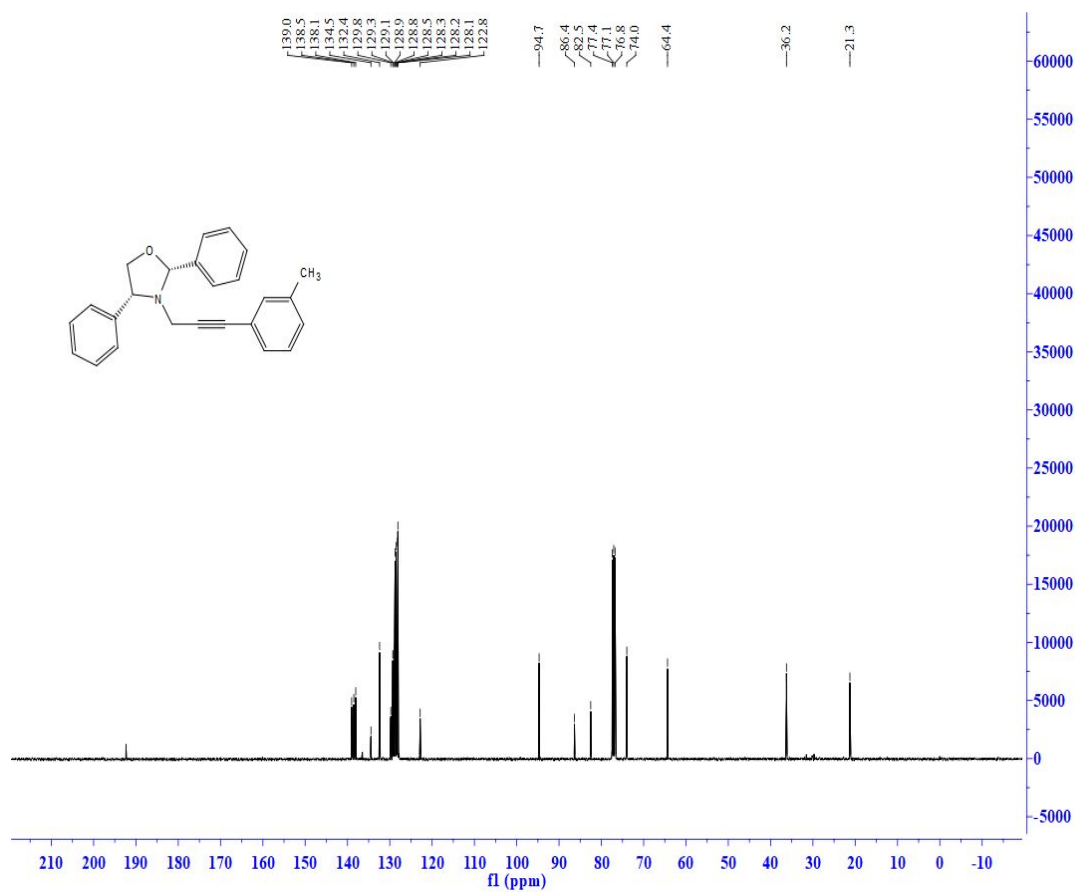
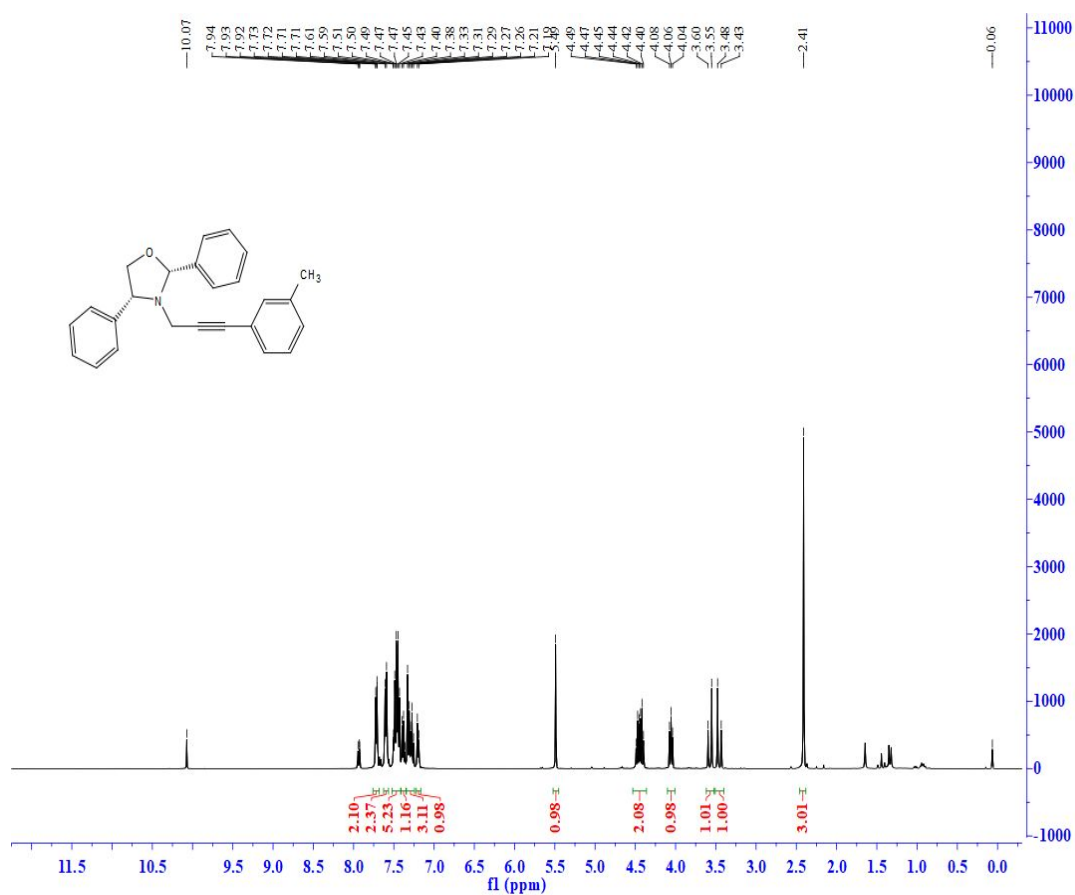
(2*S*,4*S*)-2,4-diphenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5f)



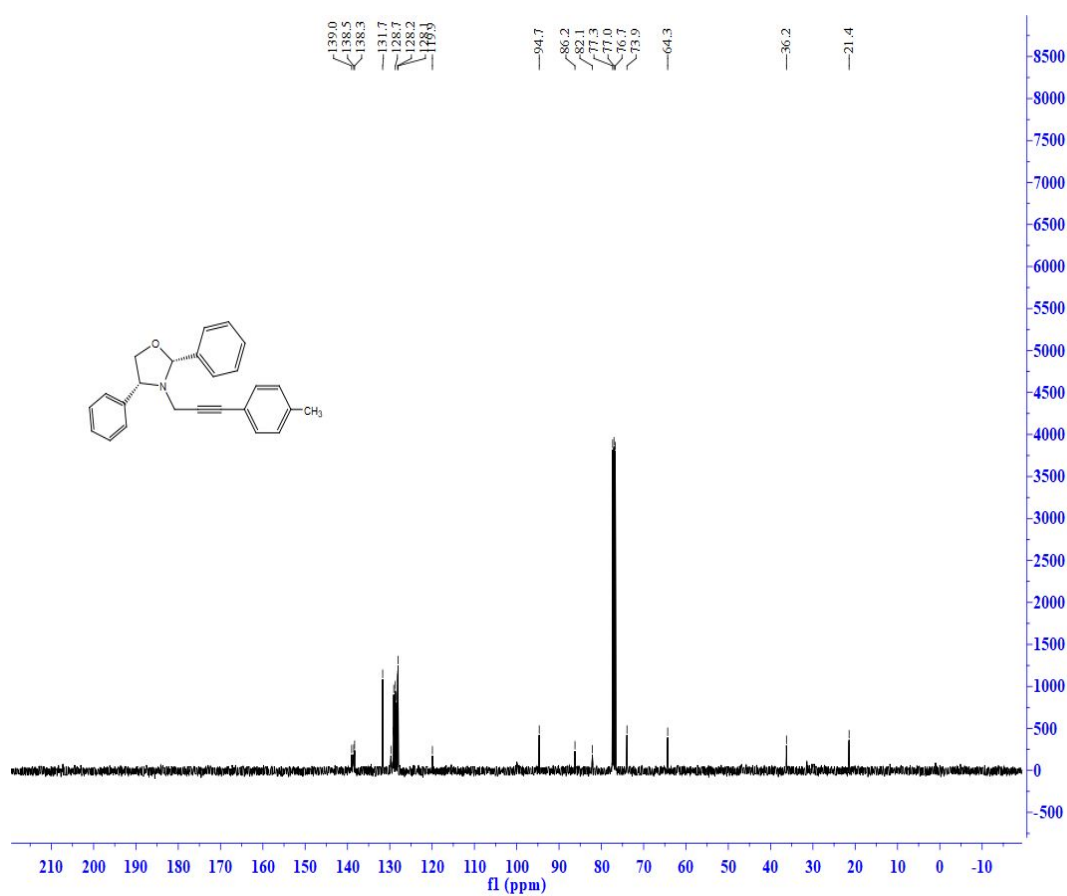
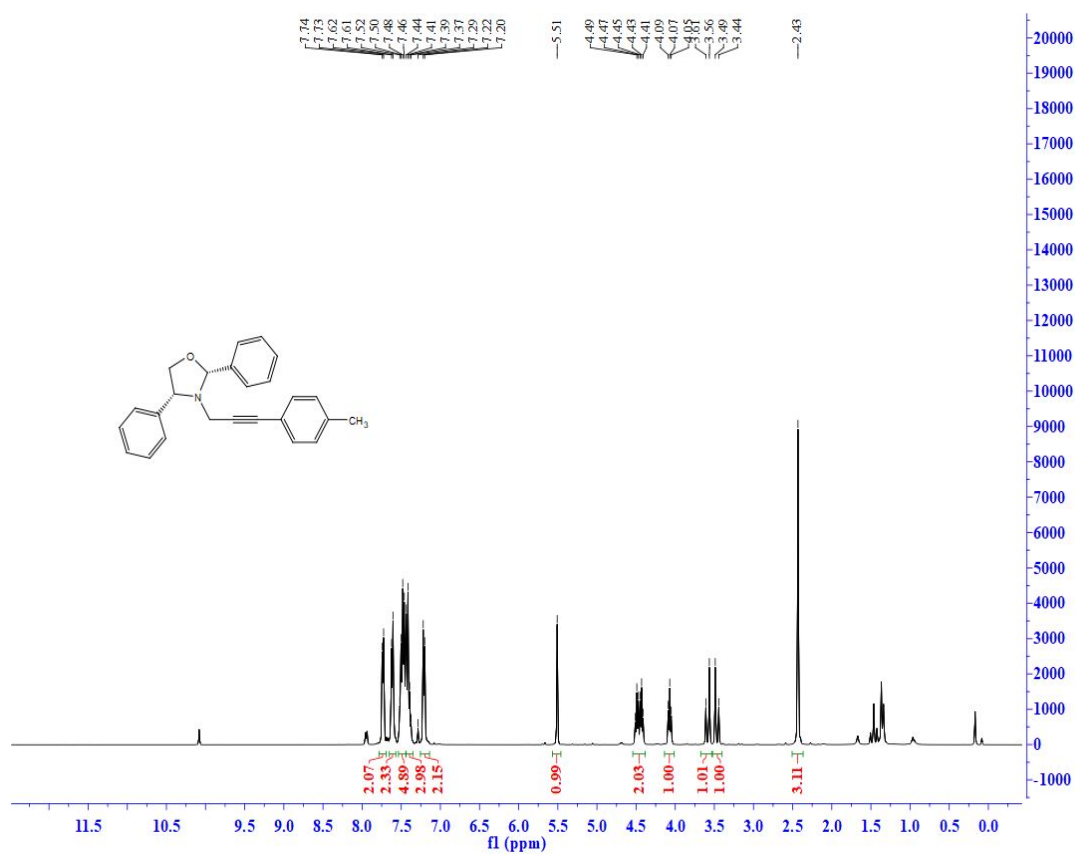
(2*R*,4*R*)-3-(3-(2-methoxyphenyl)prop-2-yn-1-yl)-2,4-diphenyloxazolidine (5g)



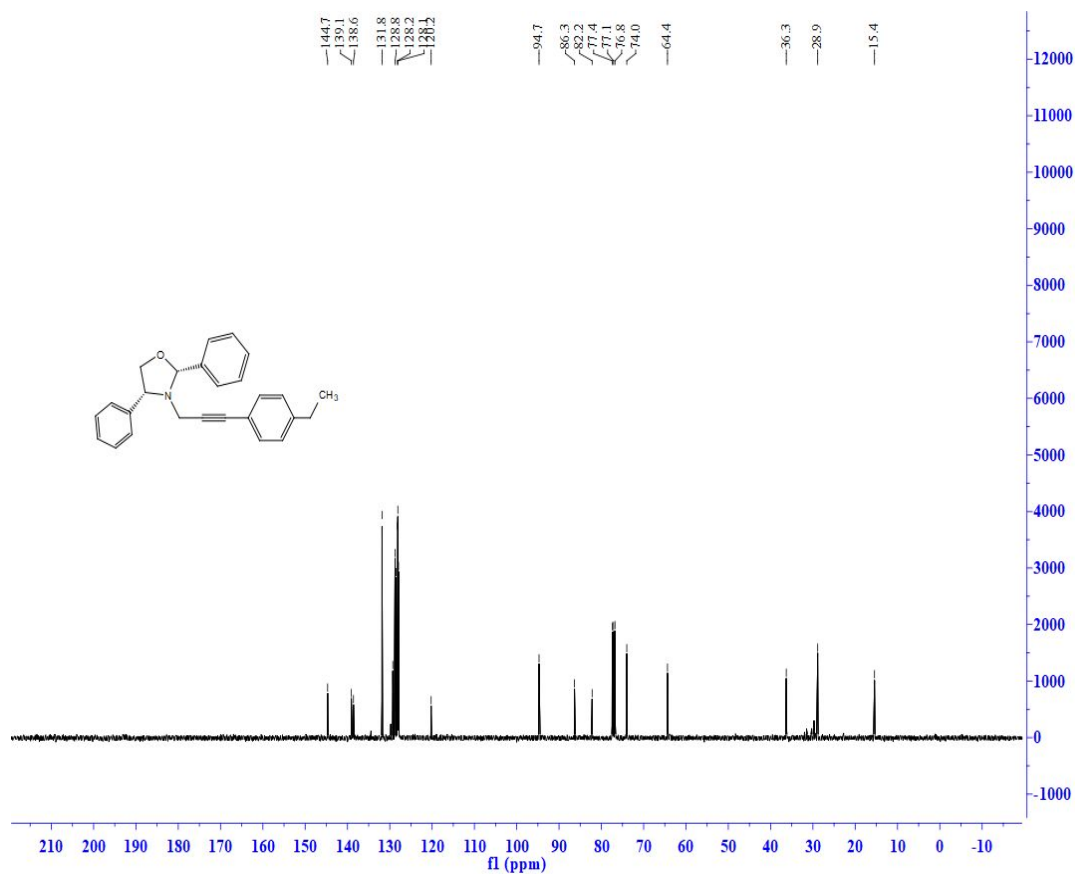
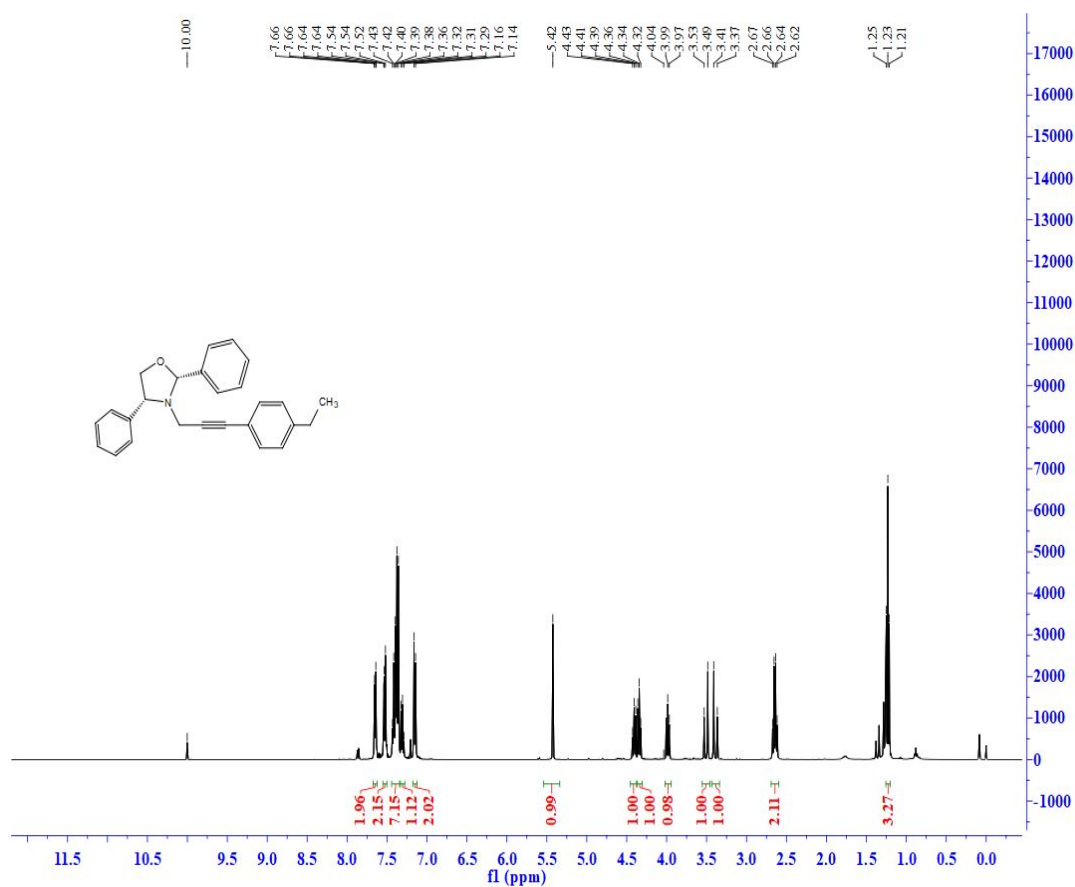
(2*R*,4*R*)-2,4-diphenyl-3-(3-(*m*-tolyl)prop-2-yn-1-yl)oxazolidine (5h)



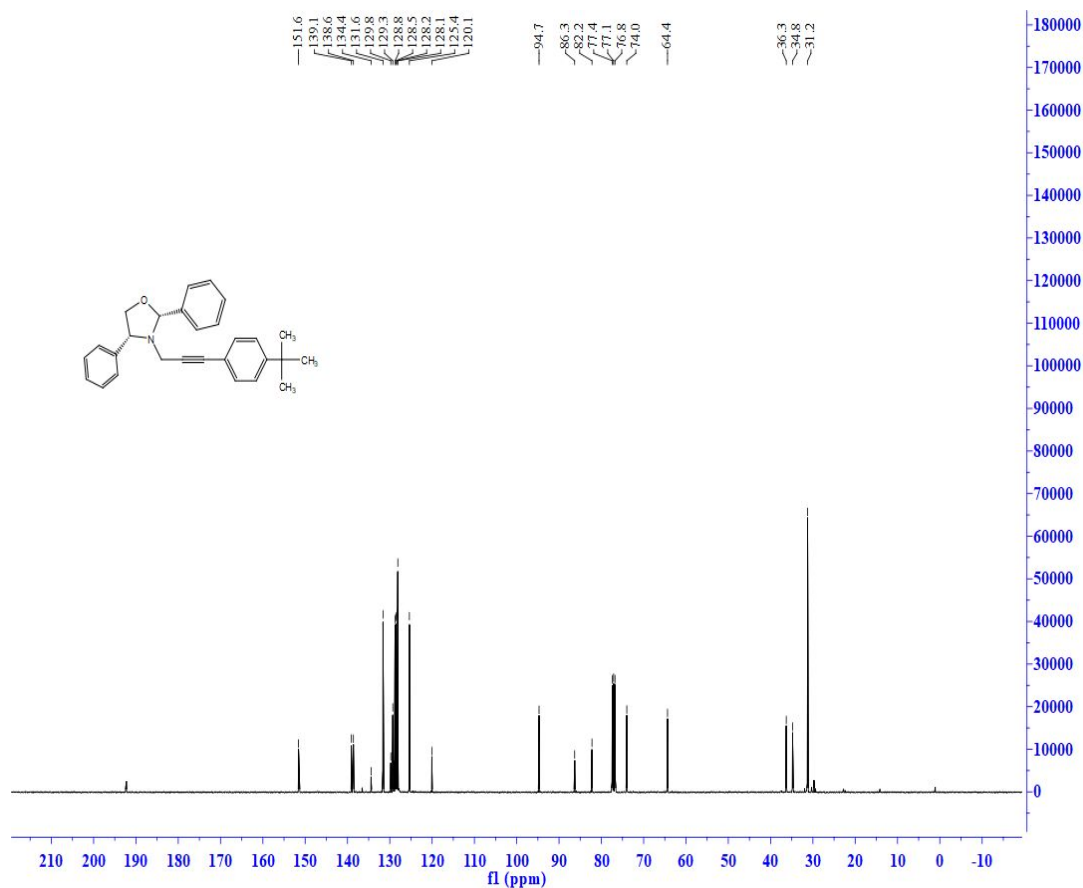
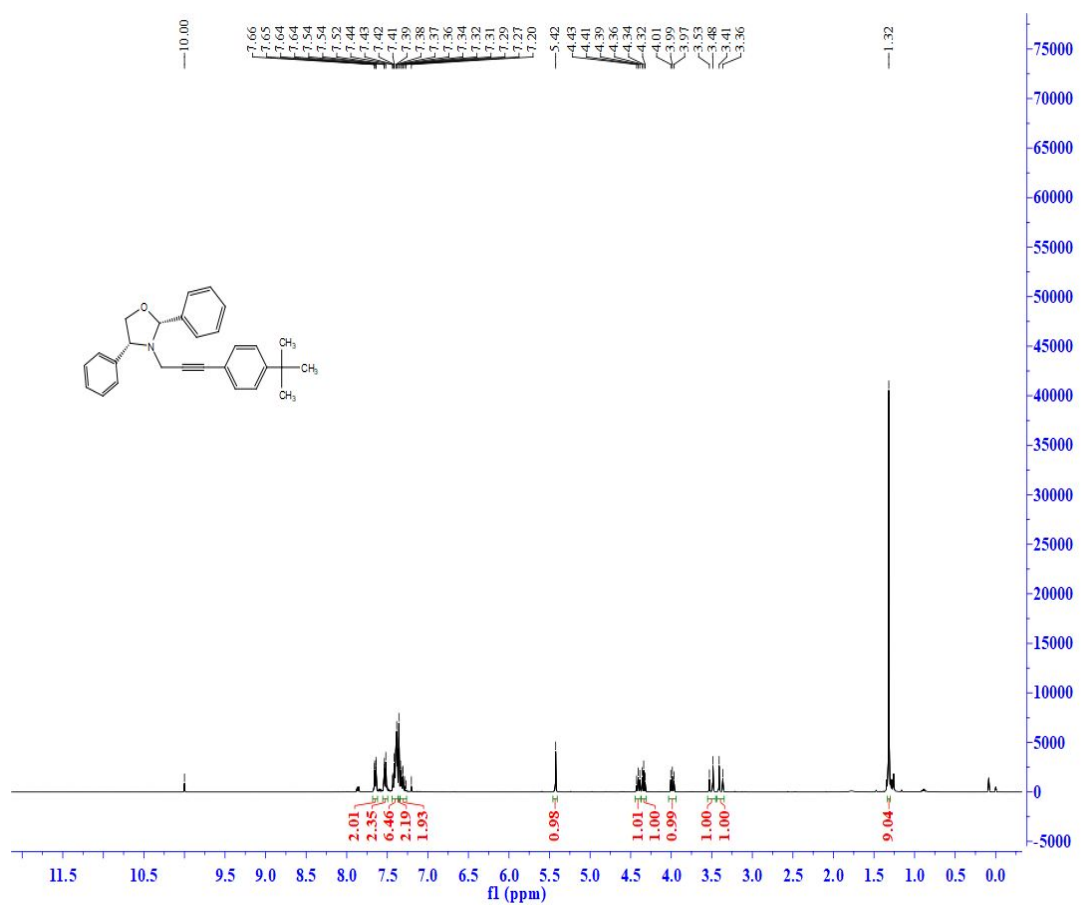
(2*R*,4*R*)-2,4-diphenyl-3-(3-(*p*-tolyl)prop-2-yn-1-yl)oxazolidine (5i)



