Supporting Information

Alkenylazaarenes as Dipolarophiles in 1,3-Dipolar Cycloaddition of Nitrones: Regioselectivity-Switchable and Highly Diastereoselective Synthesis of Multisubstituted Isoxazolidines

Mengchao Tong,[†] Yong Zhang,[†] Cong Qin,[†] Yiwei Fu,[†] Yonghai Liu,[†]
Hao Li*[†] and Wei Wang*[†,‡]

[†]*State Key Laboratory of Bioengineering Reactor, Shanghai Key Laboratory of New Drug Design, and School of Pharmacy, East China University of Science and Technology, 130 Mei-long Road, Shanghai 200237, China*

[‡]*Department of Chemistry and Chemical Biology, University of New Mexico, Albuquerque, NM 87131-0001, USA*

Table of contents

I. General Information S2

II. Synthesis of starting materials.....S3

III. General Procedure for the Synthesis of Compounds 3 and their Characterization Data S4

IV. General Procedure for the Synthesis of Compounds 4 and their Characterization Data S15

V. Scale up experiment and Synthetic transformation of cycloaddition adduct *cis*-3a.....S31

VI. Crystal data and structural refinement for racemic *cis*-3a and *trans*-4i S33

VII. Reference S39

VIII. ^{1}H NMR and ^{13}C NMR spectra.....S40

IX. HPLC spectra of the compound *cis*-3x (Table S1, enrty 3) S92

I. General Information

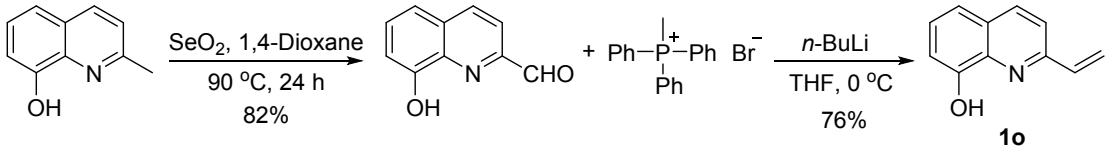
Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise specified, all other reagents were purchased from Acros, Aldrich, Adamas-beta Co. Ltd. or TCI and used without further purification. ^{1}H NMR spectra was recorded at 400 MHz, ^{13}C NMR spectra was recorded at 100 MHz. ^{1}H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) as internal reference; ^{13}C NMR spectra was recorded with $CDCl_3$ (δ = 77.00 ppm) as internal reference. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Chromatography was carried out with silica gel (200-300 mesh) using mixtures of petroleum ether (b.p. 60-80 ºC) and ethyl acetate as eluents. The enantiomeric excess of products was detected on HPLC (Shimadzu LC-LabSolutions). Mass Spectra were obtained from East China University of Science and Technology mass spectral facility.

II. Synthesis of starting materials

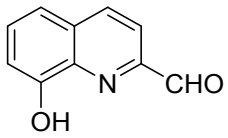
2.1 General procedure for the preparation of alkenylazaarenes **1**

Alkenylazaarenes **1a**, **1f-n** were prepared according to a previously reported method.[1]
Alkenylazaarenes **1b-e** were prepared according to a previously reported method.[2]

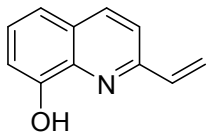
Synthesis of compound **1o**



Scheme S1. Synthesis of 2-vinylquinolin-8-ol **1o**



8-Hydroxyquinoline-2-carbaldehyde[3]: To an oven-dried 150 mL two-necked round-bottomed flask equipped with a magnetic stirring bar was charged with selenium dioxide (2.21 g, 20 mmol) and 1,4-dioxane (30 mL). The reaction was heated to 60 ℃. Then, 2-methylquinolin-8-ol (1.73 g, 10 mmol) dissolved in dioxane (30 mL) was added dropwise over a period of 1 h and was refluxed at 90 ℃ for 24 h. The reaction mixture was cooled to r.t., filtered through a pad of celite and then concentrated under vacuum. The residue was purified by flash column chromatography on silica gel to afford the desired compound 8-hydroxyquinoline-2-carbaldehyde in 82% yield.



2-Vinylquinolin-8-ol (1o)[4]: To an oven-dried 100 mL two-necked flask equipped with a stir bar was added 25 mL anhydrous THF and methyltriphenylphosphonium bromide (2.27 g, 6.35 mmol) at 0 °C under N_2 atmosphere. Then 2.5 M *n*-BuLi in hexane (2.6 mL, 6.5 mmol) was added slowly via syringe. The mixture was stirred for half an hour at 0 °C. Then 8-hydroxyquinoline-2-carbaldehyde (1 g, 5.77 mmol) in 15 mL anhydrous THF was added slowly via syringe and the reaction was stirred at room temperature for 12 h. After this time, the reaction was quenched with water (15 mL) and extracted with EtOAc (25 mL × 3). The combined organic extracts were washed with brine (20 mL ×

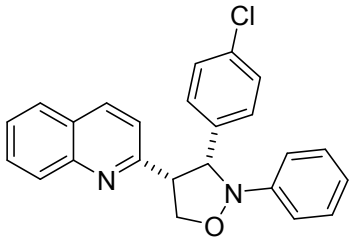
2), dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give 2-vinylquinolin-8-ol (**1o**) in 76% yield as a yellow solid (750 mg).

2.2 General procedure for the preparation of nitrones **2**

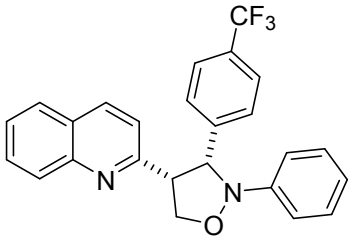
Nitrones **2a**-**b**, **2i** were prepared according to a previously reported method.[5]
Nitrones **2c**-**h**, **2k**-**l** were prepared according to a previously reported method.[6]
Nitrone **2j** was prepared according to a previously reported method.[7]

III. General Procedure for the Synthesis of Compounds 3

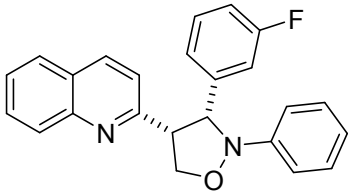
To a solution of alkenylazaarenes **1** (0.2 mmol) and nitrones **2** (0.3 mmol) in DCM (0.5 mL) was added the catalyst TMSOTf (0.01 mmol). The resulting solution was stirred at room temperature for indicated time. The reaction mixture was concentrated and the residue was directly purified by column chromatography on silica gel to give the corresponding products **3**.



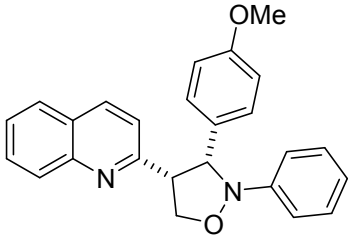
3-(4-Chlorophenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3a): Following the general procedure, the title compound was isolated in 89% yield. ***cis*-3a**: pale yellow solid, ^{1}H (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.68 (dd, *J* = 15.8, 8.2 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 3H), 7.06-6.97 (m, 3H), 5.28-5.20 (m, 1H), 4.67-4.49 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.9, 151.5, 147.2, 136.7, 136.1, 132.8, 129.6, 129.1, 129.0, 128.8, 128.1, 127.5, 126.8, 126.4, 122.3, 121.1, 114.8, 73.6, 71.2, 56.9; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1181.



2-Phenyl-4-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*cis*-3b): Following the general procedure, the title compound was isolated in 71% yield. ***cis*-3b**: yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.66 (dd, J = 13.1, 7.7 Hz, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.31 (dd, J = 14.7, 8.0 Hz, 4H), 7.09 (dd, J = 10.3, 8.8 Hz, 3H), 7.03 (t, J = 7.3 Hz, 1H), 5.31 (d, J = 6.1 Hz, 1H), 4.61 (dd, J = 12.1, 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 151.4, 147.3, 142.4, 136.1, 129.6, 129.3 (q, $J_{C\text{-}F}$ = 32 Hz), 129.1, 128.8, 128.0, 127.5, 126.8, 126.5, 125.3 (q, $J_{C\text{-}F}$ = 270 Hz), 124.9 ((q, $J_{C\text{-}F}$ = 4 Hz), 122.4, 120.9, 114.8, 73.8, 71.3, 56.9; HRMS (EI) m/z calcd. for $C_{25}H_{19}F_3N_2O$ $(M)^+$ 420.1449, found 420.1451.

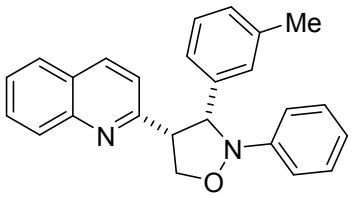


3-(3-Fluorophenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3c): Following the general procedure, the title compound was isolated in 70% yield. ***cis*-3c**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.6 Hz, 1H), 7.72-7.58 (m, 2H), 7.51-7.41 (m, 1H), 7.36-7.27 (m, 2H), 7.18-7.07 (m, 4H), 7.01 (t, J = 7.3 Hz, 1H), 6.97-6.90 (m, 2H), 6.72-6.64 (m, 1H), 5.31-5.19 (m, 1H), 4.67-4.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (d, $^1J_{C\text{-}F}$ = 242 Hz), 157.9, 151.5, 147.3, 140.9 (d, $^3J_{C\text{-}F}$ = 7 Hz), 135.9, 129.5, 129.4 (d, $^3J_{C\text{-}F}$ = 9 Hz), 129.1, 128.9, 127.4, 126.8, 126.3, 123.3 (d, $^4J_{C\text{-}F}$ = 3 Hz), 122.3, 121.0, 114.8, 114.6 (d, $^2J_{C\text{-}F}$ = 22 Hz), 113.8 (d, $^2J_{C\text{-}F}$ = 21 Hz), 73.7, 71.2, 57.0; HRMS (EI) m/z calcd. for $C_{24}H_{19}FN_2O$ $(M)^+$ 370.1481, found 370.1480.

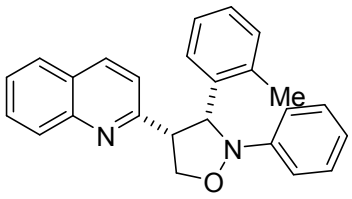


3-(4-Methoxyphenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3d): Following the general procedure, the title compound was isolated in 82% yield. ***cis*-3d**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H),

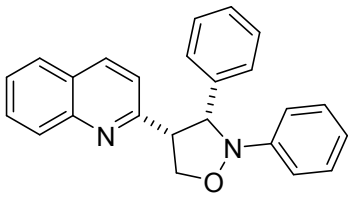
7.65 (dd, J = 14.9, 8.0 Hz, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 7.10 (dd, J = 15.1, 8.4 Hz, 3H), 6.99 (t, J = 7.3 Hz, 1H), 6.59 (d, J = 8.5 Hz, 2H), 5.21 (d, J = 7.5 Hz, 1H), 4.66-4.49 (m, 3H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 158.4, 151.8, 147.3, 135.6, 130.2, 129.3, 128.9, 128.9, 128.8, 127.5, 126.8, 126.2, 122.0, 121.3, 114.9, 113.4, 73.7, 71.1, 57.0, 55.1; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O_2$ $(M)^+$ 382.1681, found 382.1679.



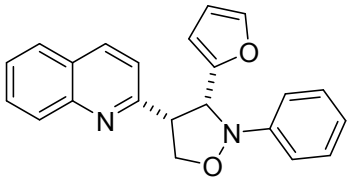
2-Phenyl-4-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*cis*-3e): Following the general procedure, the title compound was isolated in 75% yield. *cis*-**3e**: yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.6 Hz, 1H), 7.69-7.59 (m, 2H), 7.48-7.40 (m, 1H), 7.33-7.26 (m, 2H), 7.15-7.09 (m, 3H), 7.07 (d, J = 8.6 Hz, 1H), 7.04-6.96 (m, 2H), 6.91 (t, J = 7.6 Hz, 1H), 6.80 (d, J = 7.5 Hz, 1H), 5.23 (d, J = 6.5 Hz, 1H), 4.64-4.53 (m, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 151.9, 147.3, 137.9, 137.6, 135.5, 129.3, 129.0, 128.9, 128.3, 127.8, 127.7, 127.4, 126.8, 126.2, 124.7, 122.0, 121.3, 114.9, 74.3, 71.3, 57.2, 21.3; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O$ $(M)^+$ 366.1732, found 366.1734.



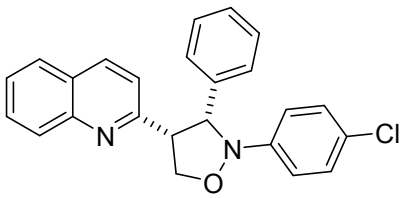
2-Phenyl-4-(quinolin-2-yl)-3-(o-tolyl)isoxazolidine (*cis*-3f): Following the general procedure, the title compound was isolated in 77% yield. *cis*-**3f**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 1H), 7.78 (t, J = 8.8 Hz, 2H), 7.62 (t, J = 9.0 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.14 (d, J = 8.6 Hz, 1H), 7.05 (d, J = 7.7 Hz, 3H), 6.98 (t, J = 7.3 Hz, 1H), 6.93 (t, J = 7.3 Hz, 1H), 6.78 (d, J = 7.4 Hz, 1H), 5.36 (d, J = 8.3 Hz, 1H), 4.70-4.63 (m, 1H), 4.60 (t, J = 7.7 Hz, 1H), 4.49-4.43 (m, 1H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 151.9, 147.0, 136.4, 135.4, 134.8, 129.9, 129.2, 129.0, 128.9, 127.8, 127.4, 127.1, 126.9, 126.2, 125.8, 121.8, 121.1, 114.6, 72.4, 71.8, 56.8, 19.8; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O$ $(M)^+$ 366.1732, found 366.1734.



2,3-Diphenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3g): Following the general procedure, the title compound was isolated in 71% yield. *cis*-**3g**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.69-7.59 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.34-7.23 (m, 4H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.09-6.96 (m, 5H), 5.30-5.24 (m, 1H), 4.68-4.51 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 151.8, 147.2, 138.1, 135.7, 129.4, 129.0, 128.9, 128.0, 127.7, 127.4, 127.0, 126.8, 126.2, 122.1, 121.2, 114.9, 74.2, 71.3, 57.2; HRMS (EI) m/z calcd. for $C_{24}H_{20}N_2O$ $(M)^+$ 352.1576, found 352.1573.

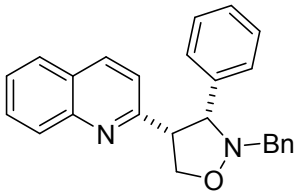


3-(Furan-2-yl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3h): Following the general procedure, the title compound was isolated in 75% yield. *cis*-**3h**: brown solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.6 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.66 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H), 7.52-7.45 (m, 1H), 7.36-7.28 (m, 2H), 7.21-7.13 (m, 3H), 7.06-6.99 (m, 2H), 6.27 (d, *J* = 3.3 Hz, 1H), 6.10 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.31 (d, *J* = 8.0 Hz, 1H), 4.79-4.71 (m, 1H), 4.66 (t, *J* = 8.0 Hz, 1H), 4.47 (dd, *J* = 15.1, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 151.4, 151.1, 147.4, 141.9, 136.0, 129.4, 129.1, 129.0, 127.5, 126.9, 126.3, 122.6, 120.5, 115.1, 110.3, 108.8, 70.7, 68.6, 55.1; HRMS (EI) m/z calcd. for $C_{22}H_{18}N_2O_2$ $(M)^+$ 342.1368, found 342.1366.

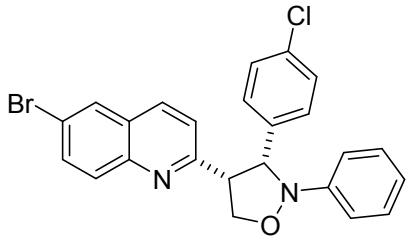


2-(4-Chlorophenyl)-3-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3i): Following the general procedure, the title compound was isolated in 73% yield. *cis*-**3i**: pale yellow

solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.64 (t, *J* = 8.5 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.28-7.19 (m, 4H), 7.09-6.96 (m, 6H), 5.19 (d, *J* = 5.8 Hz, 1H), 4.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 150.3, 147.3, 137.7, 135.7, 129.4, 128.9, 128.9, 128.1, 127.6, 127.4, 127.2, 127.0, 126.8, 126.3, 121.2, 116.3, 74.1, 71.2, 57.1; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1181.

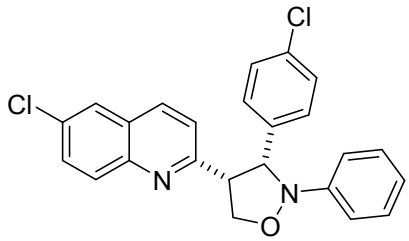


2-Benzyl-3-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3j): Following the general procedure, the title compound was isolated in 55% yield. *cis*-**3j**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.67-7.57 (m, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.44-7.39 (m, 1H), 7.39-7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.21-7.16 (m, 2H), 7.03-6.91 (m, 3H), 4.67-4.42 (m, 4H), 4.20 (d, *J* = 14.2 Hz, 1H), 3.92 (d, *J* = 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 147.1, 137.8, 136.7, 135.4, 129.1, 128.9, 128.8, 128.4, 128.2, 127.9, 127.4, 127.3, 127.1, 126.7, 126.0, 121.9, 73.7, 71.4, 60.7, 57.2; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O$ $(M)^+$ 366.1732, found 366.1735.

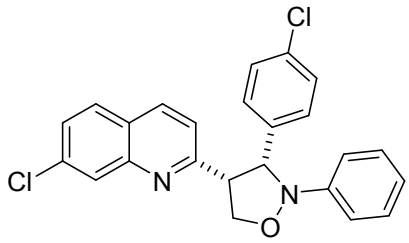


4-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-3k): Following the general procedure, the title compound was isolated in 71% yield. *cis*-**3k**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 2.1 Hz, 1H), 7.76 (dd, *J* = 11.5, 8.9 Hz, 2H), 7.70 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.34-7.26 (m, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.10-7.05 (m, 2H), 7.04-6.97 (m, 3H), 5.21 (d, *J* = 7.7 Hz, 1H), 4.61-4.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 151.4, 145.8, 136.6, 134.9, 133.0, 132.9, 130.6, 129.5, 129.1, 129.0, 128.2, 127.9, 122.3, 122.0, 120.2, 114.8, 73.5, 71.1, 57.0; HRMS (EI) m/z calcd. for $C_{24}H_{18}BrClN_2O$ $(M)^+$

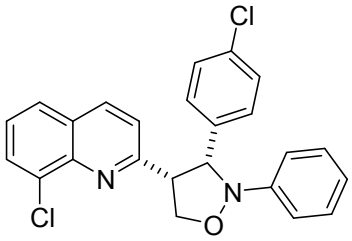
464.0291, found 464.0289.



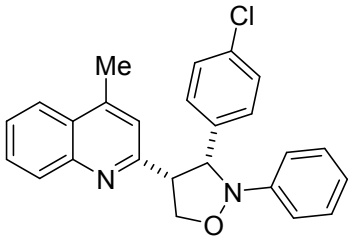
3-(4-Chlorophenyl)-4-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3l): Following the general procedure, the title compound was isolated in 77% yield. *cis*-**3l**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.66 (d, *J* = 2.3 Hz, 1H), 7.58 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.35-7.37 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.11-7.05 (m, 2H), 7.05-6.97 (m, 3H), 5.21 (d, *J* = 7.6 Hz, 1H), 4.62-4.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 151.4, 145.6, 136.6, 135.0, 132.9, 132.1, 130.5, 130.5, 129.1, 129.0, 128.2, 127.4, 126.2, 122.3, 122.0, 114.8, 73.6, 71.1, 56.9; HRMS (EI) m/z calcd. for $C_{24}H_{18}Cl_2N_2O$ $(M)^+$ 420.0796, found 420.0794.



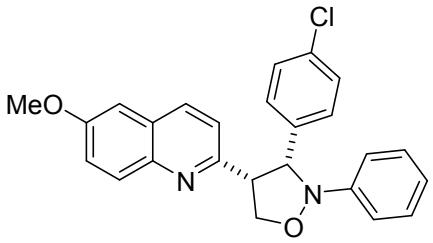
3-(4-Chlorophenyl)-4-(7-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3m): Following the general procedure, the title compound was isolated in 88% yield. *cis*-**3m**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 2.0 Hz, 1H), 7.82 (d, *J* = 8.6 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.42 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.34-7.27 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 1H), 7.10-7.06 (m, 2H), 7.05-6.96 (m, 3H), 5.22 (d, *J* = 7.7 Hz, 1H), 4.63-4.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 151.4, 147.6, 136.6, 135.7, 135.3, 132.9, 129.1, 129.0, 128.7, 128.2, 128.0, 127.4, 125.1, 122.3, 121.3, 114.8, 73.5, 71.1, 56.9; HRMS (EI) m/z calcd. for $C_{24}H_{18}Cl_2N_2O$ $(M)^+$ 420.0796, found 420.0794.



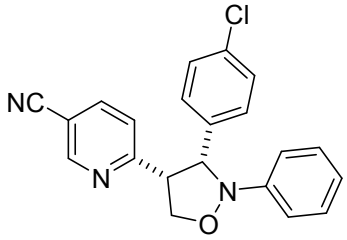
3-(4-Chlorophenyl)-4-(8-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3n): Following the general procedure, the title compound was isolated in 90% yield. *cis*-**3n**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 1H), 7.76 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.34-7.27 (m, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.05-6.97 (m, 3H), 5.25 (d, *J* = 7.8 Hz, 1H), 4.71-4.59 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 151.4, 143.4, 136.7, 136.3, 133.2, 132.8, 129.6, 129.2, 129.1, 128.1, 128.0, 126.6, 126.2, 122.2, 121.9, 114.8, 73.6, 71.3, 56.9; HRMS (EI) m/z calcd. for $C_{24}H_{18}Cl_2N_2O$ $(M)^+$ 420.0796, found 420.0798.



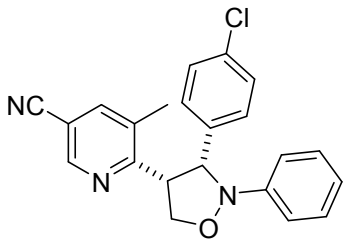
3-(4-Chlorophenyl)-4-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3o): Following the general procedure, the title compound was isolated in 84% yield. *cis*-**3o**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.88 (m, 1H), 7.85 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.64 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.33-7.27 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.13-7.06 (m, 2H), 7.04-6.97 (m, 3H), 6.89 (s, 1H), 5.22 (d, *J* = 7.7 Hz, 1H), 4.62-4.48 (m, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 151.5, 147.0, 144.2, 136.9, 132.7, 129.3, 129.2, 129.0, 129.0, 127.9, 126.9, 126.1, 123.6, 122.2, 121.8, 114.8, 73.6, 71.2, 56.8, 18.6; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O$ $(M)^+$ 400.1342, found 400.1345.



3-(4-Chlorophenyl)-4-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3p): Following the general procedure, the title compound was isolated in 60% yield. *cis*-**3p**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.2 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.36-7.27 (m, 3H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.12-6.97 (m, 6H), 6.95 (d, *J* = 2.6 Hz, 1H), 5.22 (d, *J* = 6.9 Hz, 1H), 4.64-4.50 (m, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 155.2, 151.5, 142.9, 136.8, 135.1, 132.7, 129.9, 129.1, 129.0, 128.1, 127.8, 122.4, 122.2, 121.3, 114.8, 105.0, 73.6, 71.2, 56.5, 55.5; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O_2$ $(M)^+$ 416.1292, found 416.1293.

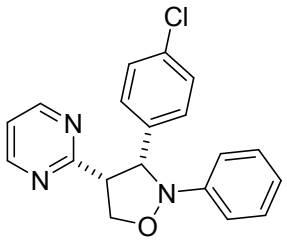


6-(3-(4-Chlorophenyl)-2-phenylisoxazolidin-4-yl)nicotinonitrile (*cis*-3q): Following the general procedure, the title compound was isolated in 85% yield. *cis*-**3q**: pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 2.1, 0.7 Hz, 1H), 7.69 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.32-7.22 (m, 3H), 7.16-7.08 (m, 4H), 7.05-6.97 (m, 3H), 5.15 (d, *J* = 8.1 Hz, 1H), 4.55-4,47 (m, 2H), 4.46-4.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 151.5, 151.1, 139.2, 136.1, 133.3, 129.1, 128.8, 128.5, 123.5, 122.5, 116.5, 114.8, 108.1, 73.6, 70.8, 56.7; HRMS (EI) m/z calcd. for $C_{21}H_{16}ClN_3O$ $(M)^+$ 361.0982, found 361.0983.

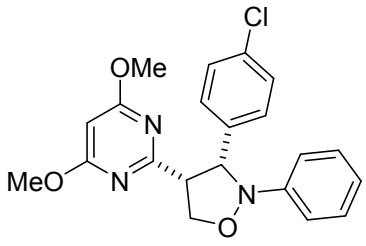


6-(3-(4-Chlorophenyl)-2-phenylisoxazolidin-4-yl)-5-methylnicotinonitrile (*cis*-3r):

Following the general procedure, the title compound was isolated in 77% yield. *cis*-**3r**: yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 1.8 Hz, 1H), 7.51 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.30-7.25 (m, 2H), 7.10-7.04 (m, 6H), 7.02-6.97 (m, 1H), 5.07-4.99 (m, 2H), 4.48 (t, *J* = 7.8 Hz, 1H), 4.41 (dt, *J* = 15.5, 7.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 150.5, 149.0, 140.1, 136.3, 133.4, 132.3, 129.1, 129.0, 128.2, 122.5, 116.7, 115.1, 107.8, 72.2, 69.4, 51.3, 18.8; HRMS (EI) m/z calcd. for $C_{22}H_{18}ClN_3O$ $(M)^+$ 375.1138, found 375.1139.

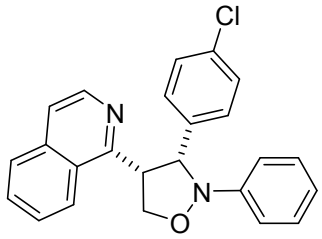


3-(4-Chlorophenyl)-2-phenyl-4-(pyrimidin-2-yl)isoxazolidine (*cis*-3s): Following the general procedure, the title compound was isolated in 83% yield. *cis*-**3s**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.9 Hz, 2H), 7.32-7.26 (m, 2H), 7.21-7.15 (m, 2H), 7.13-7.04 (m, 4H), 7.02-6.95 (m, 2H), 5.23 (d, *J* = 8.4 Hz, 1H), 4.86 (t, *J* = 7.5 Hz, 1H), 4.58 (t, *J* = 8.0 Hz, 1H), 4.50 (dd, *J* = 15.7, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 156.7, 150.9, 136.8, 132.8, 129.2, 129.0, 128.0, 122.3, 119.0, 115.1, 73.3, 69.0, 55.9; HRMS (EI) m/z calcd. for $C_{19}H_{16}ClN_3O$ $(M)^+$ 337.0982, found 337.0984.

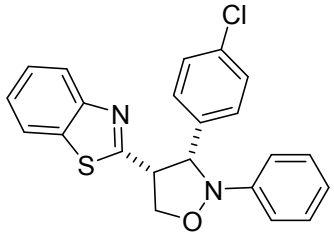


3-(4-Chlorophenyl)-4-(4,6-dimethoxypyrimidin-2-yl)-2-phenylisoxazolidine (*cis*-3t): Following the general procedure, the title compound was isolated in 75% yield. *cis*-**3t**: yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.23-7.17 (m, 2H), 7.14-7.07 (m, 4H), 7.00 (t, *J* = 7.3 Hz, 1H), 5.69 (s, 1H), 5.13 (d, *J* = 8.5 Hz, 1H), 4.80 (t, *J* = 8.0 Hz, 1H), 4.58-4.50 (m, 1H), 4.23 (q, *J* = 8.6 Hz, 1H), 3.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.9, 151.0, 137.1, 132.8, 129.2, 129.0, 127.8, 122.4, 115.2, 87.4, 73.3, 68.9, 55.0, 53.9; HRMS (EI) m/z calcd. for $C_{21}H_{20}ClN_3O_3$

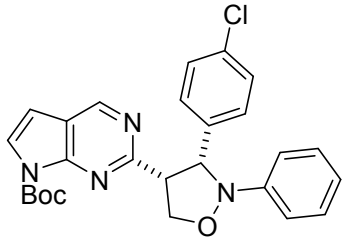
$(M)^+$ 397.1193, found 397.1194.



3-(4-Chlorophenyl)-4-(isoquinolin-1-yl)-2-phenylisoxazolidine (*cis*-3u): Following the general procedure, the title compound was isolated in 56% yield. *cis*-**3u**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 5.7 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.80-7.70 (m, 1H), 7.69-7.56 (m, 2H), 7.36 (d, *J* = 5.7 Hz, 1H), 7.35-7.29 (m, 2H), 7.18-7.09 (m, 2H), 7.07-6.98 (m, 1H), 6.94-6.88 (m, 2H), 6.87-6.80 (m, 2H), 5.31-5.23 (m, 2H), 5.01 (q, *J* = 8.5 Hz, 1H), 4.64 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 151.1, 141.5, 136.6, 135.9, 132.7, 129.8, 129.0, 129.0, 127.7, 127.6, 127.6, 127.5, 124.1, 122.2, 119.9, 115.0, 73.2, 68.9, 50.2; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1181.



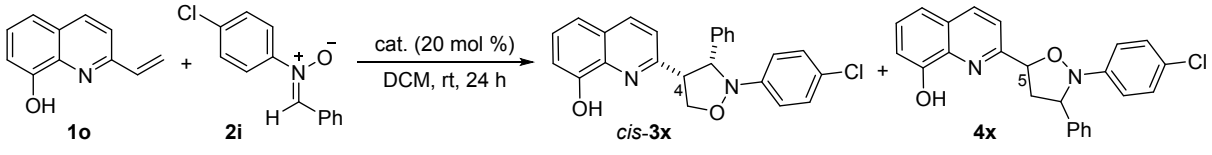
4-(Benzo[*d*]thiazol-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-3v): Following the general procedure, the title compound was isolated in 64% yield. *cis*-**3v**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 1H), 7.77-7.71 (m, 1H), 7.45-7.38 (m, 1H), 7.36-7.26 (m, 5H), 7.14-7.09 (m, 2H), 7.08-6.99 (m, 3H), 5.15 (d, *J* = 7.8 Hz, 1H), 4.75-4,68 (m, 1H), 4.59 (dd, *J* = 8.4, 6.6 Hz, 1H), 4.53 (dd, *J* = 8.4, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 152.1, 151.2, 135.6, 135.1, 133.4, 129.1, 129.0, 128.5, 126.1, 125.2, 122.8, 122.6, 121.6, 114.9, 73.5, 71.2, 53.5; HRMS (EI) m/z calcd. for $C_{22}H_{17}ClN_2OS$ $(M)^+$ 392.0750, found 392.0748.

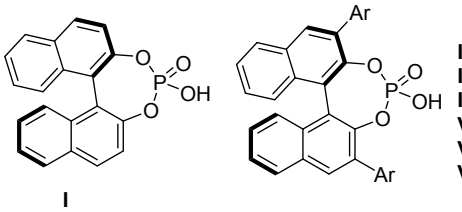


***tert*-Butyl 2-(3-(4-chlorophenyl)-2-phenylisoxazolidin-4-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-7-carboxylate (*cis*-3w):** Following the general procedure, the title compound was isolated in 77% yield. *cis*-**3w**: pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.53 (d, *J* = 4.0 Hz, 1H), 7.23-7.17 (m, 2H), 7.15-7.08 (m, 2H), 7.07-7.01 (m, 2H), 6.94-6.87 (m, 3H), 6.37 (d, *J* = 4.0 Hz, 1H), 5.19 (d, *J* = 7.8 Hz, 1H), 4.88-4.80 (m, 1H), 4.54 (dq, *J* = 16.7, 8.5 Hz, 2H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 150.5, 150.0, 148.4, 146.8, 136.0, 131.5, 128.3, 127.9, 126.6, 126.4, 121.3, 117.8, 114.1, 101.9, 83.9, 72.3, 68.1, 54.5, 27.1; HRMS (EI) m/z calcd. for $C_{26}H_{25}ClN_4O_3$ $(M)^+$ 476.1615, found 476.1617.

Screening conditions for chiral Brønsted acids catalyzed 1,3-dipolar cycloaddition reaction (4-substitute isoxazolidine)

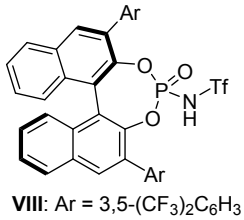
Table S1 Screening of chiral Brønsted acids [a]





I

II: Ar = 3,5-$(CF_3)_2C_6H_3$
III: Ar = 3,5-$(C_6H_5)_2C_6H_3$
IV: Ar = 3,5-(4-$FC_6H_4)_2C_6H_3$
V: Ar = 3,5-(3,4,5-$F_3C_6H_2)_2C_6H_3$
VI: Ar = 3,5-(3,5-$(CF_3)_2C_6H_3)_2C_6H_3$
VII: Ar = 2,4,6-(*i*-Pr)$_3C_6H_2$



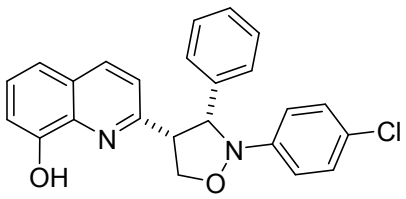
VIII: Ar = 3,5-$(CF_3)_2C_6H_3$

entry	cat.	*cis*-**3x**, yield (%)[b]	*cis*-**3x**, ee (%)[c]	**3x**, dr[d] *cis*:*trans*	Ratio[d] **3x**:**4x**
1	**I**	38	20	>20:1	3.1:1
2	**II**	42	69	>20:1	3.5:1
3	**III**	35	76	>20:1	2.5:1
4	**IV**	30	76	>20:1	2.3:1

5	**V**	32	75	>20:1	2.3:1
6	**VI**	25	69	>20:1	2.5:1
7	**VII**	35	73	>20:1	2.8:1
8	**VIII**	48	8	>20:1	5.3:1
9[e]	**III**	28	78	>20:1	2.5:1

[a] Unless otherwise specified, a mixture of **1o** (0.1 mmol, 1.0 equiv), nitrone **2i** (0.12 mmol, 1.2 equiv), acid catalyst (20 mol %) and solvent (1.0 mL) was stirred at rt for 24 h. [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] Determined by ^{1}H NMR of crude mixture. [e] The reaction was run at 0 °C.

To a solution of 2-vinylquinolin-8-ol **1o** (0.1 mmol) and nitrone **2i** (0.12 mmol) in DCM (1.0 mL) was added the Brønsted acid catalyst (0.02 mmol). The resulting solution was stirred at room temperature for 24 h. The crude reaction mixture was directly purified by column chromatography on silica gel to give the desired product *cis*-**3x**.



2-(2-(4-Chlorophenyl)-3-phenylisoxazolidin-4-yl)quinolin-8-ol (*cis*-3x): 35% yield, pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.5 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.26-7.22 (m, 2H), 7.21-7.12 (m, 4H), 7.11-6.97 (m, 6H), 5.13 (d, J = 8.0 Hz, 1H), 4.70-4.64 (m, 1H), 4.63-4.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 151.7, 150.1, 137.5, 136.2, 128.9, 128.1, 127.5, 127.4, 127.2, 126.9, 122.3, 117.5, 116.3, 110.1, 74.3, 70.9, 56.0; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O_2$ $(M)^+$ 402.1135, found 402.1132; (Chiralpak OD-3, *i*-PrOH/hexane = 15/85, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 12.37 min, t_{minor} = 16.50 min, ee = 76%.

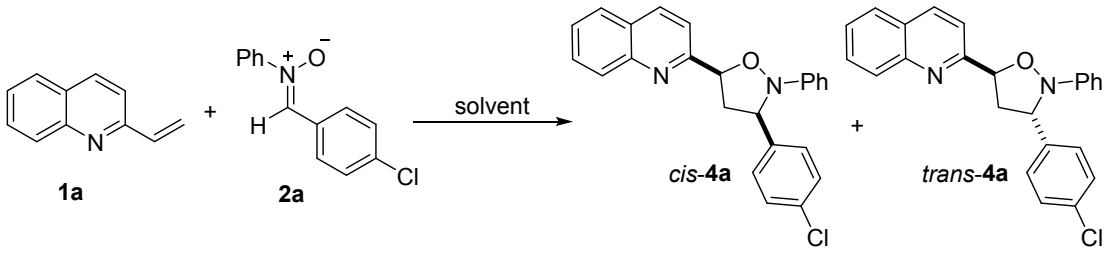
IV. General Procedure for the Synthesis of Compounds 4

To a solution of alkenylazaarenes **1** (0.2 mmol) in H_2O (1.0 mL), nitrones **2** (0.3 mmol) was added. Then the mixture was reacted under microwave irradiation at 110 ^{o}C, 100 W for 0.5 h. After the mixture was cooled to room temperature, the reaction was diluted with H_2O (5.0 mL) and extracted with EtOAc (5 mL × 3). The combined organic extracts were washed with brine, dried with Na_2SO_4, and concentrated in vacuo.

The residue was purified by flash column chromatography on silica gel to give the corresponding products **4**. The less polar compound is the *trans*-product. The more polar compound is the *cis*-product.

Optimization of reaction conditions for 5-substitute isoxazolidines

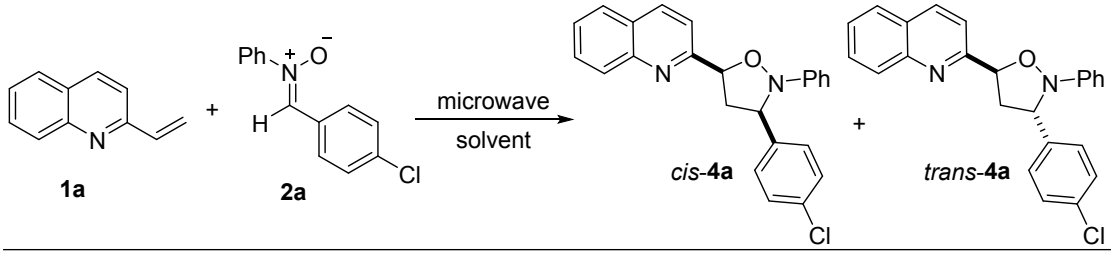
Table S2 Reaction screening studies under conventional thermal conditions [a]



entry	solvent	temperature (°C)	time (h)	**4a**, yield (%)[b]	**4a**, dr[c] *cis*:*trans*
1	DCE	60	12	65	2.1:1
2	DCE	100	15	80	2.3:1
3	THF	90	6	90	2.7:1
4	toluene	130	3	95	2:1
5	1,4-dioxane	130	5	92	2.3:1
6	EtOAc	100	18	89	2.4:1

[a] Reaction conditions: 2-vinylquinoline **1a** (0.2 mmol, 1.0 equiv), nitrone **2a** (0.3 mmol, 1.5 equiv), and solvent (2.0 mL). [b] Isolated yields. [c] Determined by ^{1}H NMR of crude mixture.