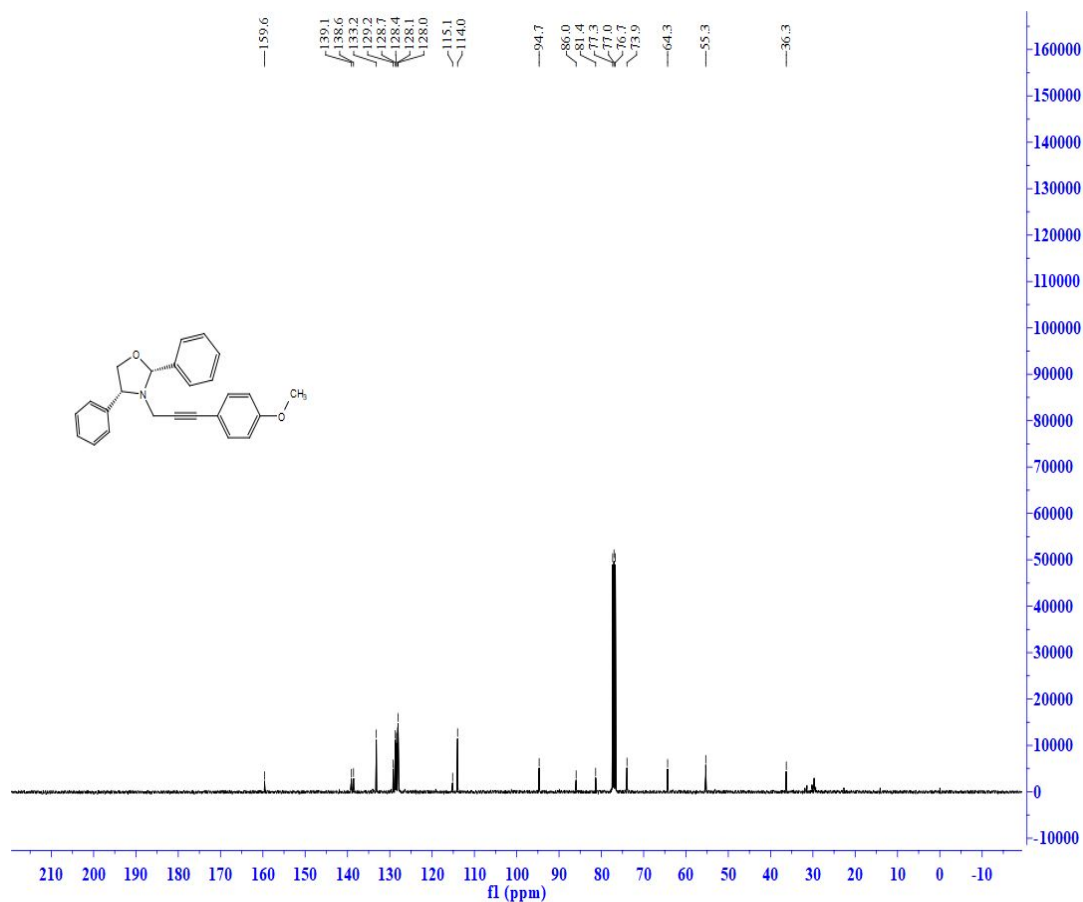
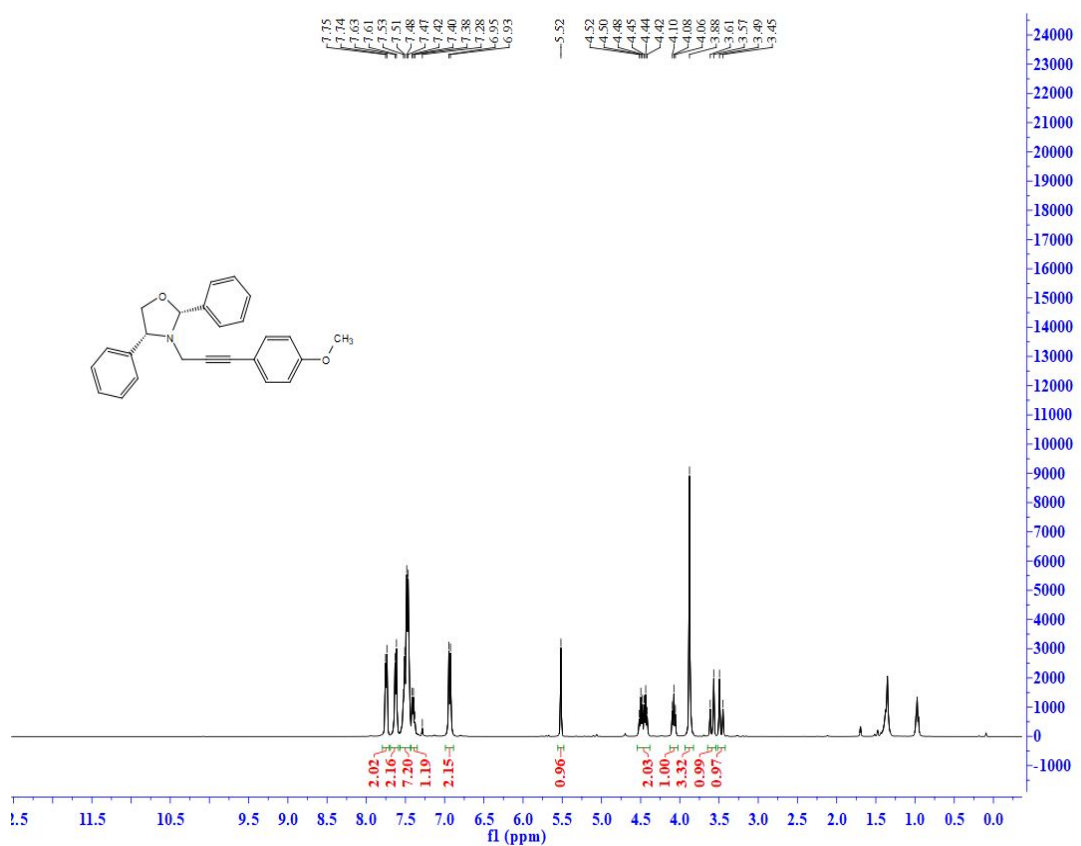
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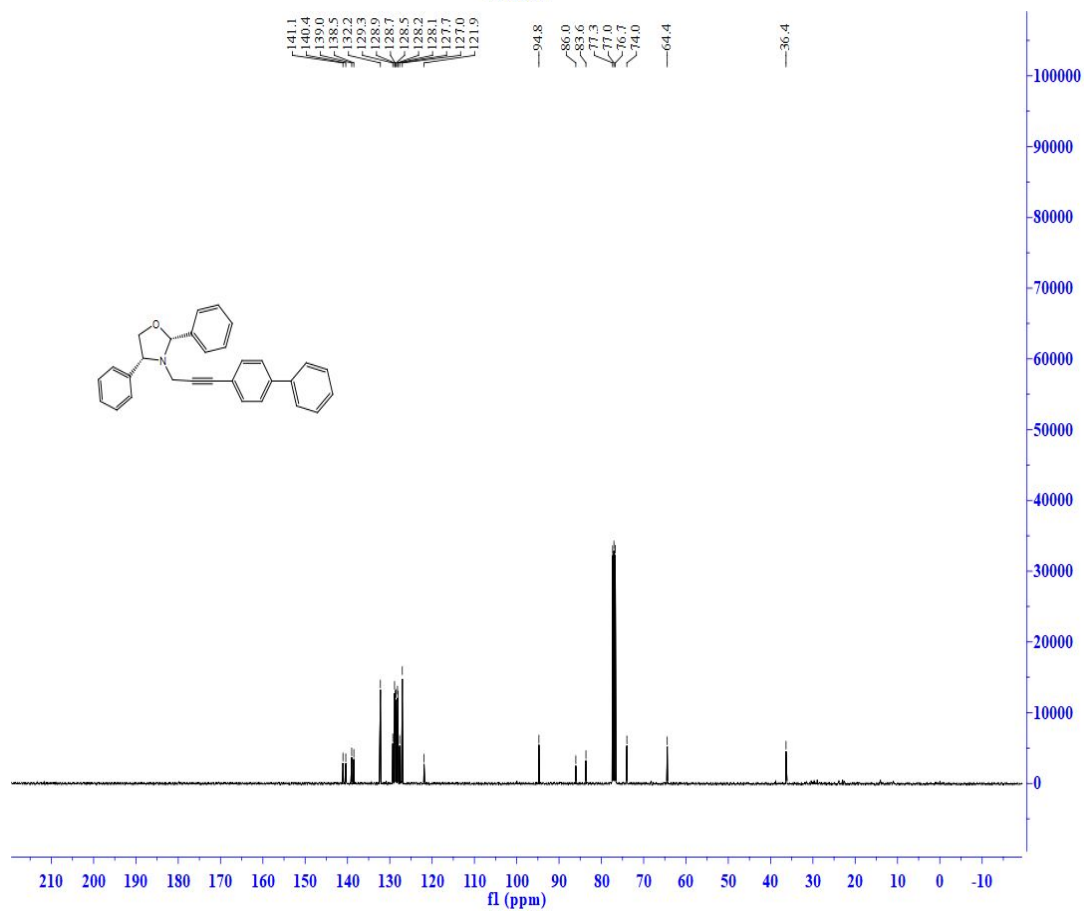
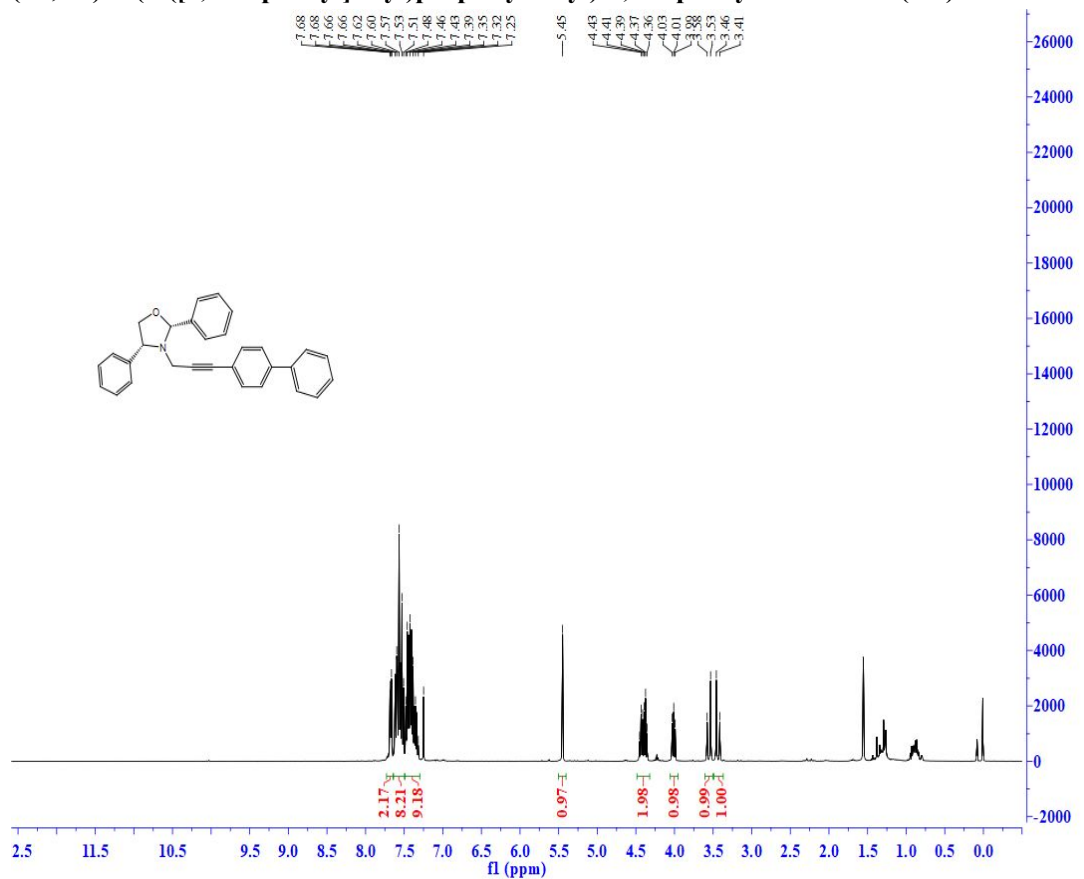
(2*R*,4*R*)-3-(3-(4-(*tert*-butyl)phenyl)prop-2-yn-1-yl)-2,4-diphenyloxazolidine (5k)



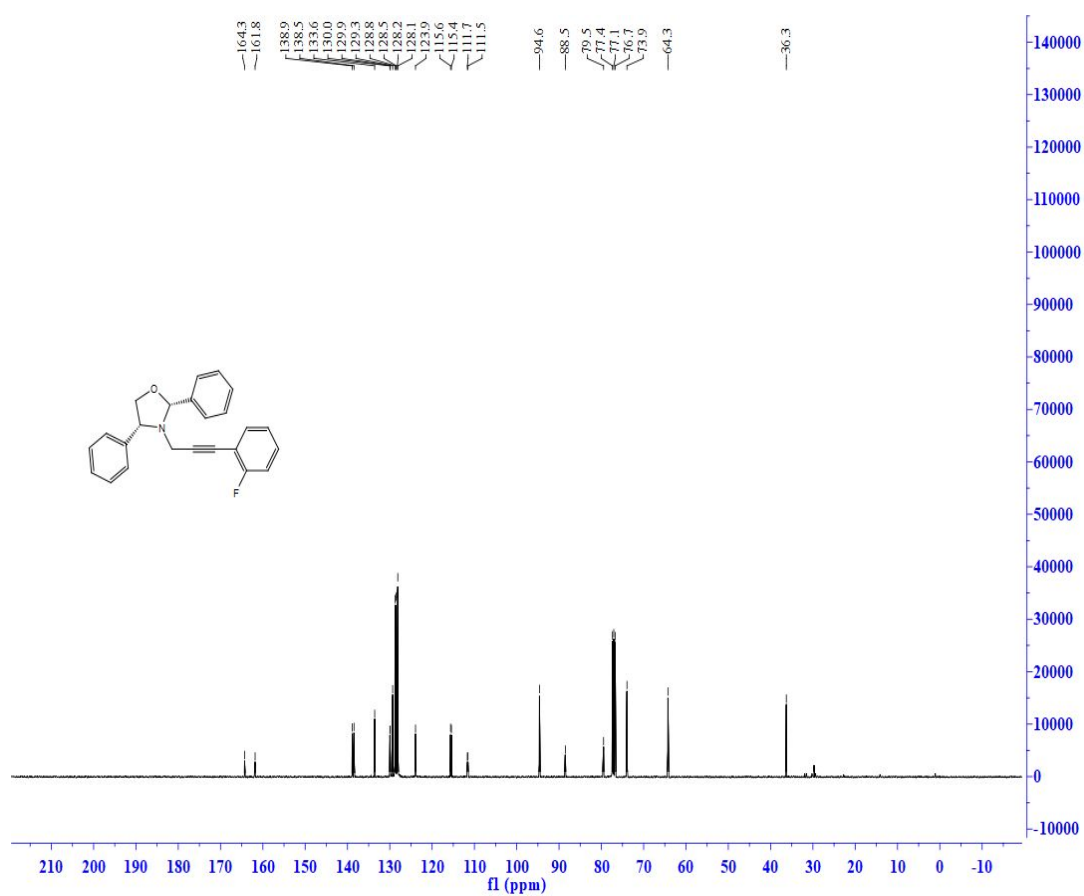
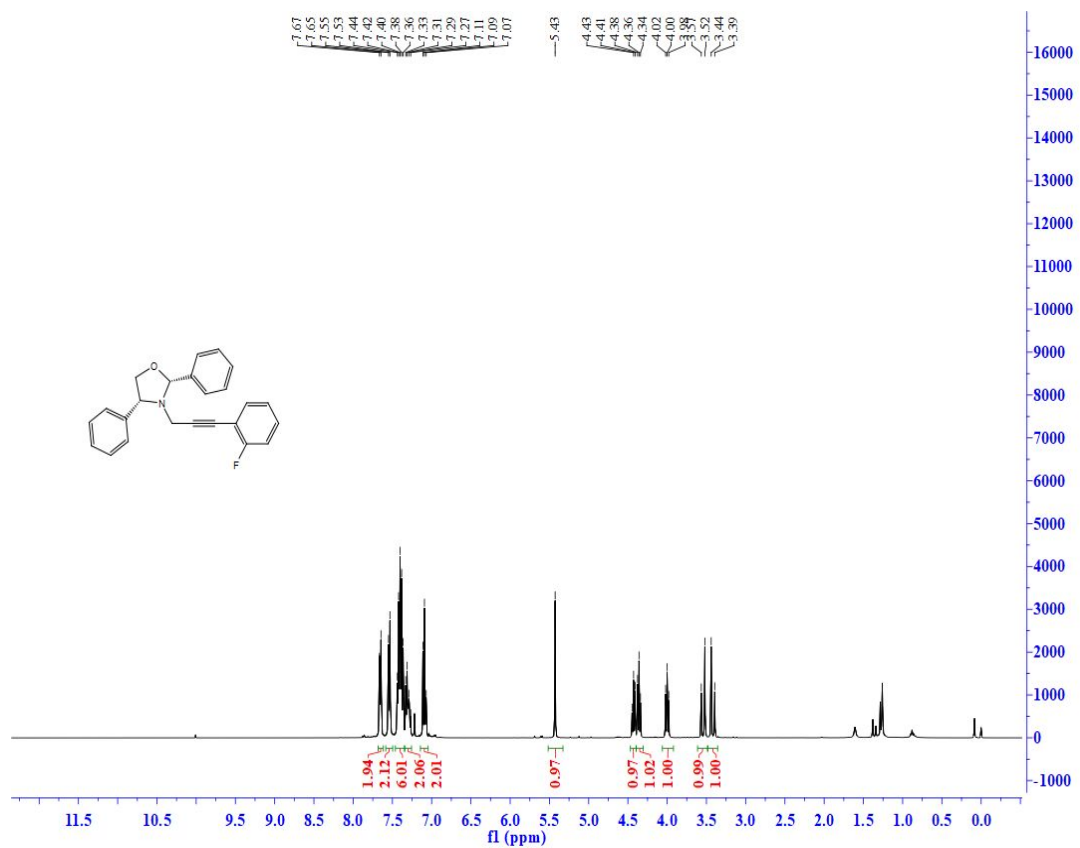
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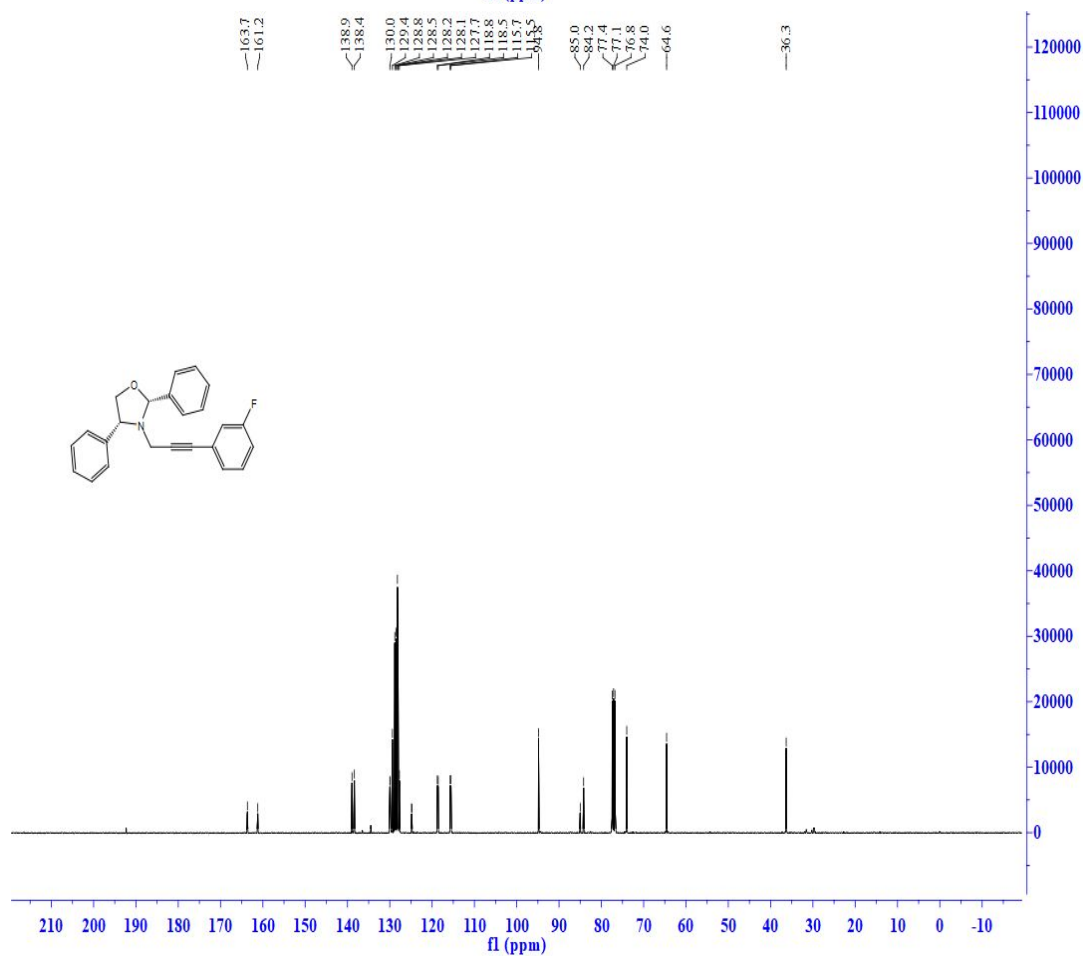
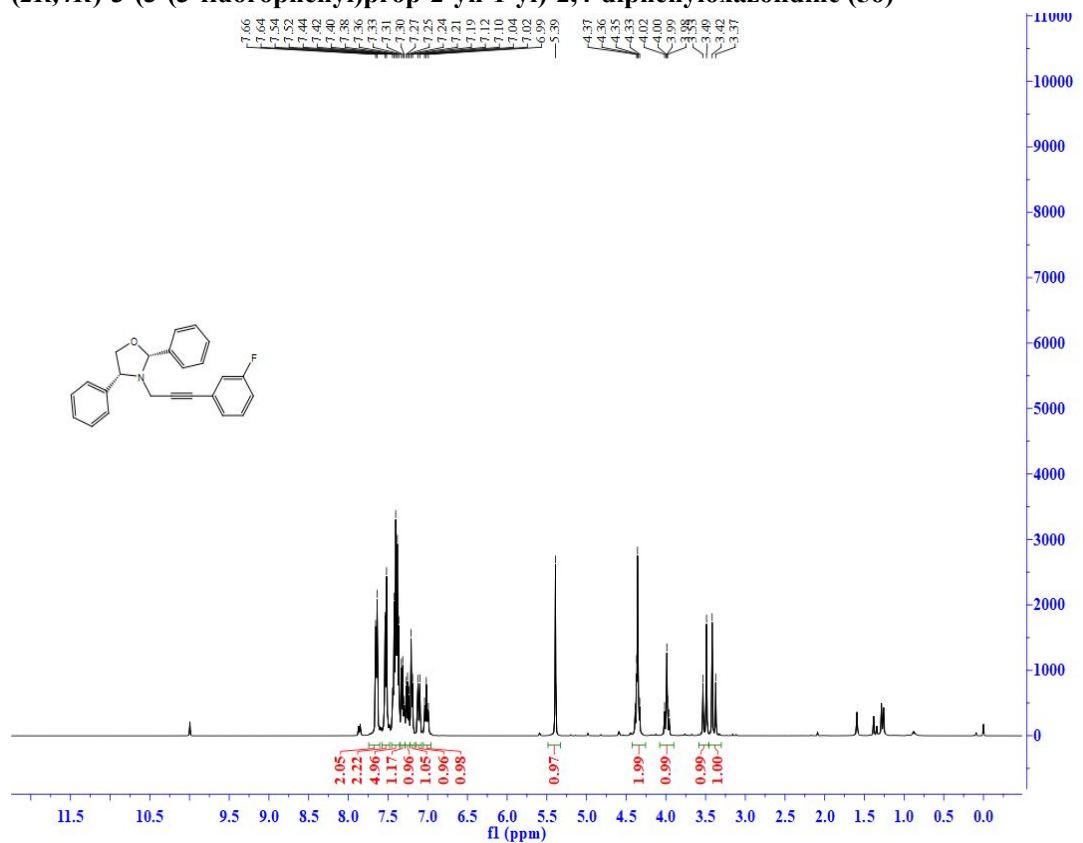
(2*R*,4*R*)-3-(3-([1,1'-biphenyl]-4-yl)prop-2-yn-1-yl)-2,4-diphenyloxazolidine (5m)



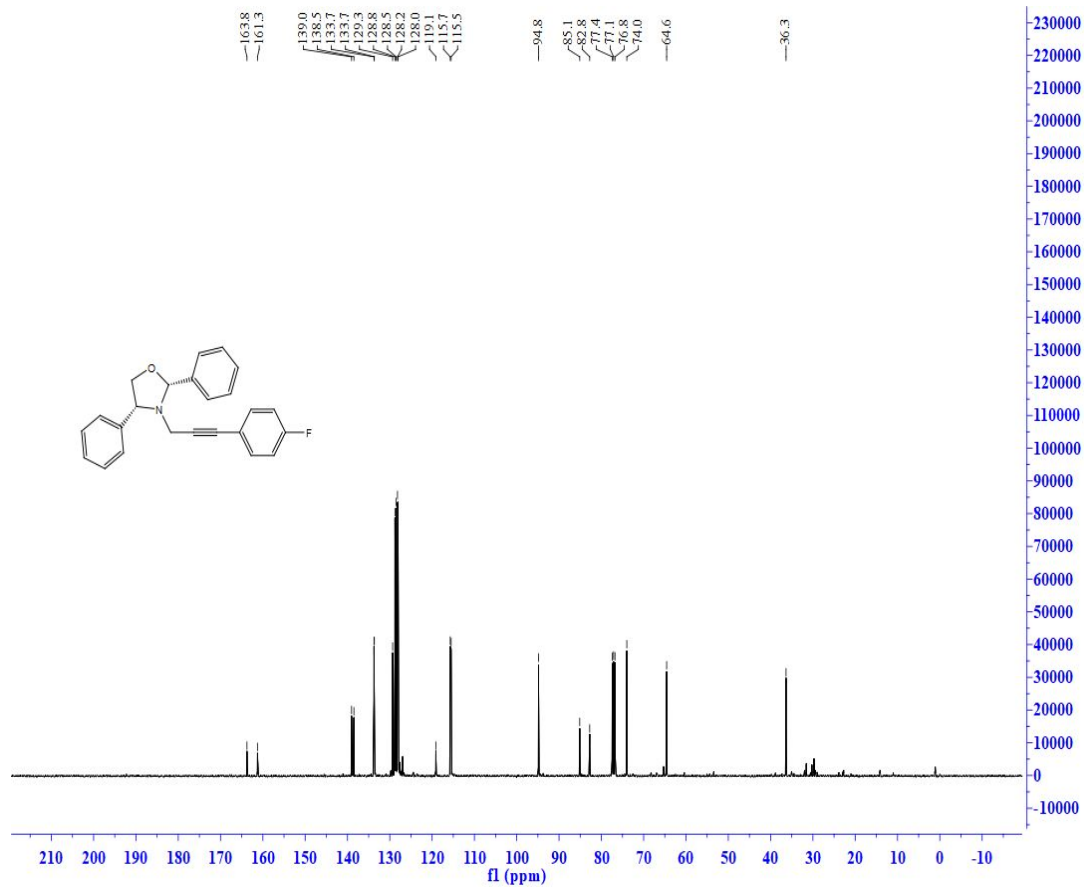
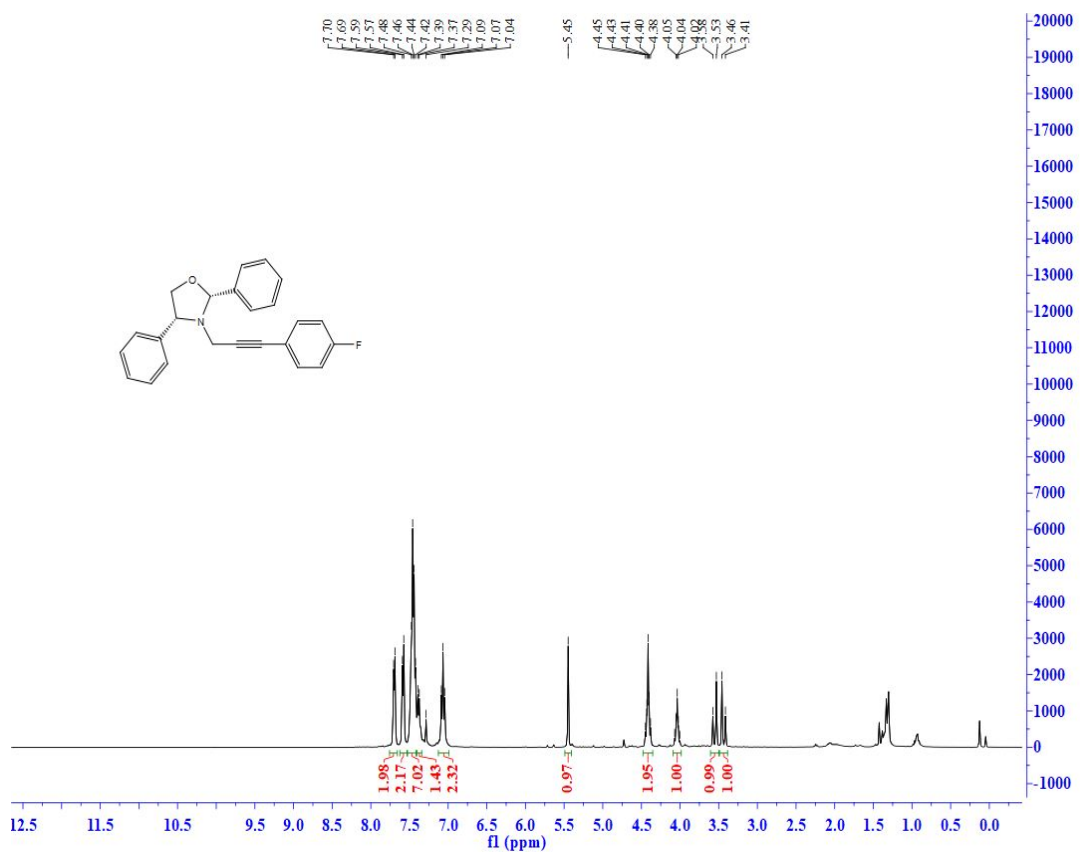
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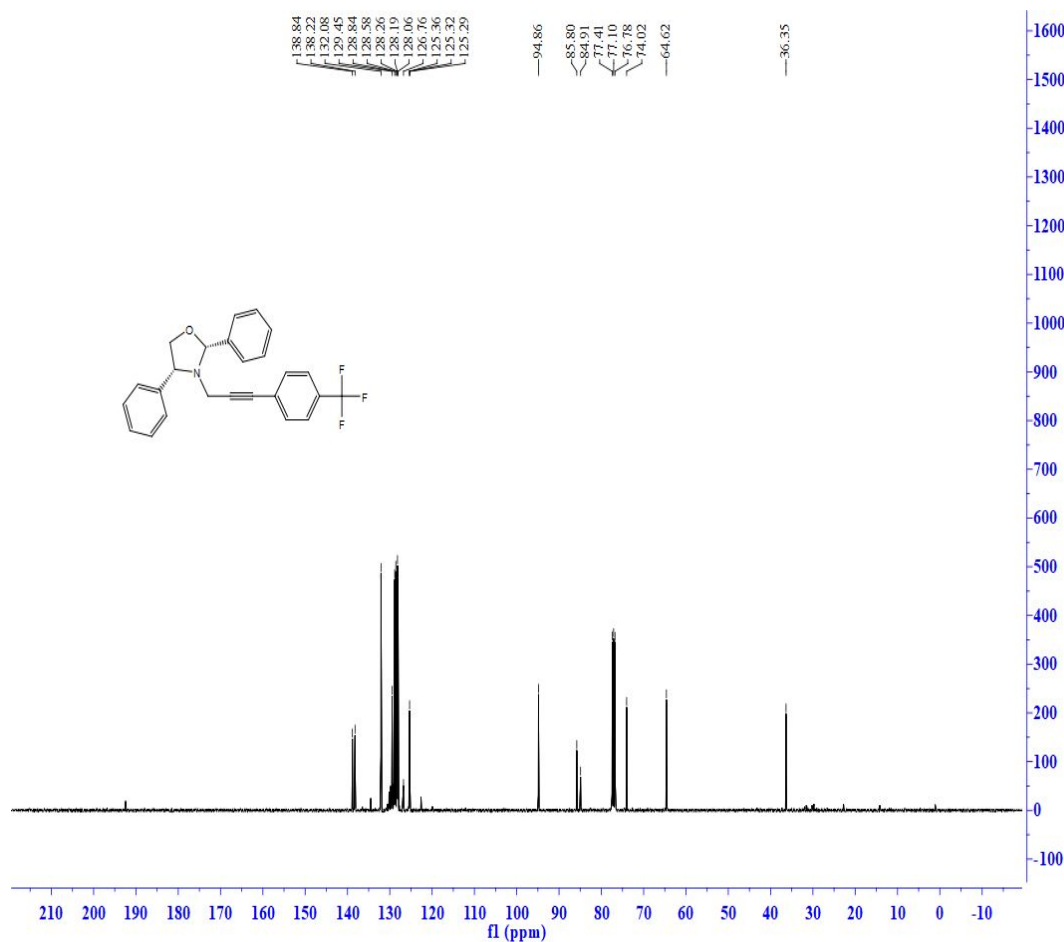
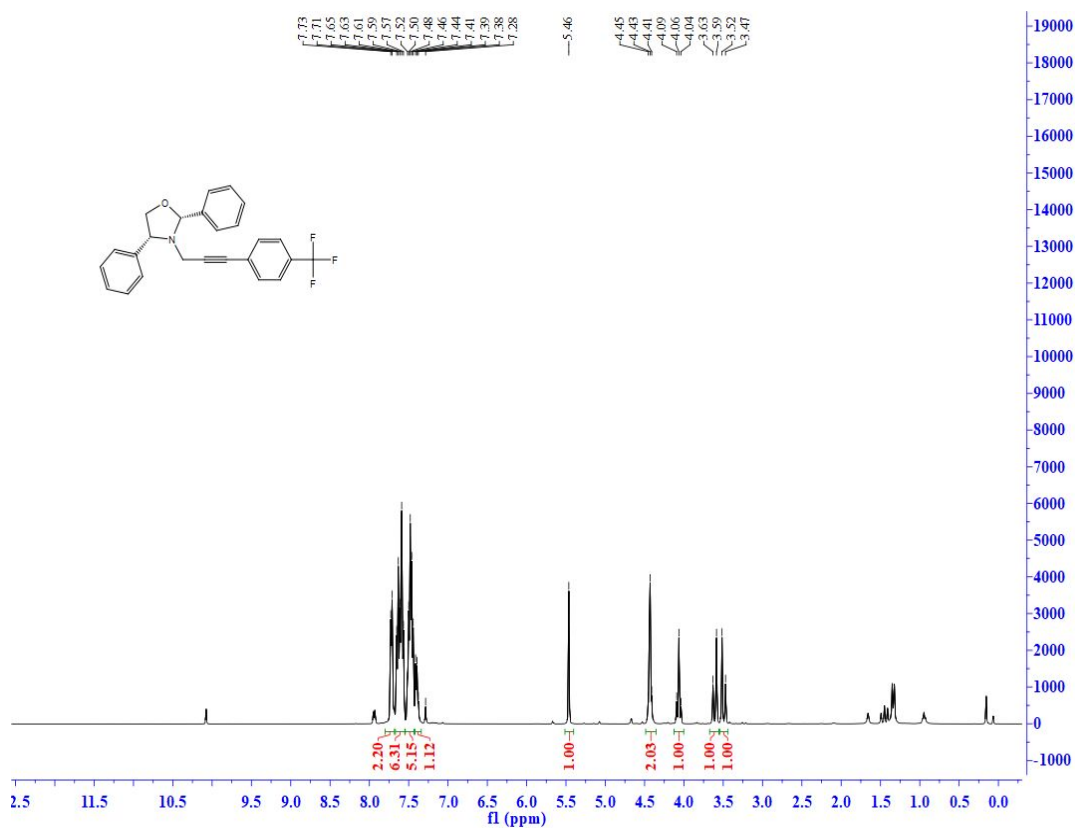
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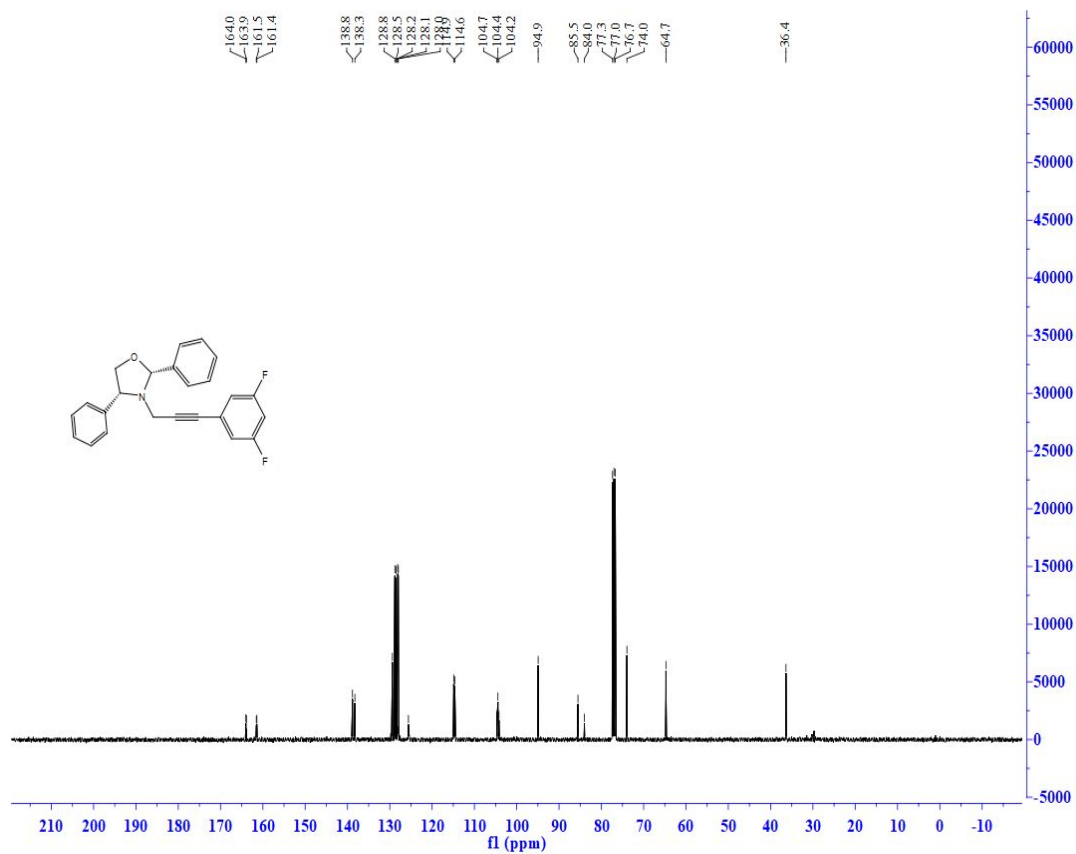
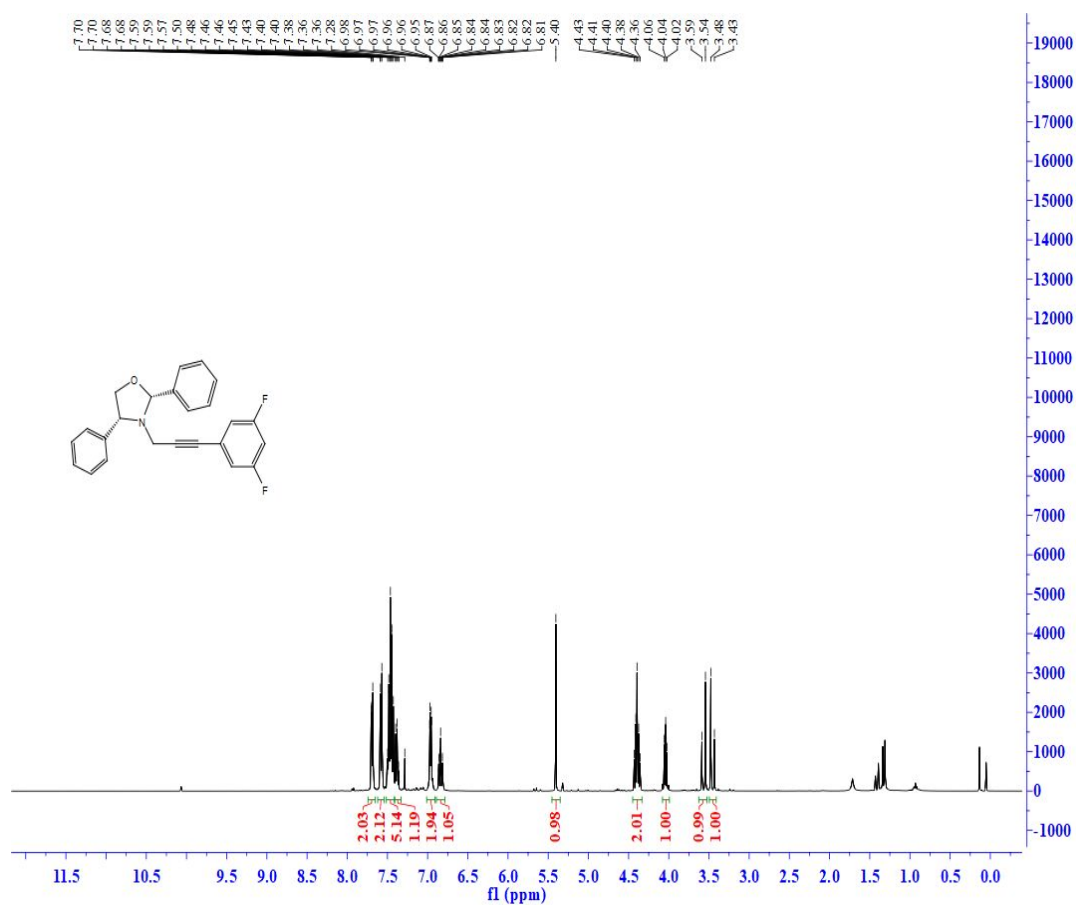
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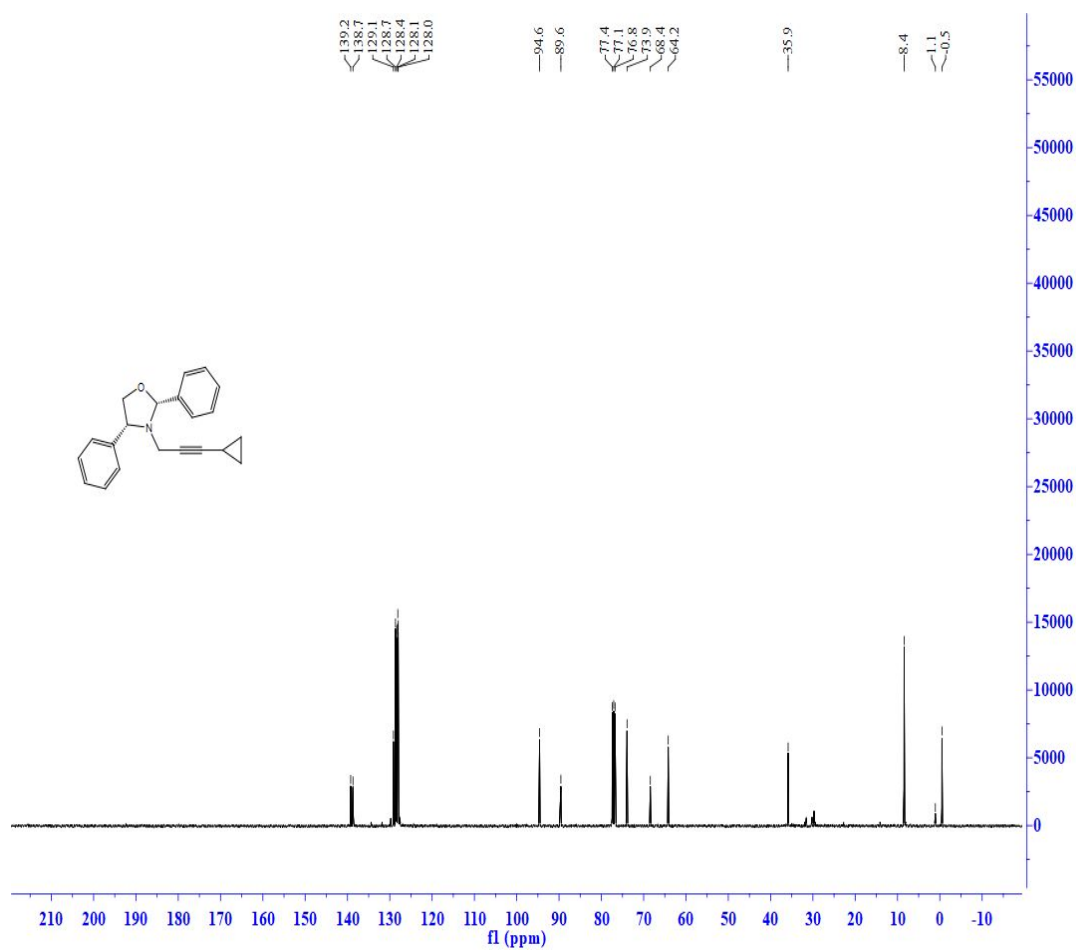
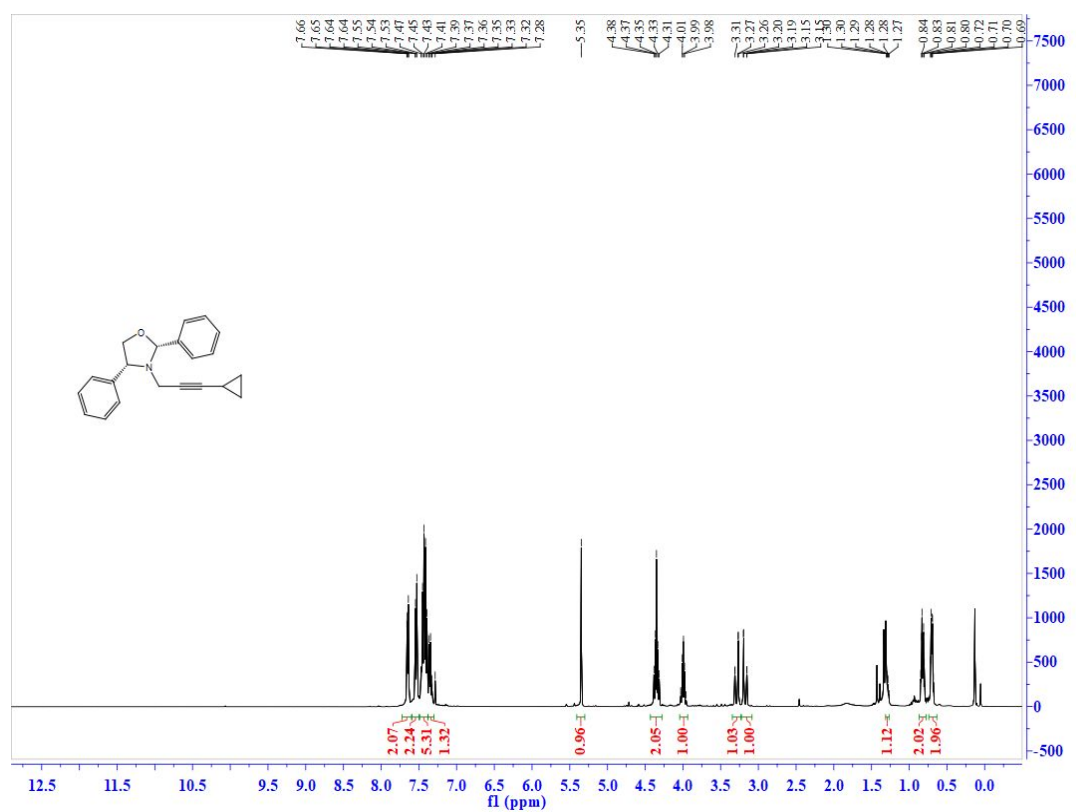
(2*R*,4*R*)-2,4-diphenyl-3-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)oxazolidine (5q)