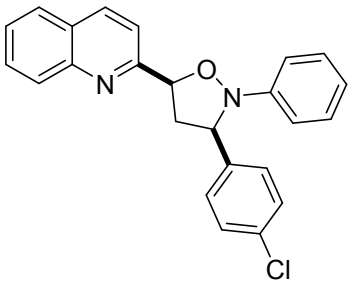
Table S3 Reaction screening studies under microwave conditions [a]



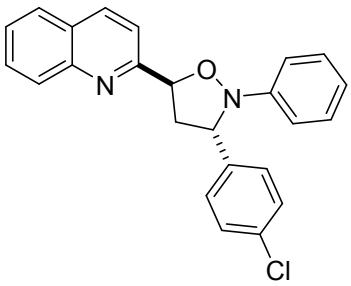
entry	solvent	temperature (°C)	power (W)	time (h)	**4a**, yield (%)[b]	**4a**, dr[c] *cis*:*trans*

1	CH_3CN	130	120	0.5	81	2:1
2	1,4-dioxane	110	100	0.5	76	2:1
3	1,4-dioxane	130	120	0.5	84	1.9:1
4	1,4-dioxane	150	130	0.5	80	1.9:1
5	toluene	150	130	0.5	81	2:1
6	DMF	150	100	0.5	83	2:1
7	H_2O	110	100	0.5	94	2.3:1

[a] Reaction conditions: 2-vinylquinoline **1a** (0.2 mmol, 1.0 equiv), nitrone **2a** (0.3 mmol, 1.5 equiv), and solvent (1.0 mL). [b] Isolated yields. [c] Determined by ^{1}H NMR of crude mixture.

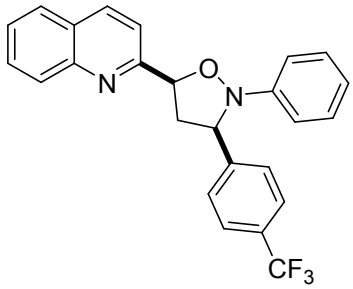


3-(4-Chlorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4a): Following the general procedure, products **4a** (72.7 mg, combined *cis*/*trans* diastereoisomers) were isolated in 94% yield. *cis*-**4a:** pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.76-7.67 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.32-7.27 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 5.55 (t, *J* = 7.5 Hz, 1H), 4.85 (t, *J* = 7.5 Hz, 1H), 3.40 (dt, *J* = 12.5, 7.8 Hz, 1H), 2.77-2.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 151.3, 147.5, 140.7, 137.1, 133.1, 129.7, 129.1, 129.0, 128.9, 128.0, 127.7, 127.7, 126.6, 122.3, 118.5, 115.1, 81.0, 70.2, 46.8; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1191.

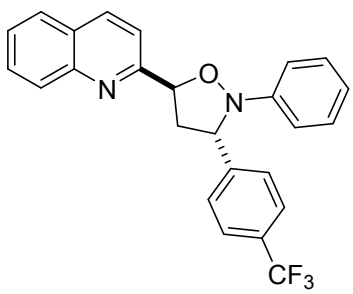


3-(4-Chlorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-4a): yellow

solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.74-7.67 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.20 (t, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.93 (t, *J* = 7.3 Hz, 1H), 5.62 (t, *J* = 7.2 Hz, 1H), 4.72 (dd, *J* = 8.4, 5.5 Hz, 1H), 3.23-3.12 (m, 1H), 2.92-2.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 150.2, 147.5, 140.1, 137.0, 133.3, 129.8, 129.1, 129.1, 128.7, 128.3, 127.7, 127.7, 126.6, 122.1, 119.0, 115.9, 80.3, 68.3, 45.6; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1191.

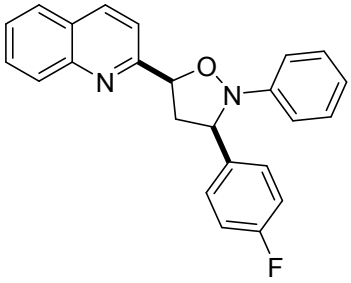


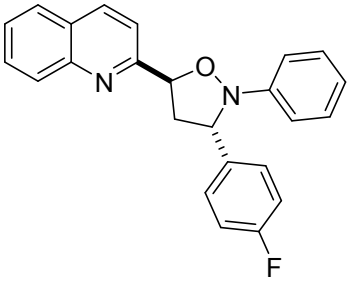
2-Phenyl-5-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*cis*-4b): Following the general procedure, products **4b** (65.5 mg, combined *cis*/*trans* diastereoisomers) were isolated in 78% yield. *cis*-**4b:** pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.71 (t, *J* = 8.1 Hz, 2H), 7.64-7.57 (m, 4H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 7.3 Hz, 1H), 5.57 (t, *J* = 7.5 Hz, 1H), 4.95 (t, *J* = 7.5 Hz, 1H), 3.44 (dt, *J* = 12.5, 7.9 Hz, 1H), 2.76 (dt, *J* = 12.8, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 151.2, 147.5, 146.4, 137.1, 130.1 (q, $J_{C\text{-}F}$ = 32 Hz), 129.8, 129.1, 129.0, 127.7, 126.9, 126.7, 125.9 (q, $J_{C\text{-}F}$ = 4 Hz), 125.5 (q, $J_{C\text{-}F}$ = 270 Hz), 122.4, 118.4, 114.9, 81.1, 70.3, 46.5; HRMS (EI) m/z calcd. for $C_{25}H_{19}F_3N_2O$ $(M)^+$ 420.1449, found 420.1454.



2-Phenyl-5-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*trans*-4b): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* =

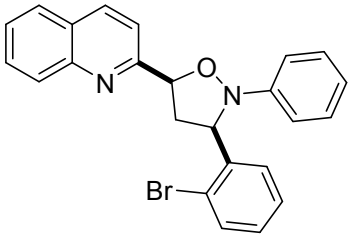
8.5 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.75-7.63 (m, 6H), 7.54 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.8 Hz, 2H), 6.99 (d, J = 8.1 Hz, 2H), 6.94 (t, J = 7.3 Hz, 1H), 5.63 (t, J = 7.2 Hz, 1H), 4.84 (dd, J = 8.3, 5.5 Hz, 1H), 3.24 (dt, J = 12.4, 8.0 Hz, 1H), 2.93-2.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 150.1, 147.5, 145.8, 137.0, 130.0 (q, $J_{C\text{-}F}$ = 32 Hz), 129.8, 129.1, 128.7, 127.7, 127.2, 126.7, 125.9 (q, $J_{C\text{-}F}$ = 4 Hz), 125.5 (q, $J_{C\text{-}F}$ = 271 Hz), 122.2, 119.0, 115.8, 80.4, 68.4, 45.4; HRMS (EI) m/z calcd. for $C_{25}H_{19}F_3N_2O$ $(M)^+$ 420.1449, found 420.1454.

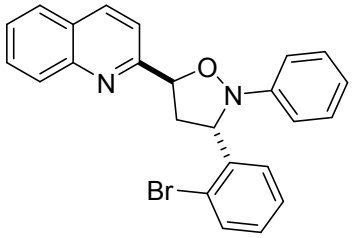


and


Following the general procedure, products **4c** (57.6 mg, combined *cis*/*trans* diastereoisomers) were isolated in 90% yield.

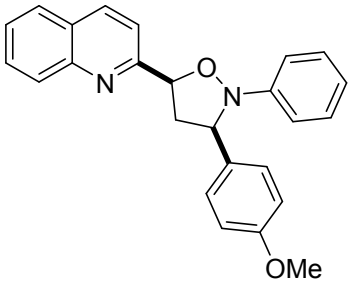
3-(4-Fluorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4c and *trans*-4c): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.12 (m, 3.3H), 8.04 (d, J = 8.4 Hz, 3.3H), 7.82-7.77 (m, 3.3H), 7.75-7.66 (m, 6.7H), 7.54-7.48 (m, 5.4H), 7.45-7.41 (m, 4.4H), 7.31-7.23 (m, 5H), 7.22-7.17 (m, 2H), 7.12-7.04 (m, 6.7H), 7.03-6.96 (m, 9H), 6.95-6.90 (m, 1H), 5.63 (t, J = 7.2 Hz, 1H), 5.55 (t, J = 7.6 Hz, 2.3H), 4.84 (t, J = 7.2 Hz, 2.3H), 4.73 (dd, J = 8.4, 5.2 Hz, 1H), 3.44-3.33 (m, 2.3H), 3.21-3.12 (m, 1H), 2.92-2.83 (m, 1H), 2.75 (dt, J = 14.8, 7.2 Hz, 2.3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, $^1J_{C\text{-}F}$ = 246 Hz), 163.3 (d, $^1J_{C\text{-}F}$ = 246 Hz), 159.9, 159.6, 151.4, 150.3, 147.5, 147.5, 137.9 (d, $^4J_{C\text{-}F}$ = 3 Hz), 137.3 (d, $^4J_{C\text{-}F}$ = 3 Hz), 137.1, 136.9, 129.8, 129.7, 129.2, 129.1, 129.0, 128.7, 128.5 (d, $^3J_{C\text{-}F}$ = 8 Hz), 128.3 (d, $^3J_{C\text{-}F}$ = 8 Hz), 127.7, 127.7, 126.6, 122.3, 122.1, 119.0, 118.5, 116.0, 115.9 (d, $^2J_{C\text{-}F}$ = 21 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 21 Hz), 115.2, 81.0, 80.3, 70.3, 68.4, 46.9, 45.7.

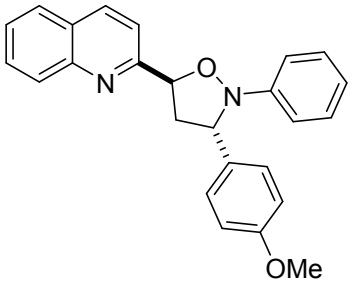


and


Following the general procedure, products **4d** (77.6 mg, combined *cis*/*trans* diastereoisomers) were isolated in 90% yield.

3-(2-Bromophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4d and *trans*-4d): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.11 (m, 3.8H), 8.06-7.98 (m, 3.8H), 7.91-7.84 (m, 3.9H), 7.81-7.75 (m, 3.8H), 7.74-7.64 (m, 7.8H), 7.62-7.58 (m, 1H), 7.58-7.53 (m, 2.8H), 7.53-7.46 (m, 4H), 7.36-7.25 (m, 9.7H), 7.25-7.20 (m, 3H), 7.19-7.07 (m, 9.7H), 7.03-6.96 (m, 4.9H), 6.95-6.89 (m, 1H), 5.62-5.50 (m, 3.8H), 5.31 (dd, *J* = 8.4, 6.4 Hz, 2.8H), 5.24 (dd, *J* = 8.8, 4.0 Hz, 1H), 3.60 (ddd, *J* = 12.6, 8.4, 7.3 Hz, 2.8H), 3.20 (dt, *J* = 12.4, 8.8 Hz, 1H), 2.79 (ddd, *J* = 12.4, 6.5, 3.9 Hz, 1H), 2.56 (ddd, *J* = 12.6, 8.4, 6.4 Hz, 2.8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.0, 151.3, 150.3, 147.5, 147.4, 141.8, 140.8, 137.1, 137.0, 132.9, 132.8, 129.8, 129.7, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.3, 128.1, 127.7, 127.7, 127.6, 126.7, 122.3, 122.2, 122.0, 121.8, 118.9, 118.6, 115.4, 114.5, 81.4, 80.4, 70.2, 68.4, 45.7, 43.9.

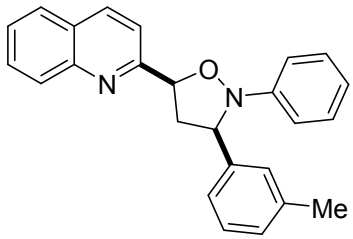


and


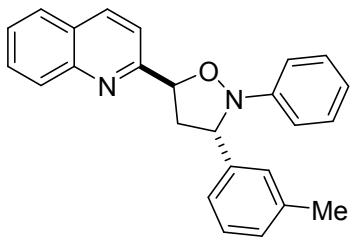
Following the general procedure, products **4e** (64.2 mg, combined *cis*/*trans* diastereoisomers) were isolated in 84% yield.

3-(4-Methoxyphenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4e and *trans*-4e): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.13 (m, 2.9H), 8.04 (d, *J* = 8.8 Hz, 2.9H), 7.83-7.76 (m, 4.8H), 7.75-7.67 (m, 4H), 7.55-7.50 (m, 2.9H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 15.6 Hz, 3.9H), 7.29-7.23 (m, 4.7H), 7.22-7.16 (m, 2H), 7.12 (d, *J* = 7.6 Hz, 3.8H), 7.04 (d, *J* = 7.6 Hz, 2H), 6.98 (t, *J* = 7.6 Hz, 2H), 6.95-6.89 (m, 3H), 6.89-6.83 (m, 4H), 5.66 (t, *J* = 7.2 Hz, 1H), 5.55 (t, *J* = 7.6 Hz, 1.9H), 4.80 (t, *J* = 7.6 Hz, 1.9H), 4.68 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 5.7H), 3.39 (dt, *J* = 12.4,

7.6 Hz, 1.9H), 3.13 (dt, *J* = 11.6, 8.0 Hz, 1H), 2.95-2.87 (m, 1H), 2.75 (dt, *J* = 12.4, 8.2 Hz, 1.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 160.0, 159.1, 158.9, 151.6, 150.4, 147.5, 147.5, 137.0, 136.9, 134.0, 133.4, 129.7, 129.6, 129.2, 129.0, 128.9, 128.5, 128.1, 127.8, 127.7, 127.6, 126.6, 126.5, 122.2, 122.0, 118.9, 118.5, 116.1, 115.3, 114.2, 114.1, 81.0, 80.3, 70.6, 68.6, 55.3, 47.2, 46.0.

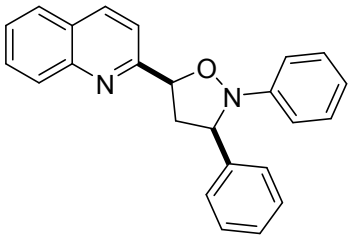


2-Phenyl-5-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*cis*-4f): Following the general procedure, products **4f** (55.0 mg, combined *cis*/*trans* diastereoisomers) were isolated in 75% yield. *cis*-**4f:** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.79 (t, *J* = 8.8 Hz, 2H), 7.72-7.66 (m, 1H), 7.56-7.48 (m, 1H), 7.34-7.19 (m, 5H), 7.15-7.09 (m, 2H), 7.07 (d, *J* = 7.3 Hz, 1H), 6.97 (t, *J* = 7.3 Hz, 1H), 5.54 (t, *J* = 7.6 Hz, 1H), 4.84 (t, *J* = 7.7 Hz, 1H), 3.39 (ddd, *J* = 12.4, 8.0, 7.2 Hz, 1H), 2.78-2.69 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 151.8, 147.5, 142.1, 138.5, 137.0, 129.7, 129.0, 128.9, 128.7, 128.2, 127.7, 127.7, 127.2, 126.6, 123.6, 122.0, 118.6, 115.0, 81.1, 71.0, 47.3, 21.5; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O$ $(M)^+$ 366.1732, found 366.1733.

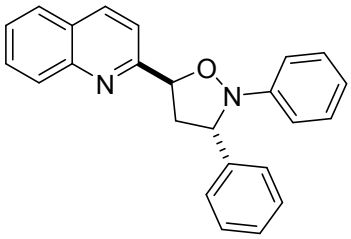


2-Phenyl-5-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*trans*-4f): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.75-7.67 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.39 (s, 1H), 7.35-7.24 (m, 2H), 7.20 (t, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.92 (t, *J* = 7.3 Hz, 1H), 5.66 (t, *J* = 7.2 Hz, 1H), 4.71 (dd, *J* = 8.3, 5.7 Hz, 1H), 3.13 (dt, *J* = 12.3, 8.0 Hz, 1H), 2.96-2.86 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 150.6, 147.5, 141.6, 138.6, 136.9, 129.7, 129.1, 128.7, 128.6, 128.4, 127.7,

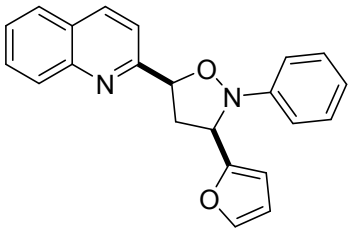
127.4, 126.6, 123.9, 121.8, 119.0, 115.8, 80.4, 69.0, 46.0, 21.5; HRMS (EI) m/z calcd. for $C_{25}H_{22}N_2O$ $(M)^+$ 366.1732, found 366.1733.

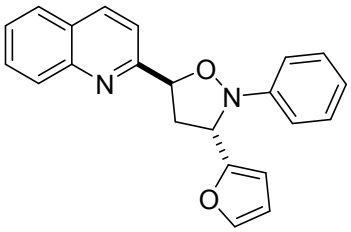


2,3-Diphenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4g): Following the general procedure, products **4g** (64.8 mg, combined *cis*/*trans* diastereoisomers) were isolated in 92% yield. ***cis*-4g:** pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.70 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.55-7.46 (m, 3H), 7.37-7.30 (m, 2H), 7.29-7.23 (m, 3H), 7.14-7.08 (m, 2H), 6.98 (t, J = 7.3 Hz, 1H), 5.56 (t, J = 7.6 Hz, 1H), 4.87 (t, J = 7.7 Hz, 1H), 3.47-3.35 (m, 1H), 2.80-2.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 151.6, 147.5, 142.1, 137.0, 129.6, 129.1, 128.9, 128.8, 127.7, 127.6, 127.4, 126.6, 126.5, 122.1, 118.5, 115.1, 81.1, 70.9, 47.2; HRMS (EI) m/z calcd. for $C_{24}H_{20}N_2O$ $(M)^+$ 352.1576, found 352.1578.



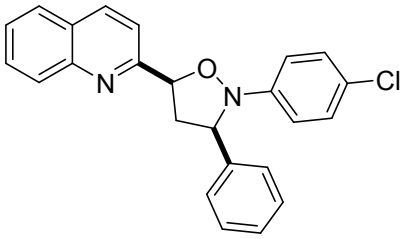
2,3-Diphenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-4g): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.78-7.67 (m, 2H), 7.59-7.49 (m, 3H), 7.39 (t, J = 7.5 Hz, 2H), 7.32 (d, J = 7.3 Hz, 1H), 7.23-7.16 (m, 2H), 7.07-7.00 (m, 2H), 6.93 (t, J = 7.3 Hz, 1H), 5.66 (t, J = 7.2 Hz, 1H), 4.75 (dd, J = 8.4, 5.6 Hz, 1H), 3.24-3.11 (m, 1H), 2.99-2.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 150.5, 147.5, 141.6, 136.9, 129.7, 129.2, 128.9, 128.6, 127.7, 127.6, 126.9, 126.5, 121.9, 119.0, 115.9, 80.4, 69.0, 45.9; HRMS (EI) m/z calcd. for $C_{24}H_{20}N_2O$ $(M)^+$ 352.1576, found 352.1578.



and


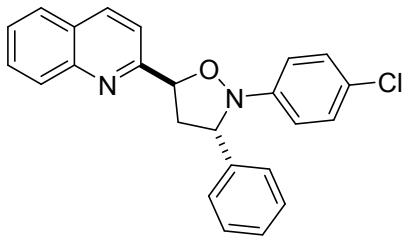
Following the general procedure, products **4h** (58.9 mg, combined *cis*/*trans* diastereoisomers) were isolated in 86% yield.

3-(Furan-2-yl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4h and *trans*-4h): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 2.9H), 8.08-8.02 (m, 2.8H), 7.84-7.78 (m, 2.9H), 7.77-7.67 (m, 5.8H), 7.56-7.50 (m, 2.9H), 7.44-7.40 (m, 1H), 7.40-7.36 (m, 1.8H), 7.35-7.28 (m, 3.8H), 7.27-7.19 (m, 6.3H), 7.13-7.07 (m, 2H), 7.02 (t, *J* = 7.3 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.38-6.33 (m, 2H), 6.33-6.29 (m, 3.6H), 5.70 (t, *J* = 7.5 Hz, 1H), 5.58 (t, *J* = 7.8 Hz, 1.9H), 5.00 (dd, *J* = 8.3, 5.6 Hz, 1.9H), 4.90 (dd, *J* = 8.4, 4.2 Hz, 1H), 3.22 (dt, *J* = 12.6, 8.2 Hz, 1.9H), 3.13 (ddd, *J* = 11.5, 7.2, 4.2 Hz, 1H), 3.03 (dt, *J* = 12.4, 8.1 Hz, 1H), 2.95 (ddd, *J* = 12.9, 7.6, 5.6 Hz, 1.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.7, 153.9, 153.1, 151.1, 149.9, 147.5, 147.4, 142.4, 142.3, 137.0, 136.9, 129.7, 129.6, 129.2, 129.1, 129.0, 128.6, 127.8, 127.7, 127.7, 127.6, 126.6, 122.6, 122.4, 118.9, 118.6, 116.3, 115.2, 110.5, 110.4, 107.9, 107.2, 81.0, 80.4, 65.0, 63.5, 41.7, 41.4.

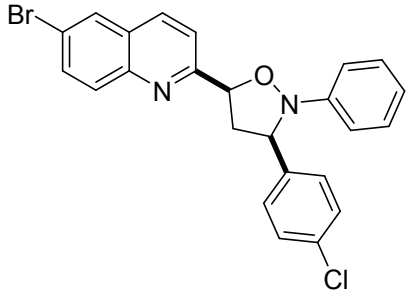


2-(4-Chlorophenyl)-3-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4i): Following the general procedure, products **4i** (56.5 mg, combined *cis*/*trans* diastereoisomers) were isolated in 73% yield. ***cis*-4i:** pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.73-7.67 (m, 1H), 7.56-7.50 (m, 1H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.29-7.24 (m, 1H), 7.23-7.17 (m, 2H), 7.05-6.98 (m, 2H), 5.53 (t, *J* = 7.6 Hz, 1H), 4.78 (t, *J* = 7.8 Hz, 1H), 3.41 (dt, *J* = 12.5, 7.7 Hz, 1H), 2.76 (dt, *J* = 12.5, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 150.2, 147.5, 141.6, 137.1, 129.7, 129.1, 128.9, 128.8, 127.7, 127.7, 127.6, 127.1, 126.6, 126.6, 118.4, 116.5, 81.2, 71.2, 47.3; HRMS

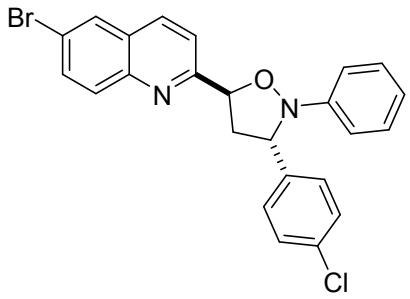
(EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1190.



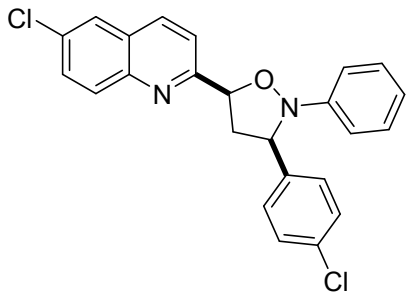
2-(4-Chlorophenyl)-3-phenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-**4i)**: pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.75-7.66 (m, 2H), 7.58-7.49 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.35-7.29 (m, 1H), 7.16-7.09 (m, 2H), 6.97-6.90 (m, 2H), 5.65 (t, *J* = 7.1 Hz, 1H), 4.70 (dd, *J* = 8.3, 5.8 Hz, 1H), 3.21 (ddd, *J* = 12.4, 8.4, 7.0 Hz, 1H), 2.97-2.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 149.0, 147.5, 141.1, 136.9, 129.8, 129.1, 128.9, 128.5, 127.8, 127.6, 126.9, 126.8, 126.6, 118.9, 117.2, 80.5, 69.1, 45.7; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1190.



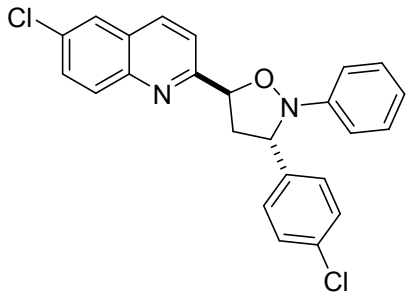
5-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-**4j)**: Following the general procedure, products **4j** (69.8 mg, combined *cis*/*trans* diastereoisomers) were isolated in 75% yield. *cis*-**4j:** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 2.1 Hz, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 7.80-7.72 (m, 2H), 7.42-7.36 (m, 2H), 7.32-7.24 (m, 5H), 7.08 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 5.52 (t, *J* = 7.5 Hz, 1H), 4.88-4.78 (m, 1H), 3.44-3.32 (m, 1H), 2.79-2.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 151.1, 146.1, 140.5, 136.0, 133.2, 133.1, 130.8, 129.7, 129.0, 128.9, 128.7, 128.0, 122.4, 120.4, 119.4, 115.2, 80.7, 70.1, 46.5; HRMS (EI) m/z calcd. for $C_{24}H_{18}BrClN_2O$ $(M)^+$ 464.0291, found 464.0293.



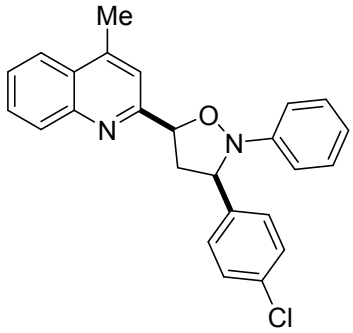
5-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*trans*-4j): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 2.1 Hz, 1H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.77 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.39-7.33 (m, 2H), 7.23-7.16 (m, 2H), 6.98 (dd, *J* = 8.7, 1.0 Hz, 2H), 6.96-6.91 (m, 1H), 5.59 (t, *J* = 7.2 Hz, 1H), 4.73 (dd, *J* = 8.4, 5.5 Hz, 1H), 3.19 (ddd, *J* = 12.4, 8.4, 7.2 Hz, 1H), 2.87 (ddd, *J* = 12.5, 7.2, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 150.0, 146.1, 139.9, 135.9, 133.4, 133.2, 130.9, 129.7, 129.0, 128.7, 128.6, 128.2, 122.2, 120.4, 119.9, 115.9, 80.1, 68.3, 45.4; HRMS (EI) m/z calcd. for $C_{24}H_{18}BrClN_2O$ $(M)^+$ 464.0291, found 464.0293.



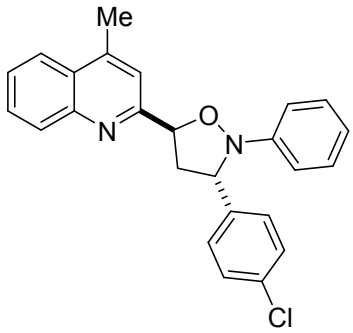
3-(4-Chlorophenyl)-5-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4k): Following the general procedure, products **4k** (69.9 mg, combined *cis*/*trans* diastereoisomers) were isolated in 83% yield. *cis*-**4k:** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 2.3 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.63 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.32-7.24 (m, 4H), 7.08 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 5.53 (t, *J* = 7.5 Hz, 1H), 4.88-4.79 (m, 1H), 3.44-3.33 (m, 1H), 2.79-2.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 151.1, 145.9, 140.5, 136.0, 133.2, 132.3, 130.7, 130.6, 129.0, 128.9, 128.2, 127.9, 126.3, 122.4, 119.4, 115.1, 80.7, 70.1, 46.5; HRMS (EI) m/z calcd. for $C_{24}H_{18}Cl_2N_2O$ $(M)^+$ 420.0796, found 420.0793.



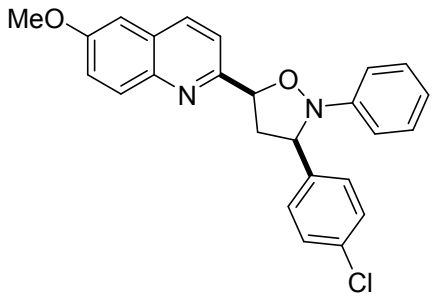
3-(4-Chlorophenyl)-5-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4k): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 2.3 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.64 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.51-7.45 (m, 2H), 7.39-7.34 (m, 2H), 7.23-7.16 (m, 2H), 7.01-6.96 (m, 2H), 6.96-6.90 (m, 1H), 5.60 (t, *J* = 7.2 Hz, 1H), 4.73 (dd, *J* = 8.4, 5.5 Hz, 1H), 3.19 (ddd, *J* = 12.4, 8.4, 7.2 Hz, 1H), 2.86 (ddd, *J* = 12.5, 7.2, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 150.1, 145.9, 140.0, 135.9, 133.4, 132.3, 130.8, 130.6, 129.0, 128.6, 128.3, 128.2, 126.3, 122.2, 119.9, 115.9, 80.1, 68.3, 45.4; HRMS (EI) m/z calcd. for $C_{24}H_{18}Cl_2N_2O$ $(M)^+$ 420.0796, found 420.0793.



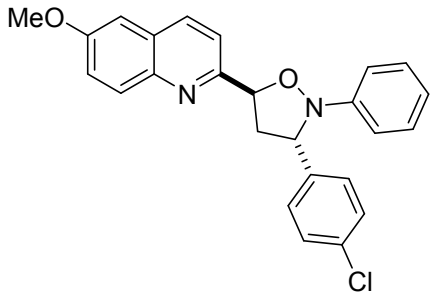
3-(4-Chlorophenyl)-5-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4l): Following the general procedure, products **4l** (72.9 mg, combined *cis*/*trans* diastereoisomers) were isolated in 91% yield. ***cis*-4l:** brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.98 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.69 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.58-7.51 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.33-7.24 (m, 4H), 7.11-7.07 (m, 2H), 7.02-6.96 (m, 1H), 5.50 (dd, *J* = 7.9, 7.4 Hz, 1H), 4.86 (t, *J* = 7.5 Hz, 1H), 3.36 (ddd, *J* = 12.5, 8.1, 7.2 Hz, 1H), 2.76-2.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 151.5, 147.3, 145.4, 140.8, 133.1, 129.6, 129.4, 129.0, 128.9, 128.0, 127.7, 126.4, 123.8, 122.2, 119.0, 114.9, 81.2, 70.4, 46.6, 18.9; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O$ $(M)^+$ 400.1342, found 400.1345.



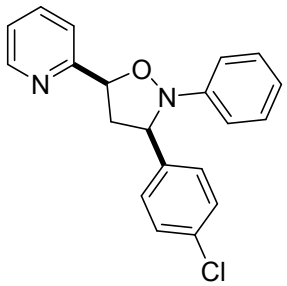
3-(4-Chlorophenyl)-5-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4l): pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.00 (m, 1H), 7.98 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.58-7.52 (m, 2H), 7.51-7.46 (m, 2H), 7.38-7.32 (m, 2H), 7.24-7.17 (m, 2H), 7.03-6.99 (m, 2H), 6.97-6.91 (m, 1H), 5.58 (t, *J* = 7.3 Hz, 1H), 4.72 (dd, *J* = 8.6, 5.3 Hz, 1H), 3.16 (ddd, *J* = 12.4, 8.5, 7.7 Hz, 1H), 2.84 (ddd, *J* = 12.4, 7.1, 5.3 Hz, 1H), 2.70 (d, *J* = 0.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 150.2, 147.3, 145.2, 140.2, 133.3, 129.7, 129.4, 129.0, 128.6, 128.3, 127.7, 126.4, 123.8, 122.1, 119.5, 116.0, 80.3, 68.4, 45.6, 18.9; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O$ $(M)^+$ 400.1342, found 400.1345.



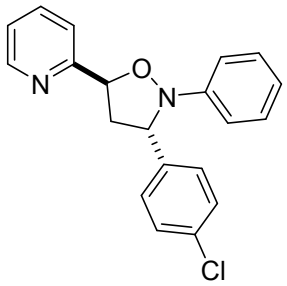
3-(4-Chlorophenyl)-5-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4m): Following the general procedure, products **4m** (79.2 mg, combined *cis*/*trans* diastereoisomers) were isolated in 95% yield. *cis*-**4m:** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.35 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.32-7.24 (m, 4H), 7.11-7.04 (m, 3H), 6.98 (t, *J* = 7.3 Hz, 1H), 5.51 (t, *J* = 7.6 Hz, 1H), 4.85 (t, *J* = 7.5 Hz, 1H), 3.92 (s, 3H), 3.36 (dt, *J* = 12.5, 7.8 Hz, 1H), 2.79-2.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 156.7, 151.4, 143.5, 140.9, 135.8, 133.1, 130.5, 129.0, 128.9, 128.7, 127.9, 122.5, 122.2, 118.8, 114.9, 105.1, 81.1, 70.3, 55.6, 46.7; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O_2$ $(M)^+$ 416.1292, found 416.1290.



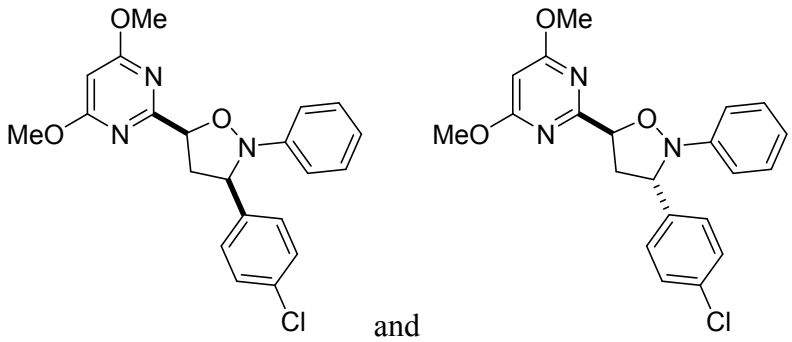
3-(4-Chlorophenyl)-5-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4m): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 9.2 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.40-7.33 (m, 3H), 7.24-7.15 (m, 2H), 7.07 (d, *J* = 2.7 Hz, 1H), 6.99 (d, *J* = 7.7 Hz, 2H), 6.93 (t, *J* = 7.3 Hz, 1H), 5.60 (t, *J* = 7.2 Hz, 1H), 4.73 (dd, *J* = 8.5, 5.4 Hz, 1H), 3.93 (s, 3H), 3.21-3.12 (m, 1H), 2.84 (ddd, *J* = 12.4, 7.0, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 156.7, 150.2, 143.5, 140.2, 135.7, 133.3, 130.5, 129.0, 128.7, 128.6, 128.2, 122.5, 122.0, 119.3, 115.9, 105.1, 80.2, 68.4, 55.6, 45.6; HRMS (EI) m/z calcd. for $C_{25}H_{21}ClN_2O_2$ $(M)^+$ 416.1292, found 416.1290.



3-(4-Chlorophenyl)-2-phenyl-5-(pyridin-2-yl)isoxazolidine (*cis*-4n): Following the general procedure, products **4n** (64.0 mg, combined *cis*/*trans* diastereoisomers) were isolated in 95% yield. *cis*-**4n:** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.3 Hz, 1H), 7.71 (td, *J* = 7.7, 1.7 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.32-7.24 (m, 4H), 7.21 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H), 7.06 (dd, *J* = 8.7, 0.9 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 5.37 (t, *J* = 7.5 Hz, 1H), 4.87-4.78 (m, 1H), 3.30 (ddd, *J* = 12.4, 8.2, 7.1 Hz, 1H), 2.62 (ddd, *J* = 12.4, 8.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 151.5, 149.1, 140.8, 136.8, 133.1, 129.0, 128.9, 127.9, 122.9, 122.1, 120.7, 114.7, 80.4, 70.2, 46.5; HRMS (EI) m/z calcd. for $C_{20}H_{17}ClN_2O$ $(M)^+$ 336.1029, found 336.1027.

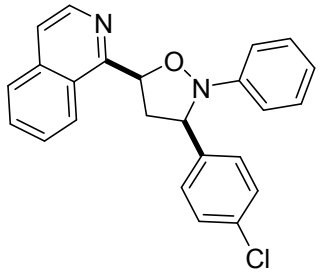


3-(4-Chlorophenyl)-2-phenyl-5-(pyridin-2-yl)isoxazolidine (*trans*-4n): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58-8.53 (m, 1H), 7.69 (td, *J* = 7.7, 1.8 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.49-7.43 (m, 2H), 7.38-7.32 (m, 2H), 7.24-7.16 (m, 3H), 6.99-6.91 (m, 3H), 5.47 (t, *J* = 7.1 Hz, 1H), 4.65 (dd, *J* = 8.4, 5.8 Hz, 1H), 3.07 (ddd, *J* = 12.3, 8.4, 7.1 Hz, 1H), 2.83-2.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 150.1, 149.2, 140.1, 136.7, 133.3, 129.0, 128.6, 128.2, 122.9, 122.2, 121.3, 116.0, 79.6, 68.3, 45.5; HRMS (EI) m/z calcd. for $C_{20}H_{17}ClN_2O$ $(M)^+$ 336.1029, found 336.1027.

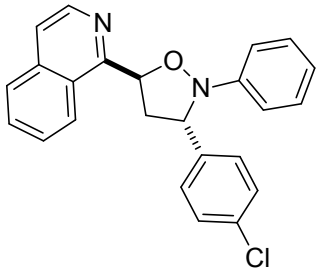


Following the general procedure, products **4o** (57.3 mg, combined *cis*/*trans* diastereoisomers) were isolated in 72% yield.

3-(4-Chlorophenyl)-5-(4,6-dimethoxypyrimidin-2-yl)-2-phenylisoxazolidine (*cis*-4o and *trans*-4o): yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2.2H), 7.41 (d, *J* = 8.4 Hz, 2.2H), 7.32-7.16 (m, 7.5H), 7.09-6.98 (m, 5H), 6.92-6.84 (m, 3.2H), 6.77 (t, *J* = 7.3 Hz, 1H), 5.88 (s, 1.2H), 5.82 (s, 1H), 5.23-5.12 (m, 2.2H), 4.90 (t, *J* = 7.3 Hz, 1H), 4.84 (dd, *J* = 8.3, 5.9 Hz, 1.2H), 3.80 (s, 7.2H), 3.66 (s, 6H), 3.09-2.98 (m, 2.2H), 2.83 (ddd, *J* = 12.3, 8.1, 5.9 Hz, 1.2H), 2.64 (dt, *J* = 12.3, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 171.4, 167.2, 165.3, 152.0, 151.4, 141.5, 140.3, 133.2, 132.8, 129.0, 129.0, 128.6, 128.3, 128.1, 127.9, 121.9, 121.4, 115.3, 114.6, 89.0, 88.9, 81.0, 81.0, 70.1, 68.7, 54.1, 54.0, 44.3, 44.1.

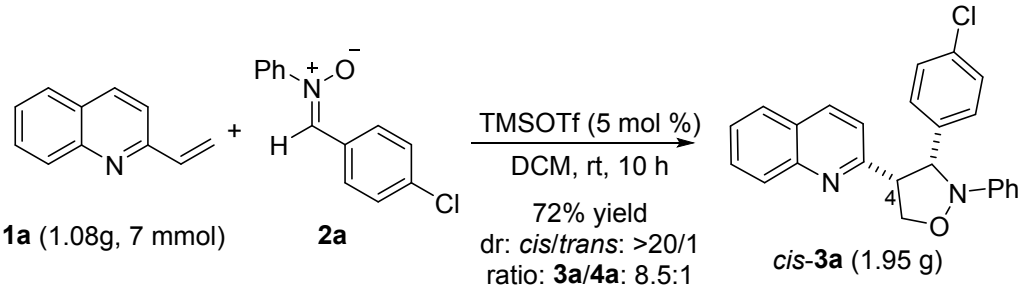


3-(4-Chlorophenyl)-5-(isoquinolin-1-yl)-2-phenylisoxazolidine (*cis*-4p): Following the general procedure, products **4p** (69.6 mg, combined *cis*/*trans* diastereoisomers) were isolated in 90% yield. *cis*-**4p:** yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.3 Hz, 1H), 8.50 (d, *J* = 5.6 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.76-7.63 (m, 3H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.39-7.28 (m, 4H), 7.17-7.08 (m, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 5.99 (dd, *J* = 9.5, 6.0 Hz, 1H), 5.01 (t, *J* = 7.9 Hz, 1H), 3.43 (ddd, *J* = 12.3, 9.5, 7.9 Hz, 1H), 3.22 (ddd, *J* = 12.4, 7.9, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 151.9, 141.6, 140.9, 136.6, 133.1, 130.1, 129.1, 128.9, 128.0, 127.6, 127.4, 125.2, 121.8, 121.6, 114.3, 79.4, 70.2, 43.9; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1188.



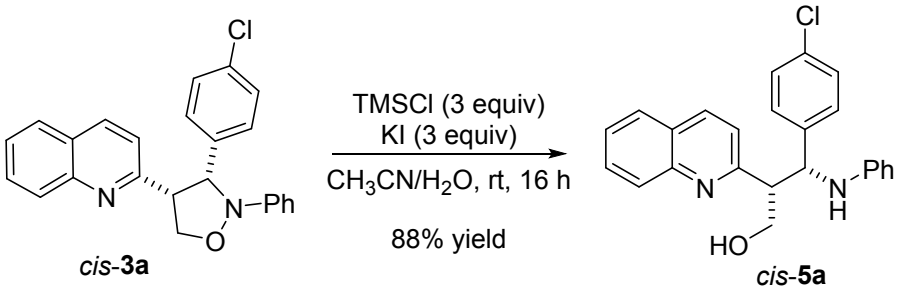
3-(4-Chlorophenyl)-5-(isoquinolin-1-yl)-2-phenylisoxazolidine (*trans*-4p): yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61-8.54 (m, 1H), 8.38 (d, *J* = 5.7 Hz, 1H), 7.85 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.76-7.67 (m, 2H), 7.62-7.55 (m, 3H), 7.44-7.38 (m, 2H), 7.02-6.94 (m, 2H), 6.81-6.75 (m, 1H), 6.71 (dd, *J* = 8.7, 1.0 Hz, 2H), 6.14 (t, *J* = 6.7 Hz, 1H), 4.97 (dd, *J* = 8.5, 5.8 Hz, 1H), 3.92 (ddd, *J* = 12.2, 8.6, 6.4 Hz, 1H), 2.68 (ddd, *J* = 12.5, 6.9, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 151.0, 141.2, 141.1, 136.5, 133.1, 130.1, 129.0, 128.3, 128.1, 127.8, 127.6, 127.2, 125.7, 121.7, 121.4, 115.3, 78.1, 69.5, 41.5; HRMS (EI) m/z calcd. for $C_{24}H_{19}ClN_2O$ $(M)^+$ 386.1186, found 386.1188.

V. Scale up experiment and Synthetic transformation of cycloaddition adduct *cis*-3a



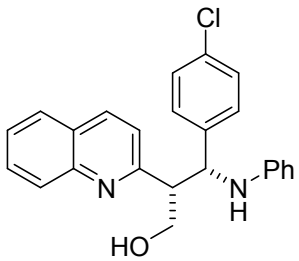
1a (1.08g, 7 mmol) **2a** *cis*-**3a** (1.95 g)

To a solution of 2-vinylquinoline **1a** (1.08 g, 7 mmol) and nitrone **2a** (2.43 g, 10.5 mmol) in DCM (20.0 mL) was added the catalyst TMSOTf (77.8 mg, 0.35 mmol). The resulting solution was stirred at room temperature for 10 h. The reaction mixture was concentrated and the residue was directly purified by column chromatography on silica gel to give the corresponding product *cis*-**3a** in 72% yield (1.95 g).



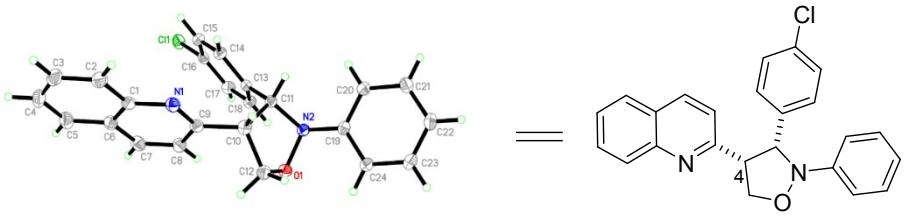
cis-**3a** *cis*-**5a**

TMSCl (65.1 mg, 0.6 mmol) and KI (99.6 mg, 0.6 mmol) were dissolved in acetonitrile (2.5 mL), and the mixture was stirred at r.t. for half an hour. To this suspension, a solution of compound *cis*-**3a** (77.5 mg, 0.2 mmol) in acetonitrile (2.5 mL) was added, followed by traces of water (5 μL). Upon stirring at r.t. for 16 h, volatiles were removed in vacuo. The brown oily residue was treated with water (10 mL) and stirred for 1 h before extracting with ethyl acetate (3×10 mL). The combined organic extracts were washed with sodium thiosulfate solution and dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by column chromatography to afford the title compound *cis*-**5a** (68.4 mg, 88%) as pale yellow oil.



3-(4-Chlorophenyl)-3-(phenylamino)-2-(quinolin-2-yl)propan-1-ol (*cis*-5a): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.22 (d, J = 8.5 Hz, 1H), 8.08 (dd, J = 8.3, 3.6 Hz, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.75 (dd, J = 11.3, 4.1 Hz, 1H), 7.61-7.51 (m, 1H), 7.48-7.37 (m, 3H), 7.33 (t, J = 6.9 Hz, 2H), 7.20 (d, J = 8.7 Hz, 1H), 6.92 (t, J = 7.8 Hz, 1H), 6.51 (t, J = 9.9 Hz, 2H), 6.44-6.33 (m, 1H), 5.11-4.99 (m, 1H), 4.71 (t, J = 5.0 Hz, 1H), 3.79-3.68 (m, 1H), 3.67-3.53 (m, 1H), 3.53-3.42 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.5, 152.6, 152.2, 147.3, 142.1, 136.4, 134.6, 134.3, 133.9, 133.7, 133.4, 133.3, 132.9, 132.0, 131.1, 128.2, 121.1, 120.7, 118.1, 67.8, 61.9, 61.1; HRMS (EI) m/z calcd. for $C_{24}H_{21}ClN_2O$ $(M)^+$ 388.1342, found 388.1345.

VI. Crystal data and structural refinement for racemic *cis*-3a and *trans*-4i



cis-**3a**

Datablock: t_a

Bond precision: C-C = 0.0019 A Wavelength=1.54178

Cell: a=5.628(2) b=19.385(4) c=17.569(4)
alpha=90 beta=91.36(3) gamma=90
Temperature: 173 K

	Calculated	Reported
Volume	1916.2(9)	1916.3(9)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C24 H19 Cl N2 O	C24 H19 Cl N2 O
Sum formula	C24 H19 Cl N2 O	C24 H19 Cl N2 O
Mr	386.86	386.86
Dx,g cm-3	1.341	1.341
Z	4	4
Mu (mm-1)	1.891	1.891
F000	808.0	808.0
F000'	811.52	
h,k,lmax	6,23,21	6,23,21
Nref	3511	3500
Tmin,Tmax	0.747,0.767	
Tmin'	0.678	

Correction method= Not given

Data completeness= 0.997 Theta(max)= 68.332

R(reflections)= 0.0300(3116) wR2(reflections)= 0.0819(3500)

S = 1.015 Npar= 253

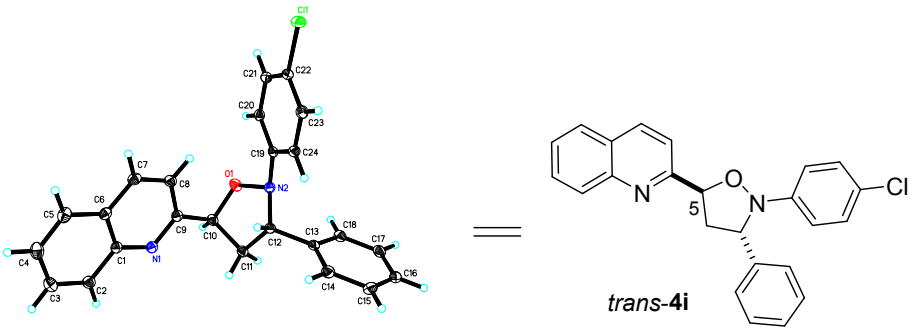


Table 1 Crystal data and structure refinement for mo_dm14659_0m.

Identification code	mo_dm14659_0m
Empirical formula	$C_{24}H_{19}ClN_2O$
Formula weight	386.86
Temperature/K	130
Crystal system	triclinic
Space group	P-1
a/Å	5.7976(9)
b/Å	9.4263(14)
c/Å	17.097(3)
α/°	87.715(3)
β/°	87.737(3)
γ/°	86.465(3)
Volume/Å^3	931.2(2)
Z	2
ρ_{calc}g/cm^3	1.380
μ/mm^{-1}	0.223
F(000)	404.0
Crystal size/mm^3	0.8 × 0.22 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.386 to 61.138
Index ranges	-8 ≤ h ≤ 8, -13 ≤ k ≤ 13, -24 ≤ l ≤ 14
Reflections collected	9492
Independent reflections	5658 [R_{int} = 0.0350, R_{sigma} = 0.0750]
Data/restraints/parameters	5658/0/253
Goodness-of-fit on F^2	1.005
Final R indexes [I>=2σ (I)]	R_1 = 0.0533, wR_2 = 0.1070
Final R indexes [all data]	R_1 = 0.1002, wR_2 = 0.1273
Largest diff. peak/hole / e Å^{-3}	0.31/-0.29

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for mo_dm14659_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	3578.6(10)	7100.9(6)	2.3(3)	35.85(15)
O1	6850(2)	10379.2(15)	-3307.6(7)	27.6(3)
N1	12276(3)	9042.2(16)	-4211.4(8)	23.3(3)
N2	7222(3)	10885.6(17)	-2528.1(8)	22.2(3)
C1	13717(3)	7841(2)	-4228.4(10)	22.2(4)
C2	15689(3)	7836(2)	-4743.7(11)	27.7(4)
C3	17175(4)	6657(2)	-4769.3(12)	33.6(5)
C4	16761(4)	5434(2)	-4301.1(12)	35.2(5)
C5	14876(4)	5408(2)	-3801.0(11)	30.5(5)
C6	13313(3)	6619(2)	-3749.7(10)	23.3(4)
C7	11333(3)	6668(2)	-3241.3(11)	26.5(4)
C8	9906(3)	7874(2)	-3227.5(10)	25.6(4)
C9	10447(3)	9048(2)	-3723.5(10)	22.3(4)
C10	9001(3)	10438(2)	-3747.2(10)	24.0(4)
C11	10179(3)	11637(2)	-3384.5(11)	26.2(4)
C12	9560(3)	11408.2(19)	-2514.4(10)	21.6(4)
C13	9546(3)	12740.8(19)	-2050.8(10)	22.3(4)
C14	11423(3)	12995(2)	-1604.6(12)	29.4(4)
C15	11403(4)	14229(2)	-1186.3(12)	33.1(5)
C16	9531(4)	15203(2)	-1203.9(12)	32.6(5)
C17	7674(4)	14957(2)	-1646.7(12)	31.0(5)
C18	7685(3)	13728(2)	-2067.3(11)	26.1(4)
C19	6505(3)	9901.9(19)	-1943.3(10)	20.0(4)
C20	4683(3)	9050.6(19)	-2076.2(11)	21.9(4)
C21	3803(3)	8192(2)	-1480.2(11)	24.1(4)
C22	4736(3)	8162(2)	-749.2(11)	24.9(4)
C23	6574(3)	8974(2)	-609.1(11)	26.1(4)
C24	7447(3)	9844(2)	-1204(1)	23.8(4)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for mo_dm14659_0m. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	47.8(3)	32.7(3)	27.7(3)	1.9(2)	8.2(2)	-15.1(2)
O1	26.5(7)	38.1(8)	18.3(7)	-1.3(6)	-1.3(5)	-2.2(6)
N1	27.2(9)	24.9(8)	18.3(8)	-1.2(6)	-1.5(6)	-4.2(7)

N2	24.8(8)	24.6(8)	17.9(7)	-2.4(6)	-0.6(6)	-4.5(7)
C1	25.4(10)	25.1(10)	17.1(9)	-3.0(7)	-2.7(7)	-4.8(8)
C2	28.7(11)	28.6(11)	25.9(10)	-0.7(8)	0.2(8)	-3.3(8)
C3	30.7(12)	39.5(12)	30.1(11)	-2.8(9)	2.2(9)	0.7(10)
C4	37.8(13)	34.1(12)	32.8(12)	-1.8(9)	-3.9(9)	8(1)
C5	41.0(13)	25.6(10)	24.7(10)	2.4(8)	-6.1(9)	1.4(9)
C6	28.4(10)	22.8(9)	19.3(9)	-0.8(7)	-3.9(7)	-4.4(8)
C7	33.8(11)	25.3(10)	21.0(9)	2.1(7)	-1.8(8)	-7.7(9)
C8	30.0(11)	28.3(10)	18.8(9)	-0.2(7)	2.4(8)	-6.1(8)
C9	25.8(10)	25(1)	16.7(9)	-2.1(7)	-2.8(7)	-3.4(8)
C10	27.5(10)	25.9(10)	17.8(9)	1.4(7)	2.8(7)	-0.2(8)
C11	29.6(11)	22.7(10)	25.4(10)	1.0(8)	7.2(8)	-1.2(8)
C12	19.8(9)	19.8(9)	24.8(9)	1.1(7)	1.9(7)	-1.3(7)
C13	24.5(10)	20.4(9)	21.7(9)	2.1(7)	4.9(7)	-3.6(8)
C14	23.3(10)	27.6(11)	37.2(11)	-2.2(9)	1.9(8)	-1.0(8)
C15	30.5(12)	35.1(12)	35.2(12)	-5.3(9)	-1.0(9)	-11.6(10)
C16	39.1(12)	25.8(11)	33.0(11)	-5.2(9)	12.7(9)	-10.7(9)
C17	30.1(11)	23.4(10)	38.0(12)	0.1(8)	10.8(9)	2.2(8)
C18	25.7(10)	26.9(10)	25.3(10)	1.8(8)	1.8(8)	-0.8(8)
C19	18.1(9)	19.2(9)	22.2(9)	-2.4(7)	3.1(7)	1.3(7)
C20	19.0(9)	22.9(9)	23.6(9)	-3.9(7)	-1.5(7)	1.5(7)
C21	21.3(10)	24(1)	27.2(10)	-3.9(8)	2.7(7)	-4.0(8)
C22	29.9(10)	21.6(9)	22.8(9)	-0.7(7)	7.3(8)	-4.4(8)
C23	30.9(11)	28.4(10)	19.3(9)	-2.3(8)	-0.3(8)	-4.0(9)
C24	24.3(10)	25.9(10)	21.8(9)	-3.0(7)	0.4(7)	-6.5(8)

Table 4 Bond Lengths for mo_dm14659_0m.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl1	C22	1.7359(19)	C9	C10	1.511(3)
O1	N2	1.4617(19)	C10	C11	1.521(3)
O1	C10	1.433(2)	C11	C12	1.527(2)
N1	C1	1.365(2)	C12	C13	1.511(2)
N1	C9	1.323(2)	C13	C14	1.391(3)
N2	C12	1.472(2)	C13	C18	1.381(3)
N2	C19	1.405(2)	C14	C15	1.389(3)
C1	C2	1.415(3)	C15	C16	1.378(3)
C1	C6	1.413(3)	C16	C17	1.377(3)
C2	C3	1.365(3)	C17	C18	1.387(3)
C3	C4	1.405(3)	C19	C20	1.396(2)
C4	C5	1.362(3)	C19	C24	1.395(3)

C5	C6	1.416(3)	C20	C21	1.378(3)
C6	C7	1.412(3)	C21	C22	1.380(3)
C7	C8	1.365(3)	C22	C23	1.384(3)
C8	C9	1.410(3)	C23	C24	1.381(3)

Table 5 Bond Angles for mo_dm14659_0m.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	O1	N2	107.26(13)	C10	C11	C12	102.26(14)
C9	N1	C1	118.10(16)	N2	C12	C11	102.29(14)
O1	N2	C12	109.07(13)	N2	C12	C13	110.82(15)
C19	N2	O1	110.89(13)	C13	C12	C11	114.04(15)
C19	N2	C12	119.41(15)	C14	C13	C12	120.31(17)
N1	C1	C2	118.29(17)	C18	C13	C12	120.67(17)
N1	C1	C6	122.42(17)	C18	C13	C14	119.02(18)
C6	C1	C2	119.29(18)	C15	C14	C13	119.87(19)
C3	C2	C1	119.73(19)	C16	C15	C14	120.61(19)
C2	C3	C4	121.1(2)	C17	C16	C15	119.66(19)
C5	C4	C3	120.5(2)	C16	C17	C18	120.0(2)
C4	C5	C6	120.1(2)	C13	C18	C17	120.81(19)
C1	C6	C5	119.35(17)	C20	C19	N2	119.83(16)
C7	C6	C1	117.61(18)	C24	C19	N2	121.01(16)
C7	C6	C5	123.04(18)	C24	C19	C20	118.92(17)
C8	C7	C6	119.52(18)	C21	C20	C19	120.35(17)
C7	C8	C9	119.05(18)	C20	C21	C22	119.95(17)
N1	C9	C8	123.29(18)	C21	C22	Cl1	119.56(15)
N1	C9	C10	113.40(16)	C21	C22	C23	120.65(17)
C8	C9	C10	123.30(17)	C23	C22	Cl1	119.78(15)
O1	C10	C9	113.44(16)	C24	C23	C22	119.48(17)
O1	C10	C11	103.66(14)	C23	C24	C19	120.62(17)
C9	C10	C11	112.73(16)				

Table 6 Torsion Angles for mo_dm14659_0m.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Cl1	C22	C23	C24	-178.32(15)	C7	C8	C9	C10	-179.28(17)
O1	N2	C12	C11	18.40(18)	C8	C9	C10	O1	-8.9(2)
O1	N2	C12	C13	140.34(15)	C8	C9	C10	C11	108.6(2)
O1	N2	C19	C20	-30.7(2)	C9	N1	C1	C2	-179.35(16)
O1	N2	C19	C24	154.89(16)	C9	N1	C1	C6	0.3(2)
O1	C10	C11	C12	39.12(18)	C9	C10	C11	C12	-83.95(18)
N1	C1	C2	C3	179.39(17)	C10	O1	N2	C12	6.15(18)

N1	C1	C6	C5	179.71(16)	C10	O1	N2	C19	-127.33(15)
N1	C1	C6	C7	0.1(3)	C10	C11	C12	N2	-34.53(18)
N1	C9	C10	O1	171.38(14)	C10	C11	C12	C13	-154.24(16)
N1	C9	C10	C11	-71.19(19)	C11	C12	C13	C14	-100.2(2)
N2	O1	C10	C9	94.35(16)	C11	C12	C13	C18	79.3(2)
N2	O1	C10	C11	-28.25(18)	C12	N2	C19	C20	-158.81(16)
N2	C12	C13	C14	144.99(17)	C12	N2	C19	C24	26.8(2)
N2	C12	C13	C18	-35.5(2)	C12	C13	C14	C15	179.41(17)
N2	C19	C20	C21	-173.11(16)	C12	C13	C18	C17	-179.54(17)
N2	C19	C24	C23	173.53(17)	C13	C14	C15	C16	0.5(3)
C1	N1	C9	C8	-0.6(3)	C14	C13	C18	C17	0.0(3)
C1	N1	C9	C10	179.17(15)	C14	C15	C16	C17	-0.7(3)
C1	C2	C3	C4	1.1(3)	C15	C16	C17	C18	0.5(3)
C1	C6	C7	C8	-0.3(3)	C16	C17	C18	C13	-0.2(3)
C2	C1	C6	C5	-0.7(3)	C18	C13	C14	C15	-0.2(3)
C2	C1	C6	C7	179.76(16)	C19	N2	C12	C11	147.31(16)
C2	C3	C4	C5	-1.0(3)	C19	N2	C12	C13	-90.76(19)
C3	C4	C5	C6	0.0(3)	C19	C20	C21	C22	-0.5(3)
C4	C5	C6	C1	0.8(3)	C20	C19	C24	C23	-0.9(3)
C4	C5	C6	C7	-179.67(18)	C20	C21	C22	Cl1	178.80(14)
C5	C6	C7	C8	-179.83(18)	C20	C21	C22	C23	-0.8(3)
C6	C1	C2	C3	-0.3(3)	C21	C22	C23	C24	1.3(3)
C6	C7	C8	C9	0.0(3)	C22	C23	C24	C19	-0.4(3)
C7	C8	C9	N1	0.4(3)	C24	C19	C20	C21	1.4(3)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for mo_dm14659_0m.

Atom	*x*	*y*	*z*	U(eq)
H2	15976	8650	-5070	33
H3	18511	6663	-5109	40
H4	17804	4619	-4334	42
H5	14609	4577	-3486	37
H7	10996	5866	-2911	32
H8	8567	7923	-2889	31
H10	8677	10714	-4305	29
H11A	9563	12579	-3585	31
H11B	11874	11552	-3487	31
H12	10642	10655	-2280	26
H14	12715	12326	-1586	35

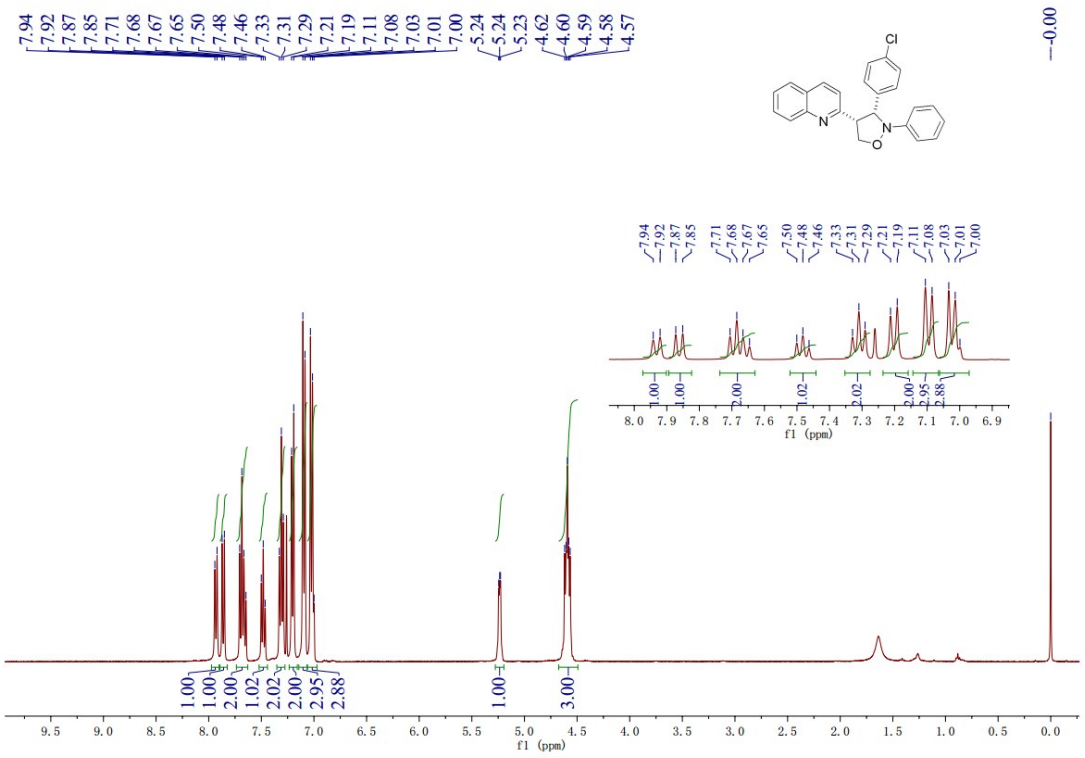
H15	12691	14404	-885	40
H16	9522	16040	-912	39
H17	6385	15629	-1664	37
H18	6396	13563	-2370	31
H20	4047	9064	-2580	26
H21	2554	7620	-1572	29
H23	7230	8934	-108	31
H24	8702	10408	-1109	29

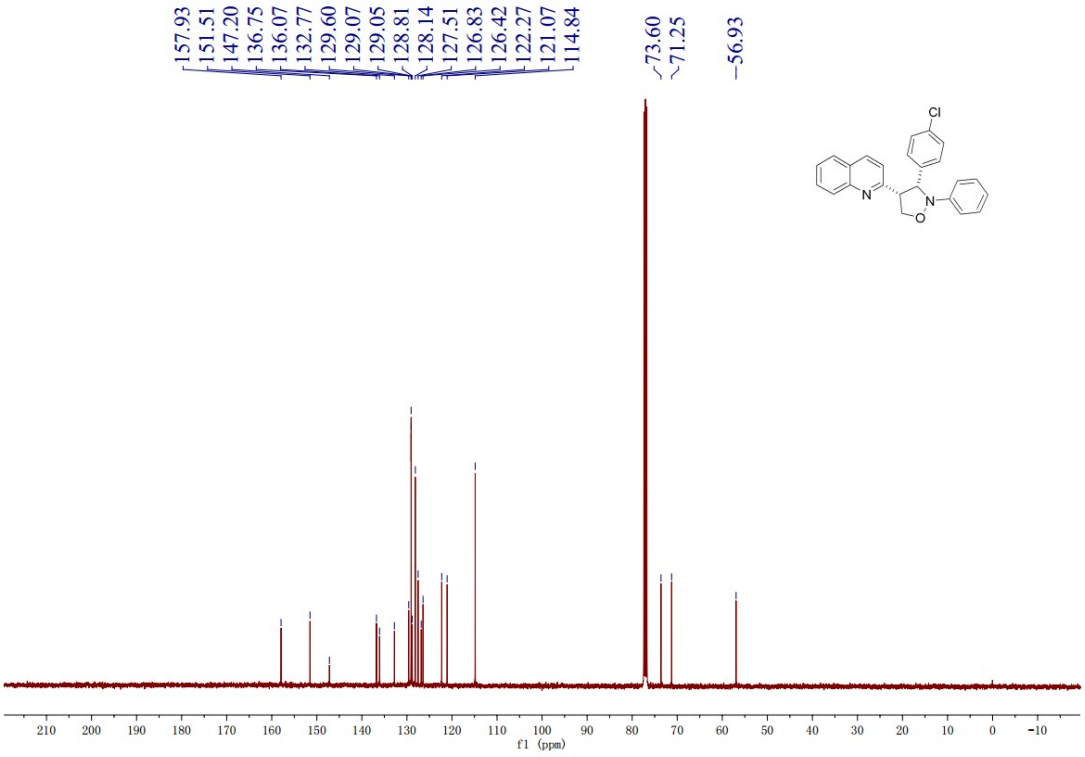
VII. References

1. A. Saxena, B. Choi and H. W. Lam, *J. Am. Chem. Soc.*, 2012, **134**, 8428-8431.
2. Y.-F. Li, F.-F. Guo, Z.-G Zha and Z.-Y. Wang, *Chem. Asian J.*, 2013, **8**, 534-537.
3. V. Chandrasekhar, S. Hossain, S. Das, S. Biswas and J.-P. Sutter, *Inorg. Chem.*, 2013, **52**, 6346-6353.
4. V. Corcé, S. Renaud, I. Cannie, K. Julienne, S. G. Gouin, O. Loréal, F. Gaboriau and D. Deniaud, *Bioconjugate Chem.*, 2014, **25**, 320-334.
5. P. Jiao, D. Nakashima and H. Yamamoto, *Angew. Chem. Int. Ed.*, 2008, **47**, 2411-2413.
6. G. K. S. Prakash, Z. Zhang, F. Wang, M. Rahm, C.-F. Ni, M. Iuliucci, R. Haiges and G. A. Olah, *Chem. Eur. J.*, 2014, **20**, 831-838.
7. F. Nikbakht and A. Heydari, *Tetrahedron Lett*, 2014, **55**, 2513–2516.

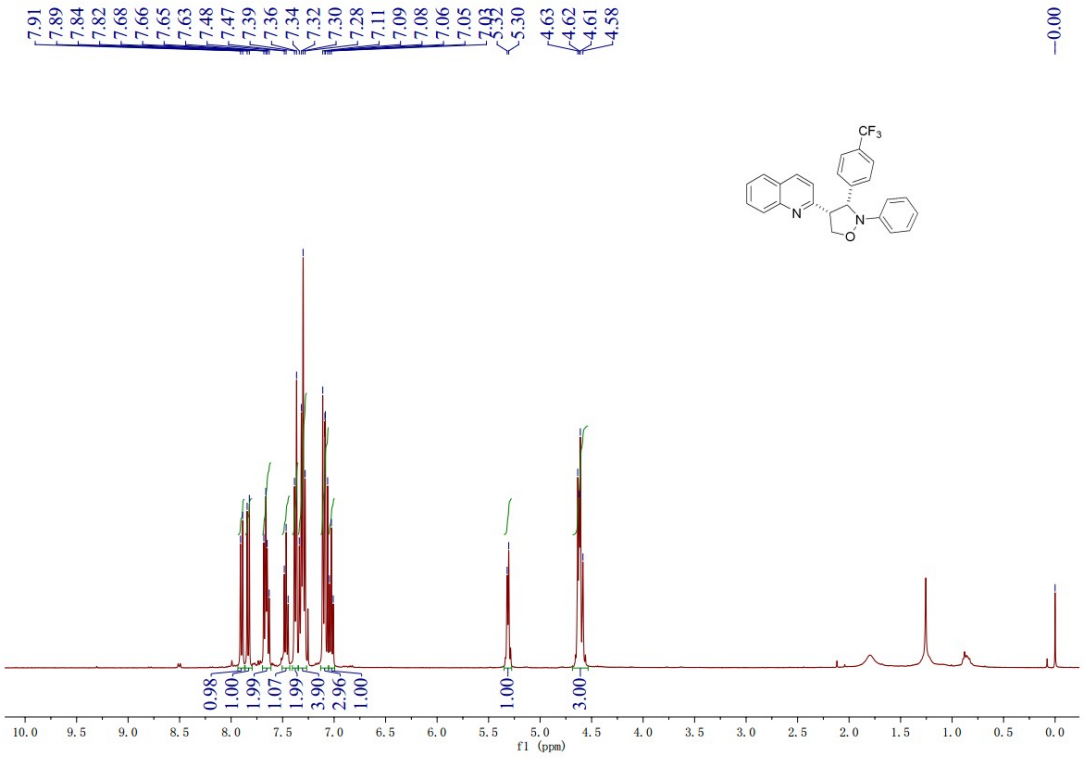
VIII. ^{1}H NMR and ^{13}C NMR spectra

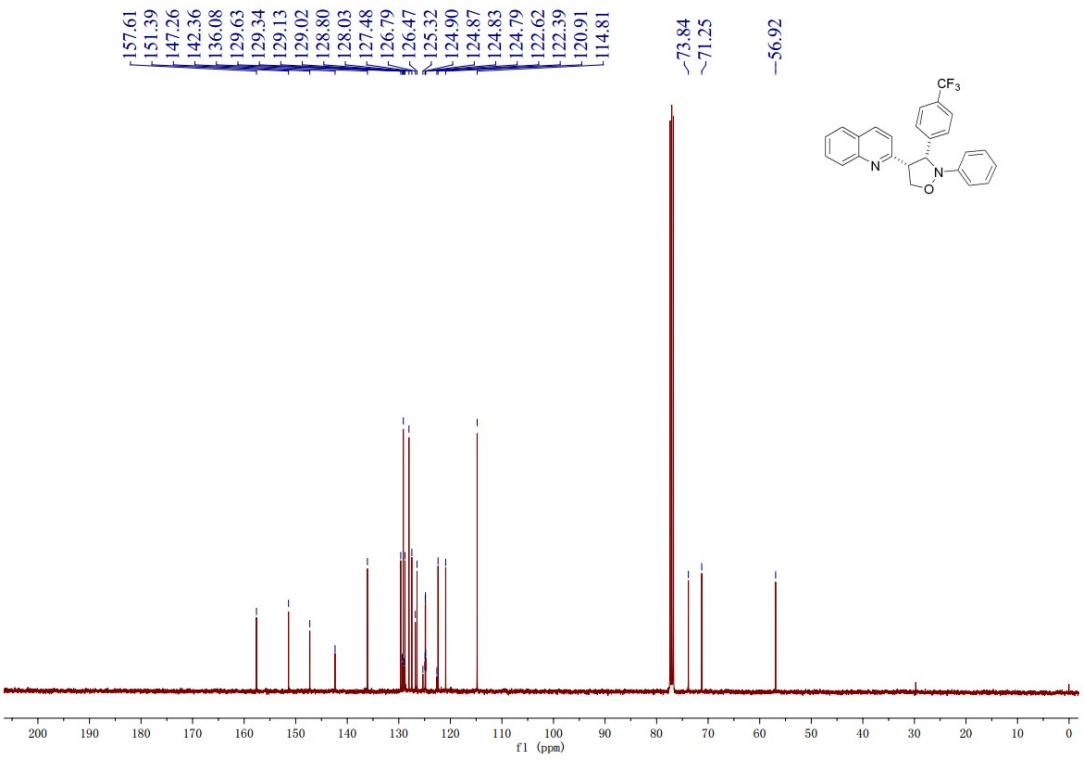
3-(4-Chlorophenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3a)



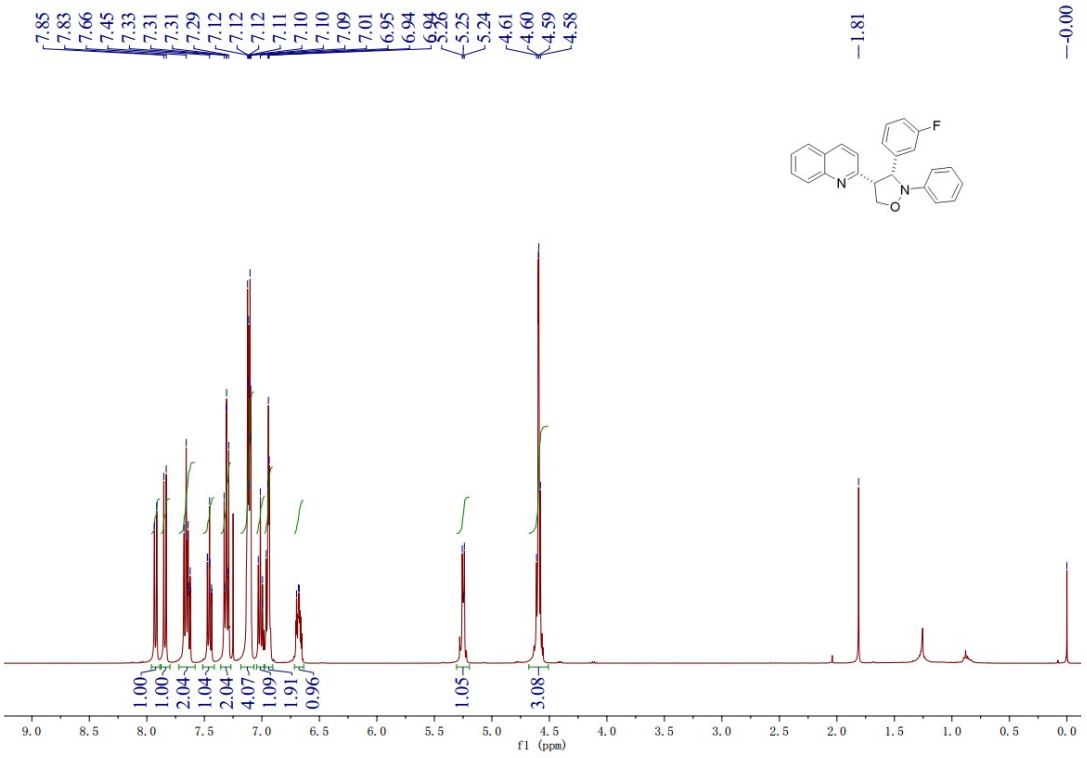


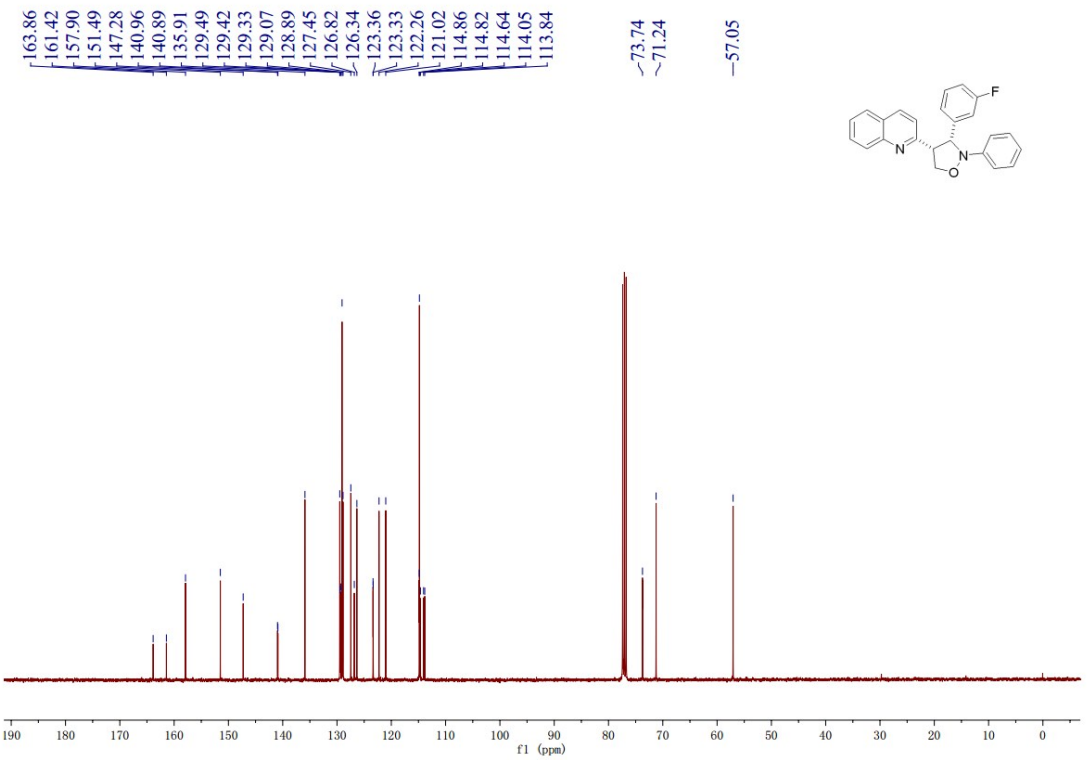
2-Phenyl-4-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*cis*-3b)