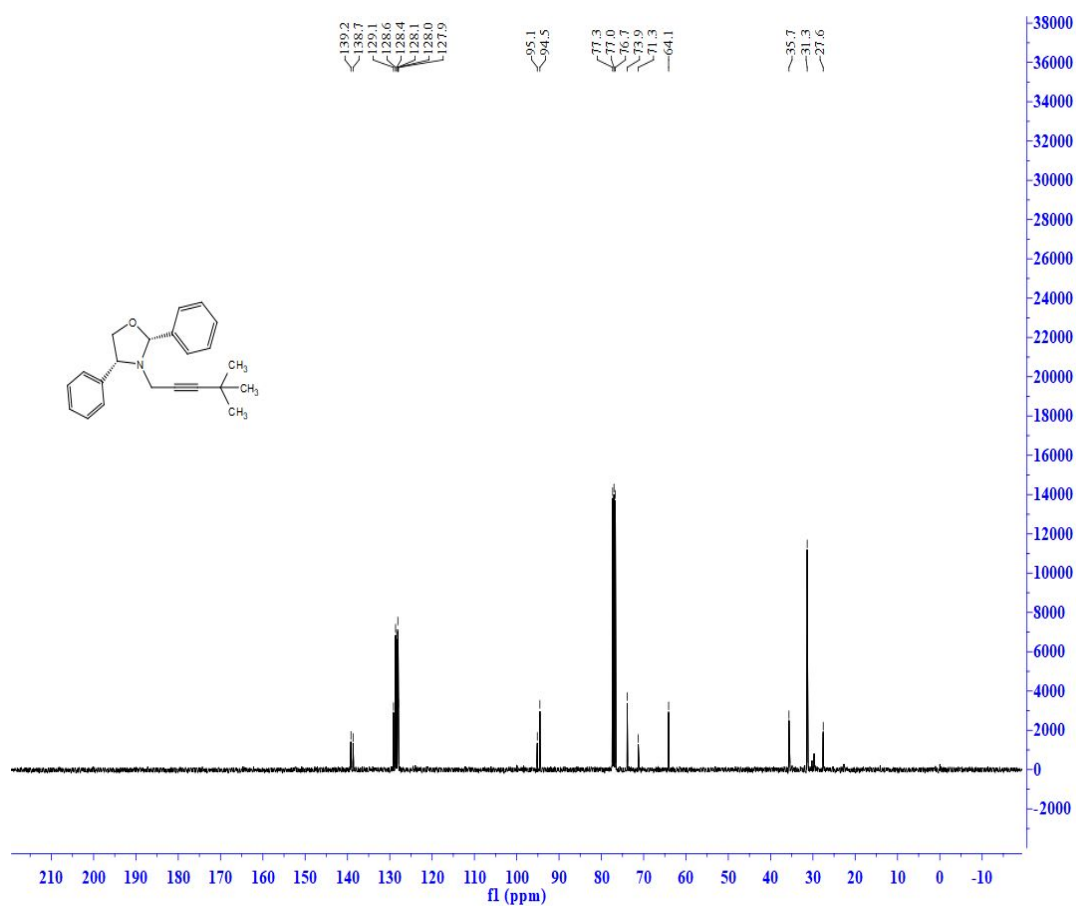
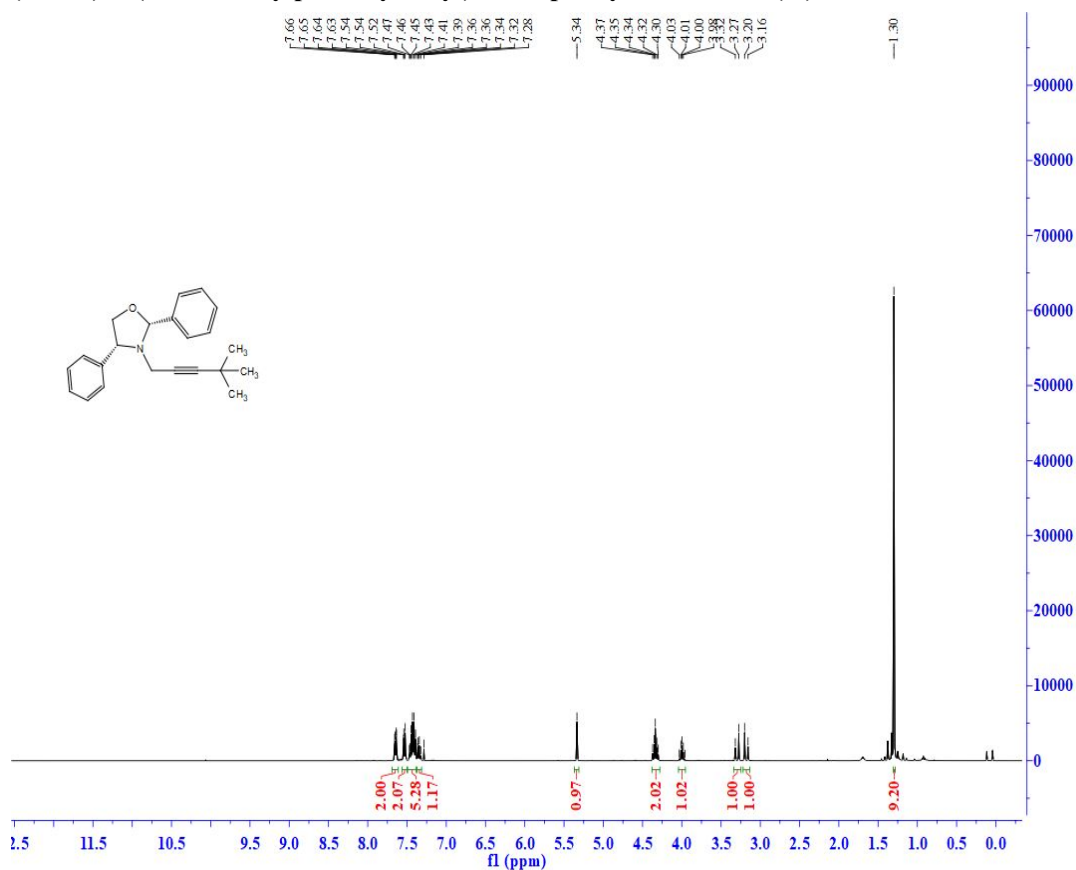
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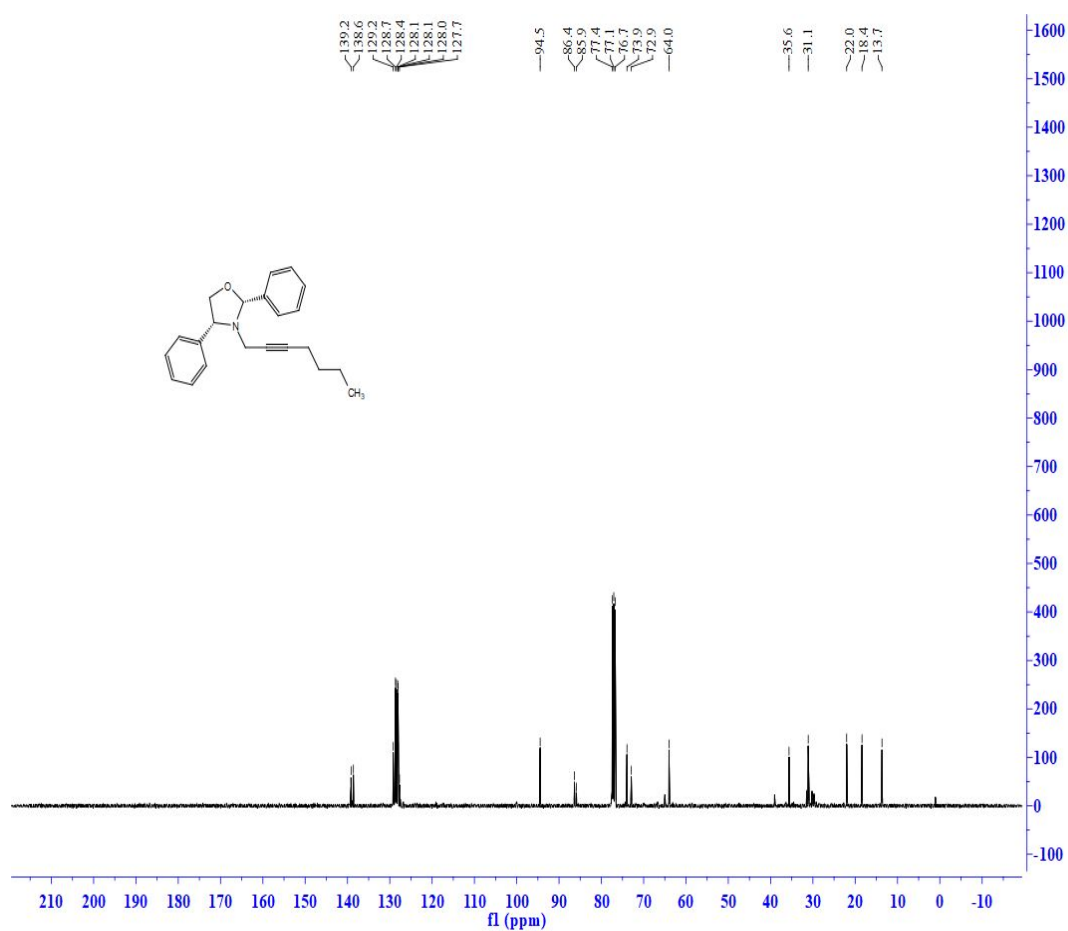
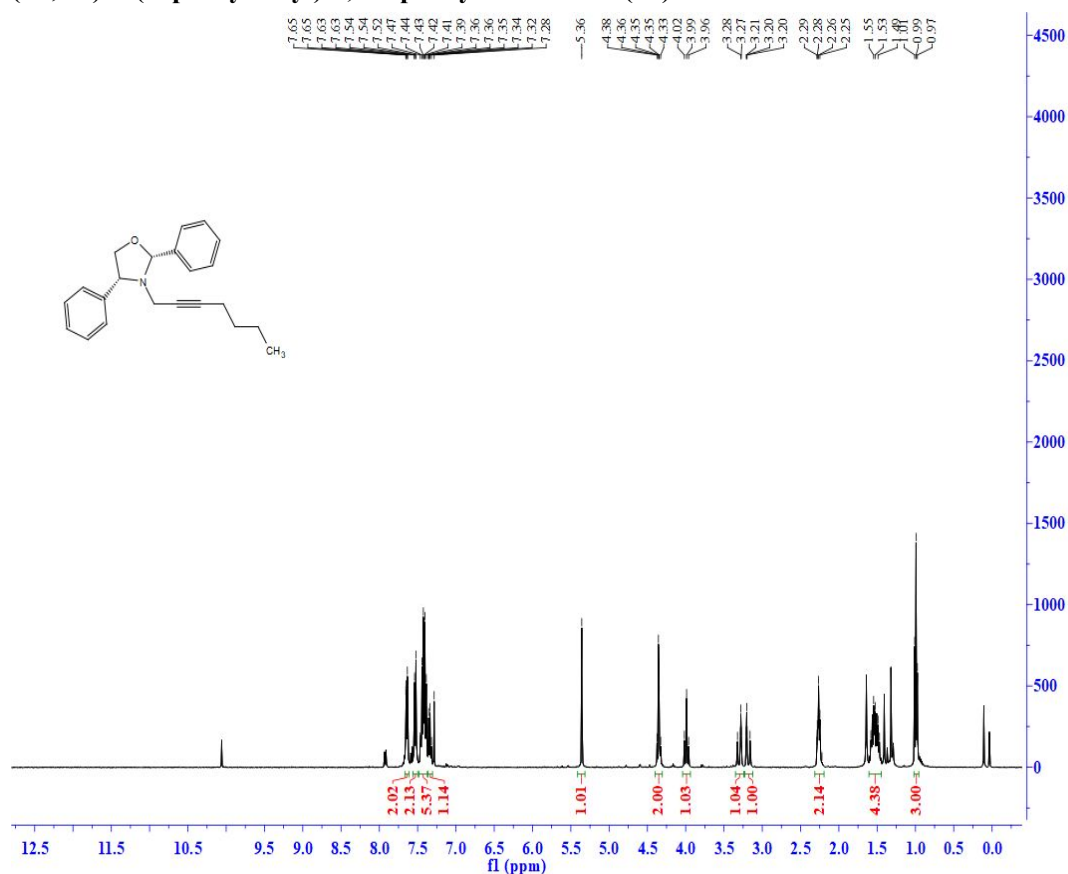
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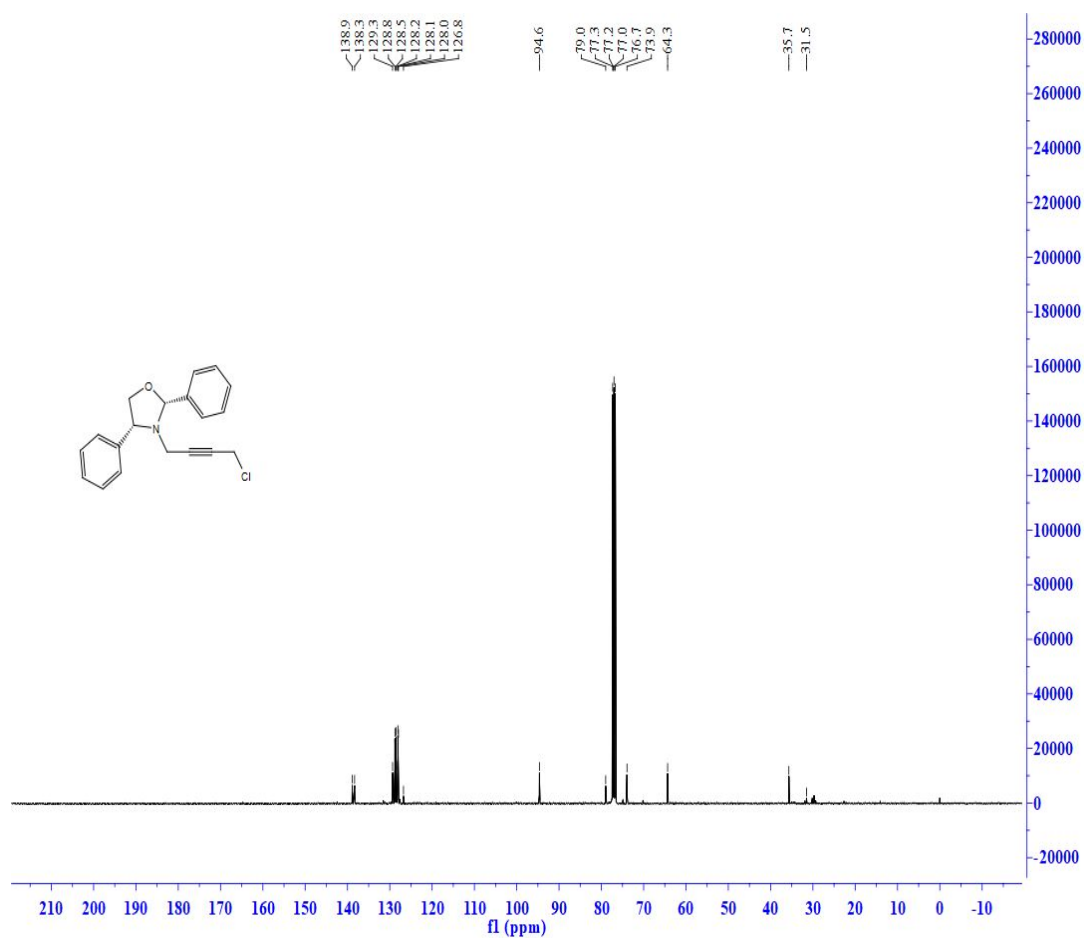
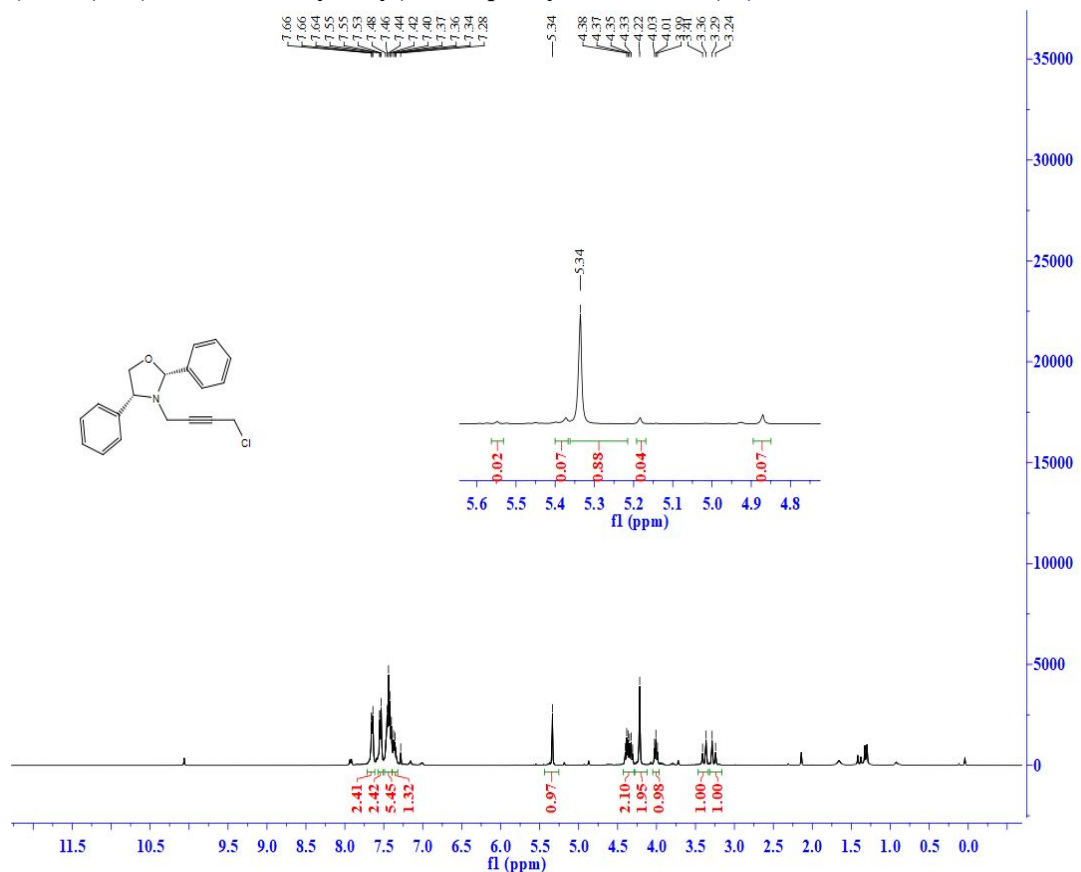
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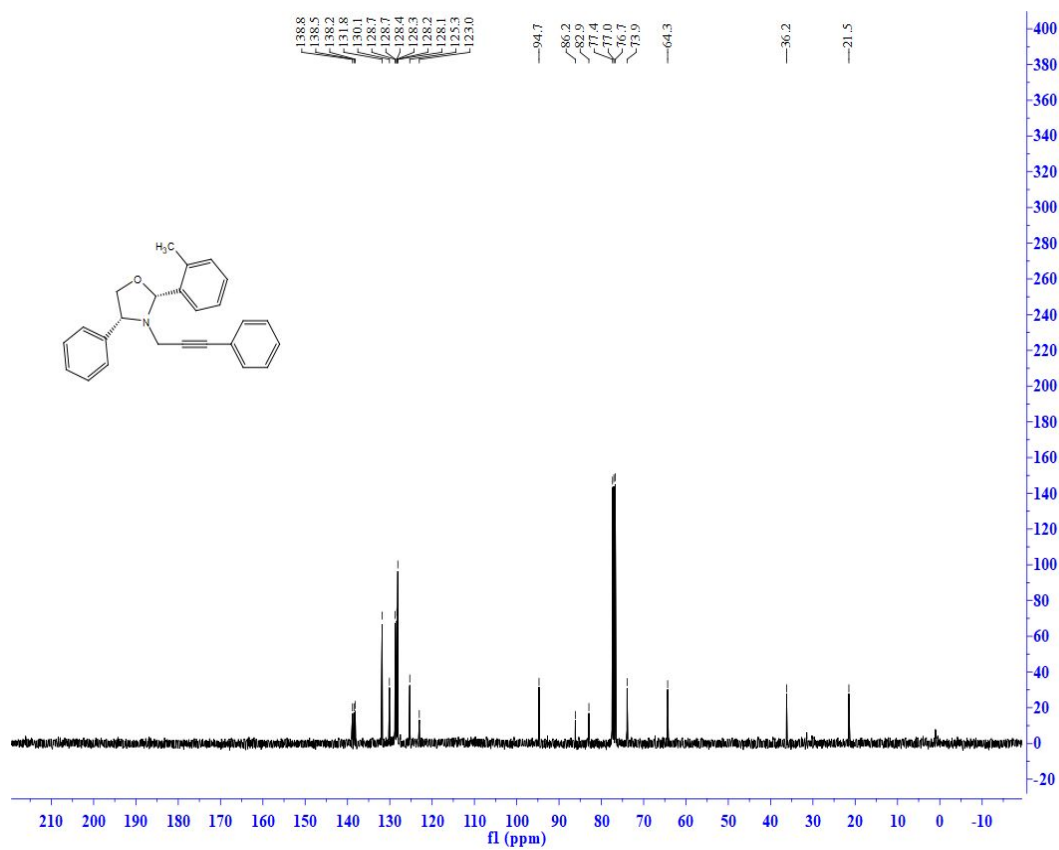
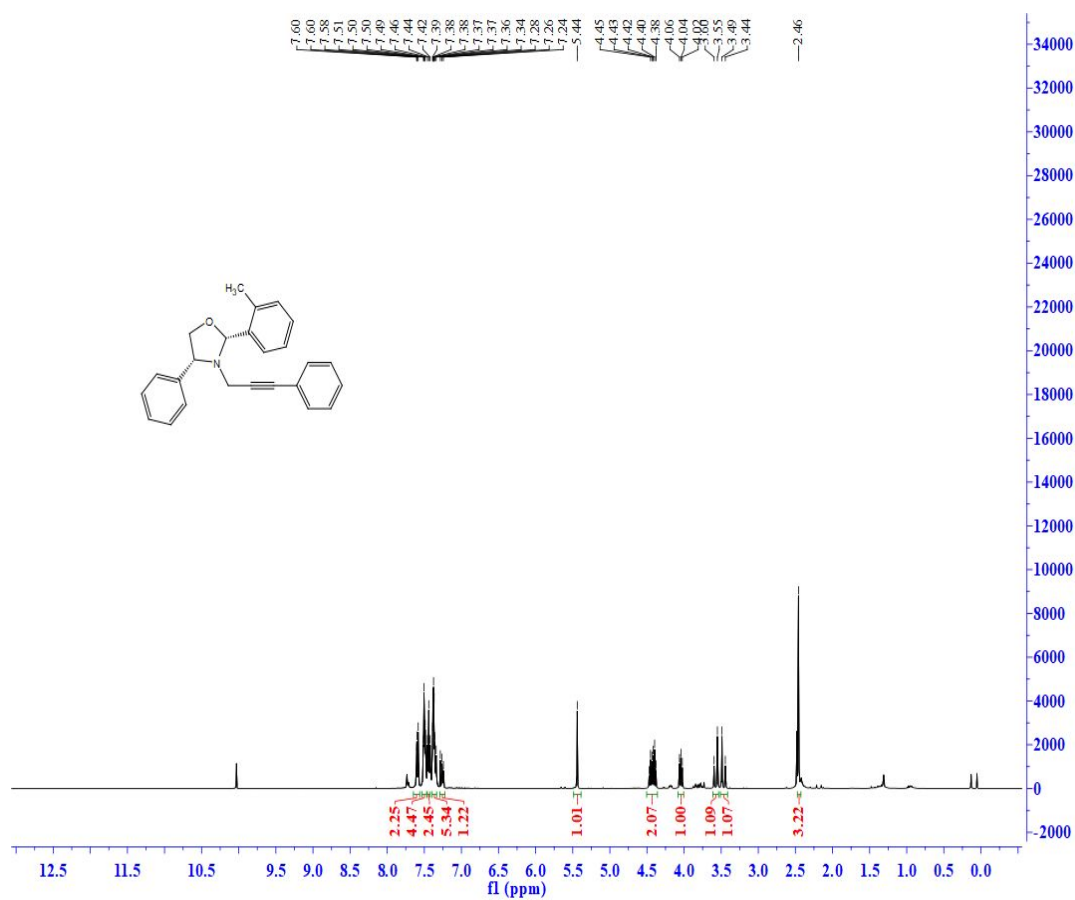
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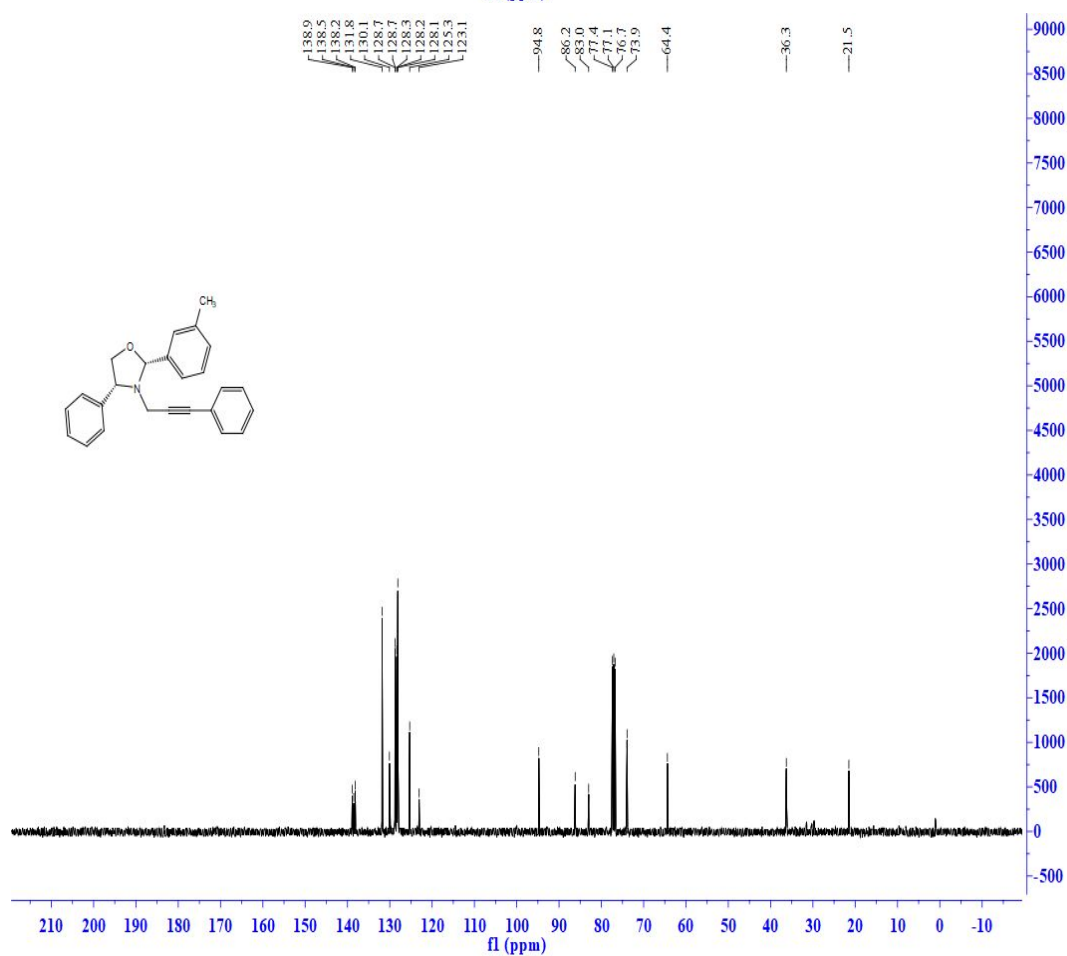
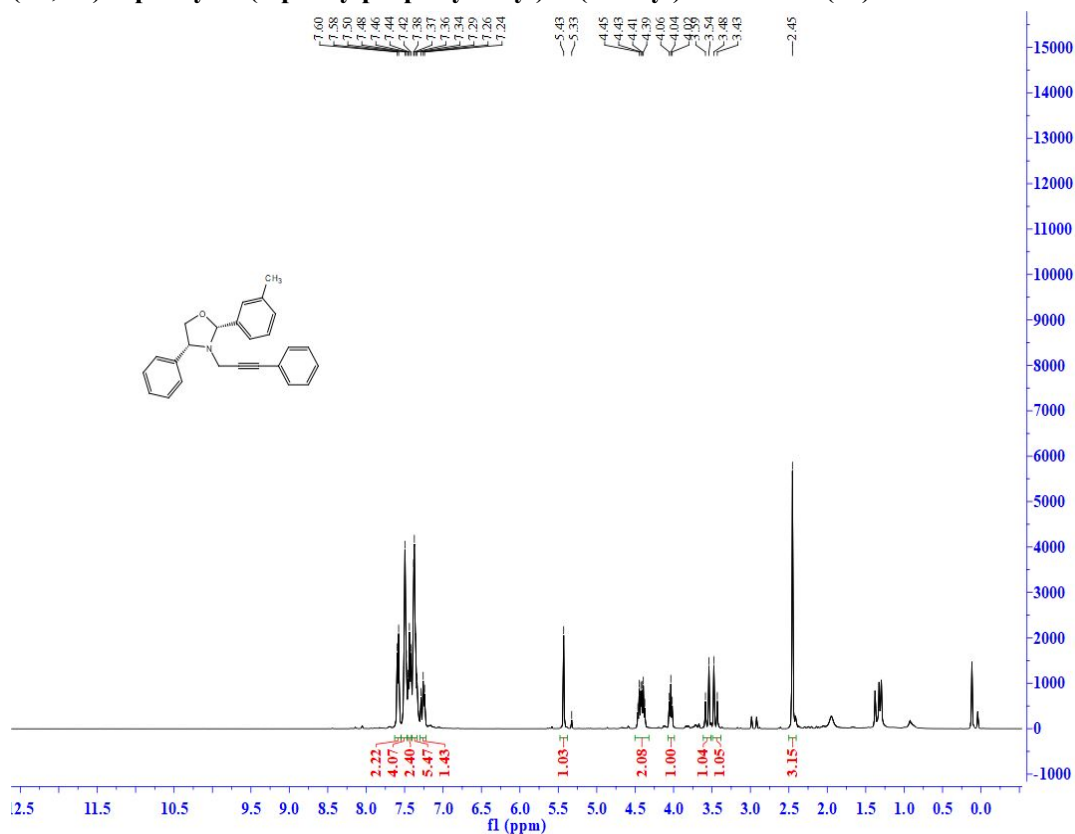
(2*R*,4*R*)-3-(4-chlorobut-2-yn-1-yl)-2,4-diphenyloxazolidine (5v)