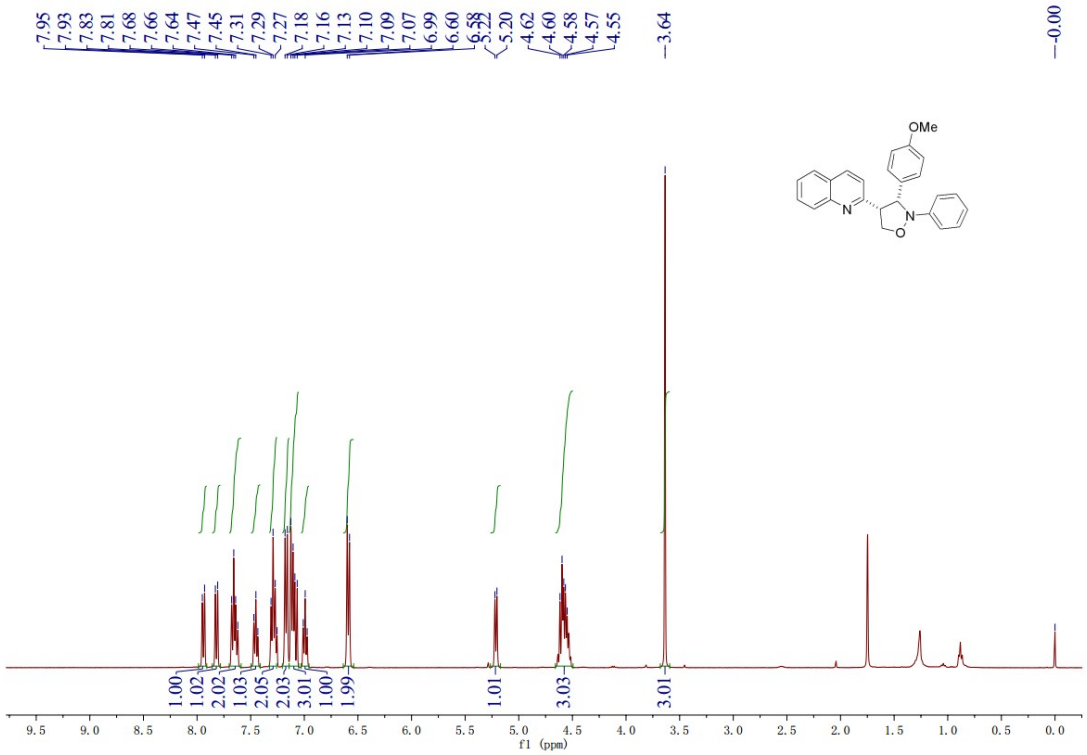


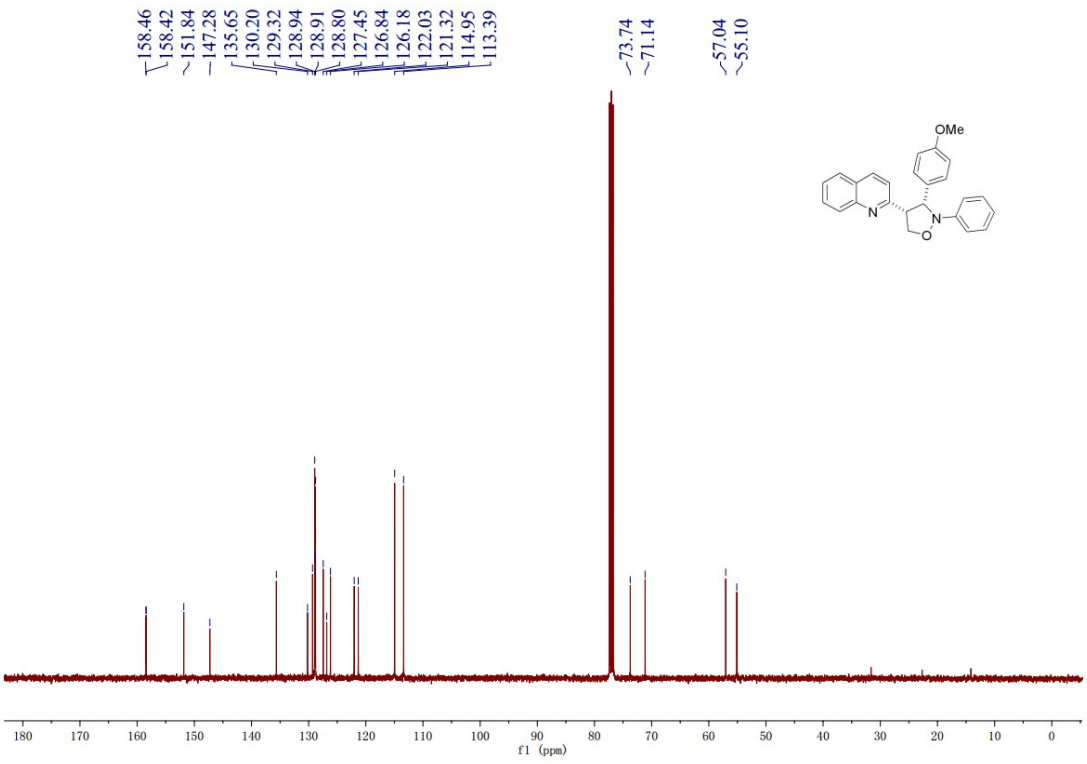
3-(3-Fluorophenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3c)



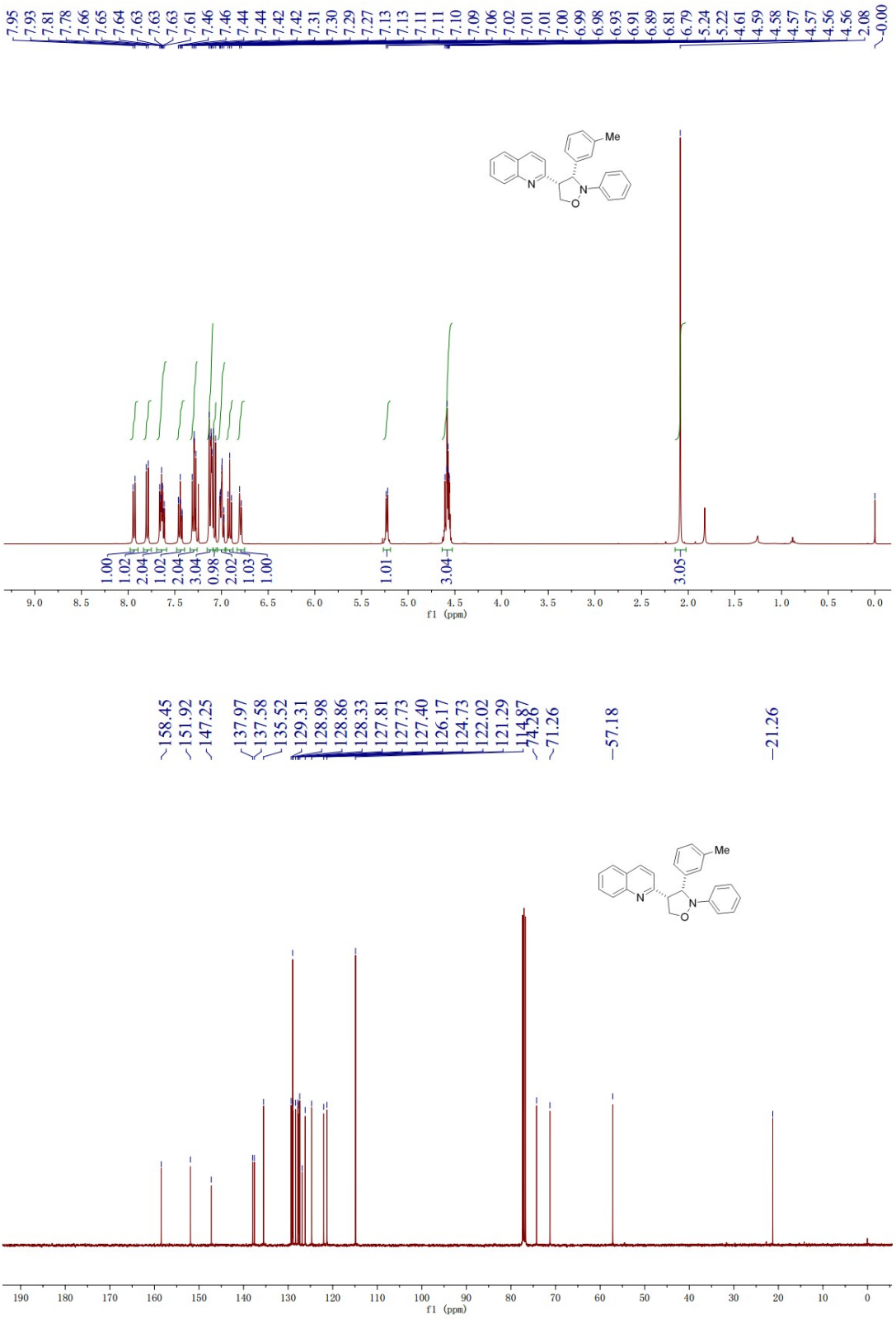


3-(4-Methoxyphenyl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3d)

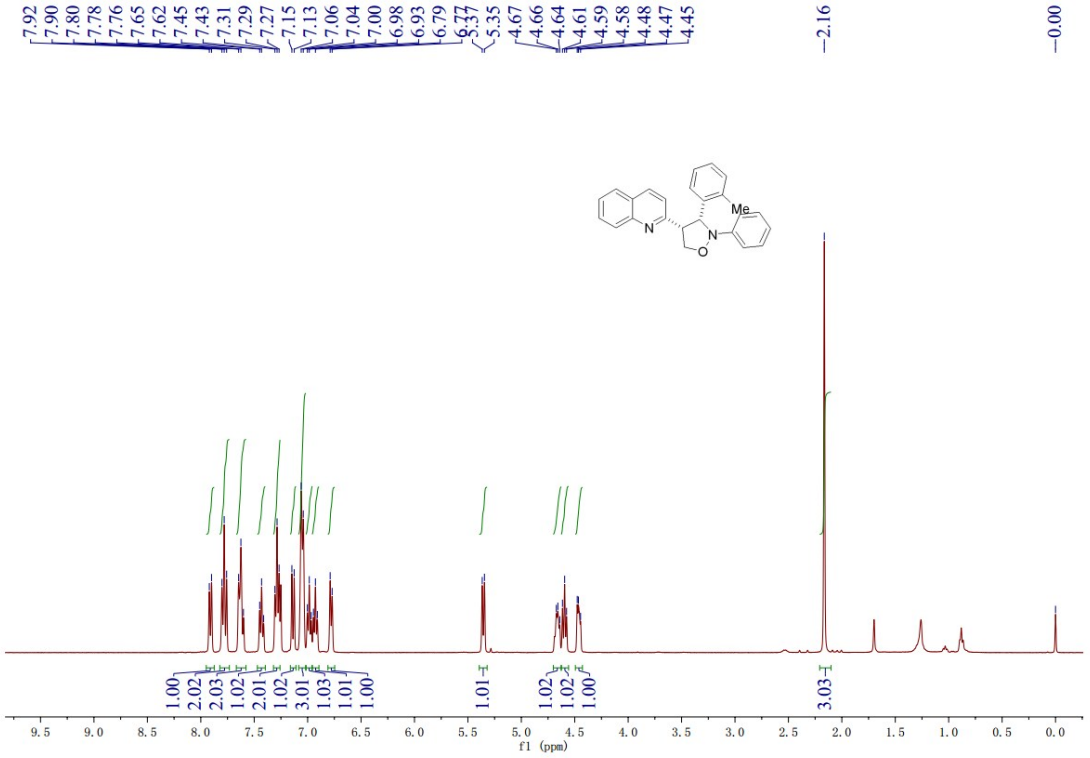


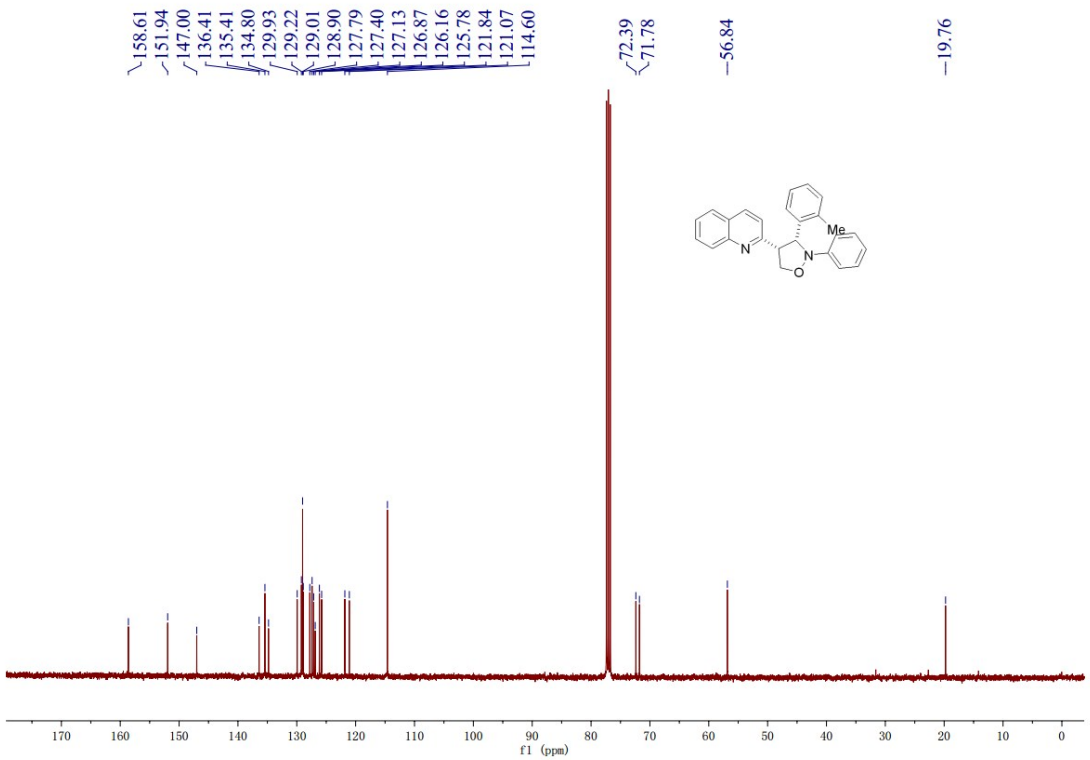


2-Phenyl-4-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*cis*-3e)

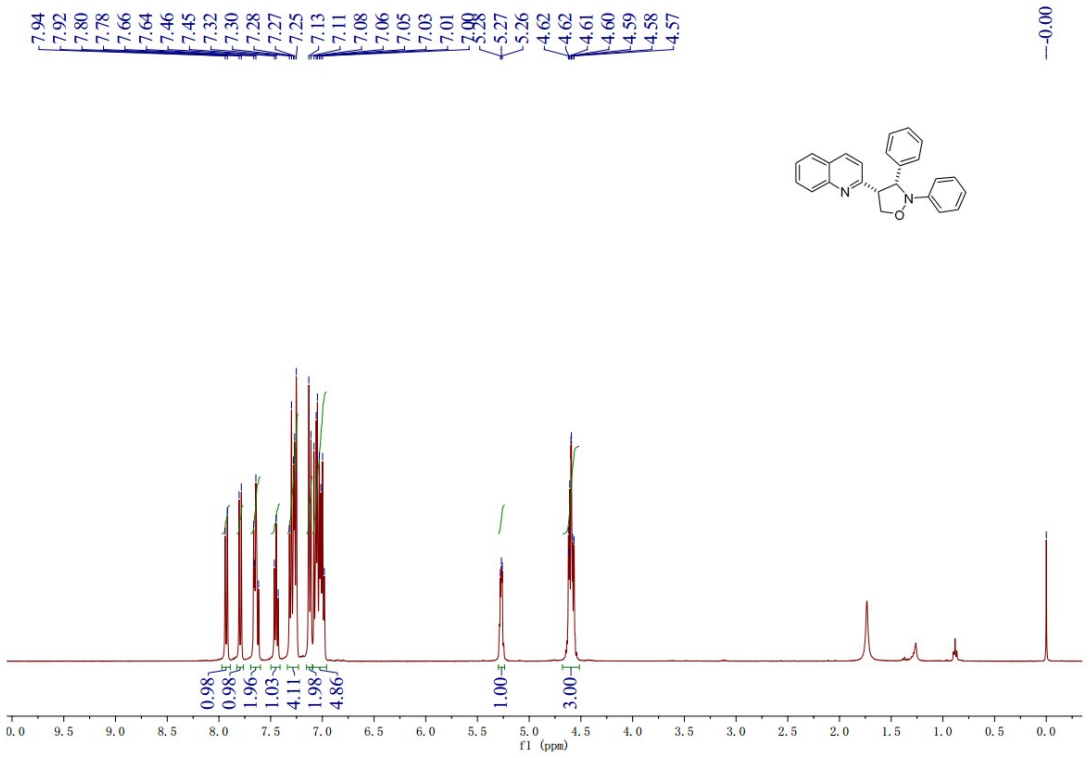


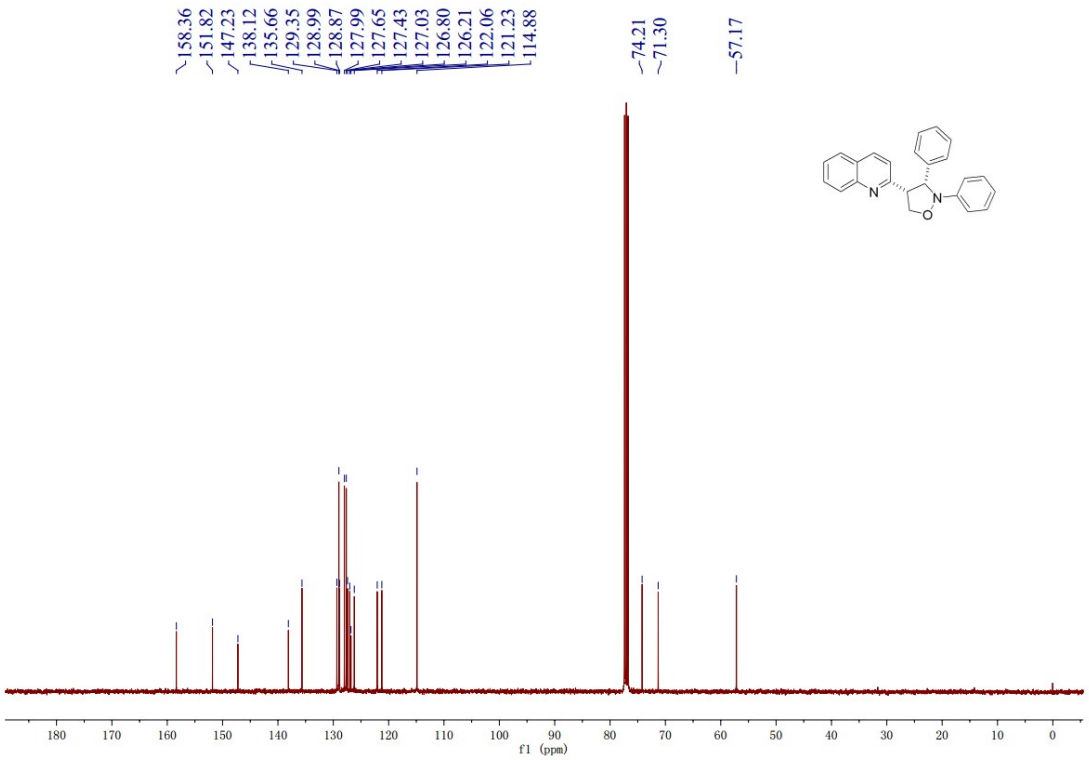
2-Phenyl-4-(quinolin-2-yl)-3-(o-tolyl)isoxazolidine (*cis*-3f)



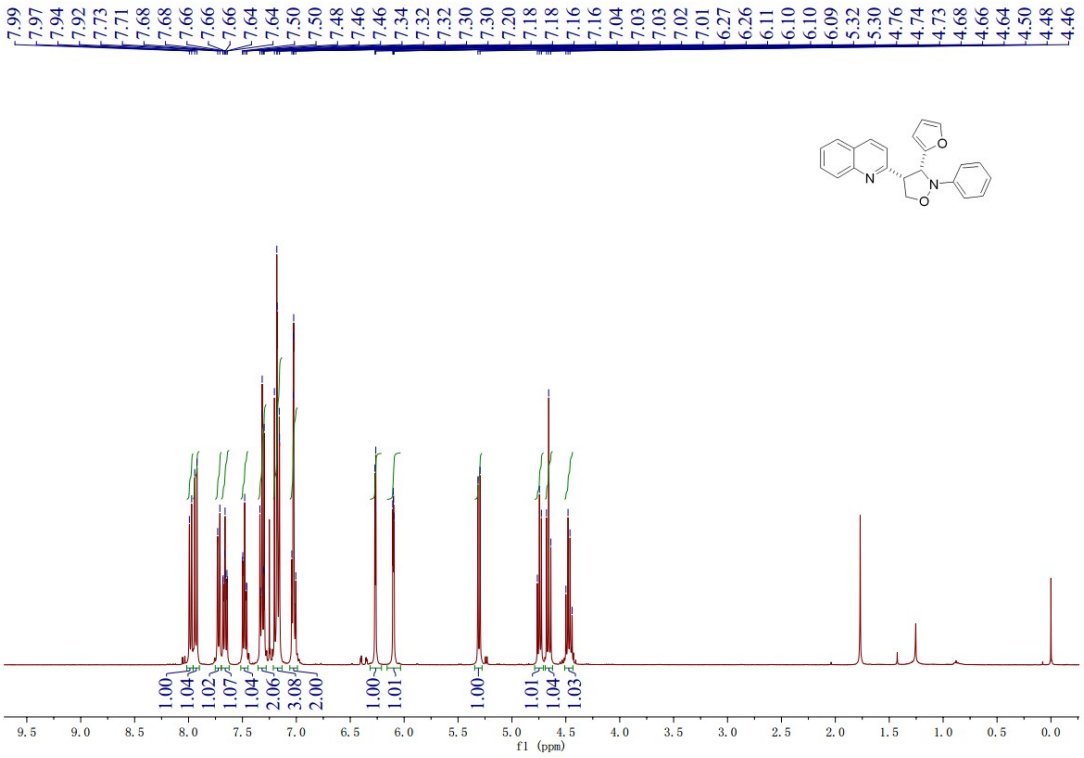


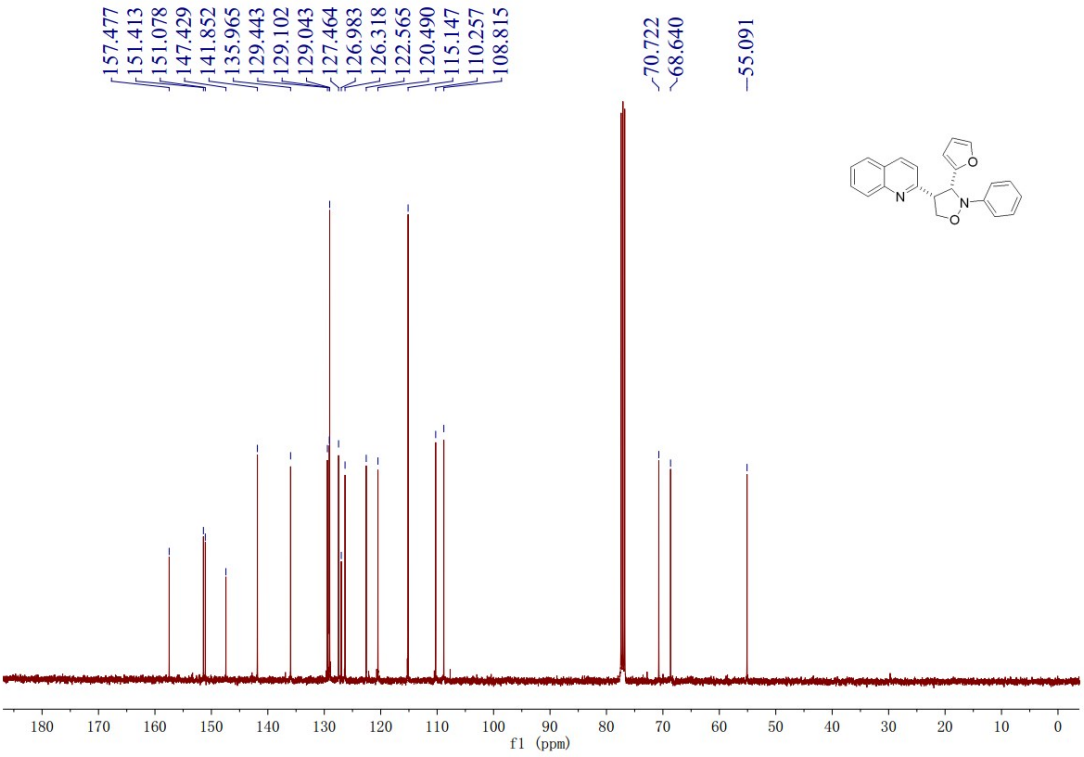
2,3-Diphenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3g)



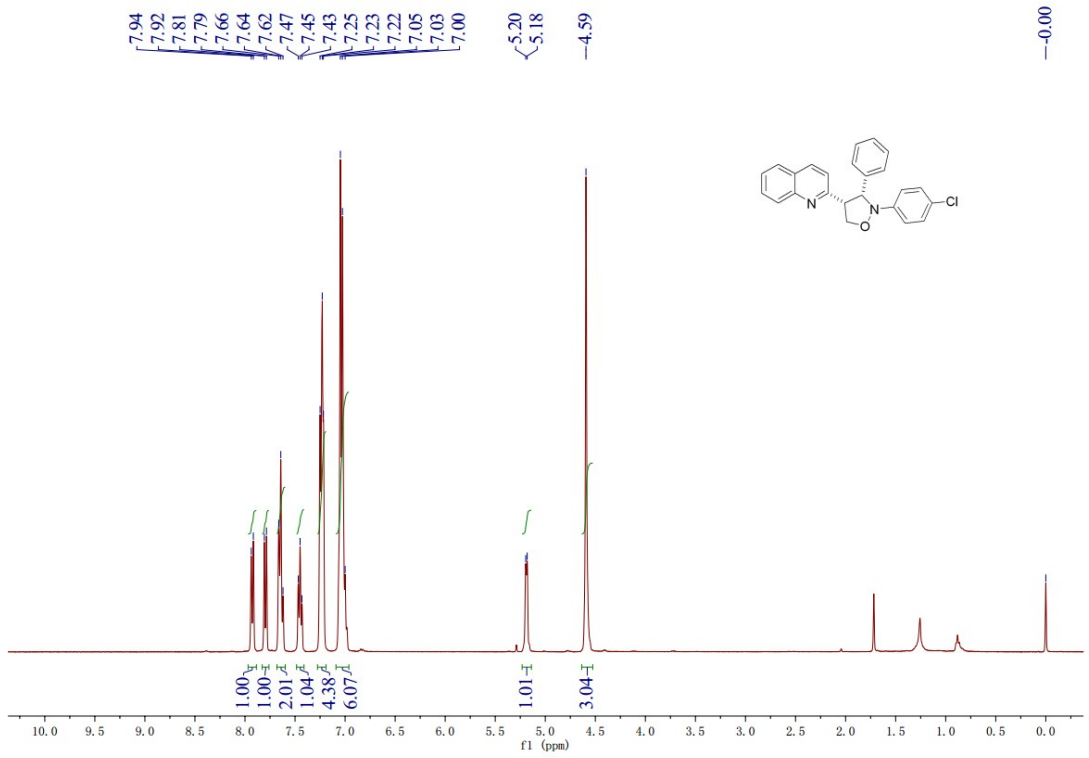


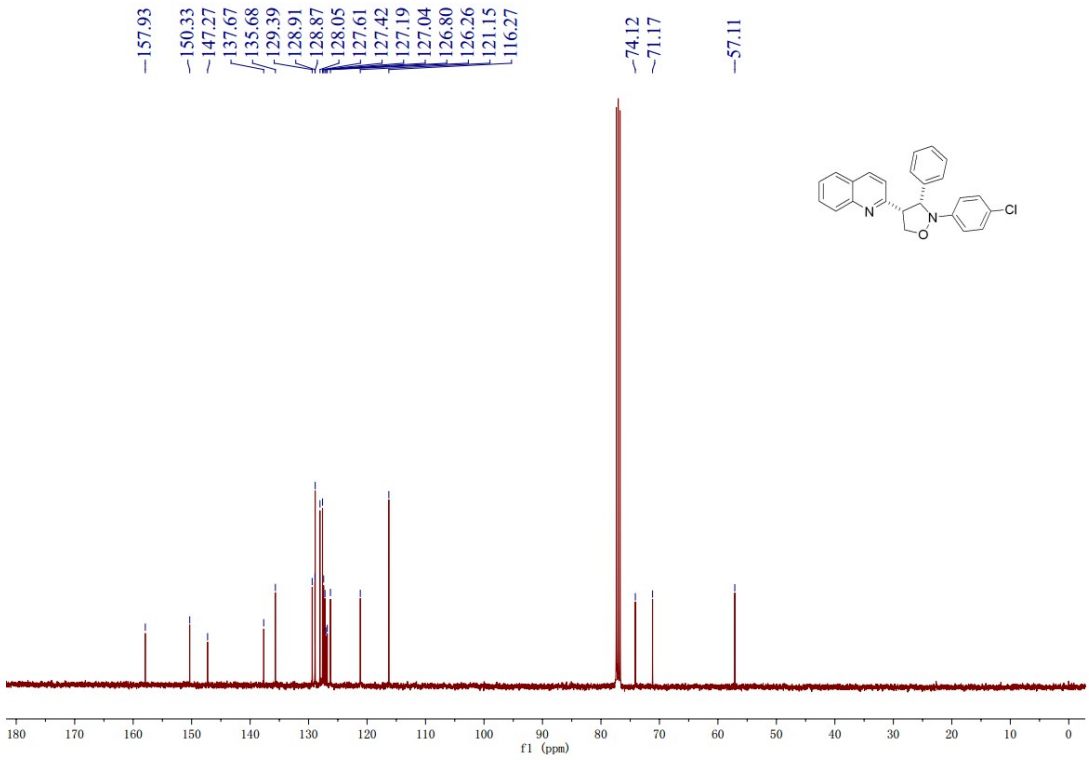
3-(Furan-2-yl)-2-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3h)



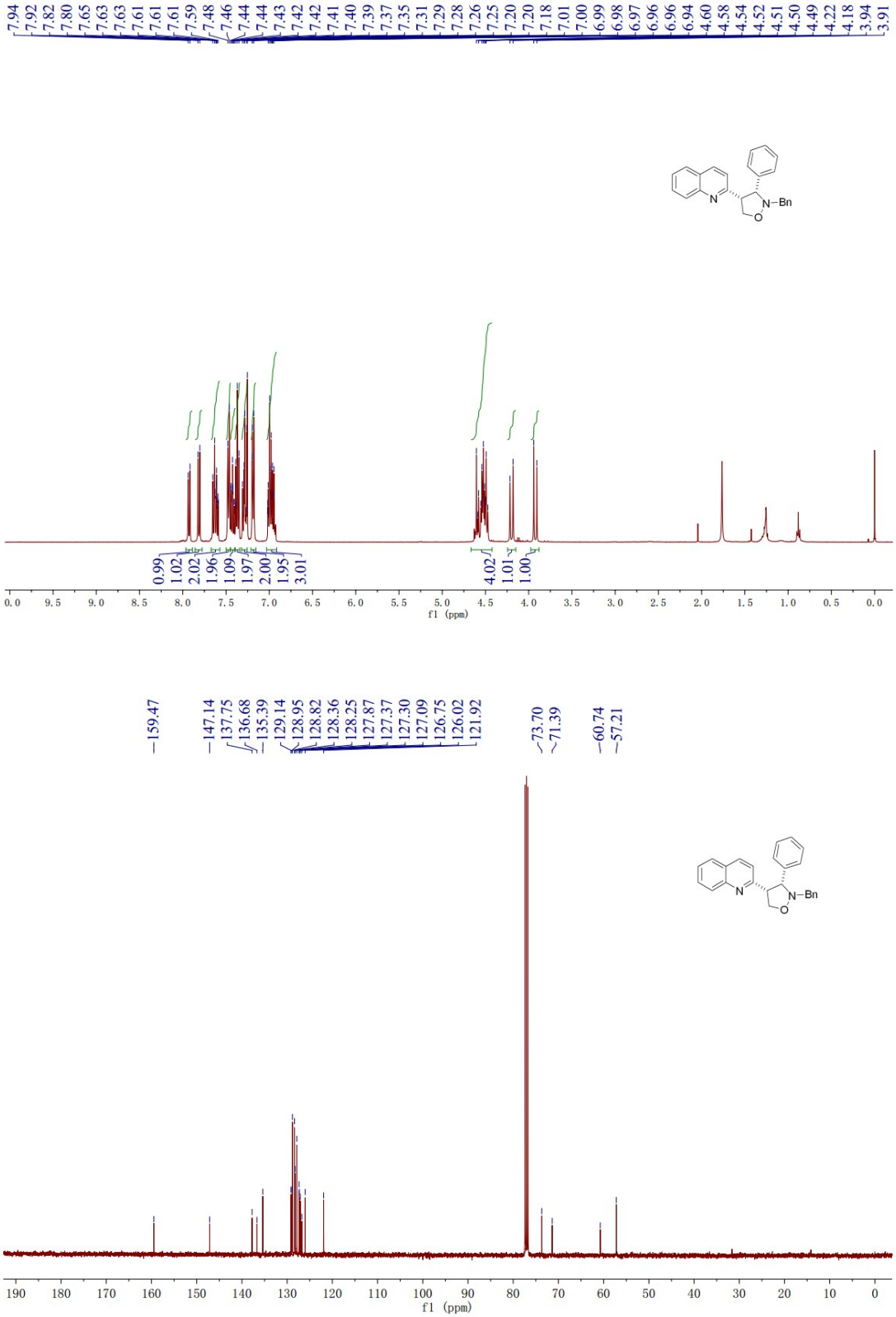


2-(4-Chlorophenyl)-3-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3i)