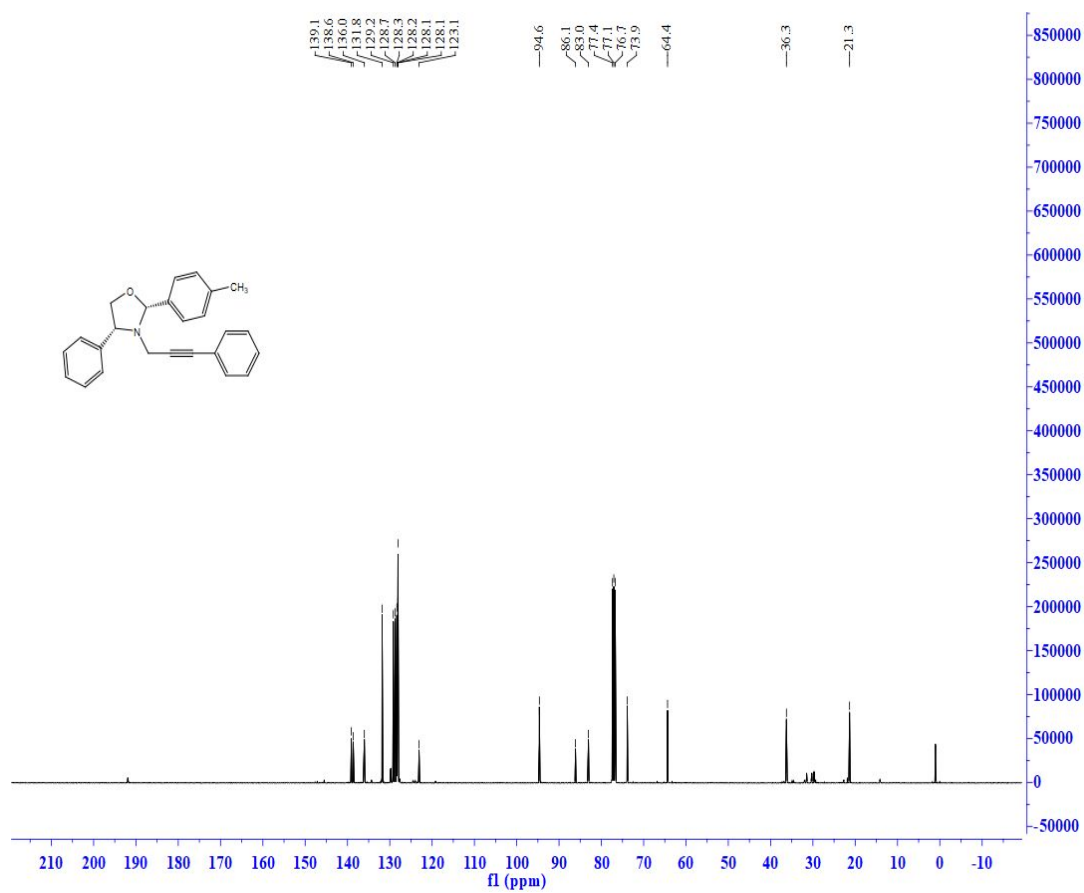
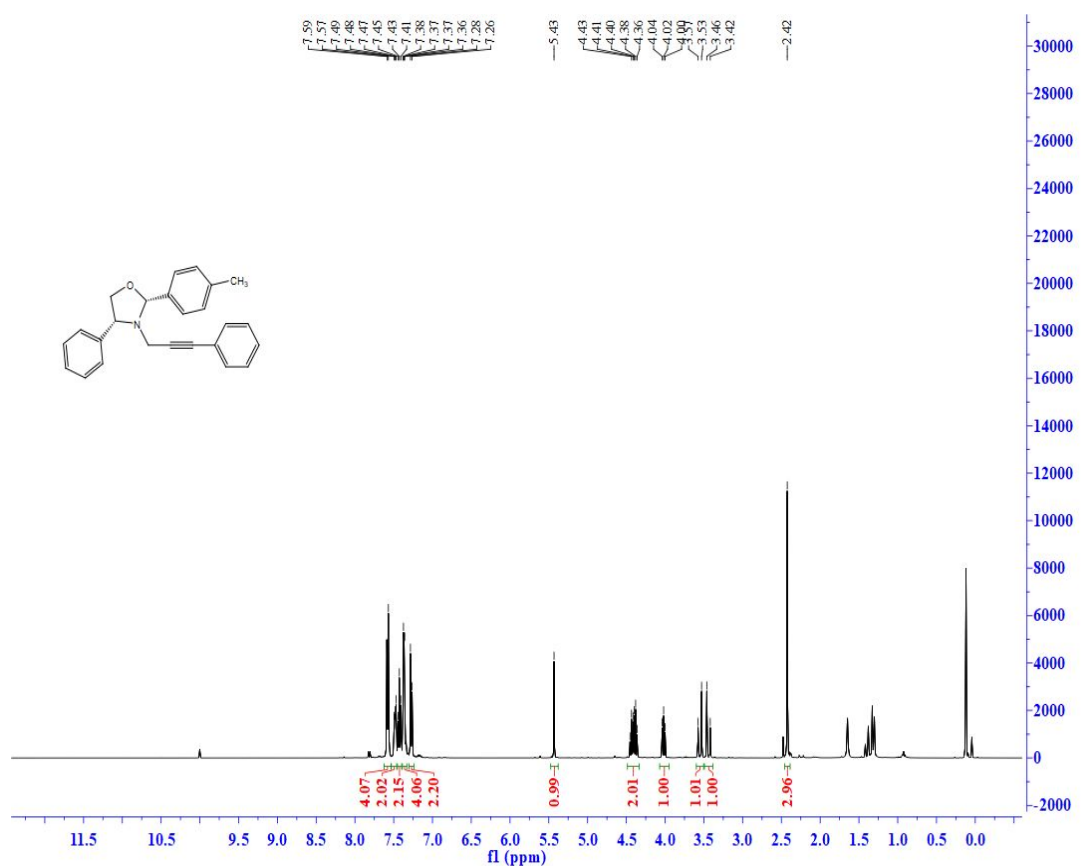
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(*o*-tolyl)oxazolidine (5w)



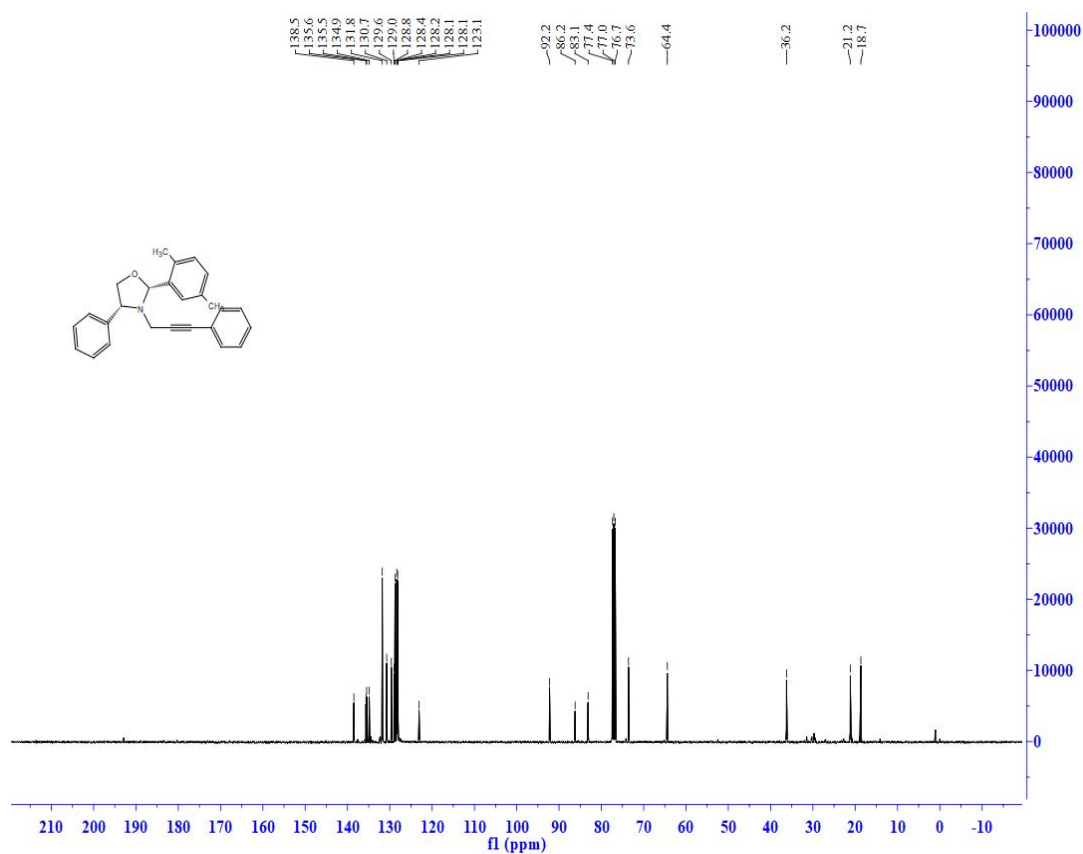
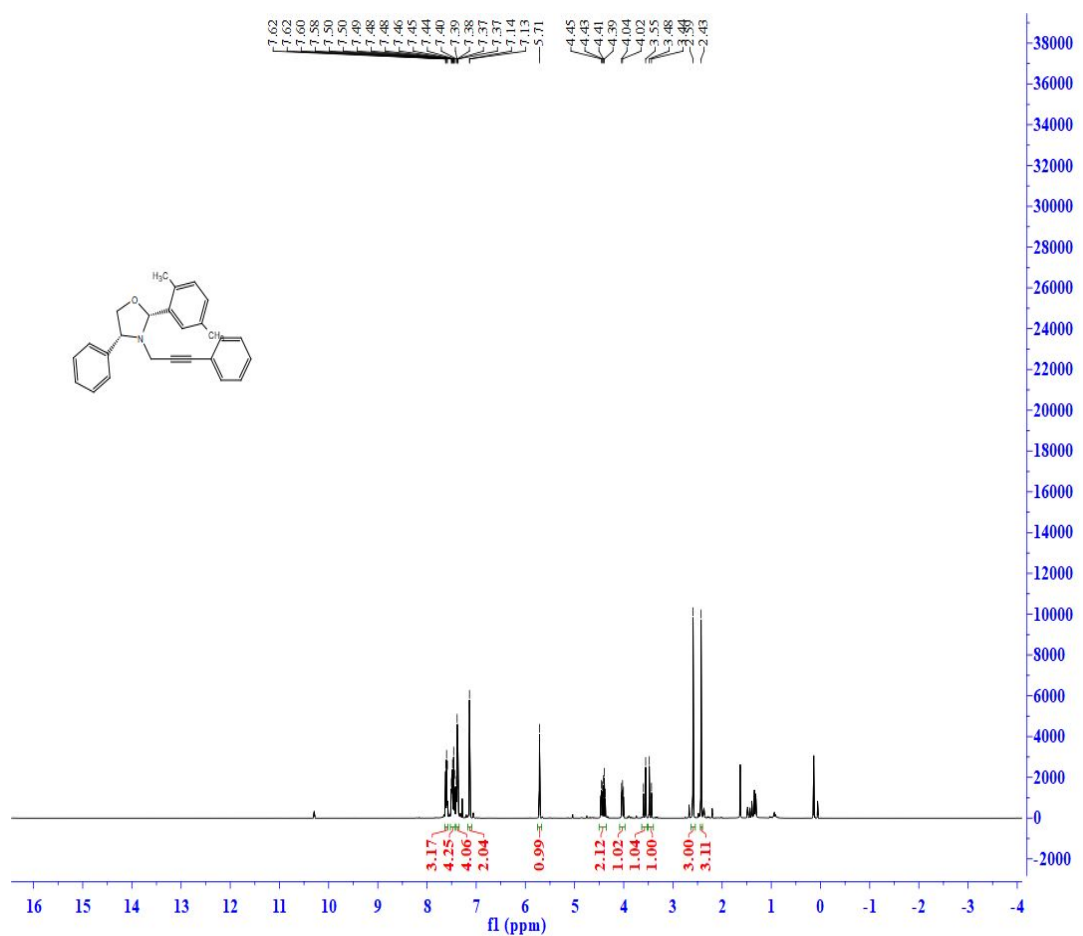
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(*m*-tolyl)oxazolidine (5x)



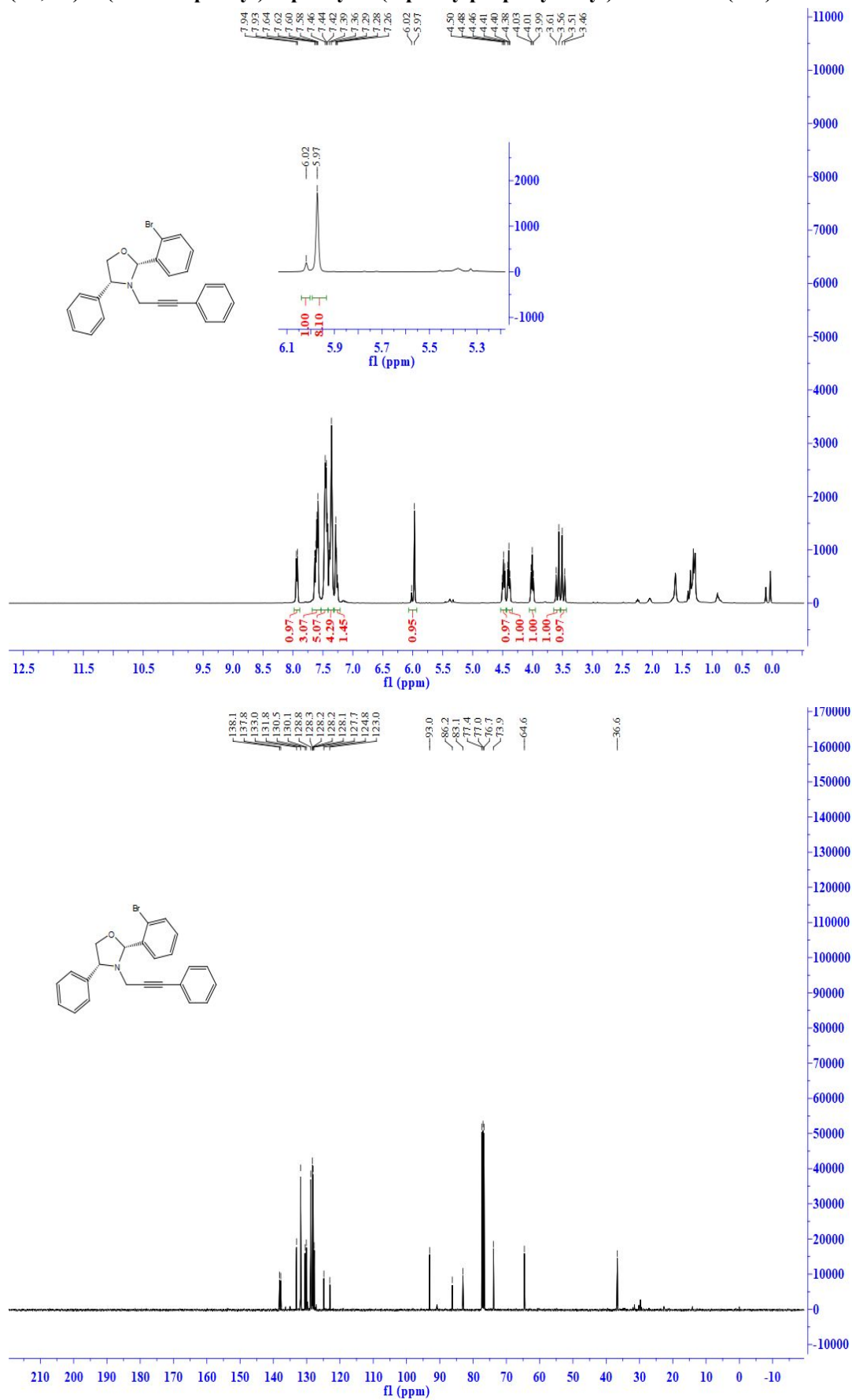
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(p-tolyl)oxazolidine (5y)



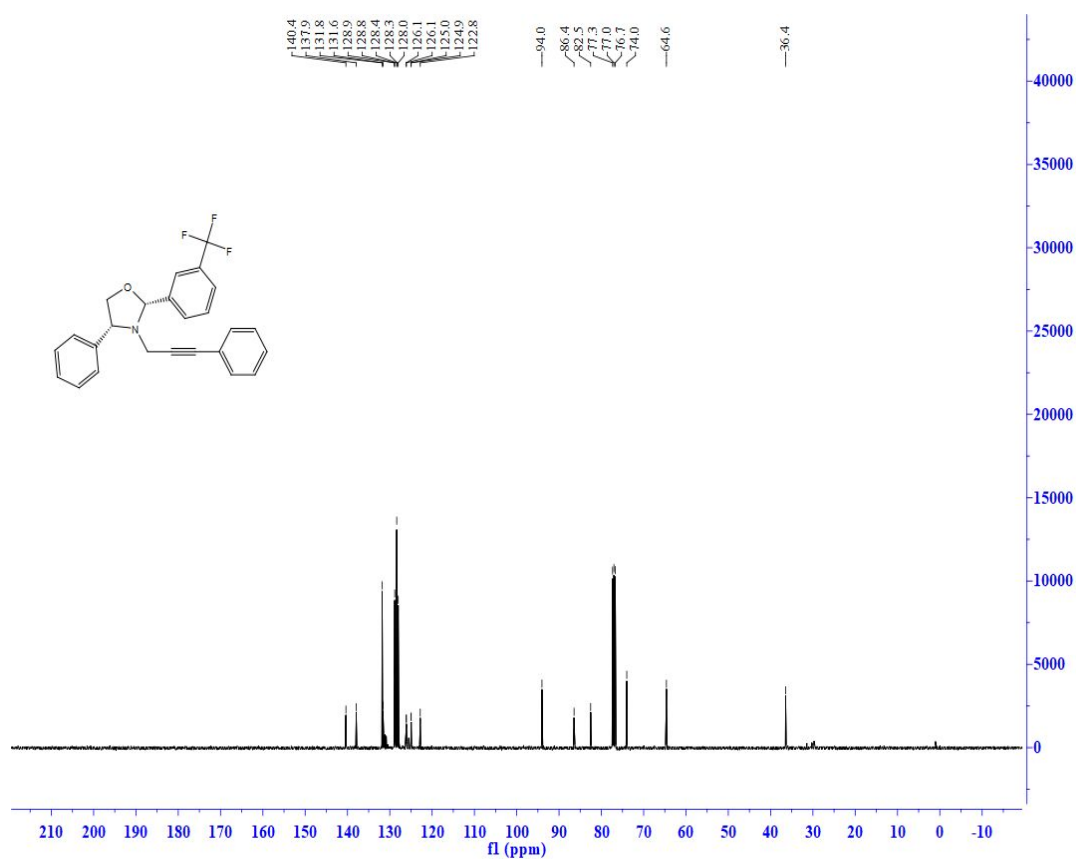
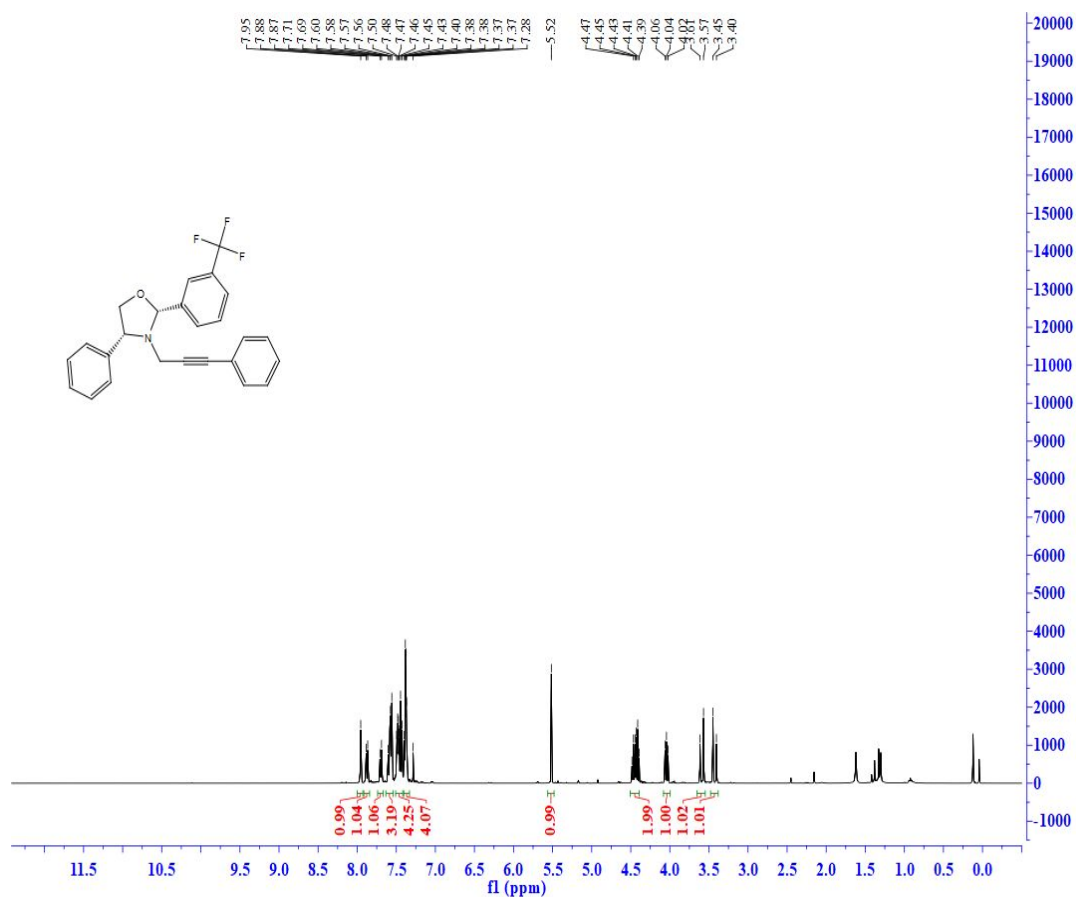
(2*R*,4*R*)-2-(2,5-dimethylphenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5z)



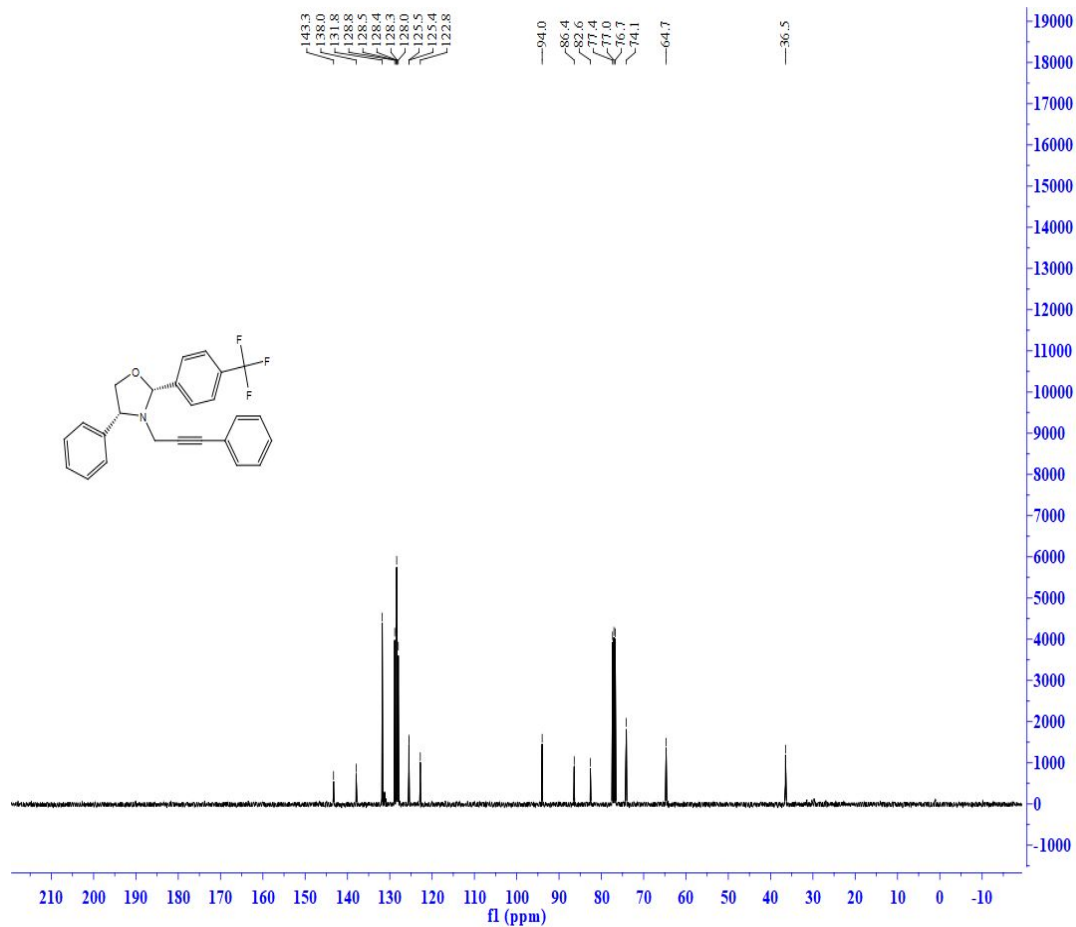
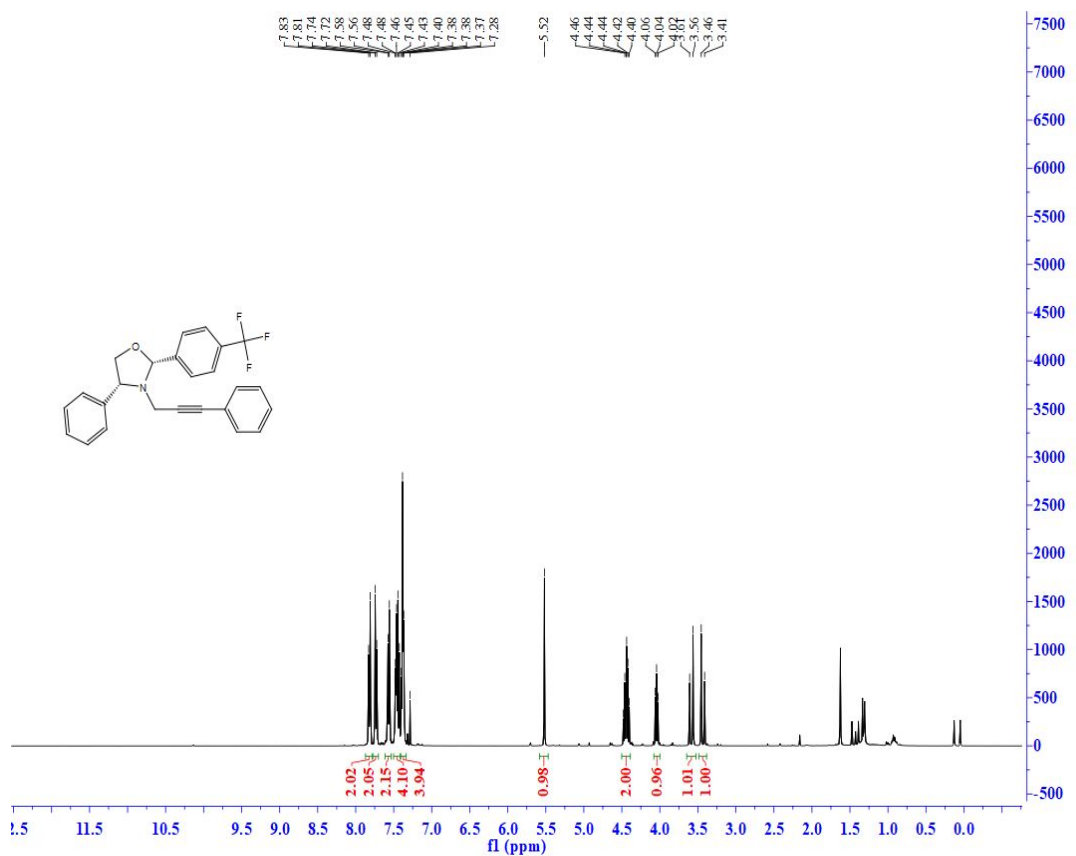
(2*R*,4*R*)-2-(2-bromophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5za)



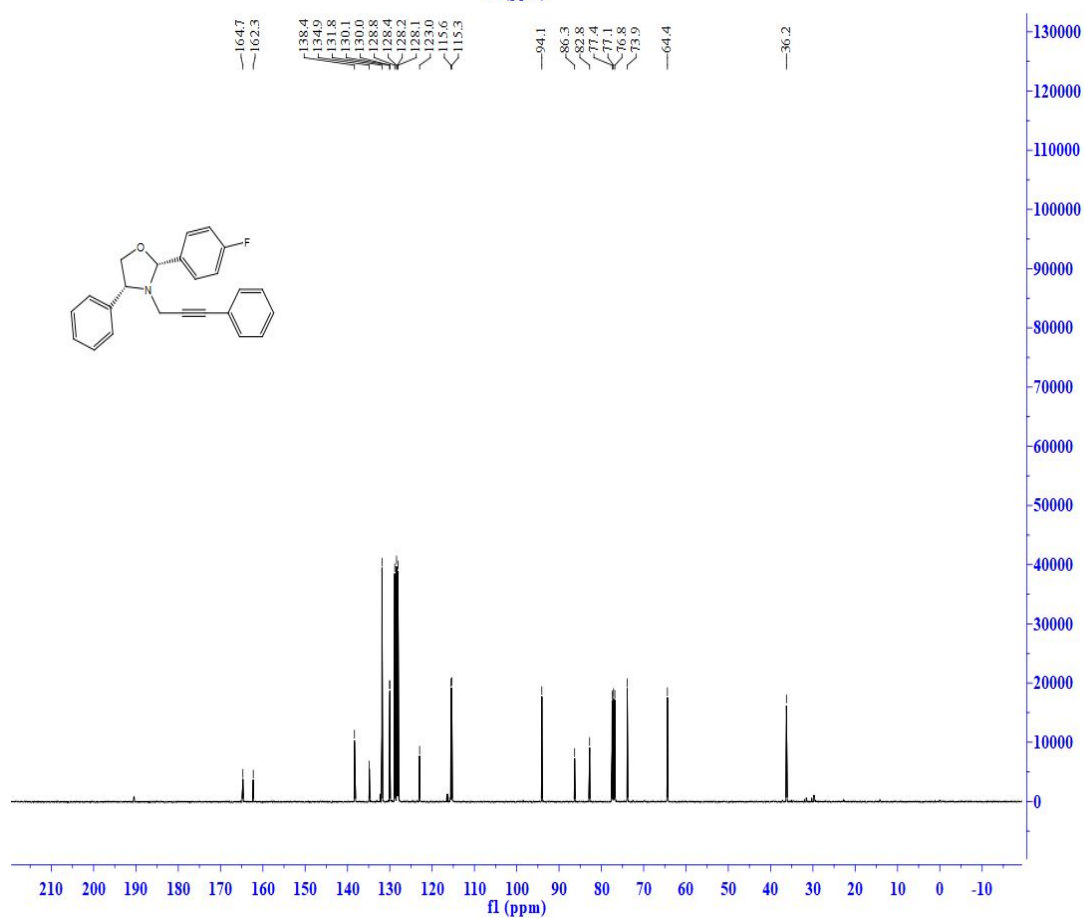
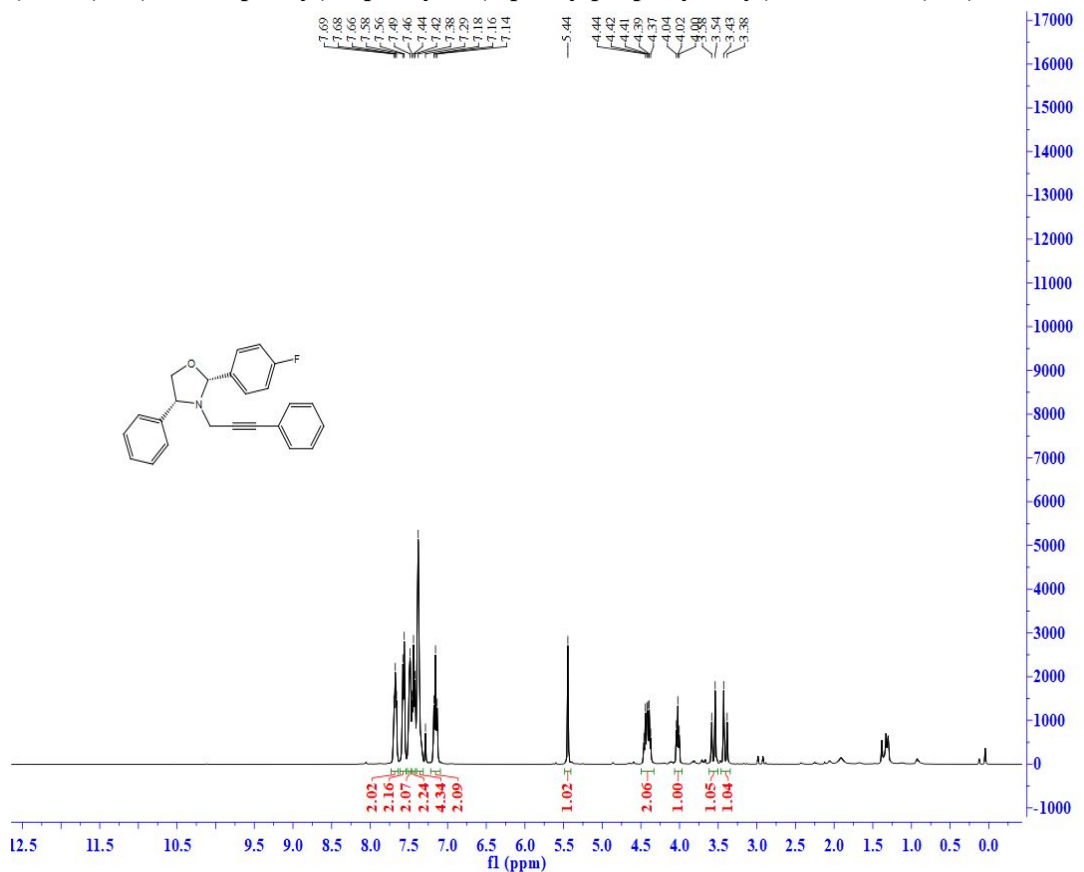
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(3-(trifluoromethyl)phenyl)oxazolidine (5zb)



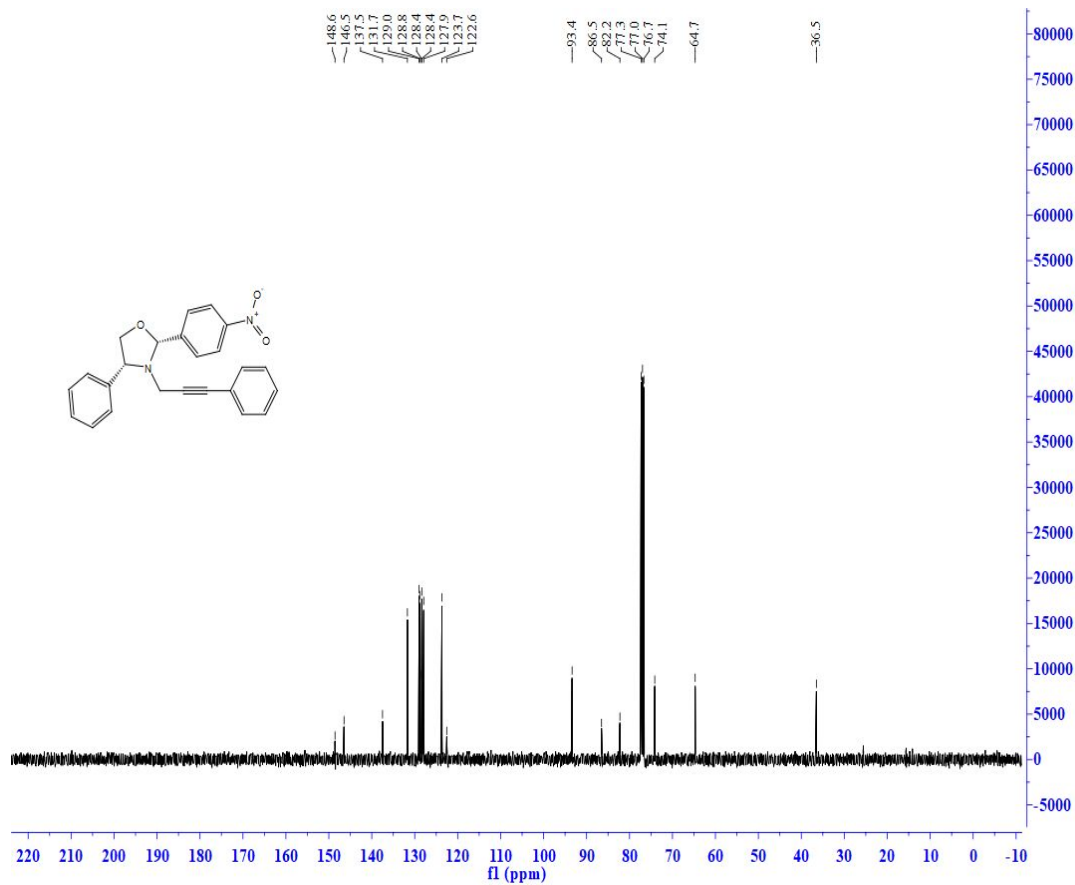
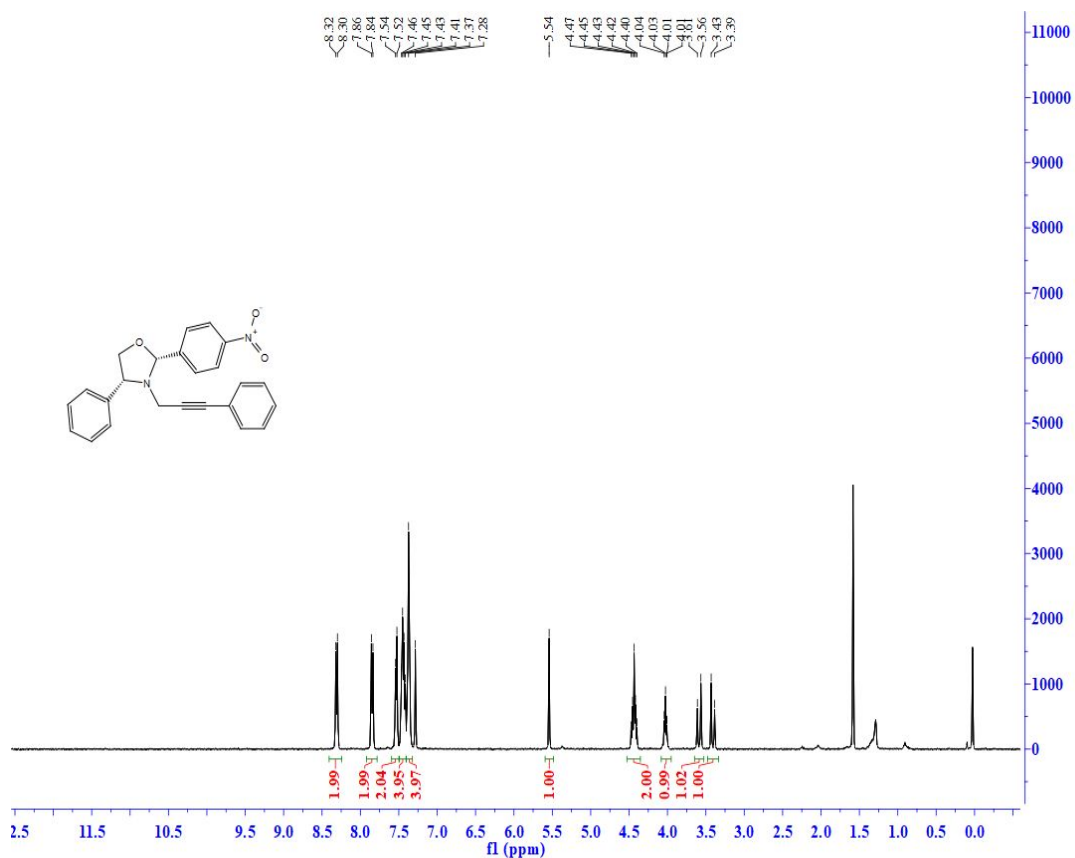
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(4-(trifluoromethyl)phenyl)oxazolidine (5zc)



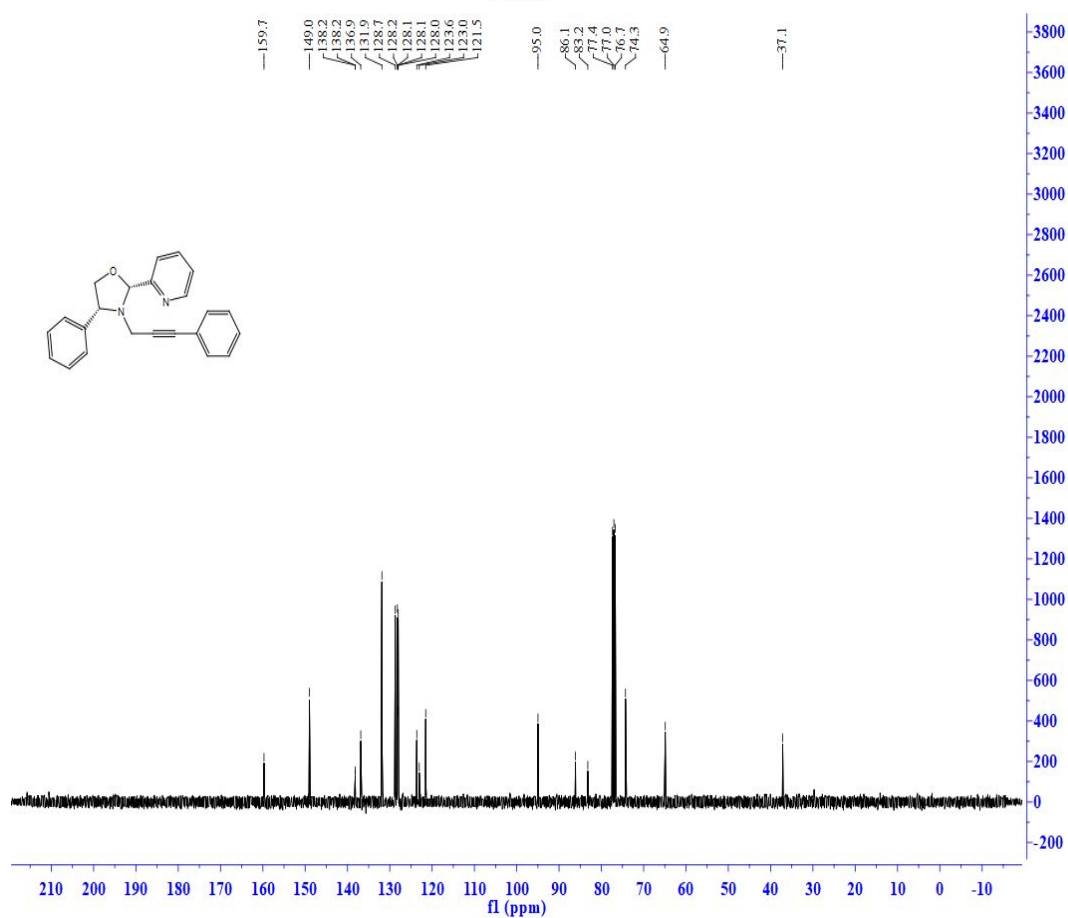
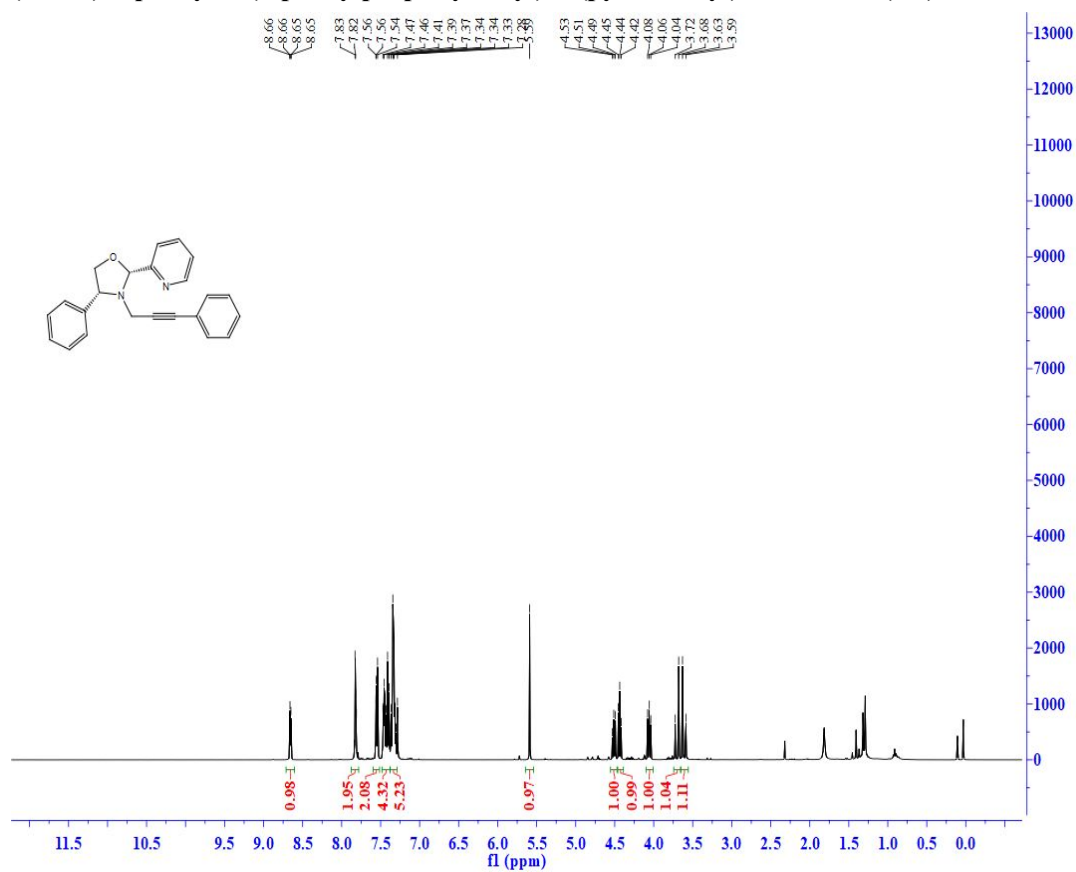
(2*R*,4*R*)-2-(4-fluorophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zd)



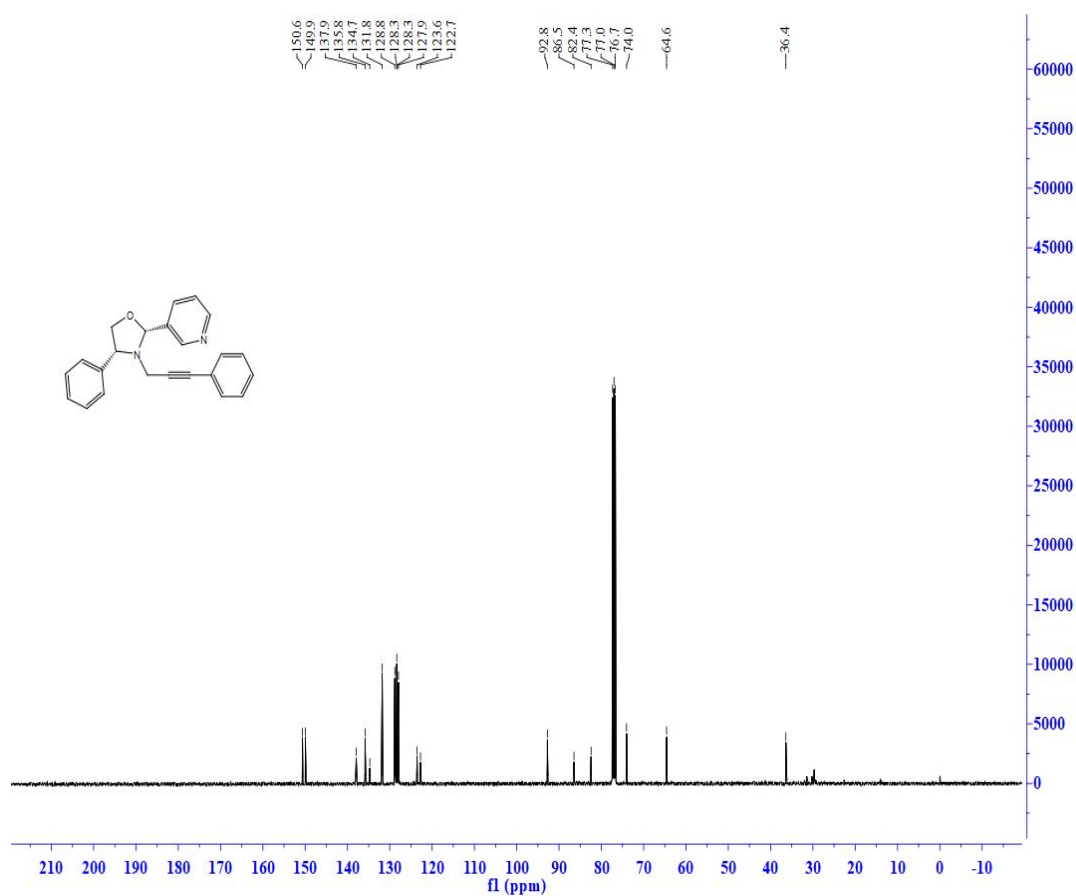
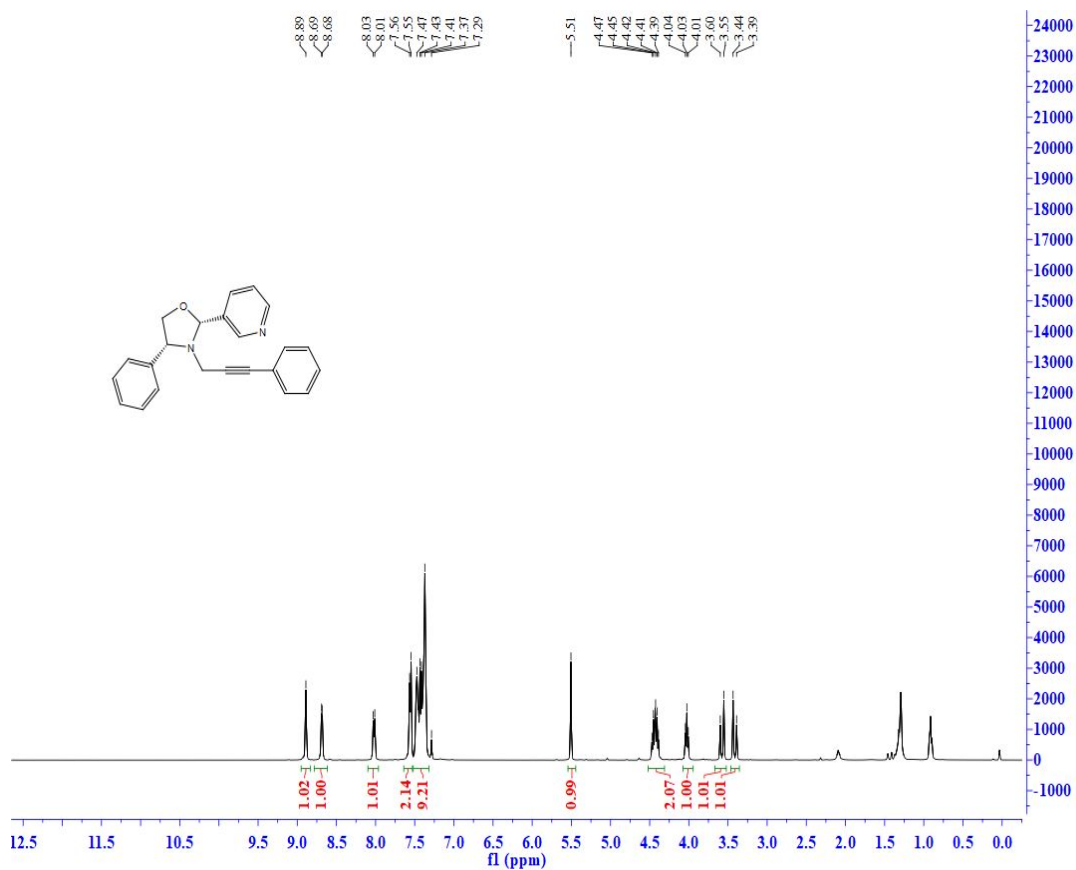
(2*R*,4*R*)-2-(4-nitrophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5ze)