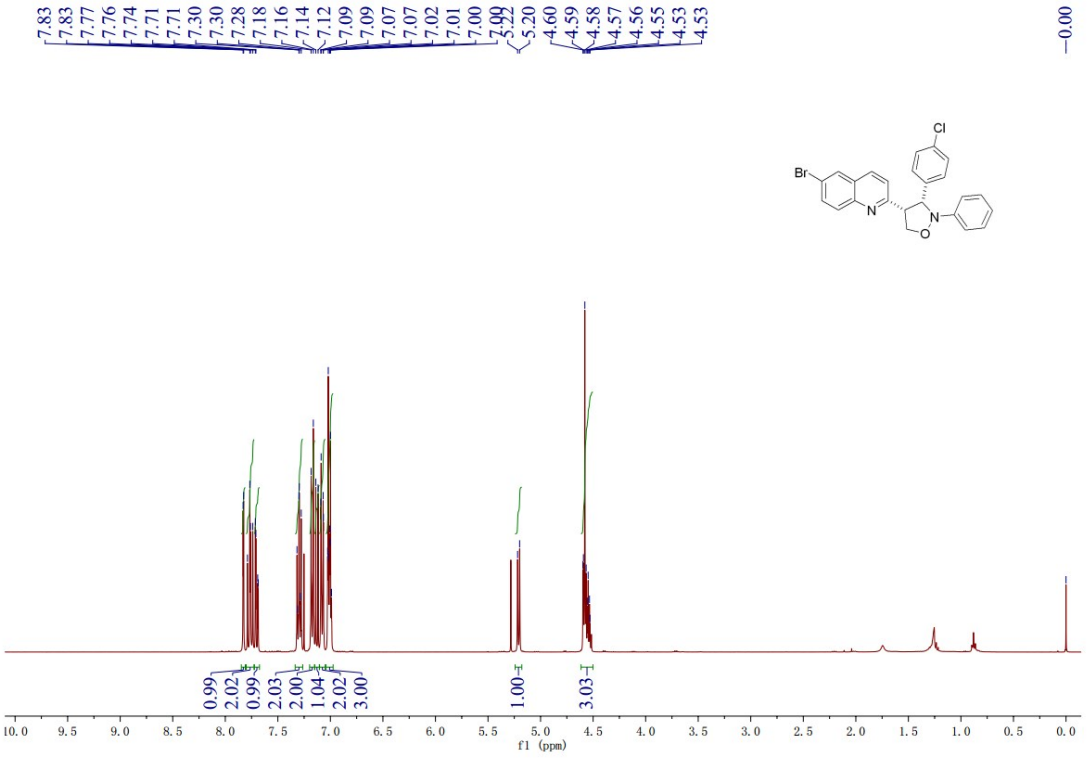


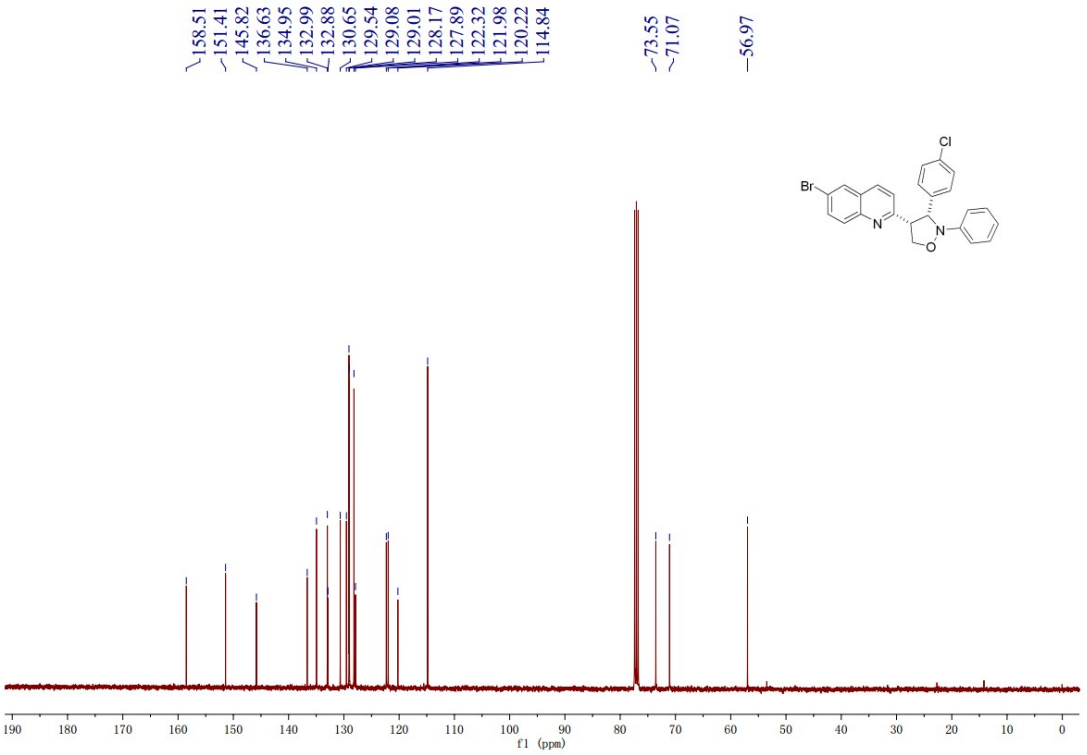


2-Benzyl-3-phenyl-4-(quinolin-2-yl)isoxazolidine (*cis*-3j)

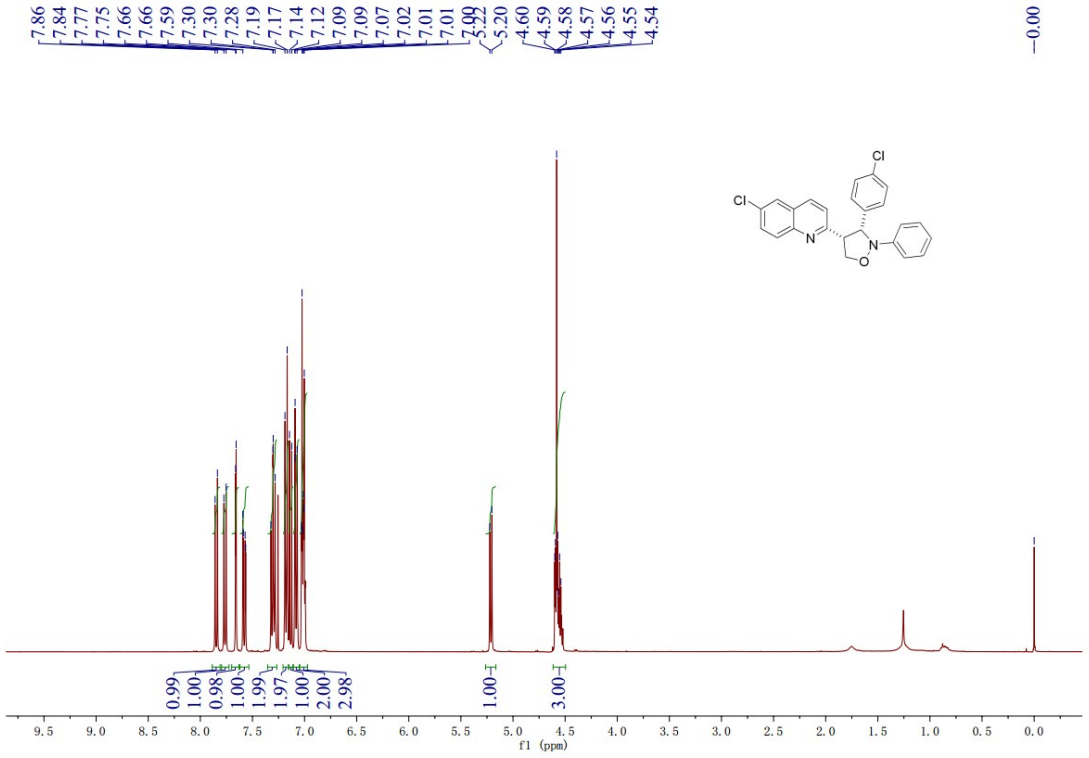


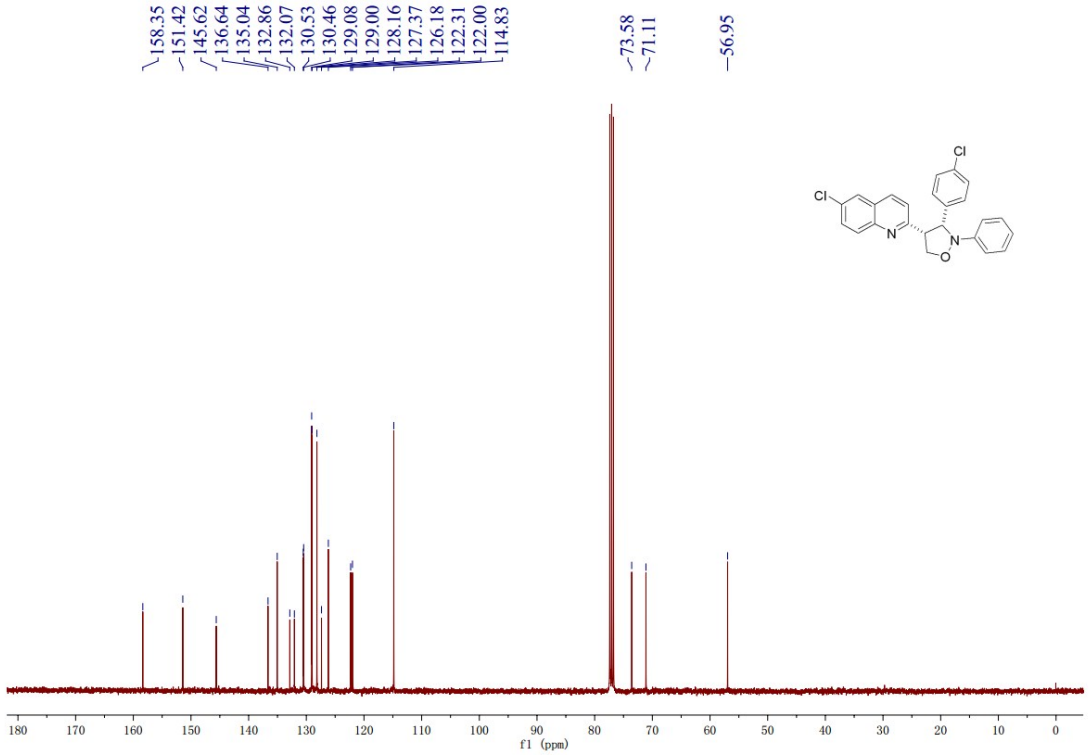
4-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-3k)



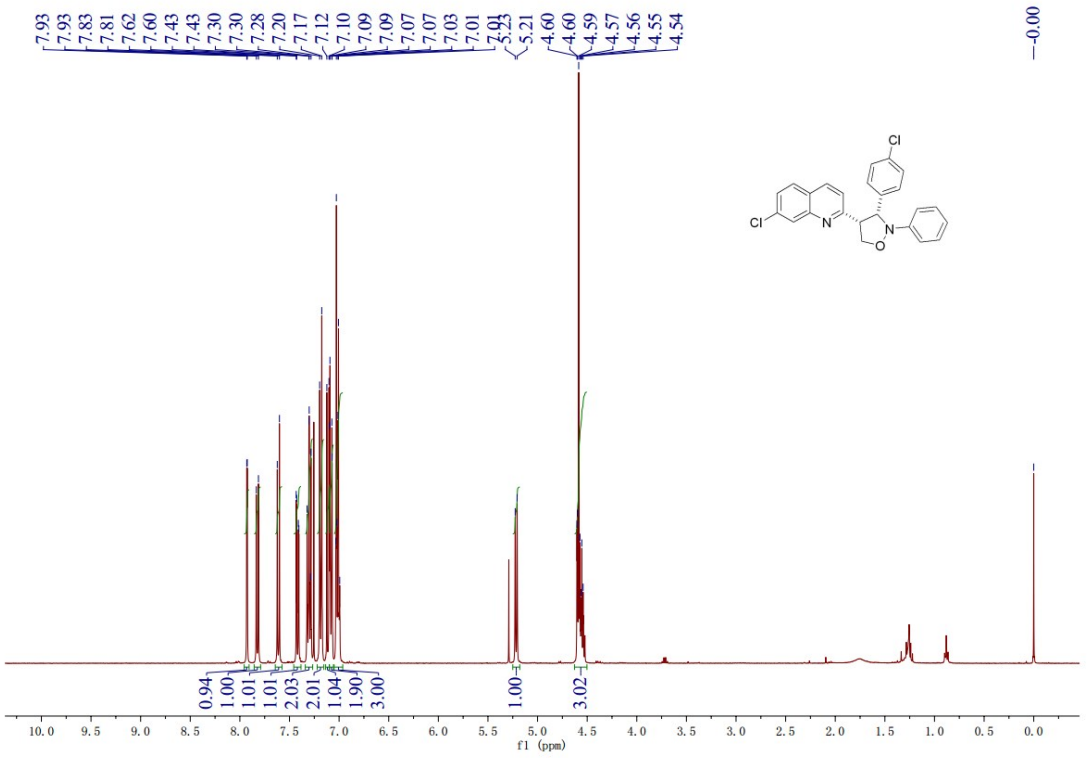


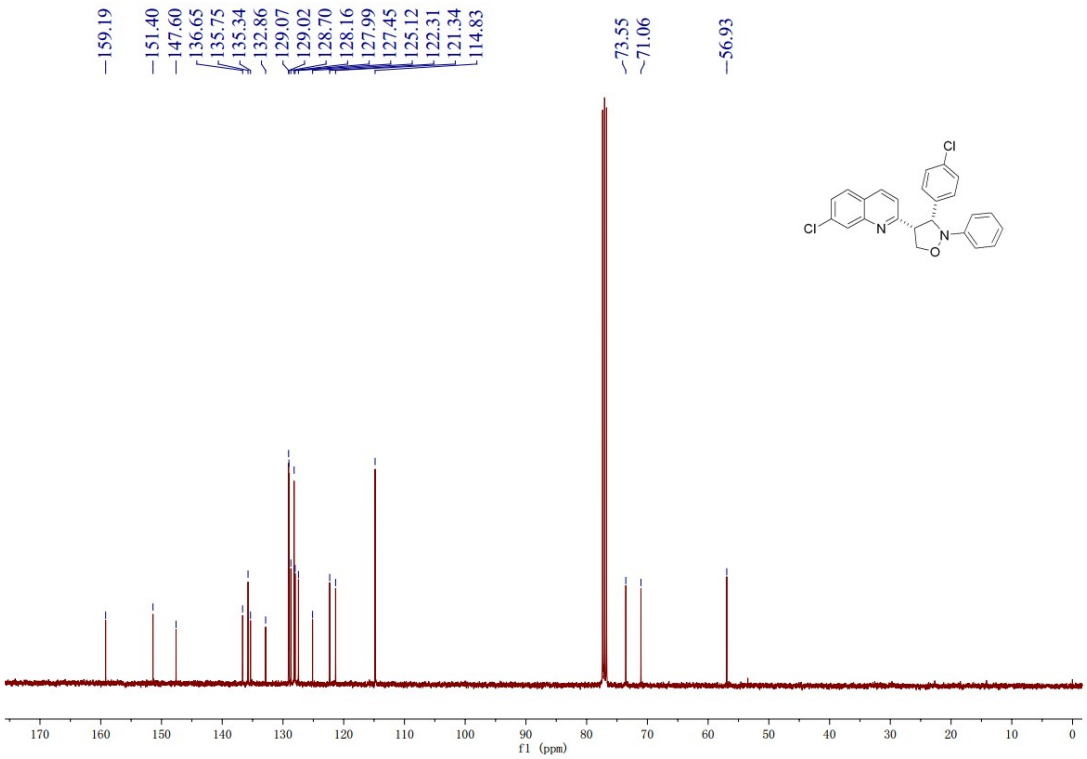
3-(4-Chlorophenyl)-4-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3l)



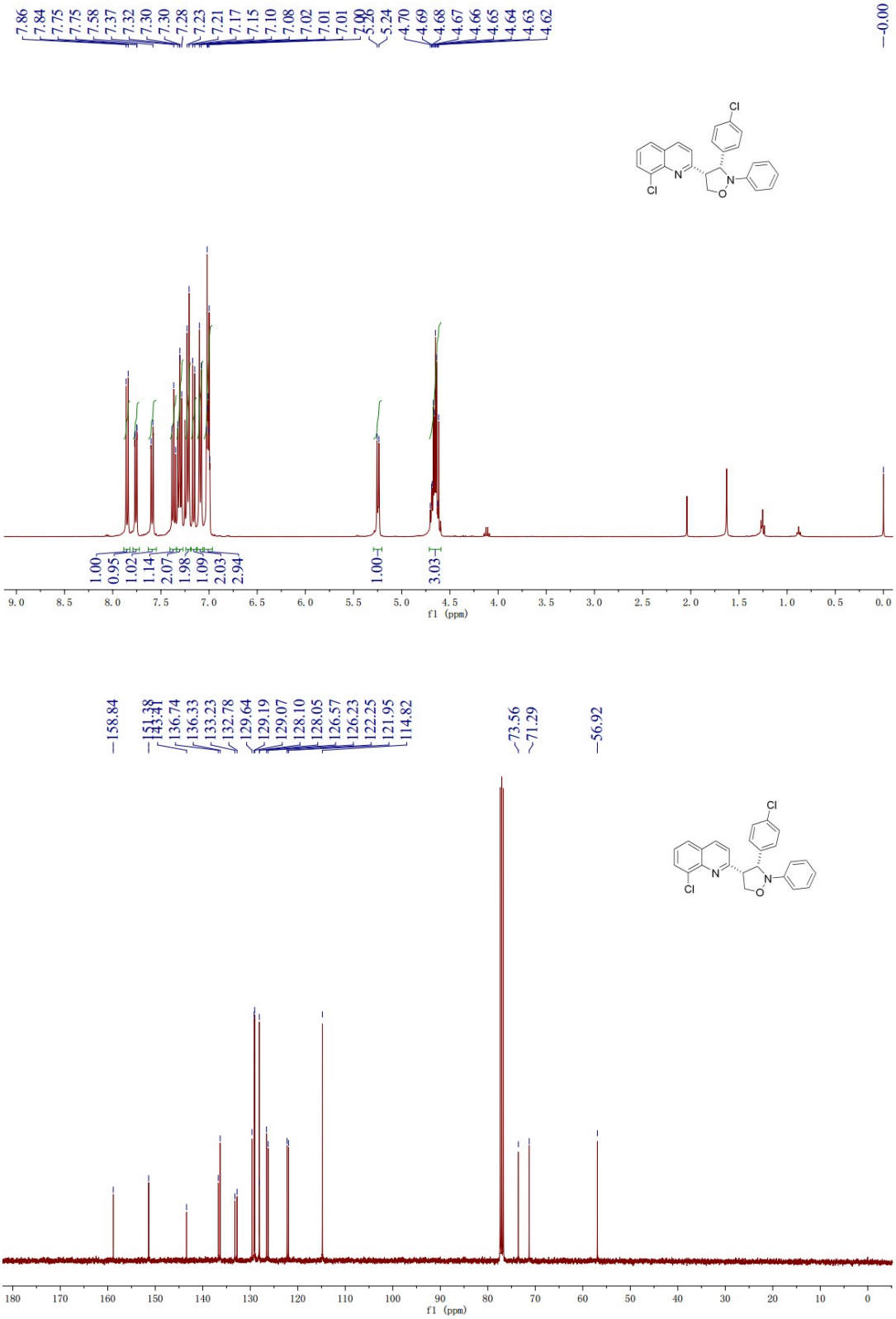


3-(4-Chlorophenyl)-4-(7-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3m)

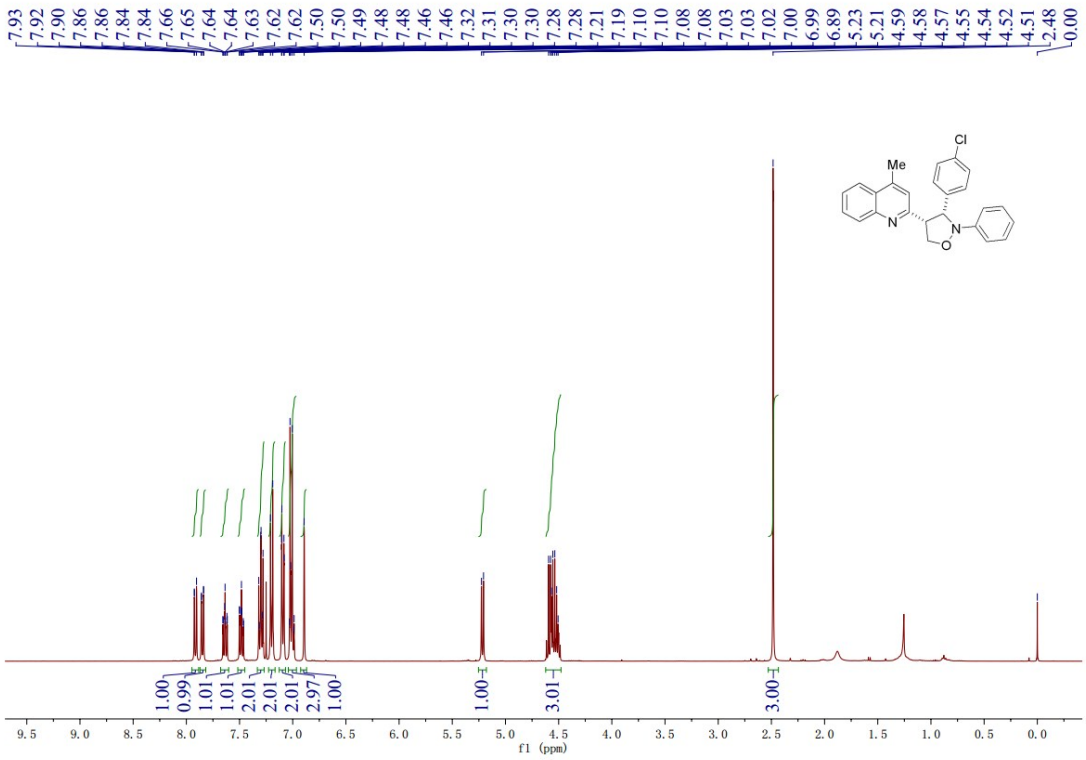


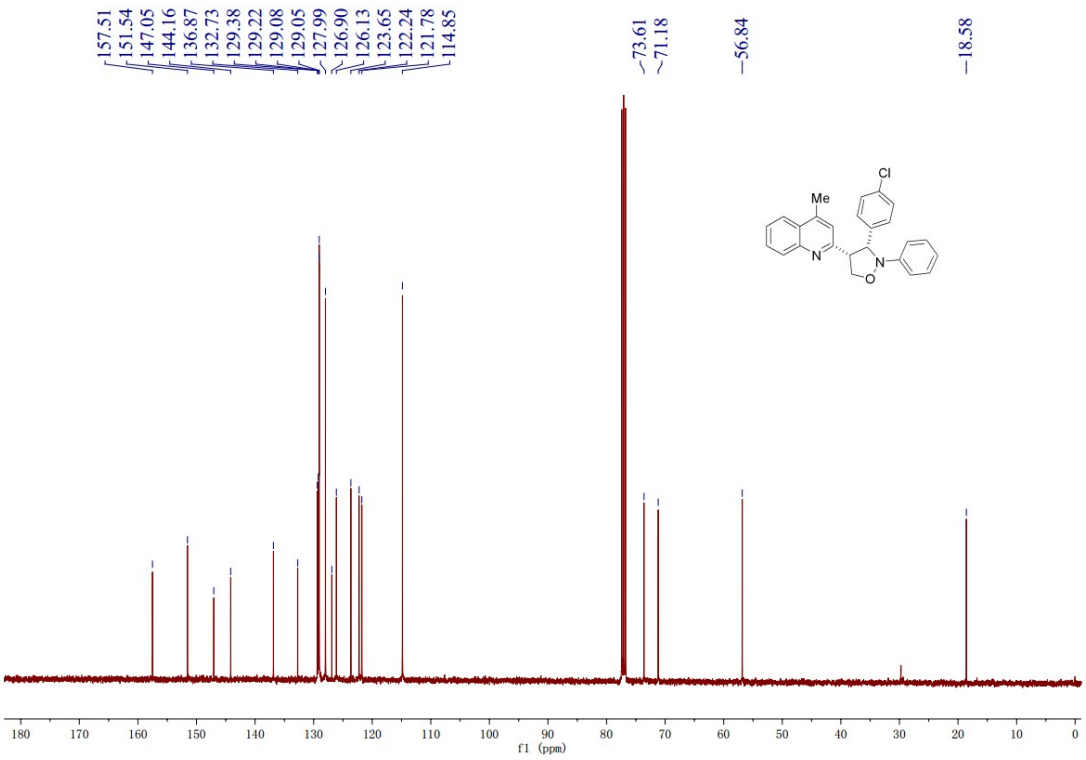


3-(4-Chlorophenyl)-4-(8-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3n)

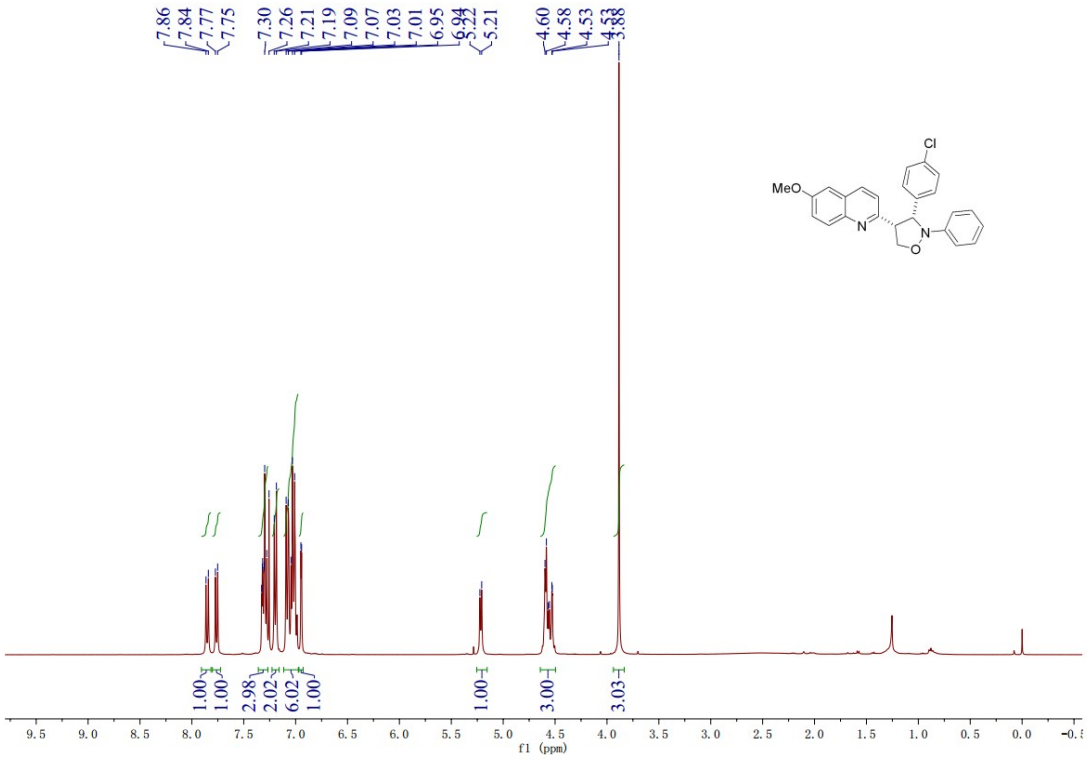


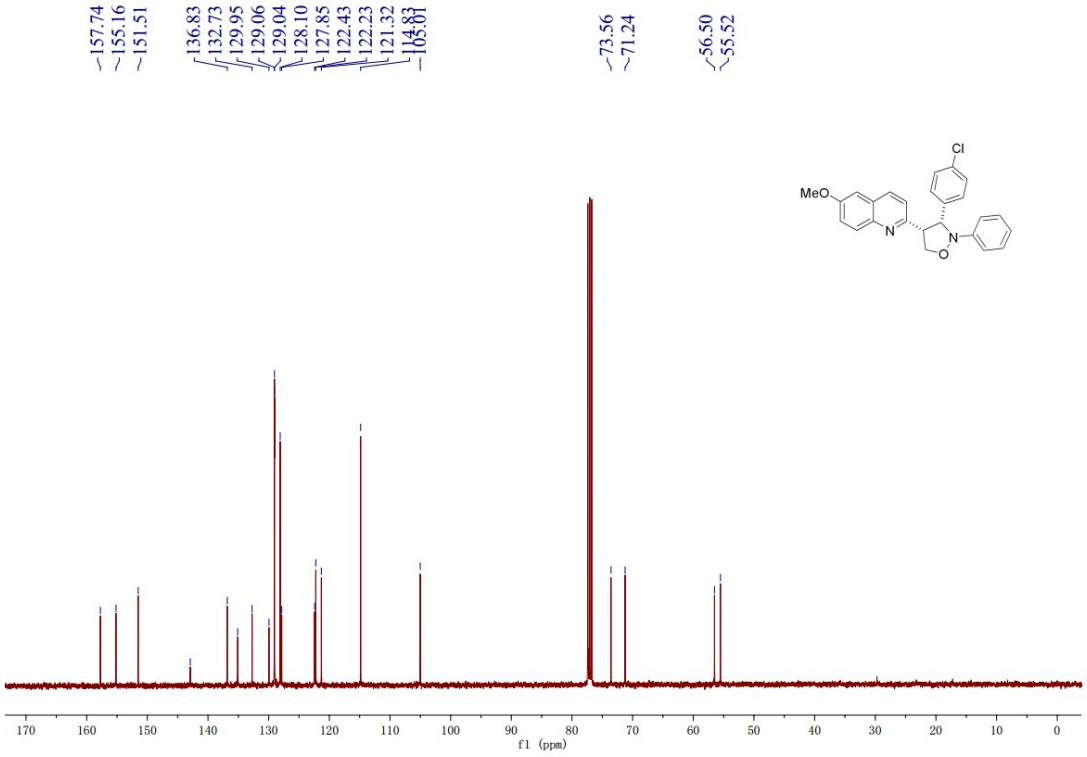
3-(4-Chlorophenyl)-4-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3o)



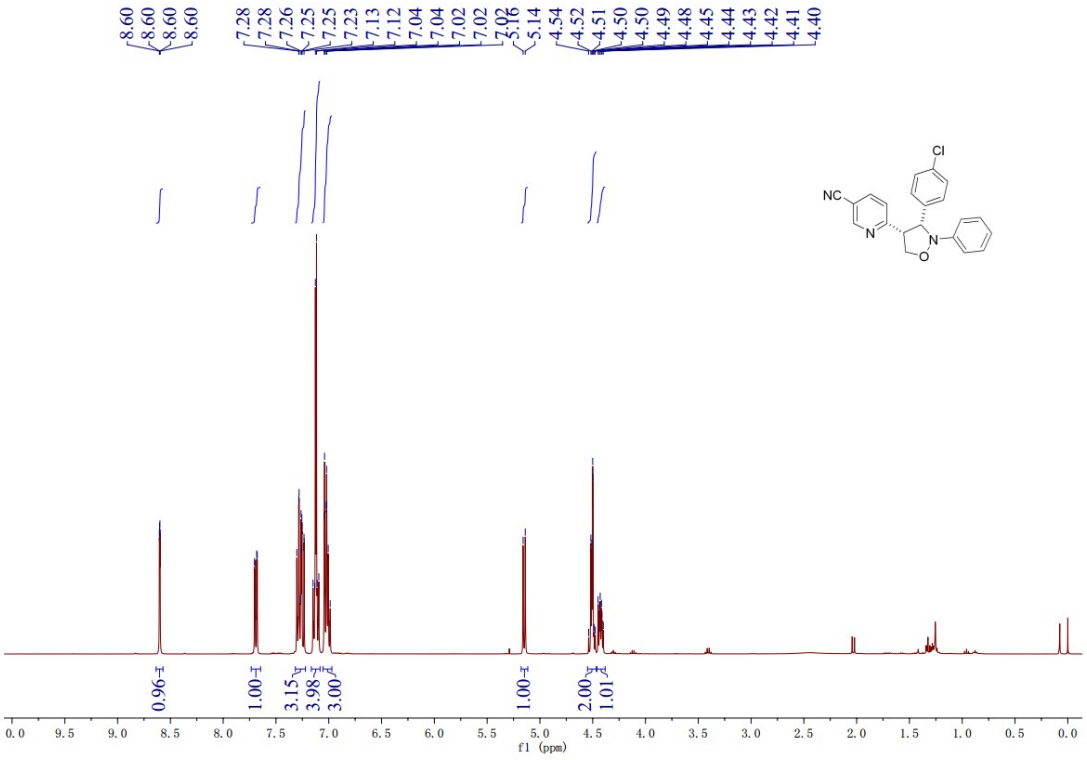


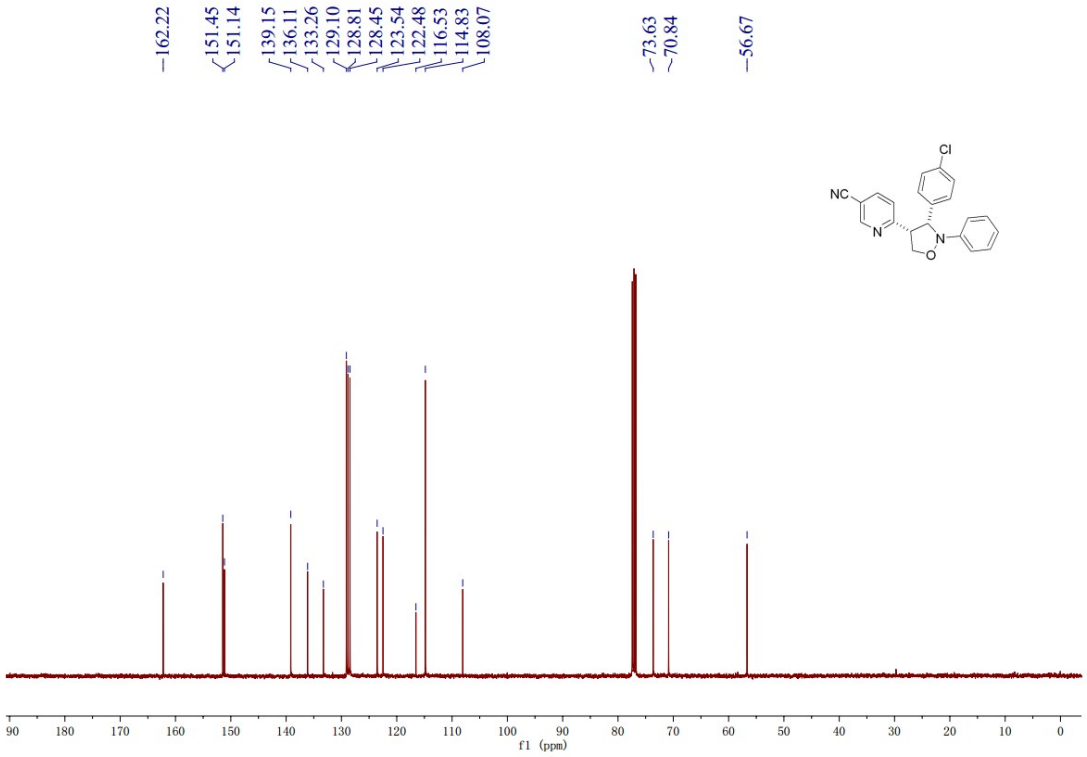
3-(4-Chlorophenyl)-4-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*cis*-3p)



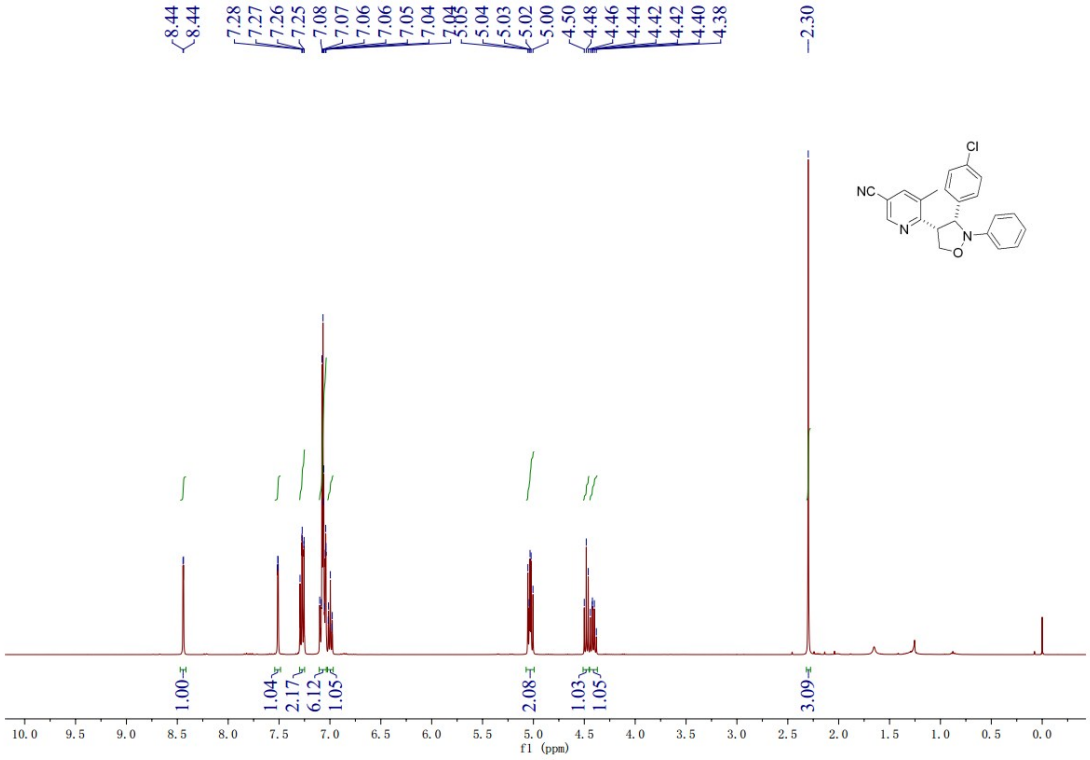


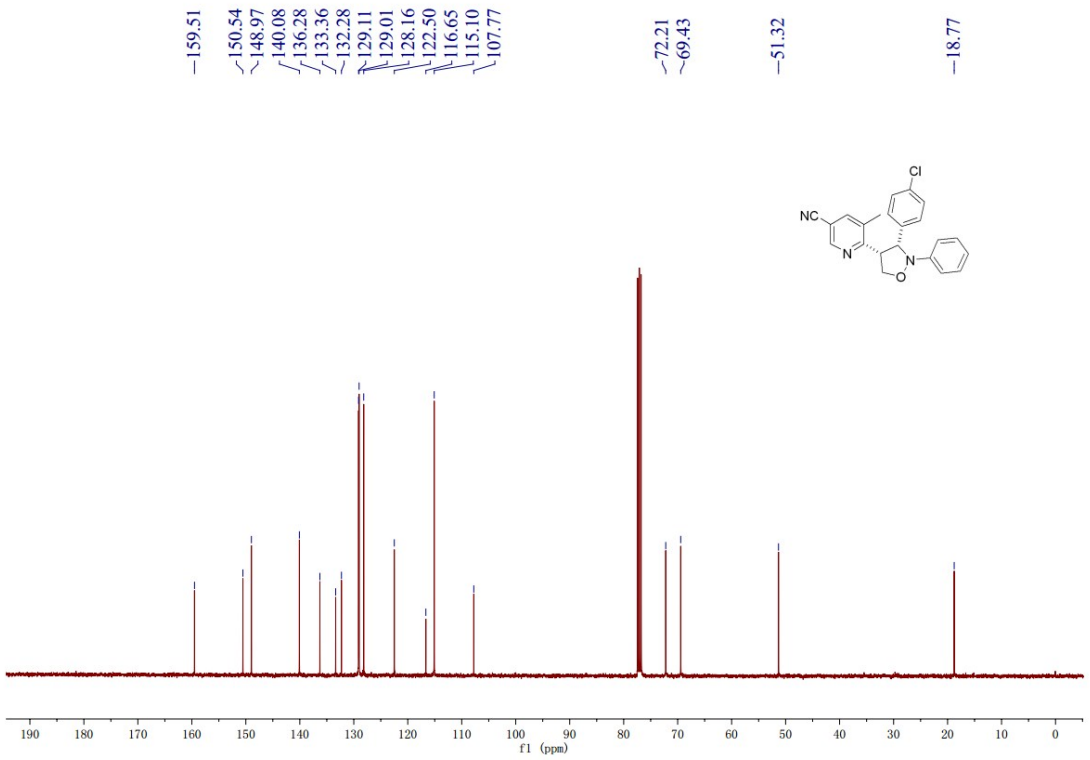
6-(3-(4-Chlorophenyl)-2-phenylisoxazolidin-4-yl)nicotinonitrile (*cis*-3q)



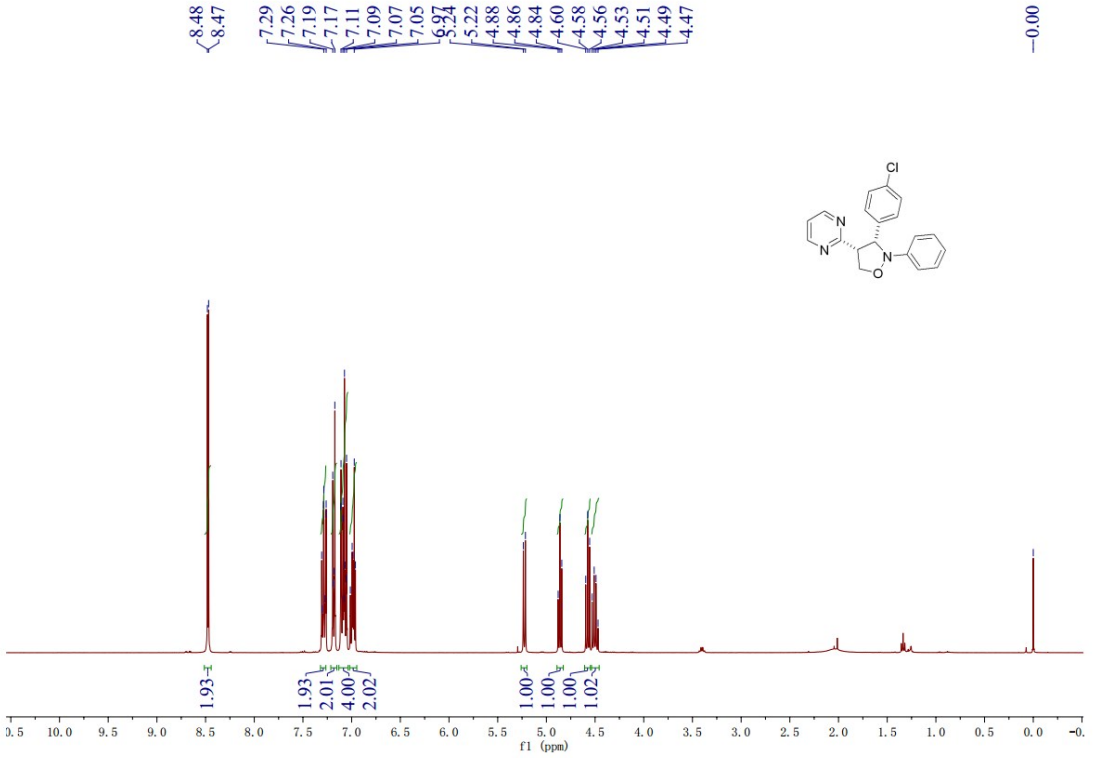


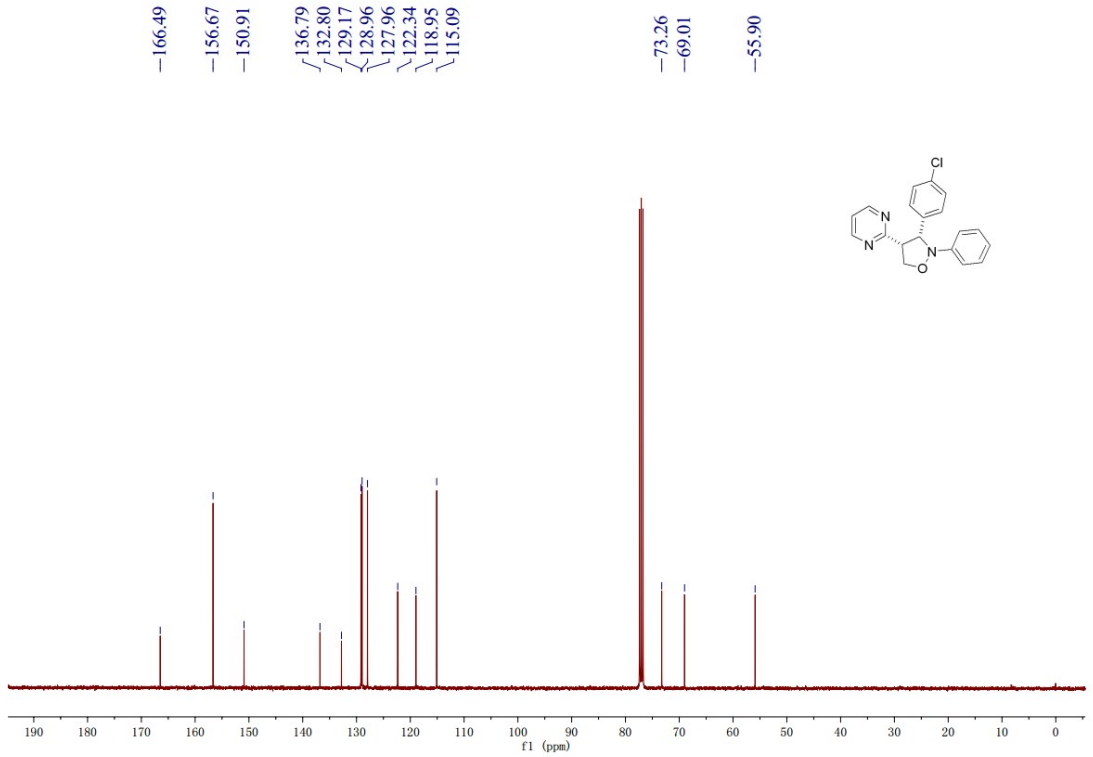
6-(3-(4-Chlorophenyl)-2-phenylisoxazolidin-4-yl)-5-methylnicotinonitrile (*cis*-3r)



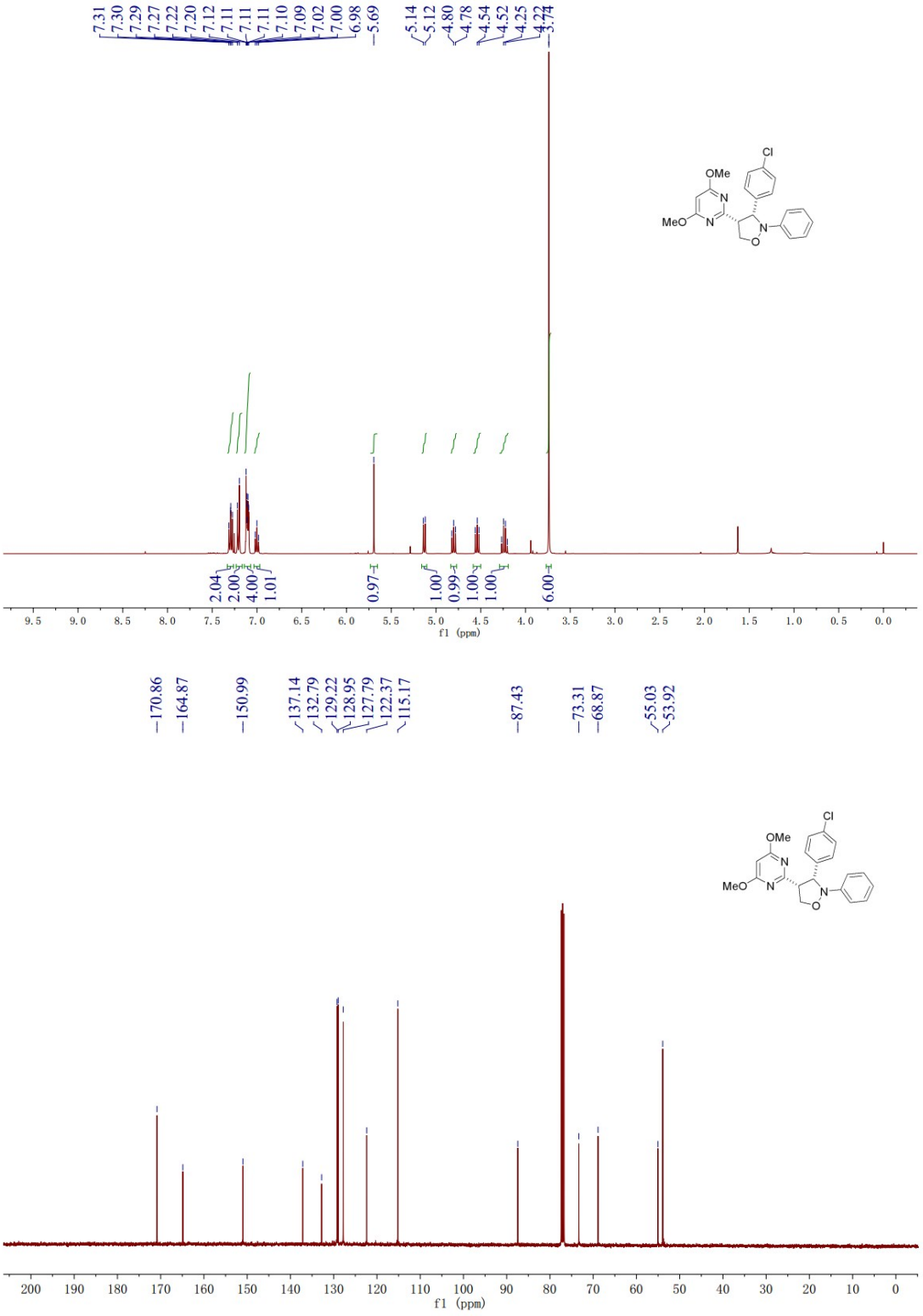


3-(4-Chlorophenyl)-2-phenyl-4-(pyrimidin-2-yl)isoxazolidine (*cis*-3s)

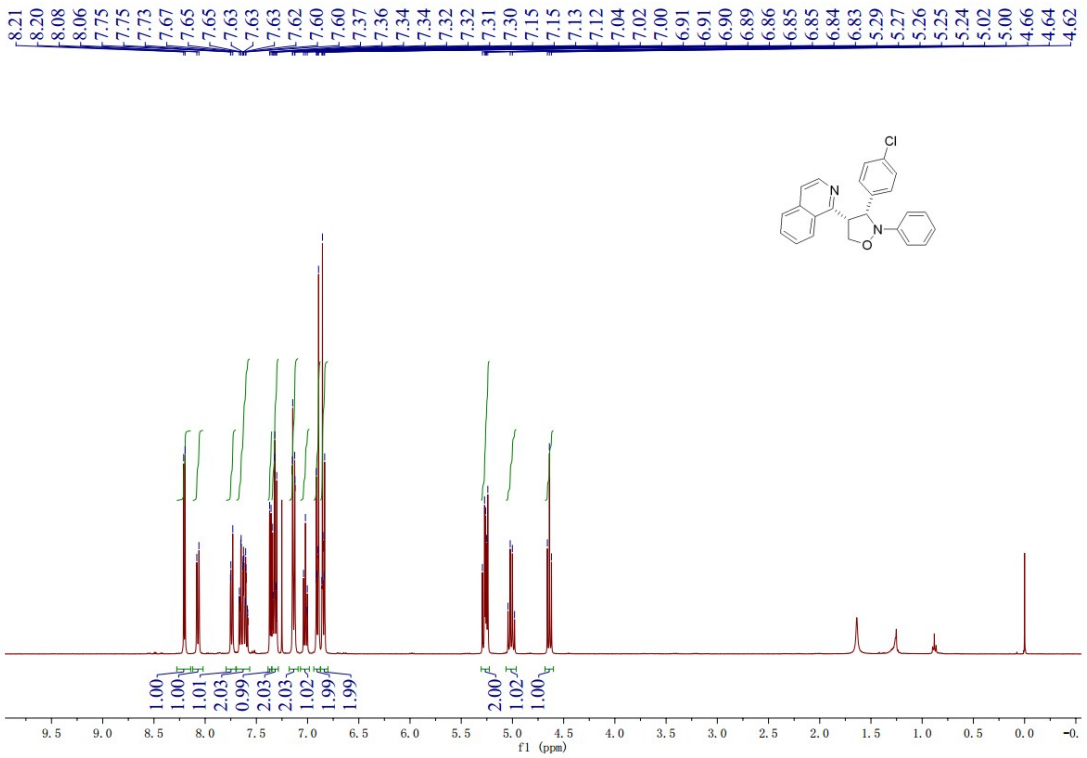


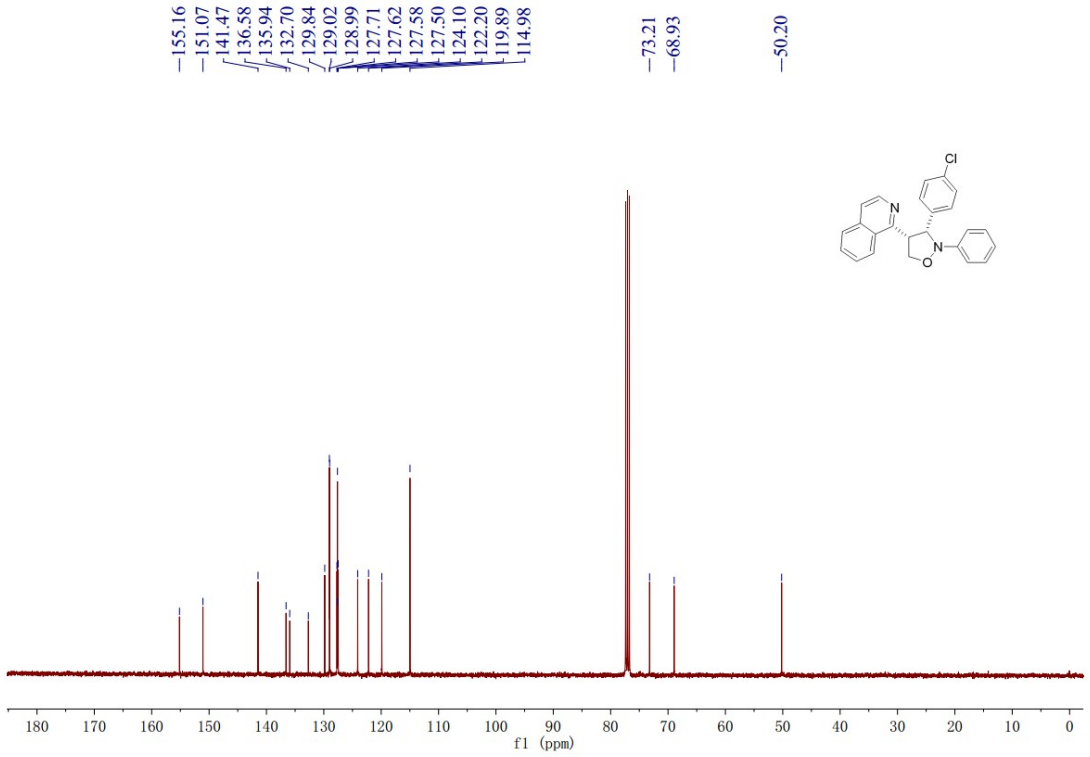


3-(4-Chlorophenyl)-4-(4,6-dimethoxypyrimidin-2-yl)-2-phenylisoxazolidine (*cis*-3t)

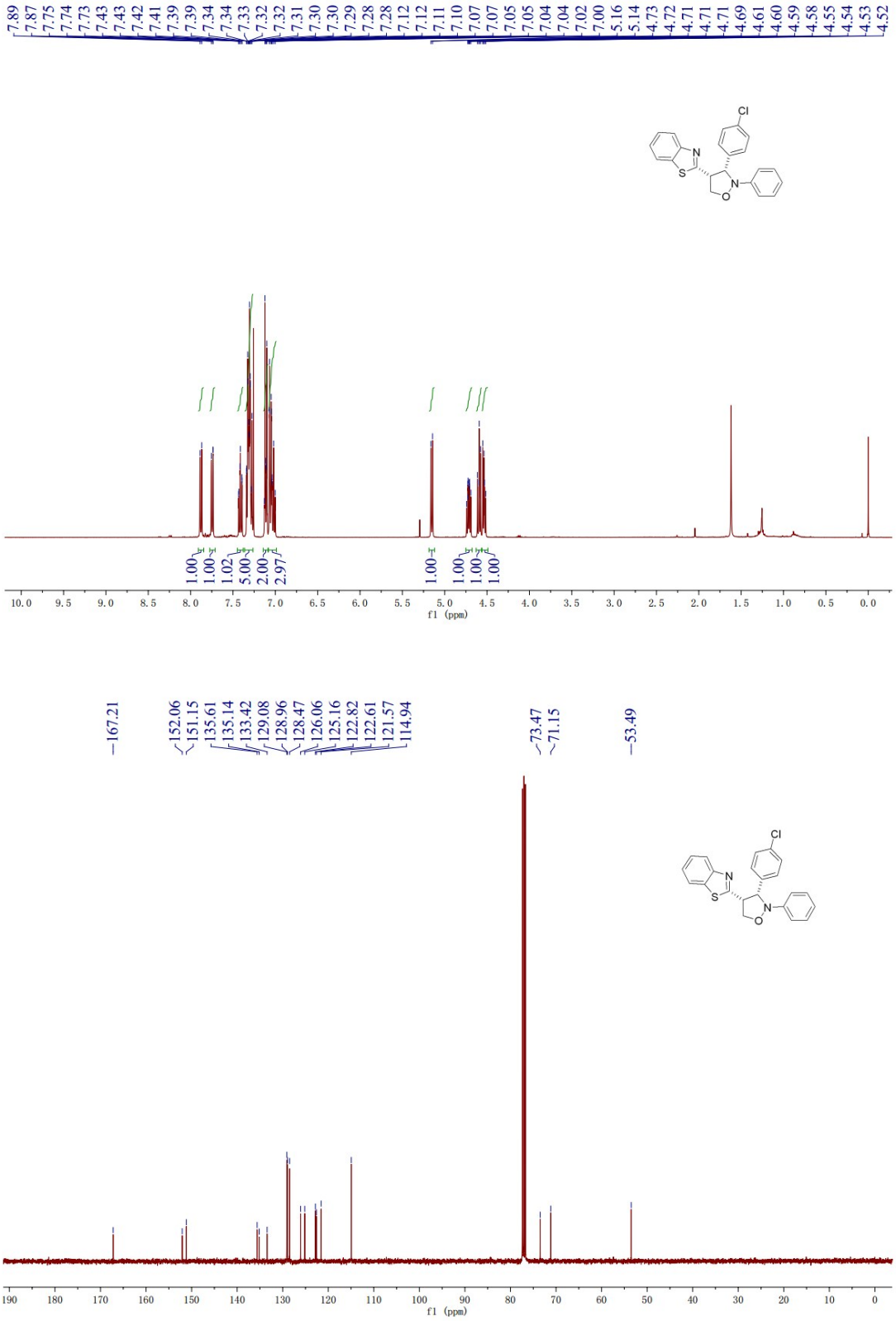


3-(4-Chlorophenyl)-4-(isoquinolin-1-yl)-2-phenylisoxazolidine (*cis*-3u)

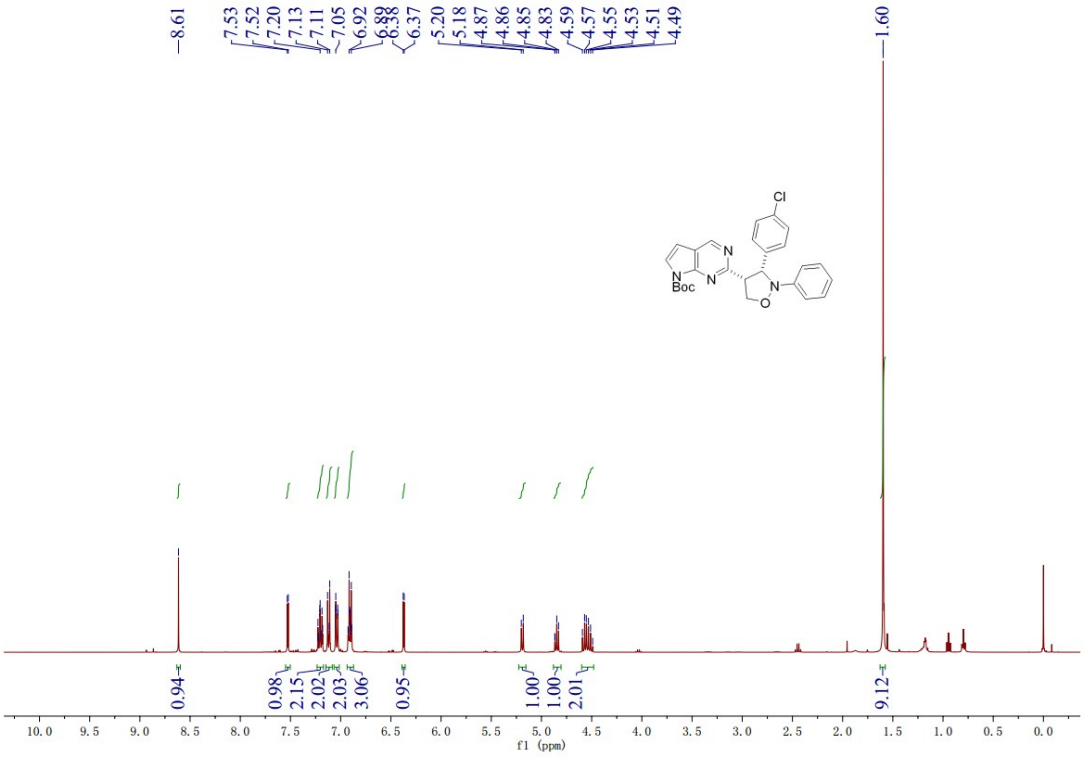


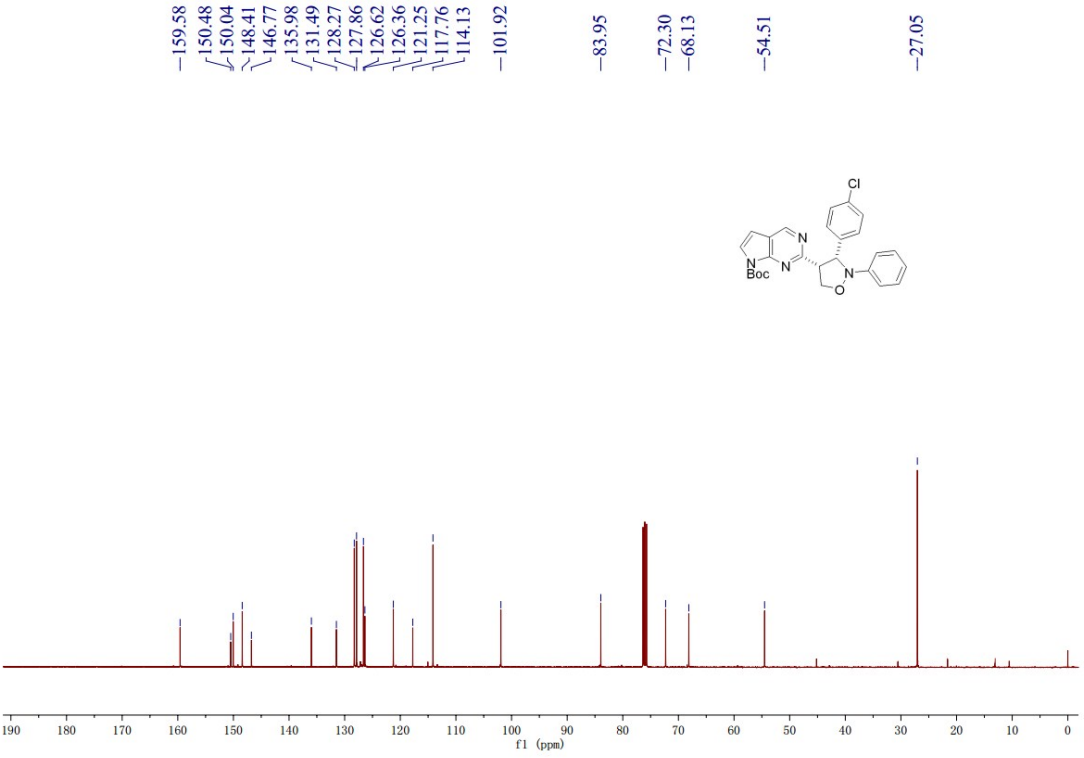


4-(Benzo[*d*]thiazol-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-3v)

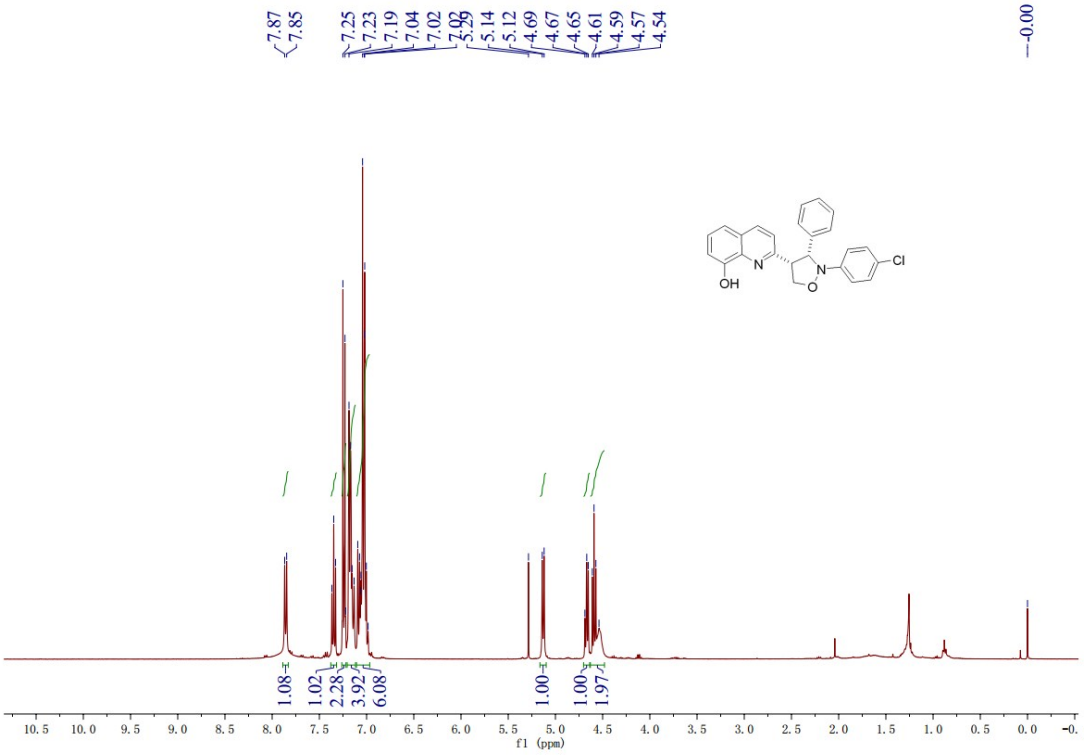


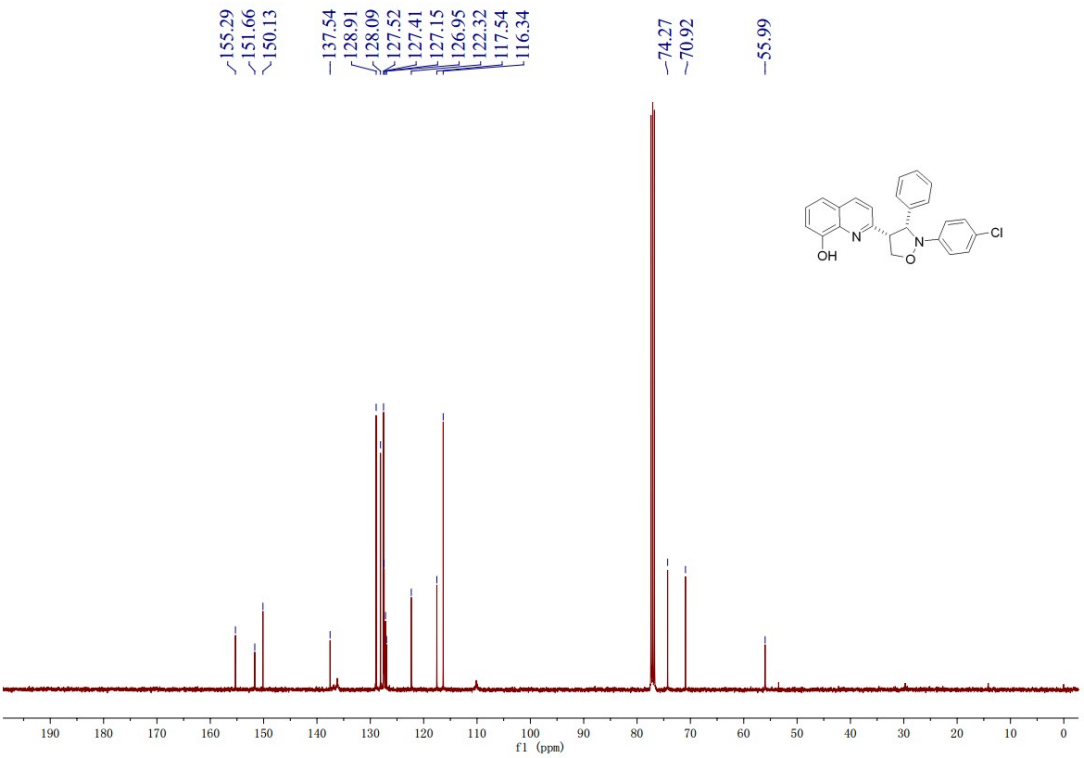
***tert*-Butyl 2-(3-(4-chlorophenyl)-2-phenylisoxazolidin-4-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-7-carboxylate (*cis*-3w)**



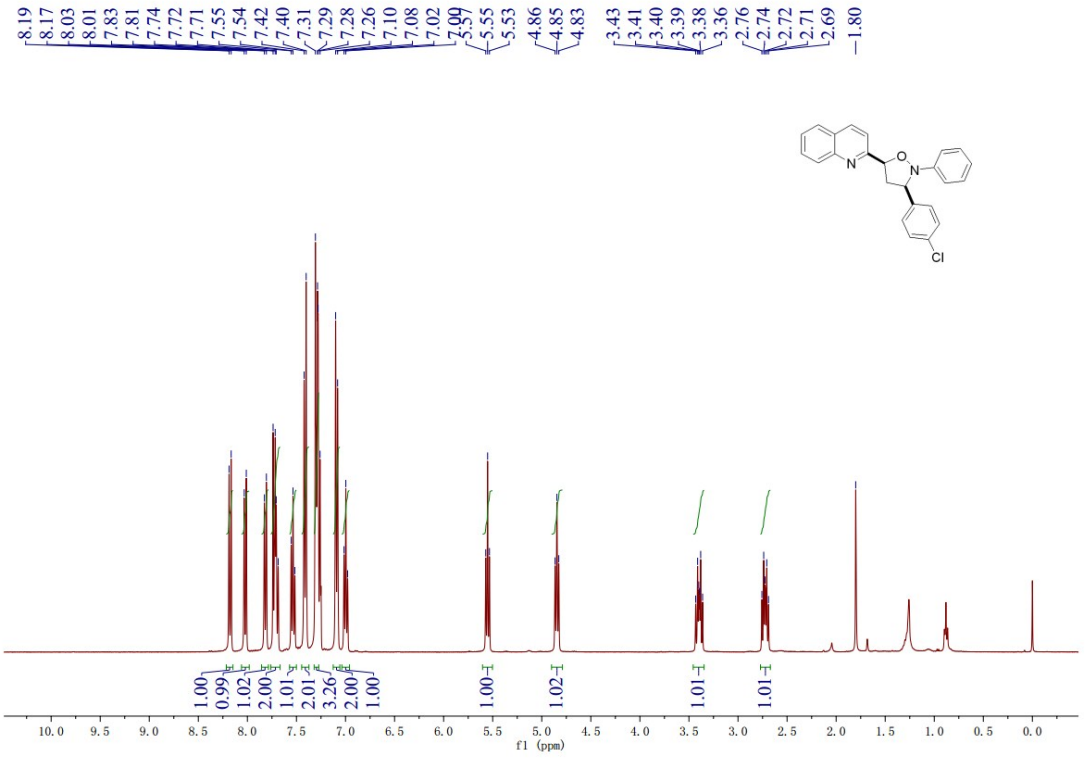


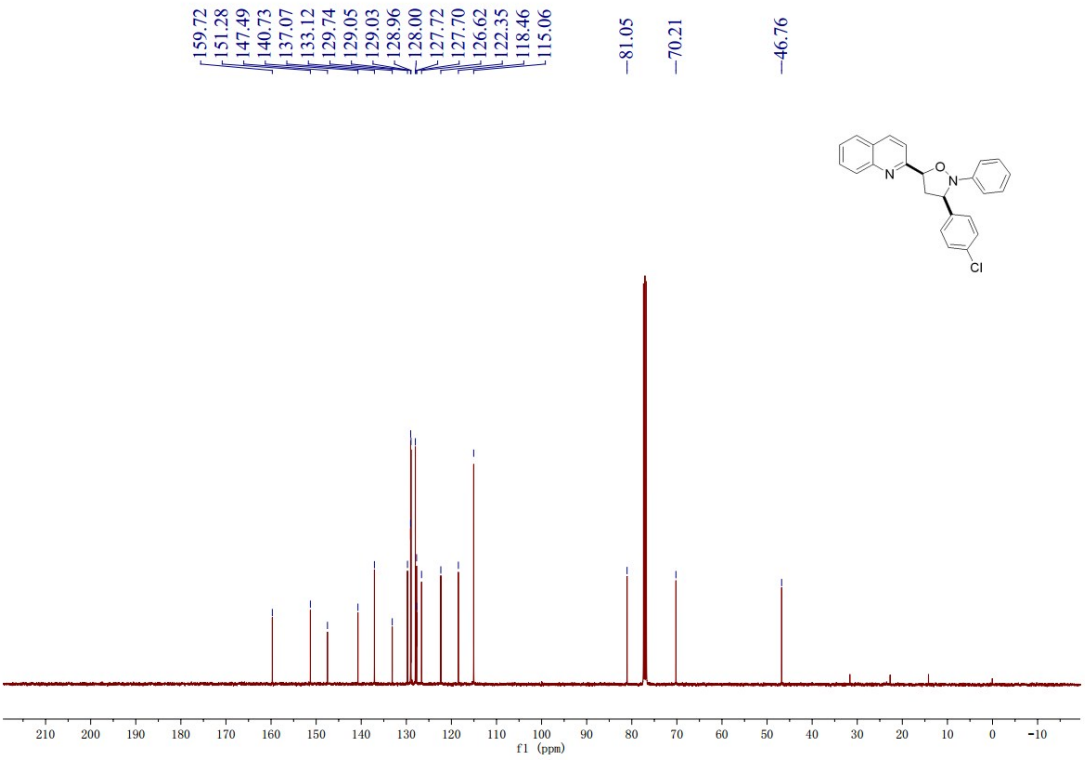
2-(2-(4-Chlorophenyl)-3-phenylisoxazolidin-4-yl)quinolin-8-ol (*cis*-3x)



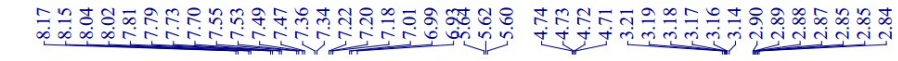


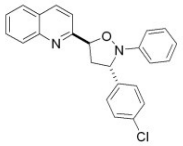
3-(4-Chlorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4a)

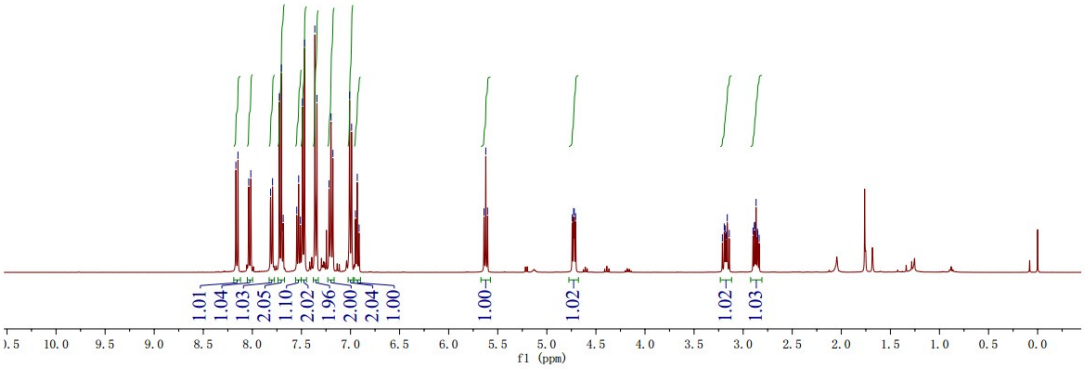


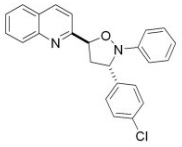


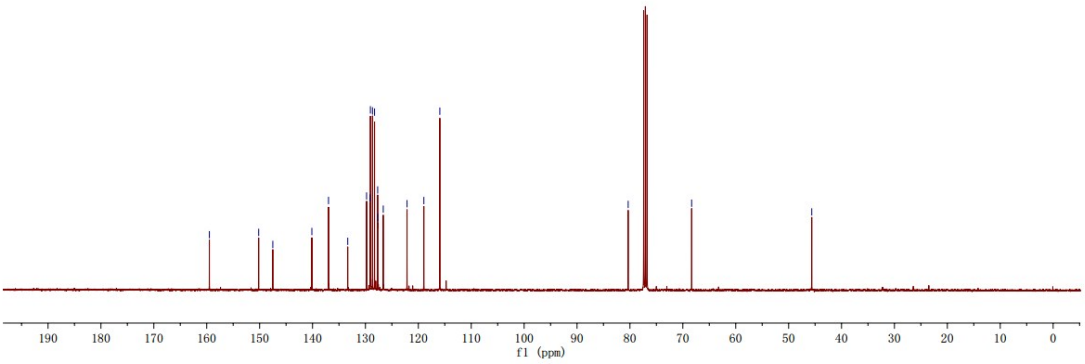
3-(4-Chlorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-4a)