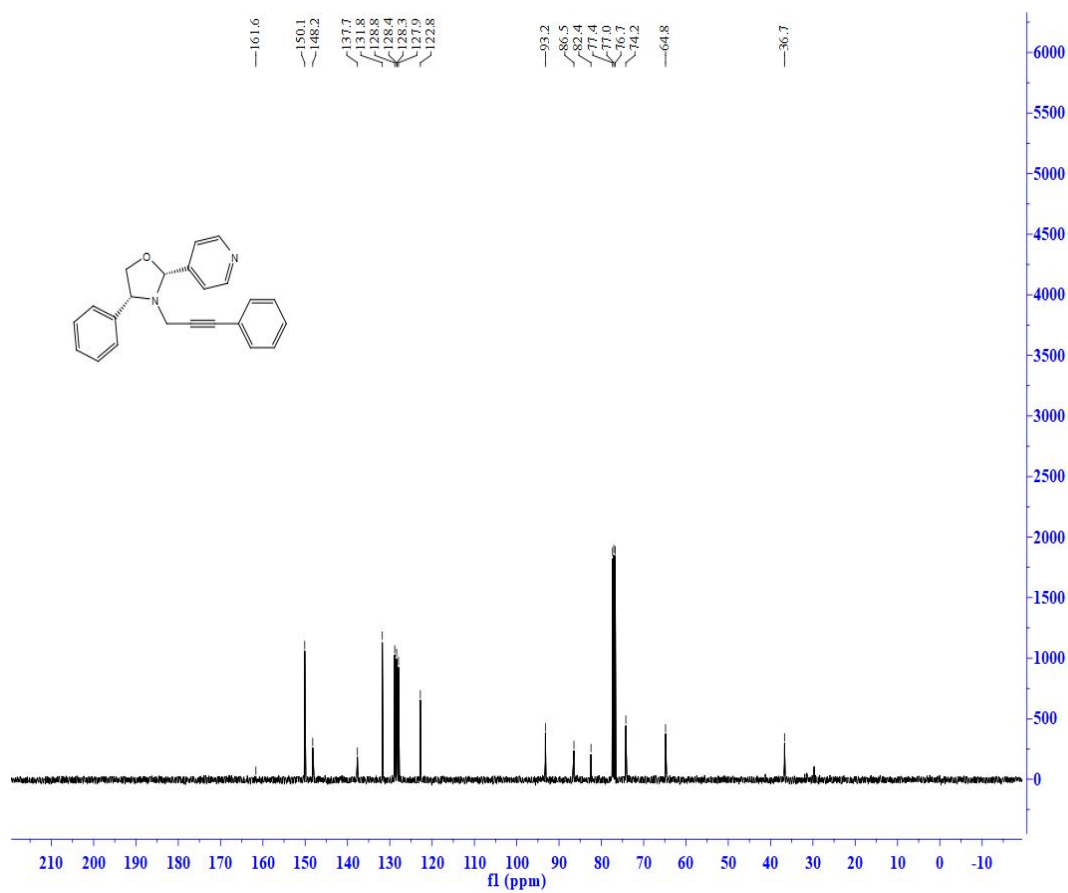
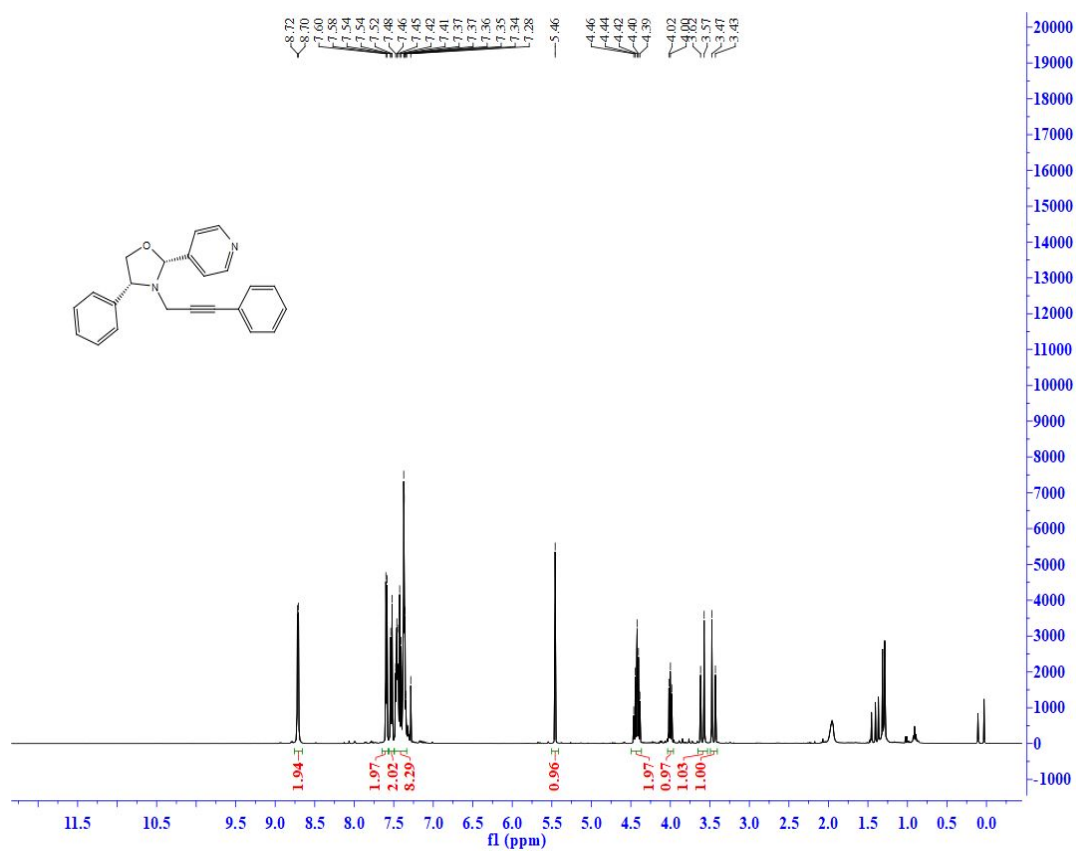
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(pyridin-2-yl)oxazolidine (5zf)



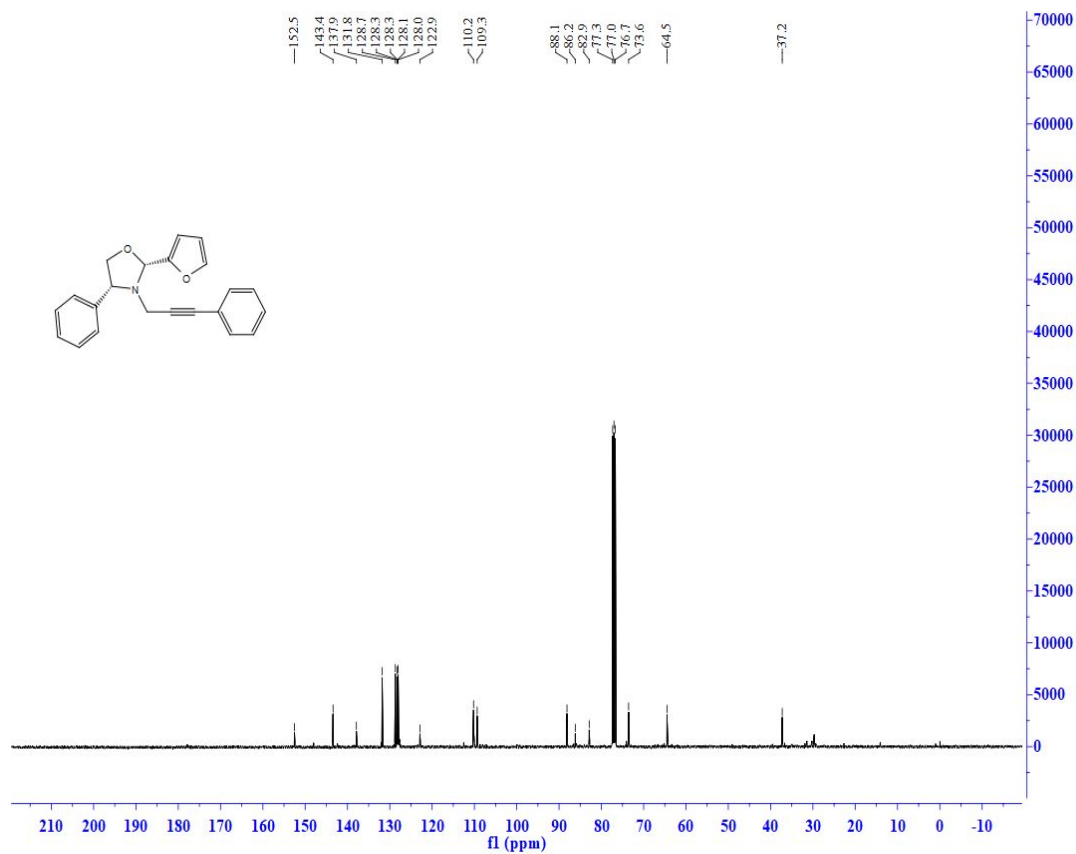
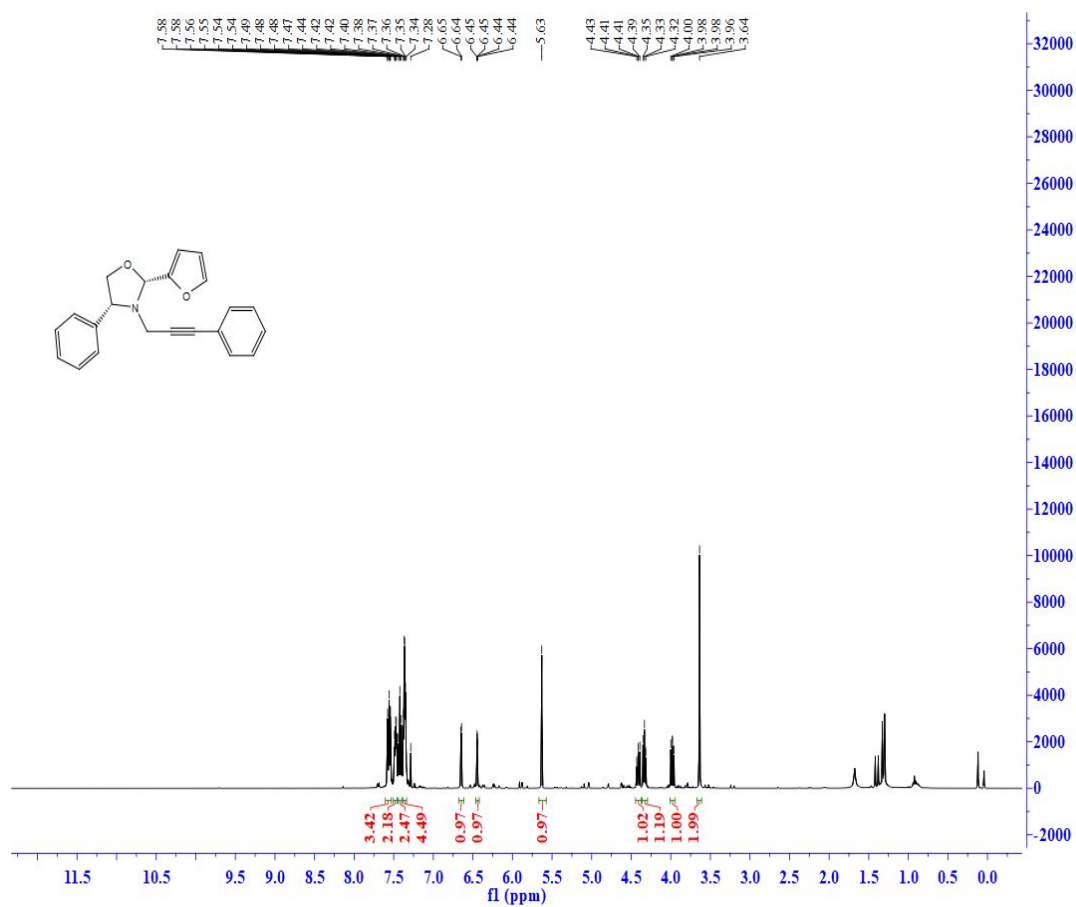
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(pyridin-3-yl)oxazolidine (5zg)



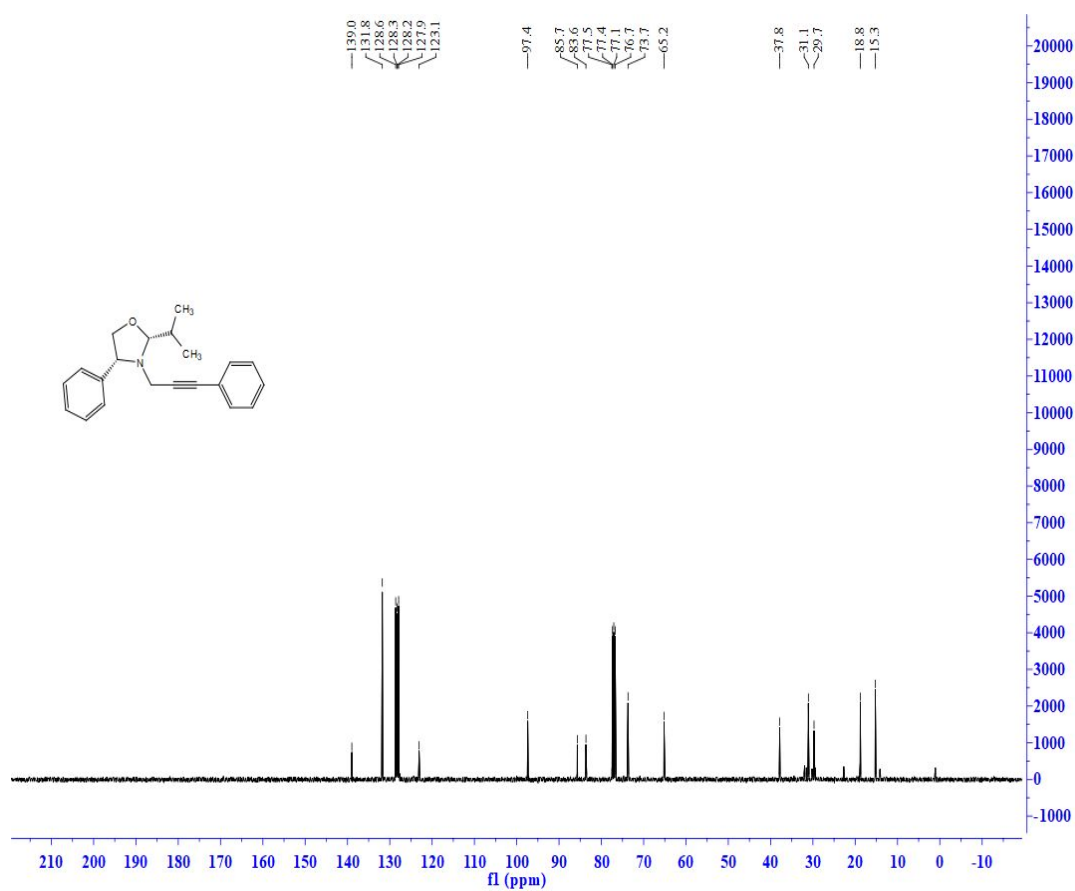
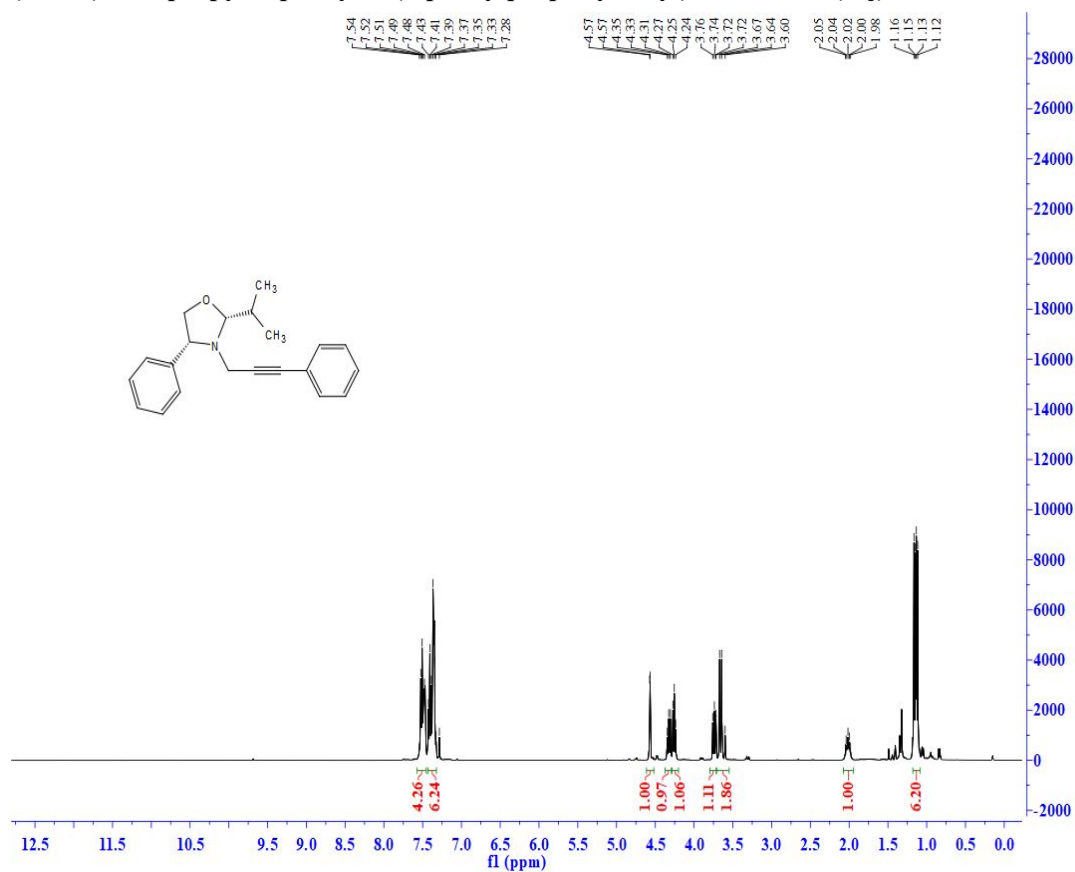
(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(pyridin-4-yl)oxazolidine (5zh)



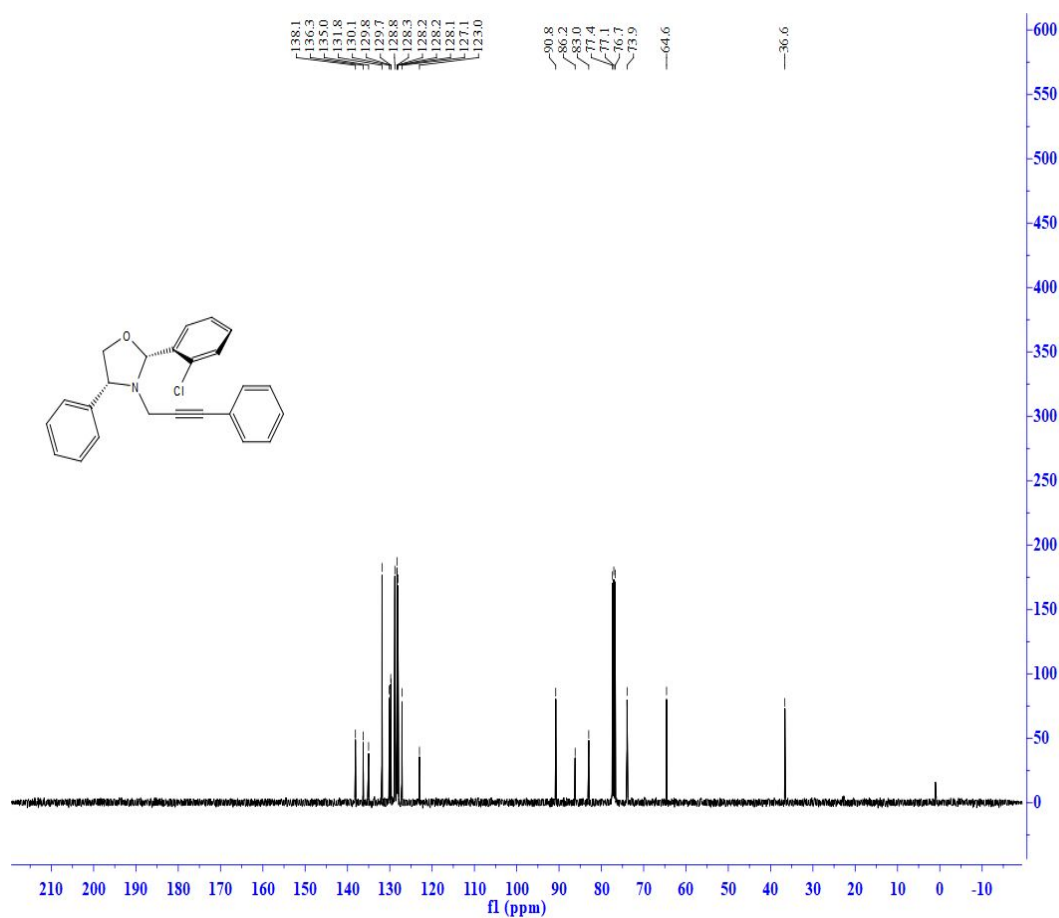
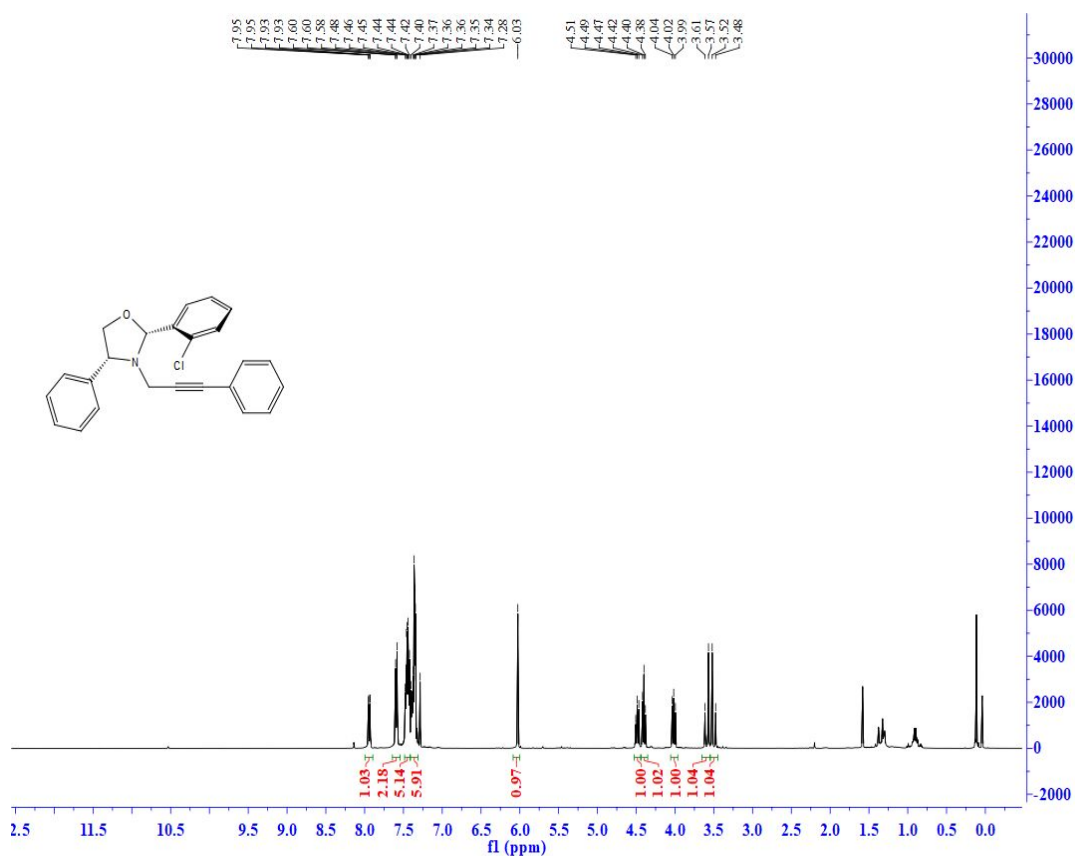
(2*R*,4*R*)-2-(furan-2-yl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zi)