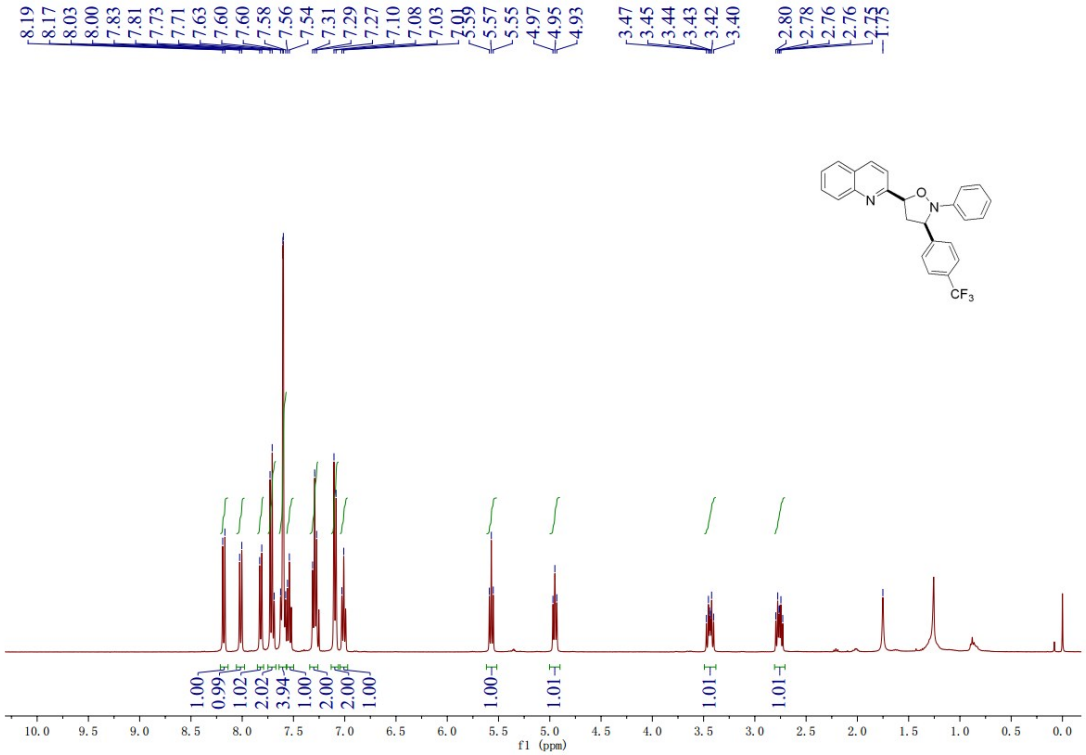


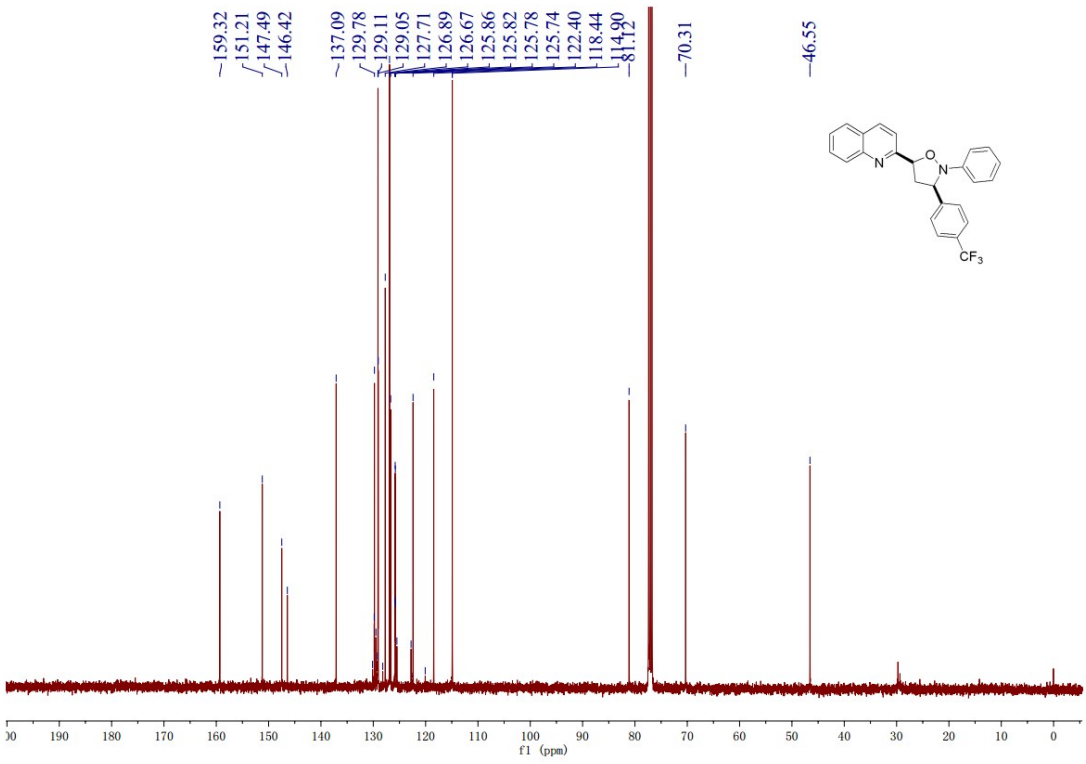




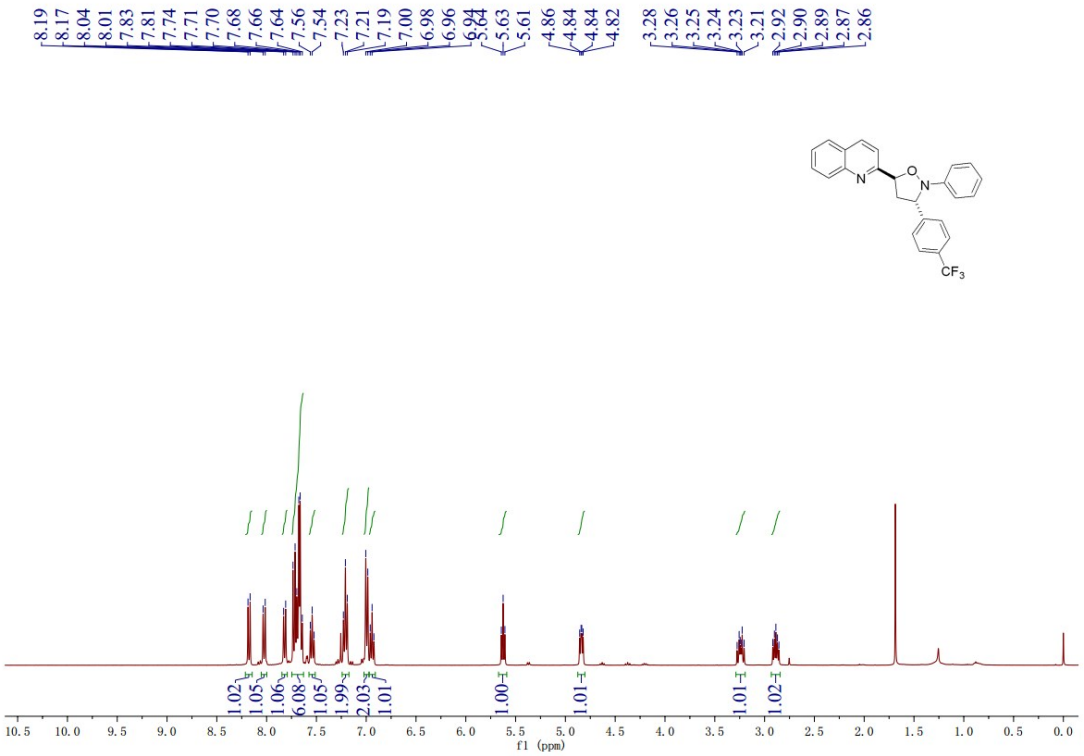


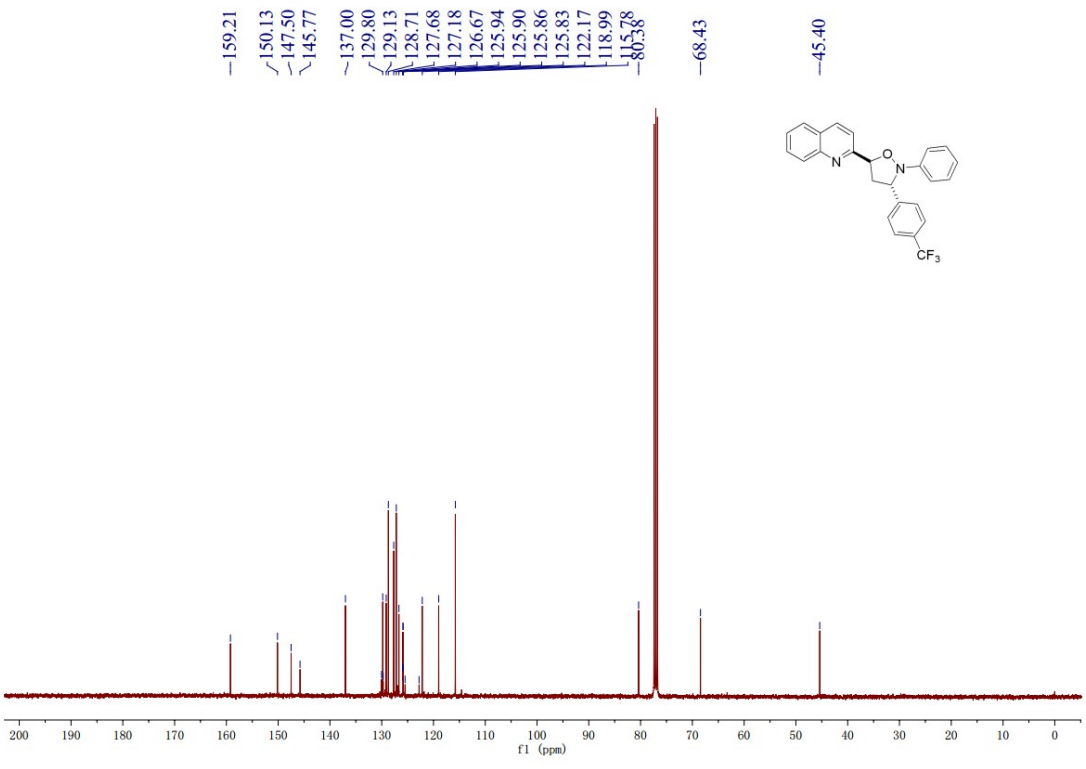
2-Phenyl-5-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*cis*-4b)



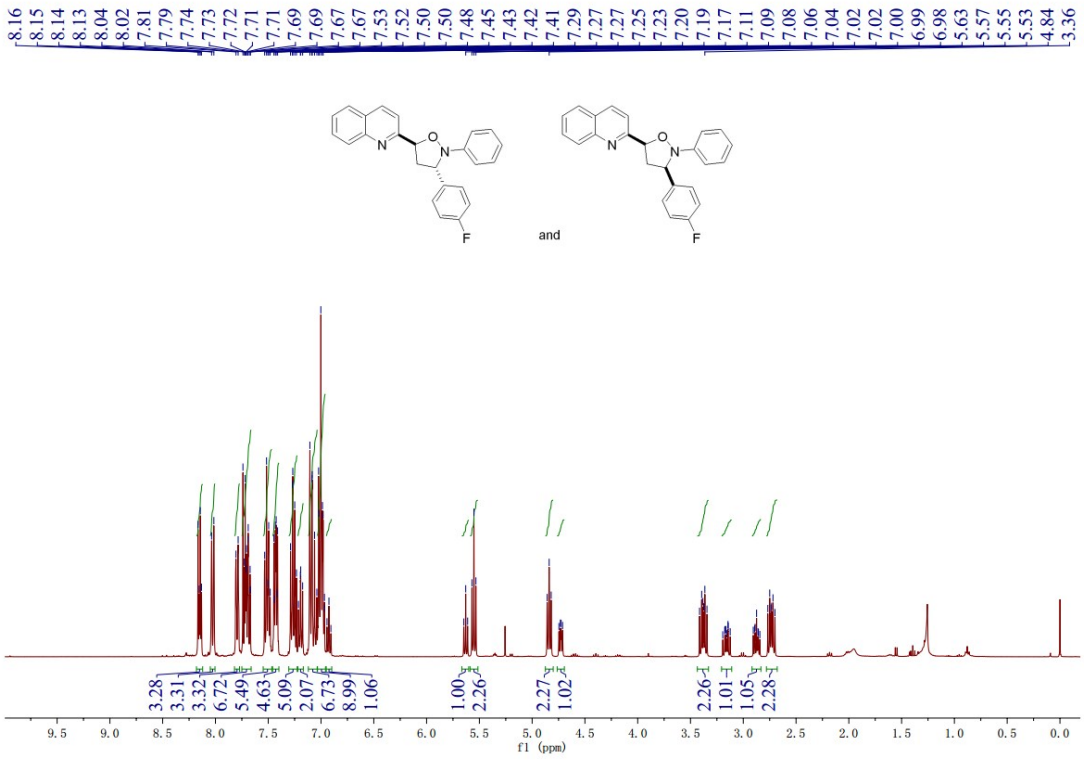


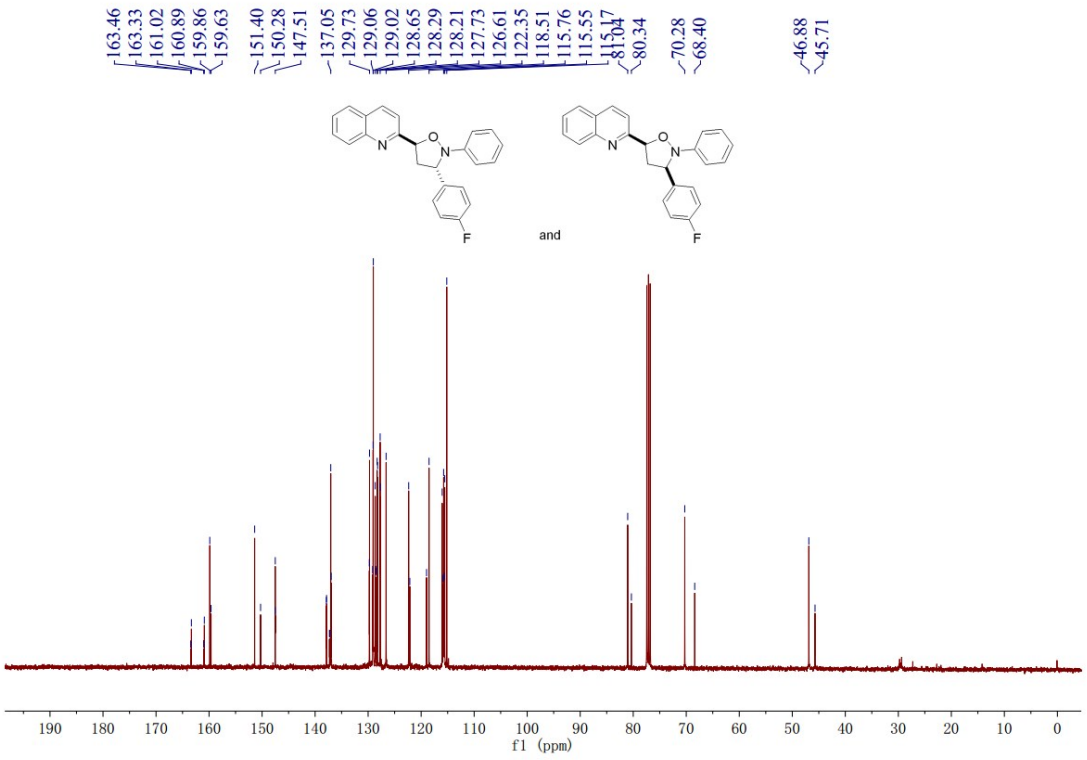
2-Phenyl-5-(quinolin-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazolidine (*trans*-4b)



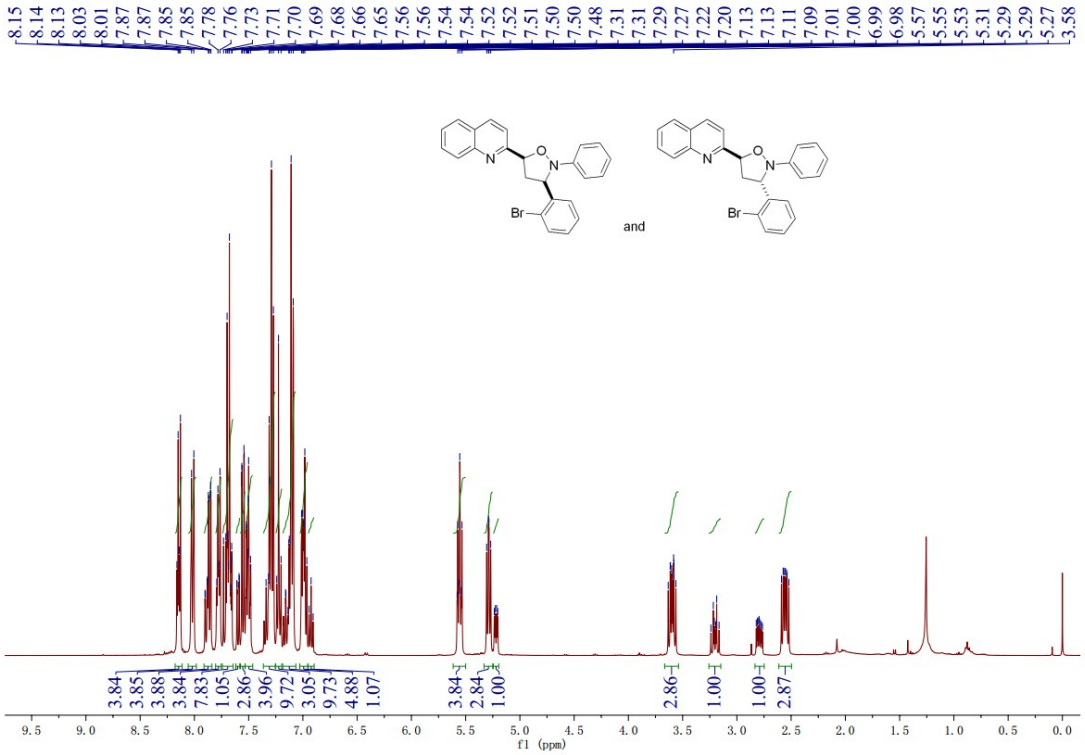


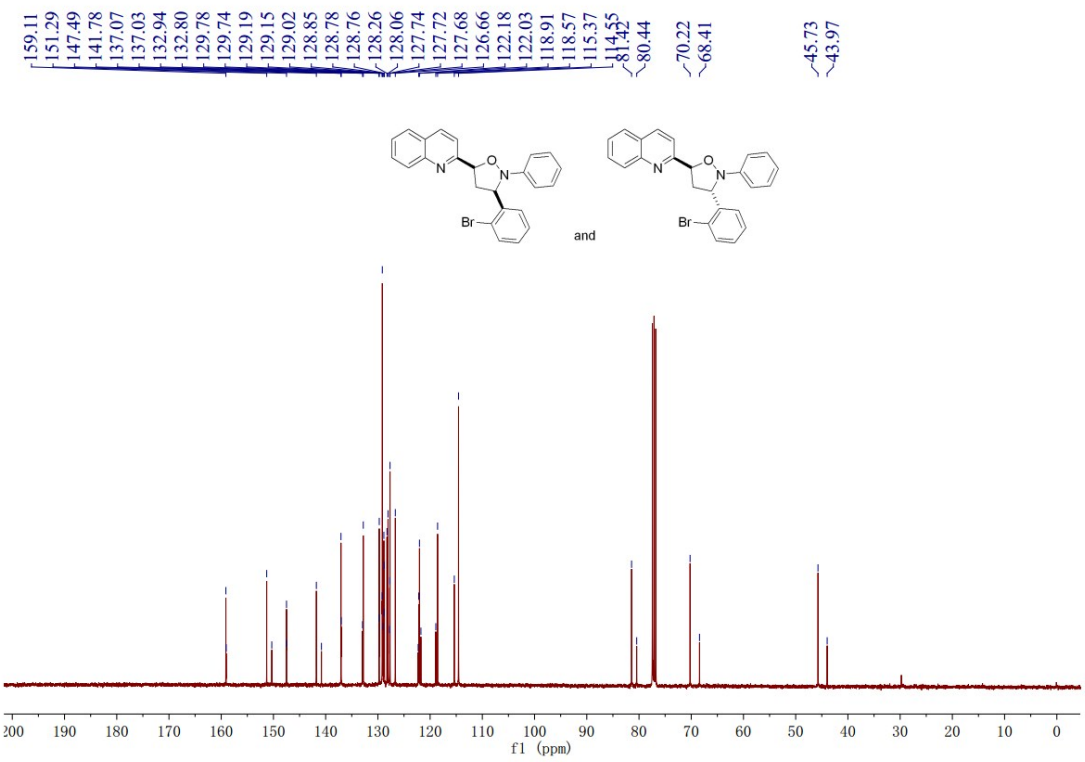
3-(4-Fluorophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4c and *trans*-4c)



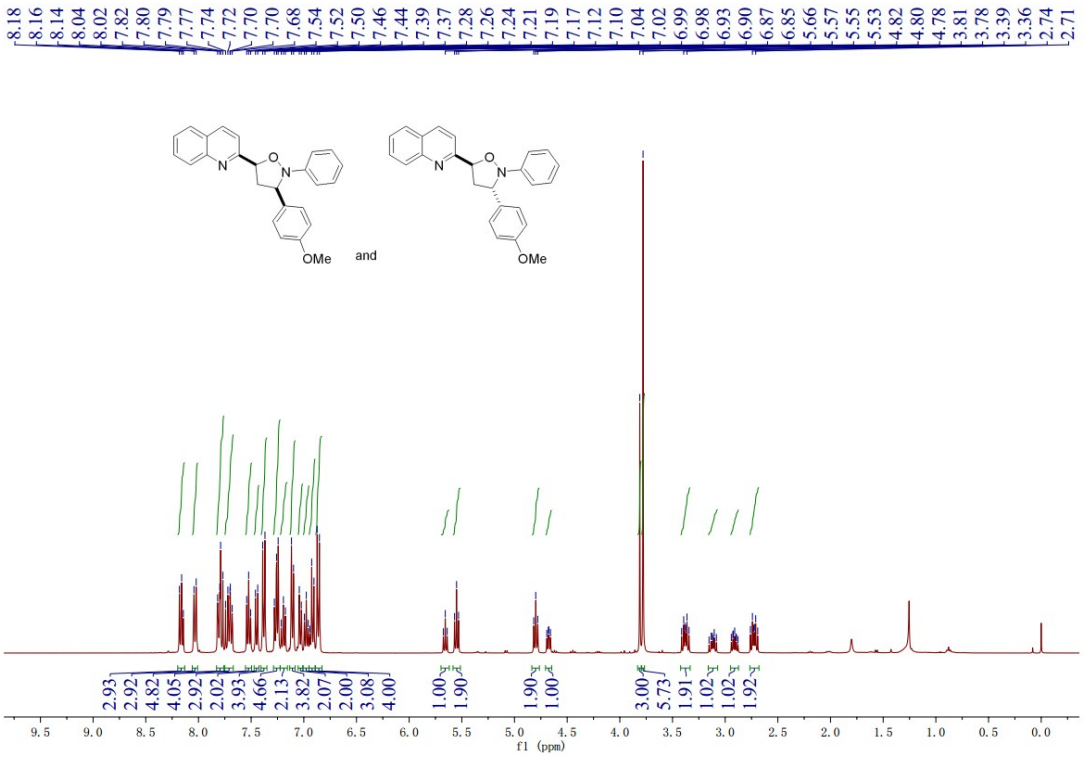


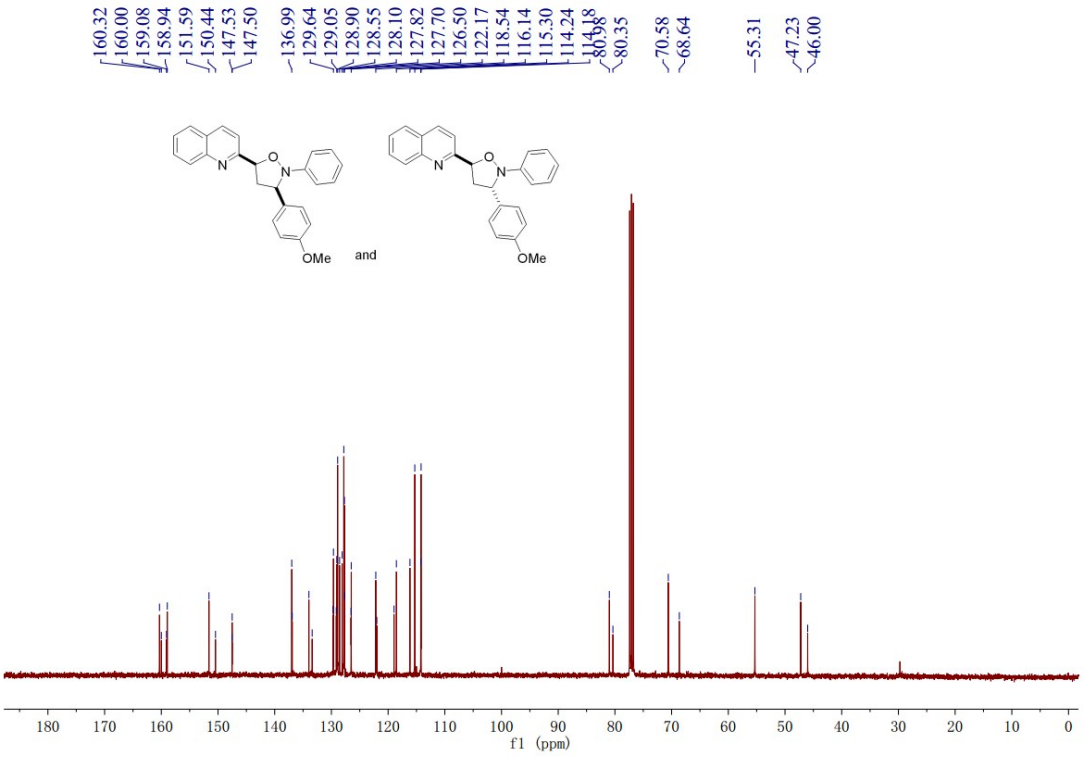
3-(2-Bromophenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4d and *trans*-4d)



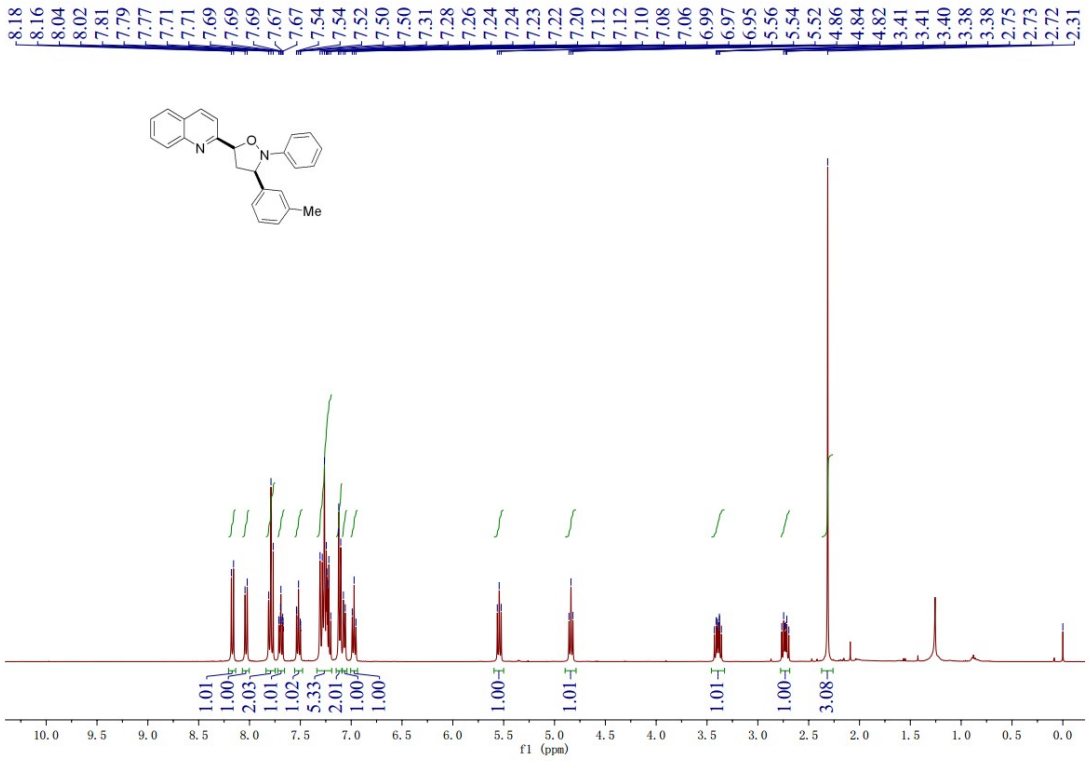


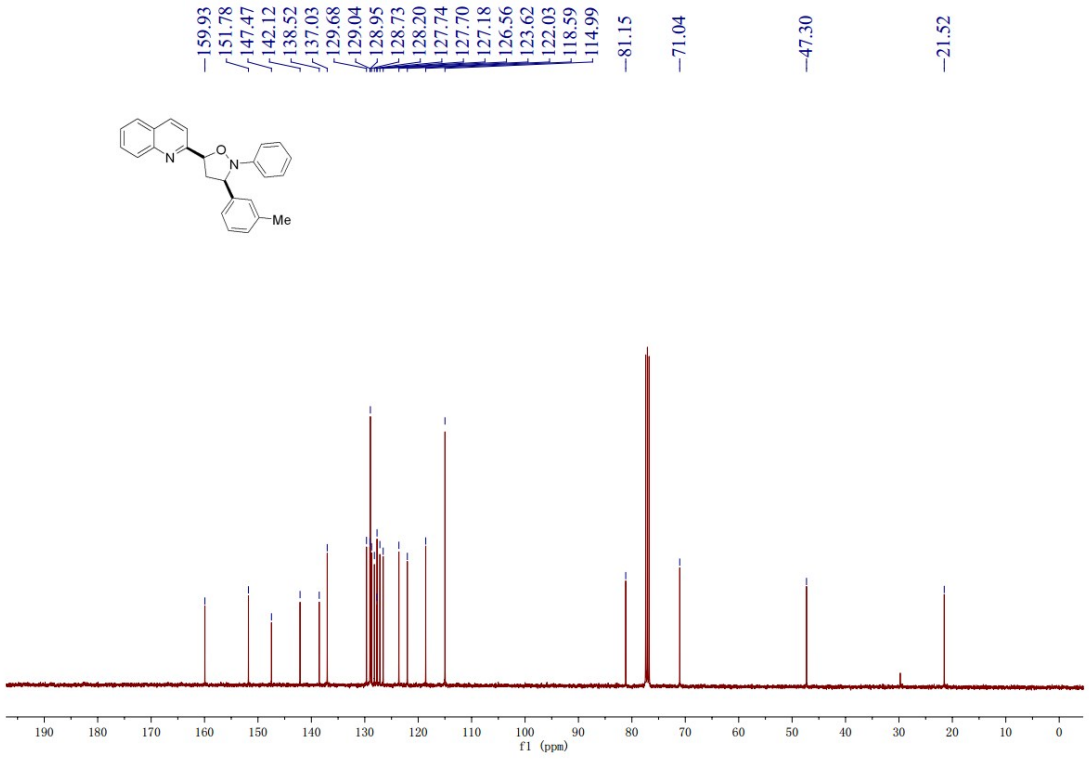
3-(4-Methoxyphenyl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4e and *trans*-4e)



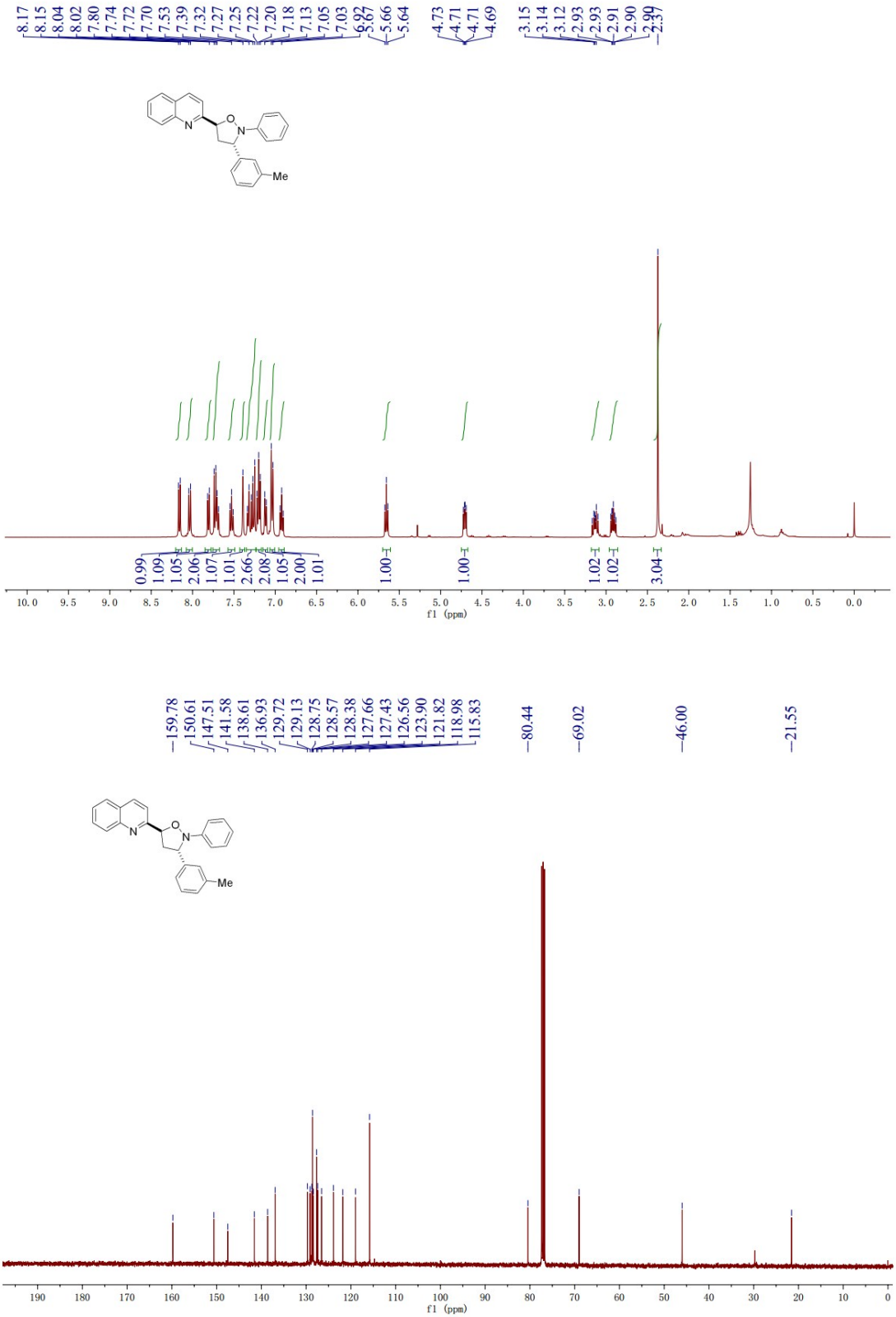


2-Phenyl-5-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*cis*-4f)