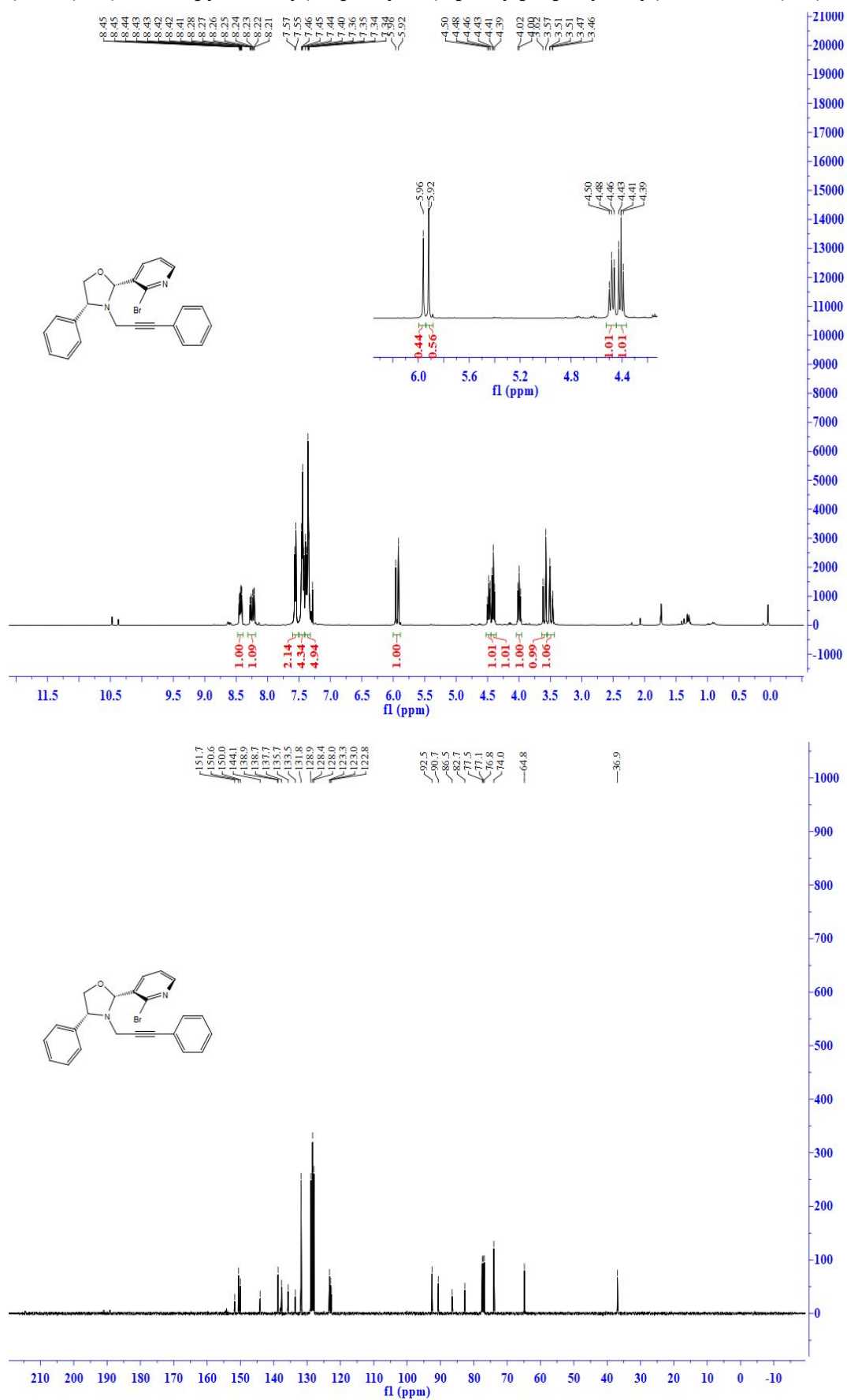
(2*R*,4*R*)-2-isopropyl-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zj)



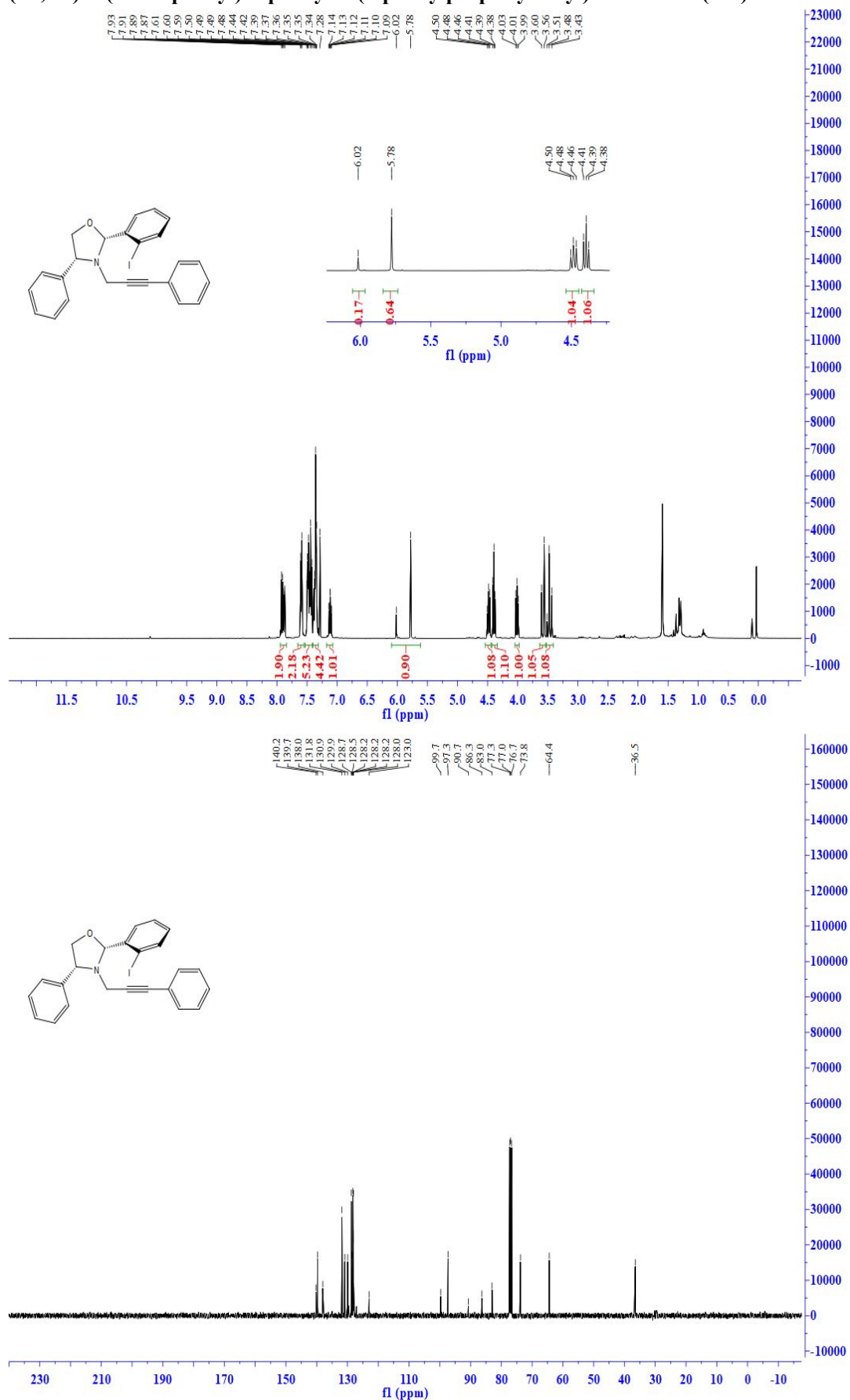
(2*R*,4*R*)-2-(2-chlorophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zm)



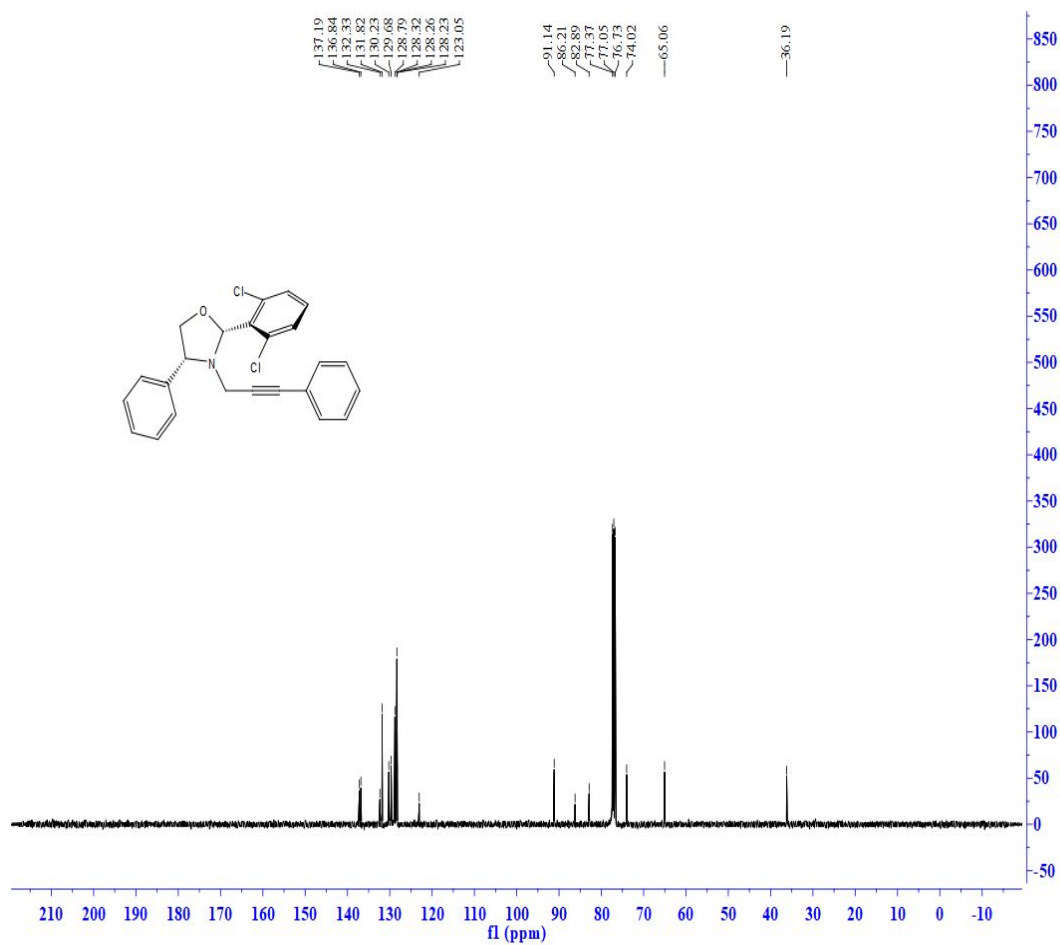
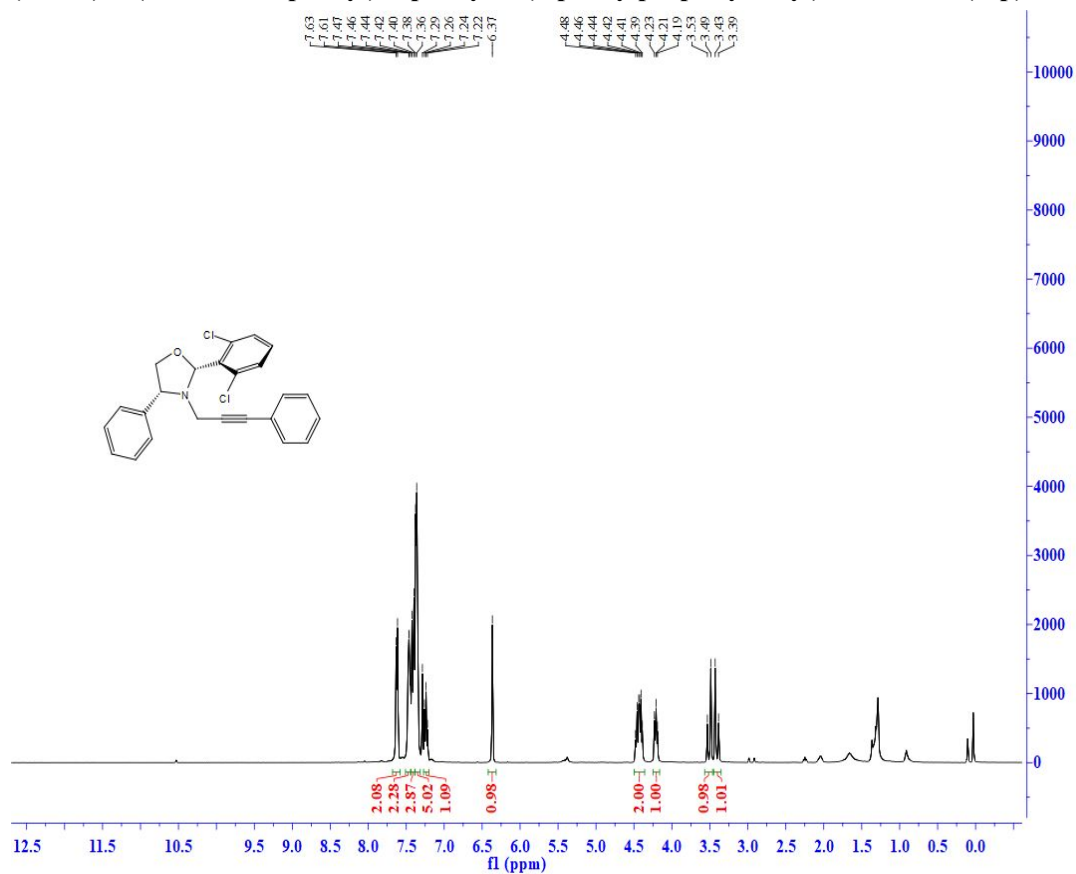
(2*R*,4*R*)-2-(2-bromopyridin-3-yl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zn)



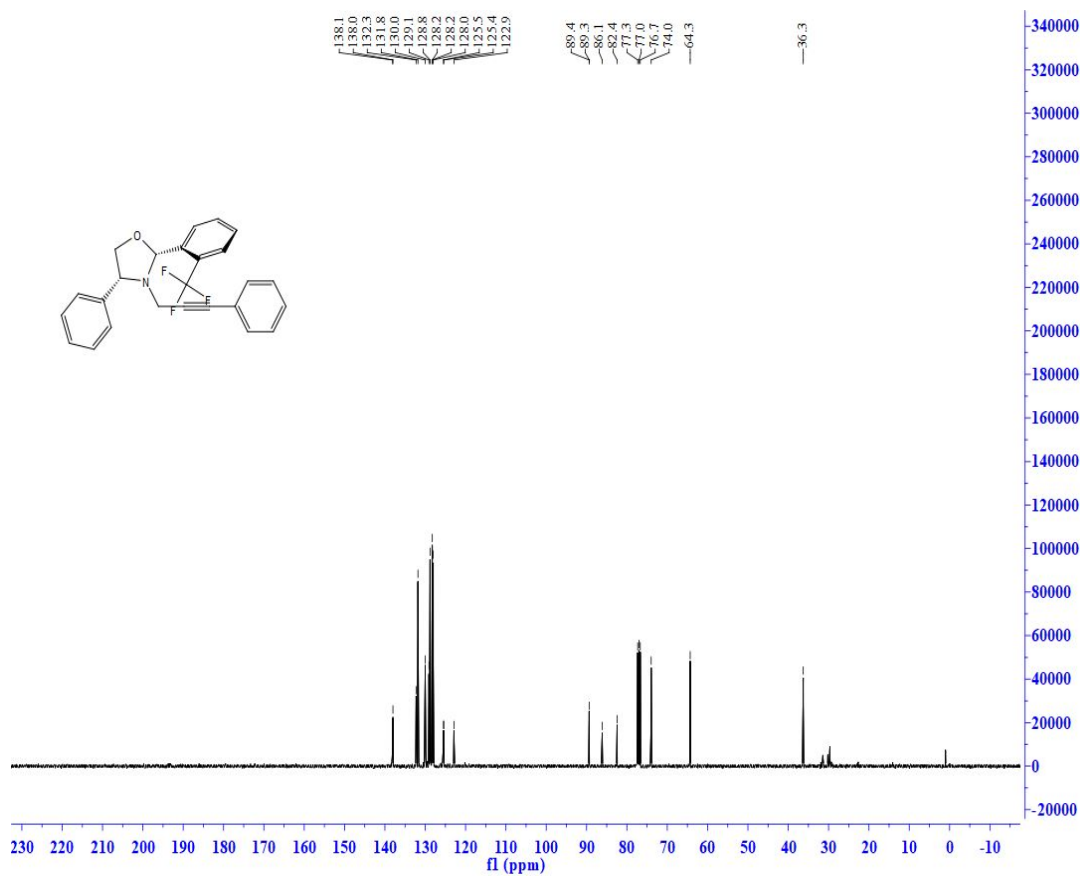
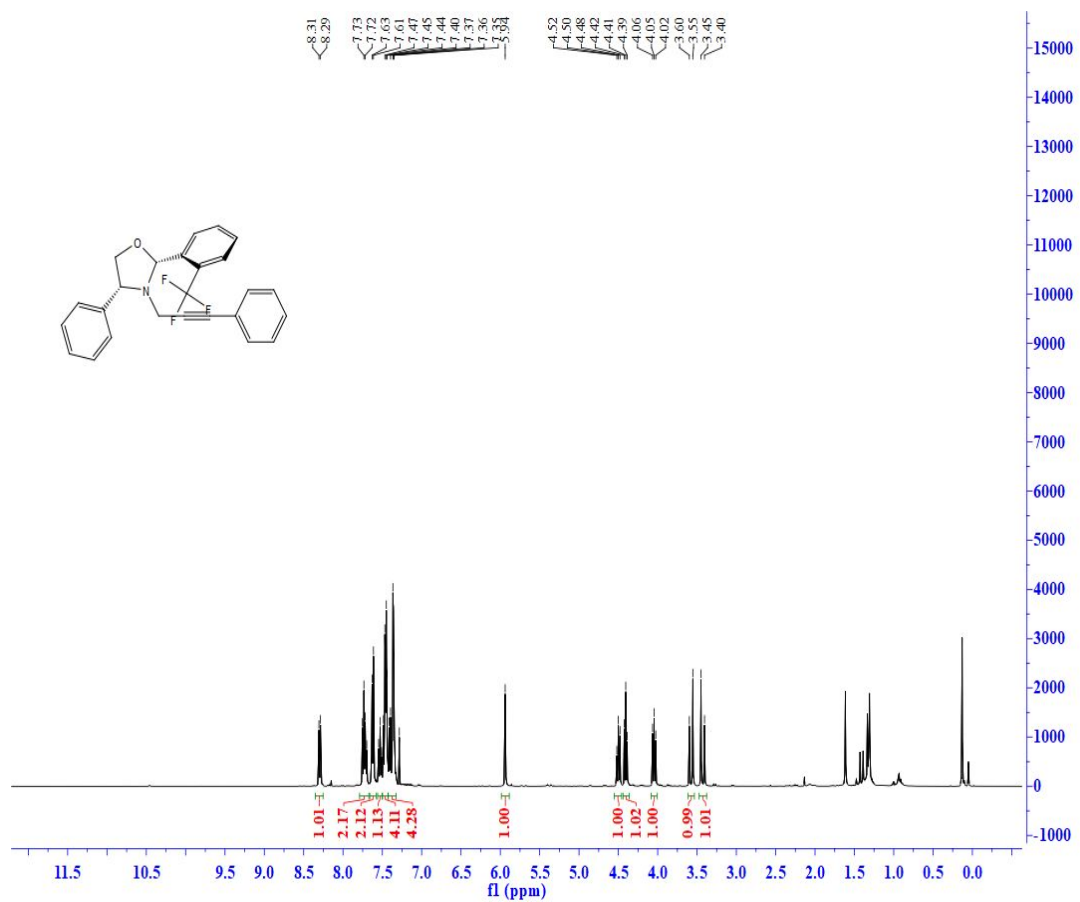
(2*R*,4*R*)-2-(2-iodophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zo)



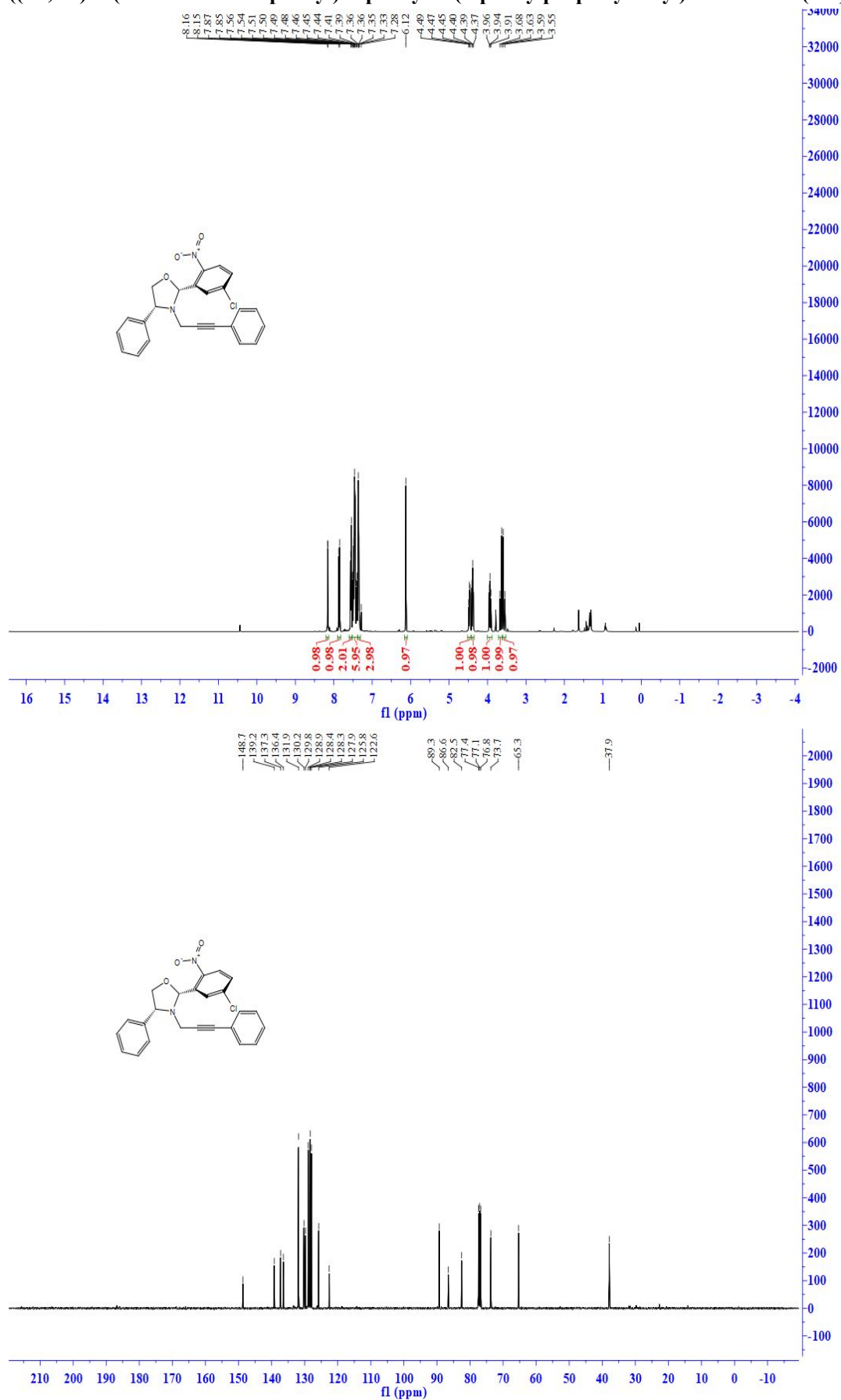
(2*R*,4*R*)-2-(2,6-dichlorophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zp)



(2*R*,4*R*)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)-2-(2-(trifluoromethyl)phenyl)oxazolidine (5zq)



((2*R*,4*R*)-2-(5-chloro-2-nitrophenyl)-4-phenyl-3-(3-phenylprop-2-yn-1-yl)oxazolidine (5zr)



(R)-2-(benzyl(3-phenylprop-2-yn-1-yl)amino)-2-phenylethan-1-ol (5zt)