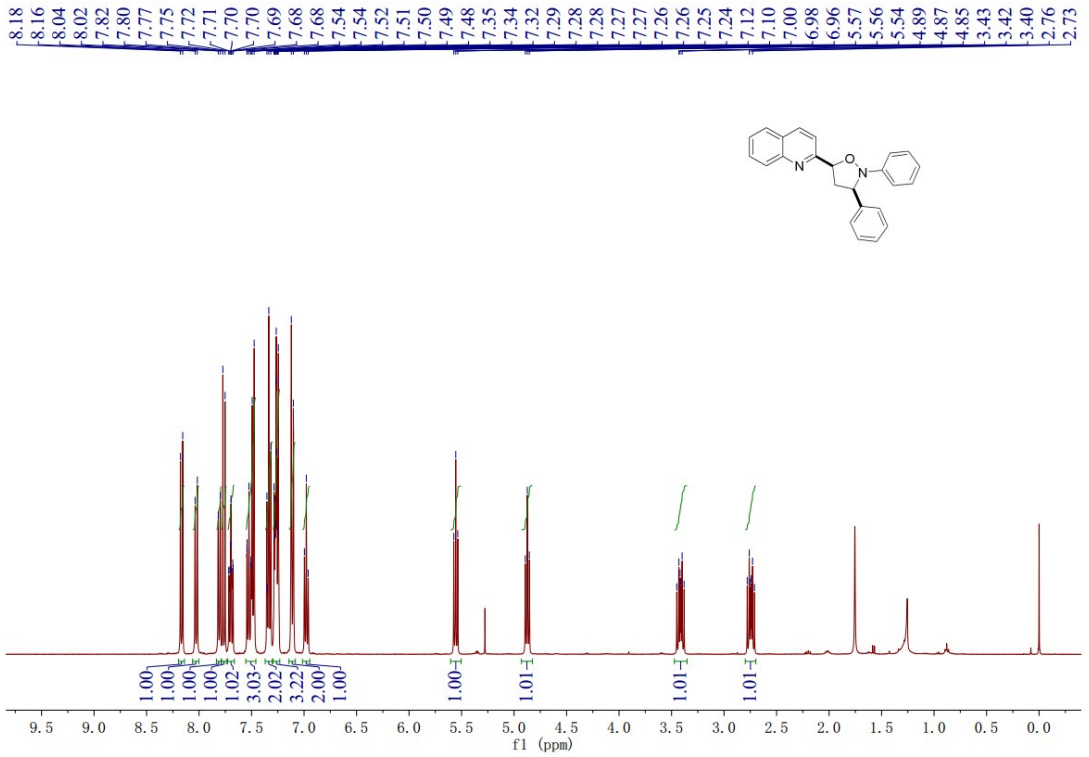


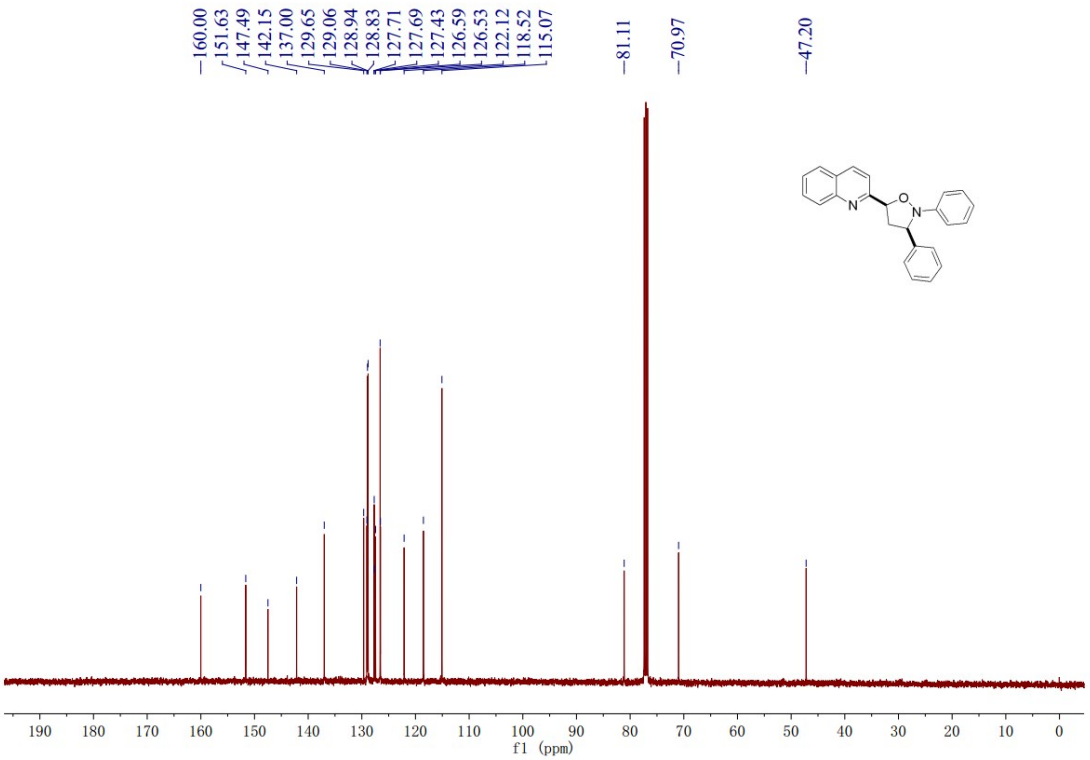


2-Phenyl-5-(quinolin-2-yl)-3-(m-tolyl)isoxazolidine (*trans*-4f)

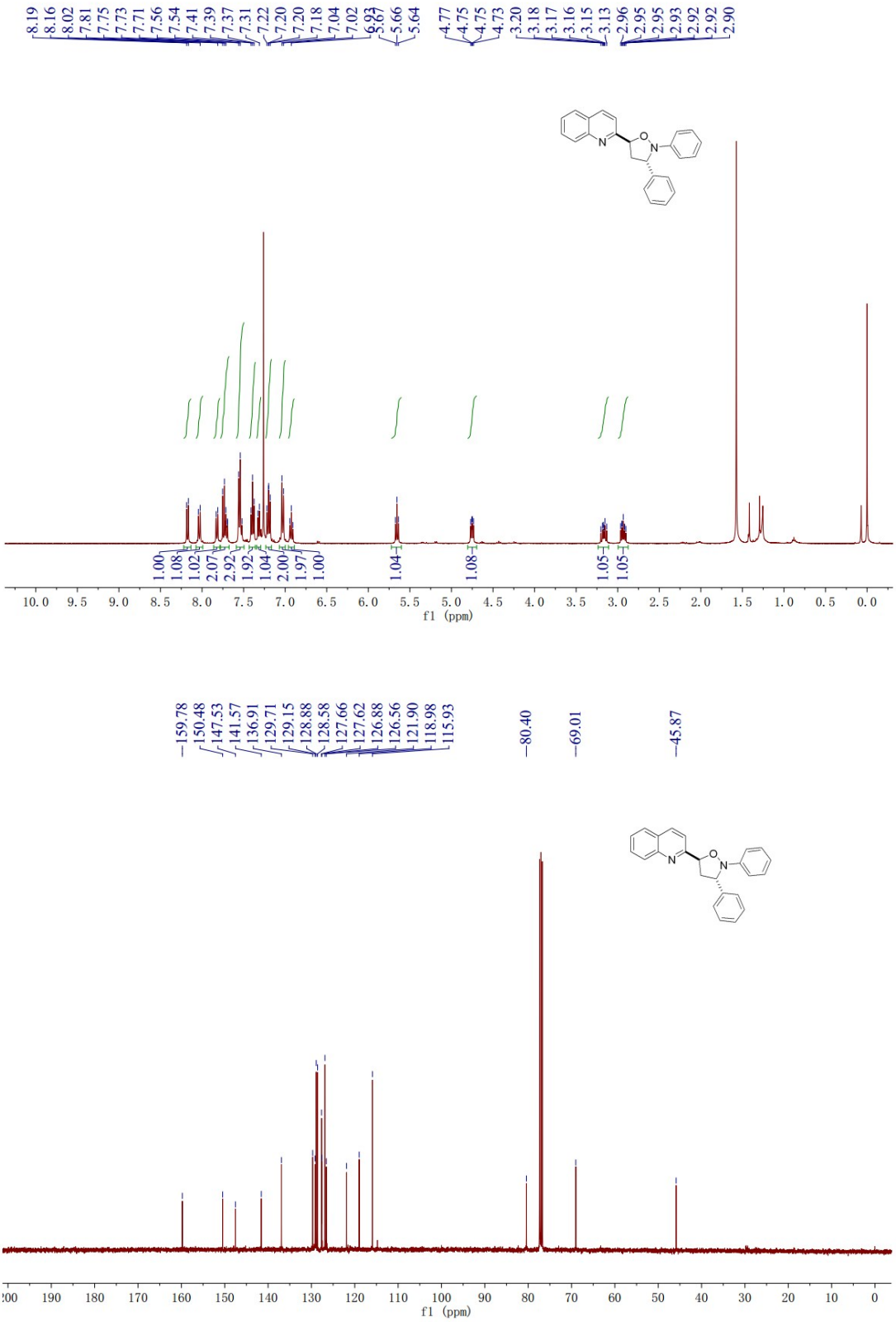


2,3-Diphenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4g)

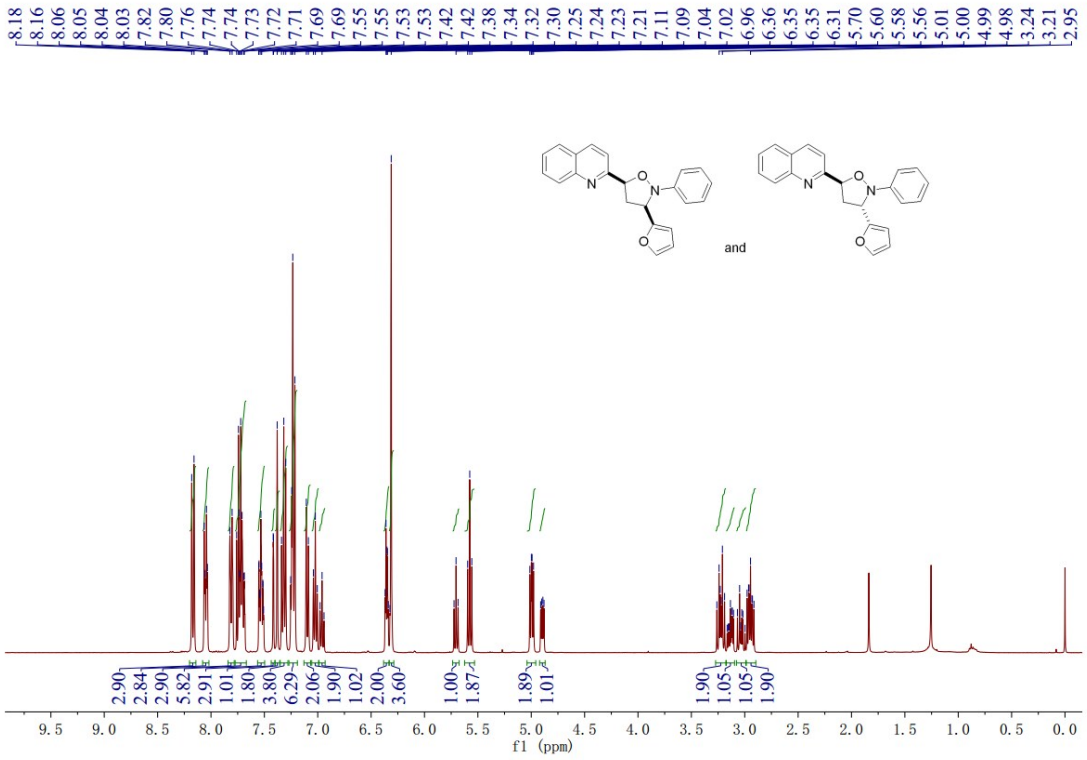


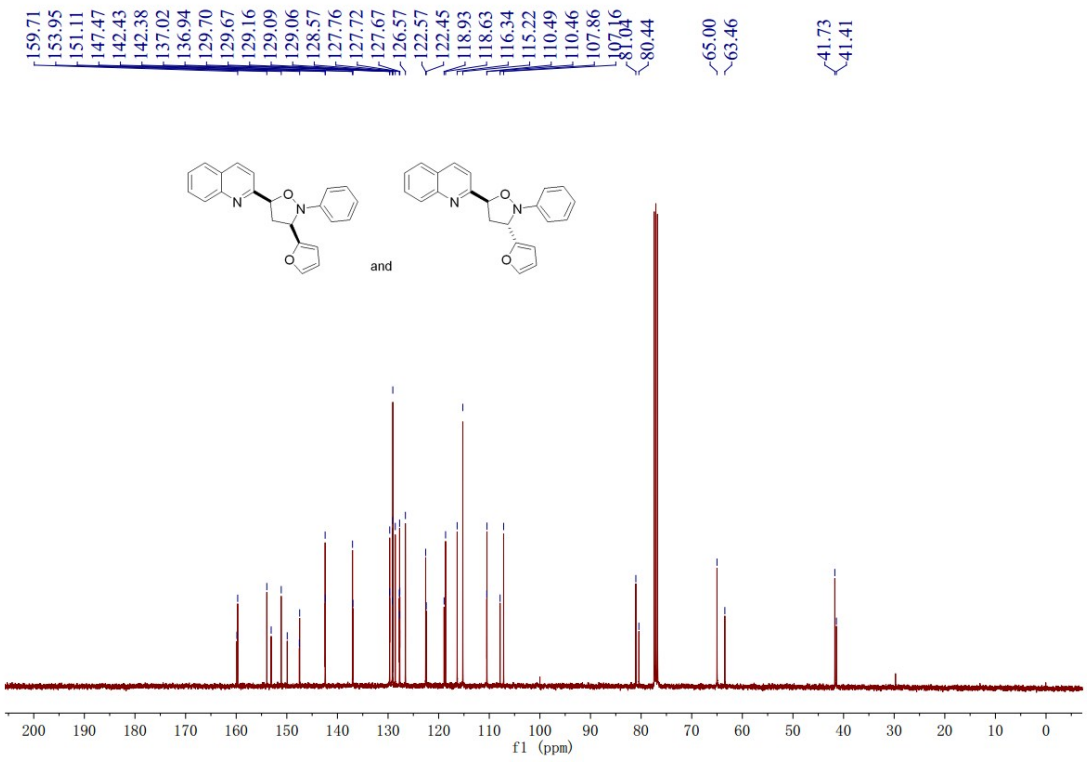


2,3-Diphenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-4g)

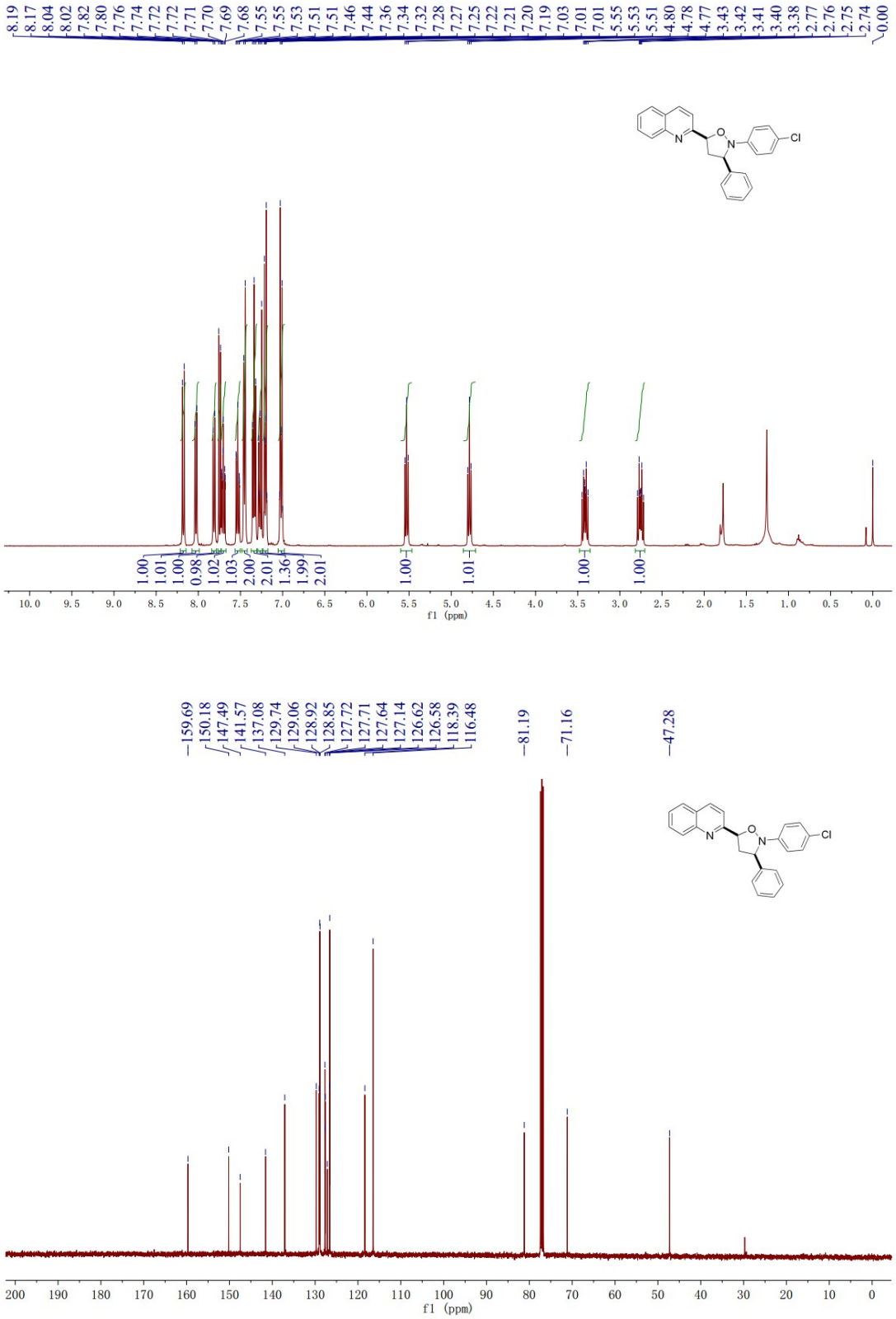


3-(Furan-2-yl)-2-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4h and *trans*-4h)

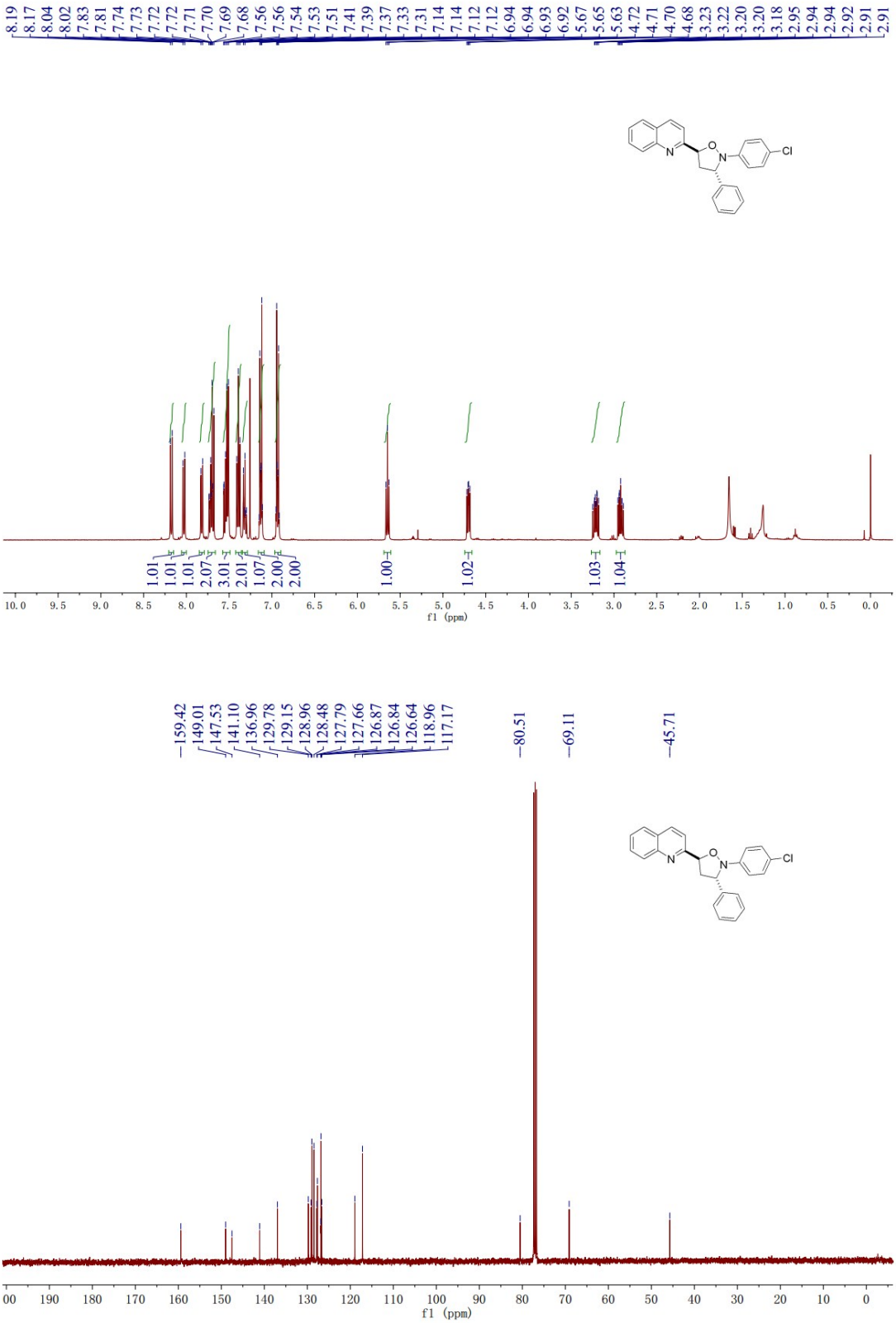




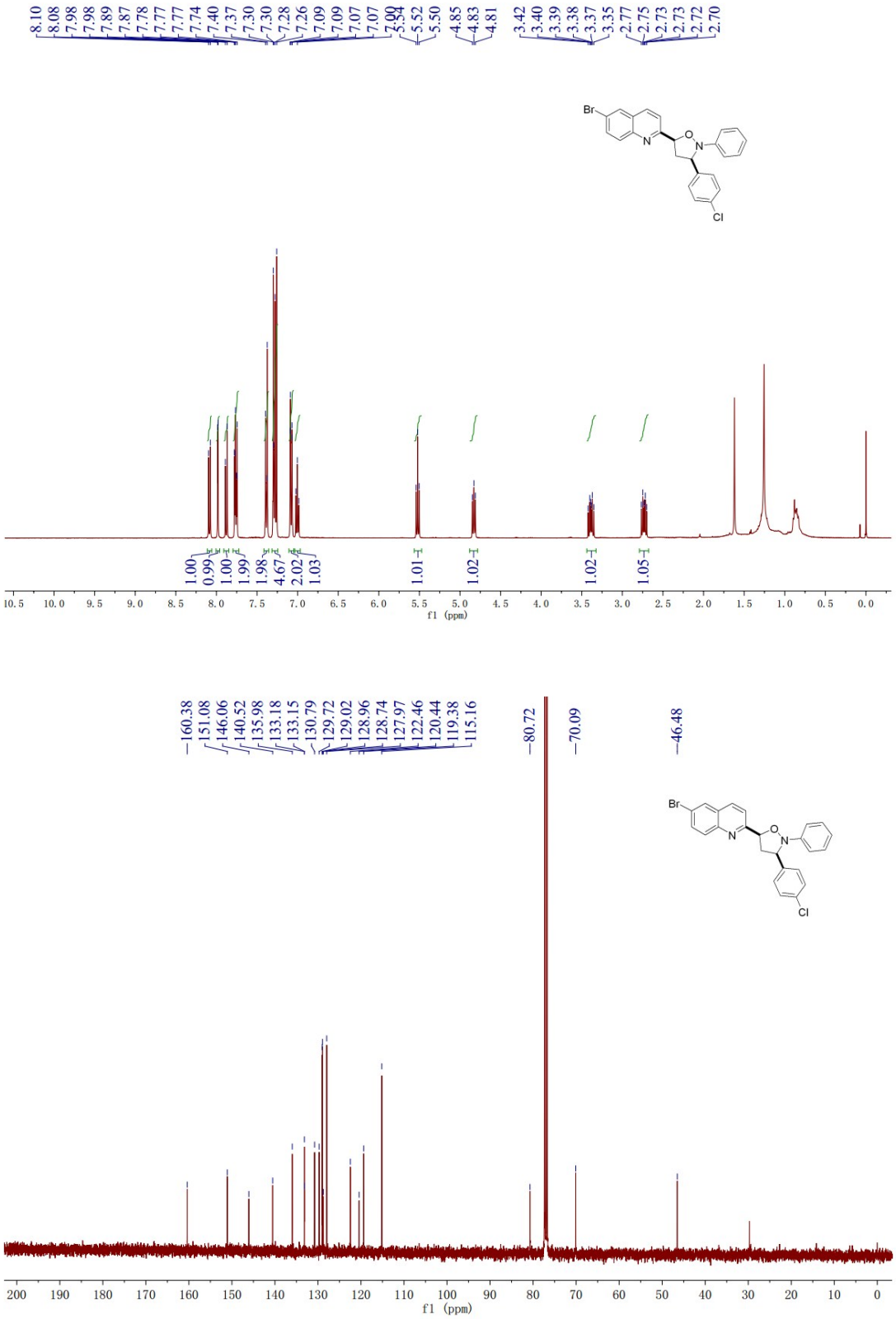
2-(4-Chlorophenyl)-3-phenyl-5-(quinolin-2-yl)isoxazolidine (*cis*-4i)



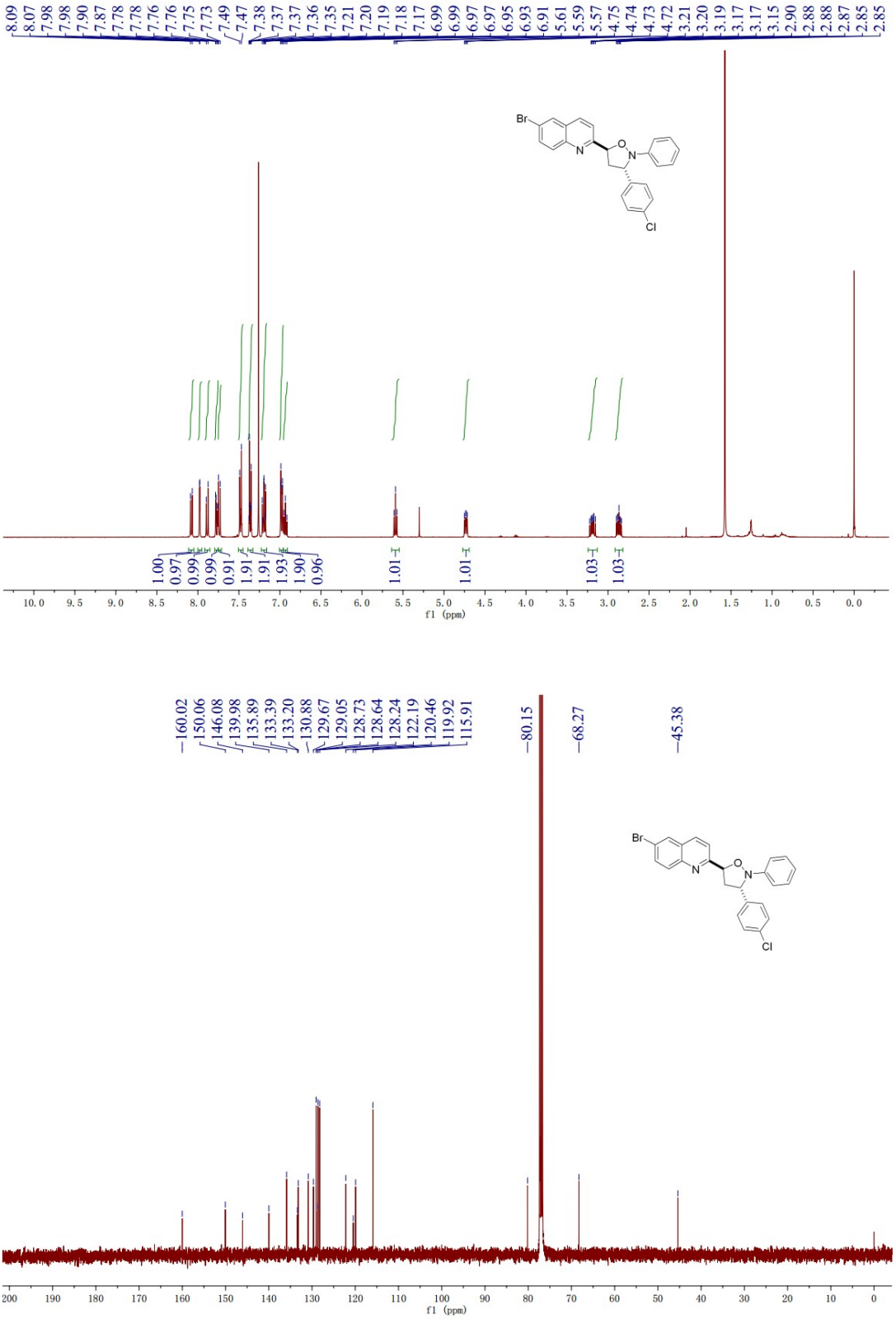
2-(4-Chlorophenyl)-3-phenyl-5-(quinolin-2-yl)isoxazolidine (*trans*-4i)



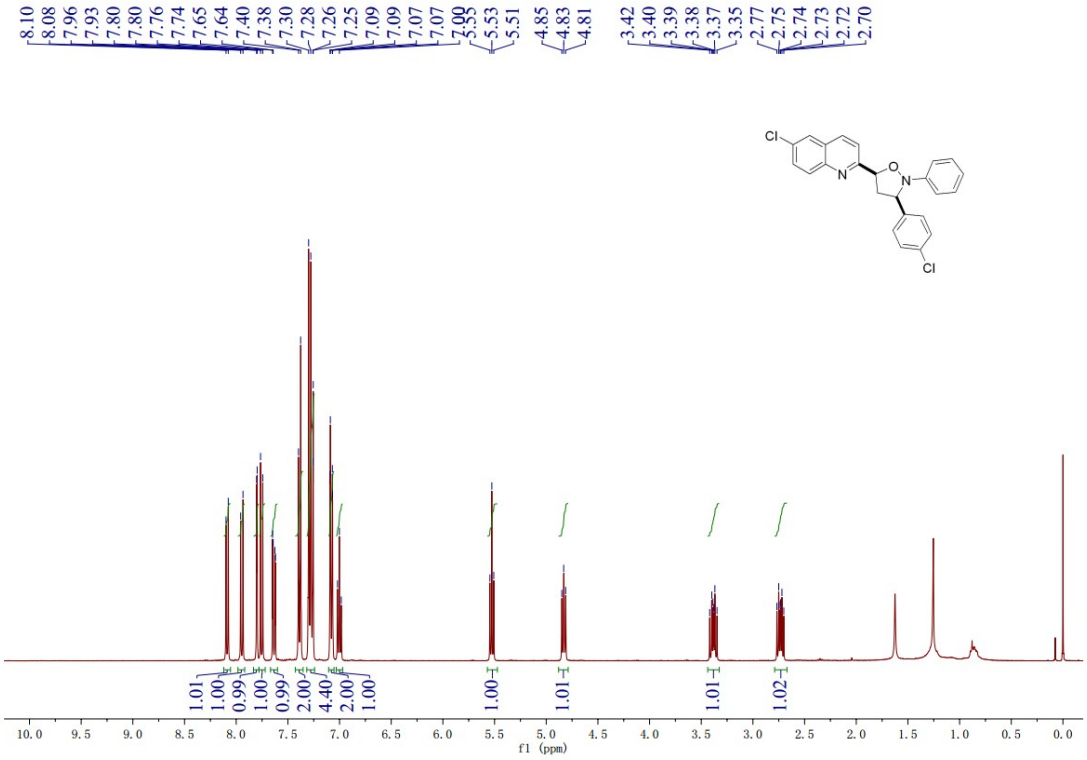
5-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*cis*-4j)

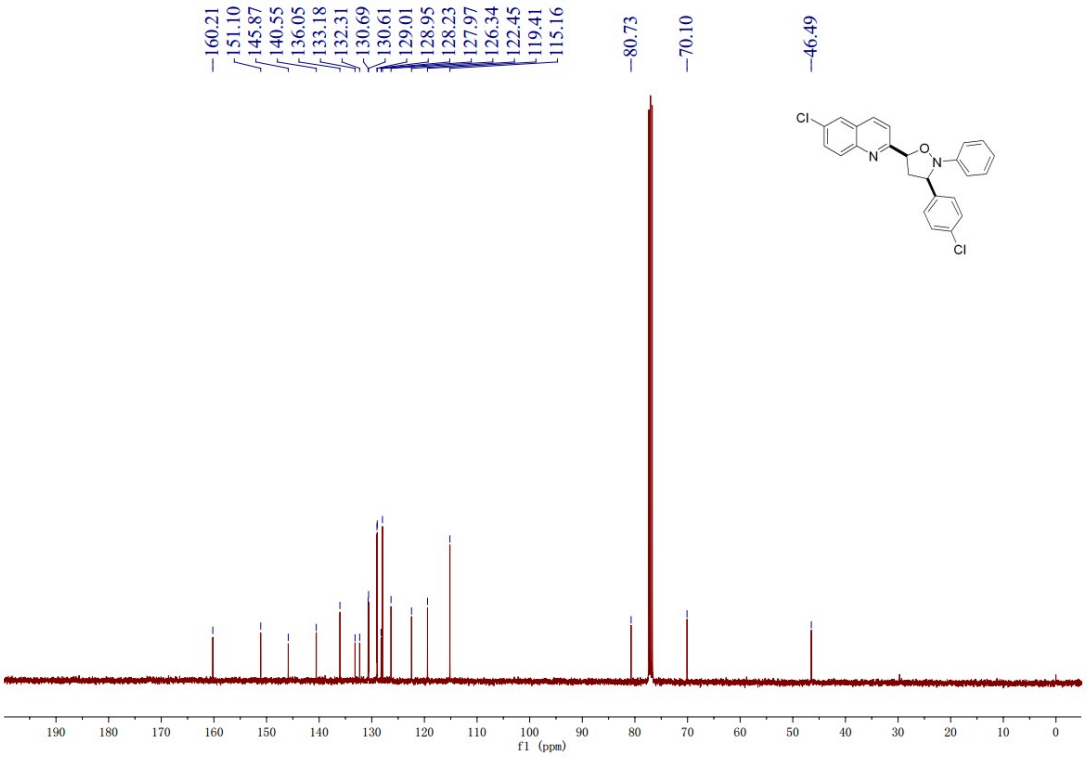


5-(6-Bromoquinolin-2-yl)-3-(4-chlorophenyl)-2-phenylisoxazolidine (*trans*-4j)

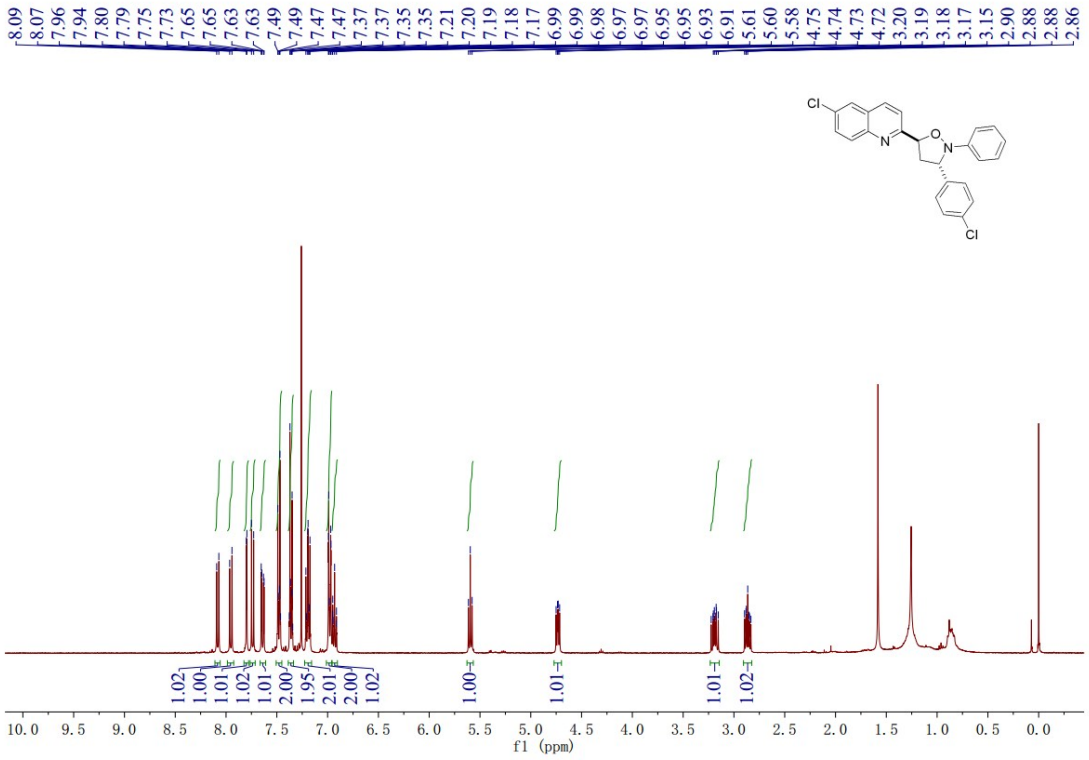


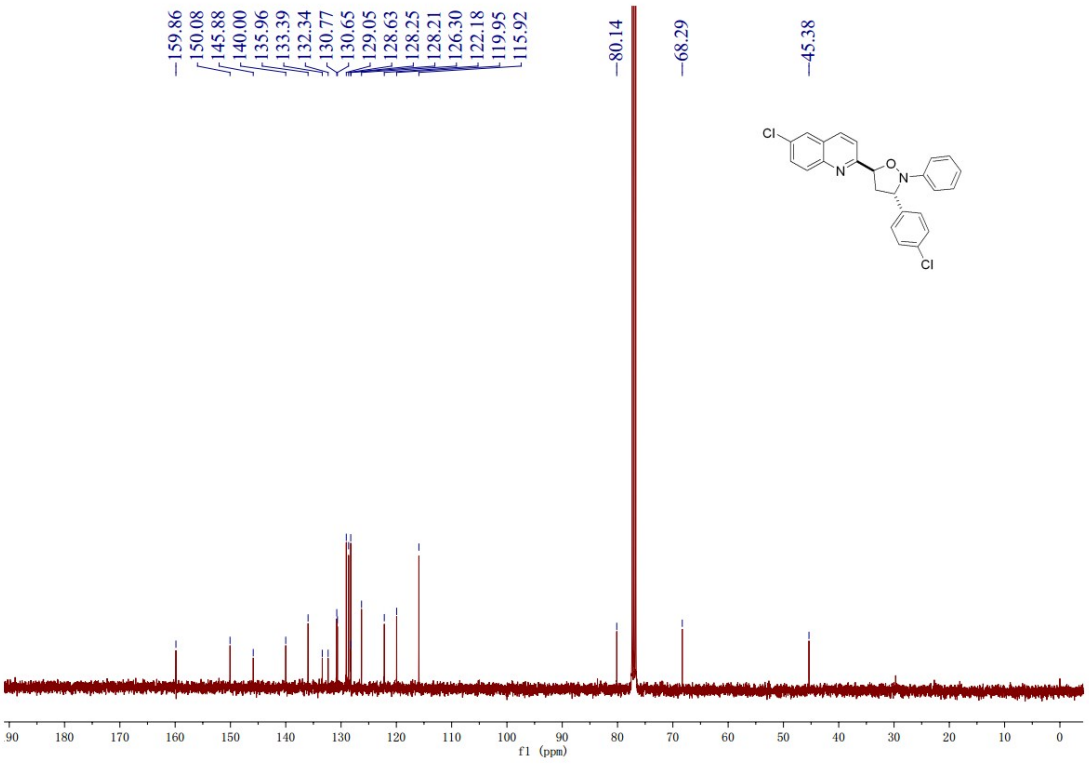
3-(4-Chlorophenyl)-5-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4k)



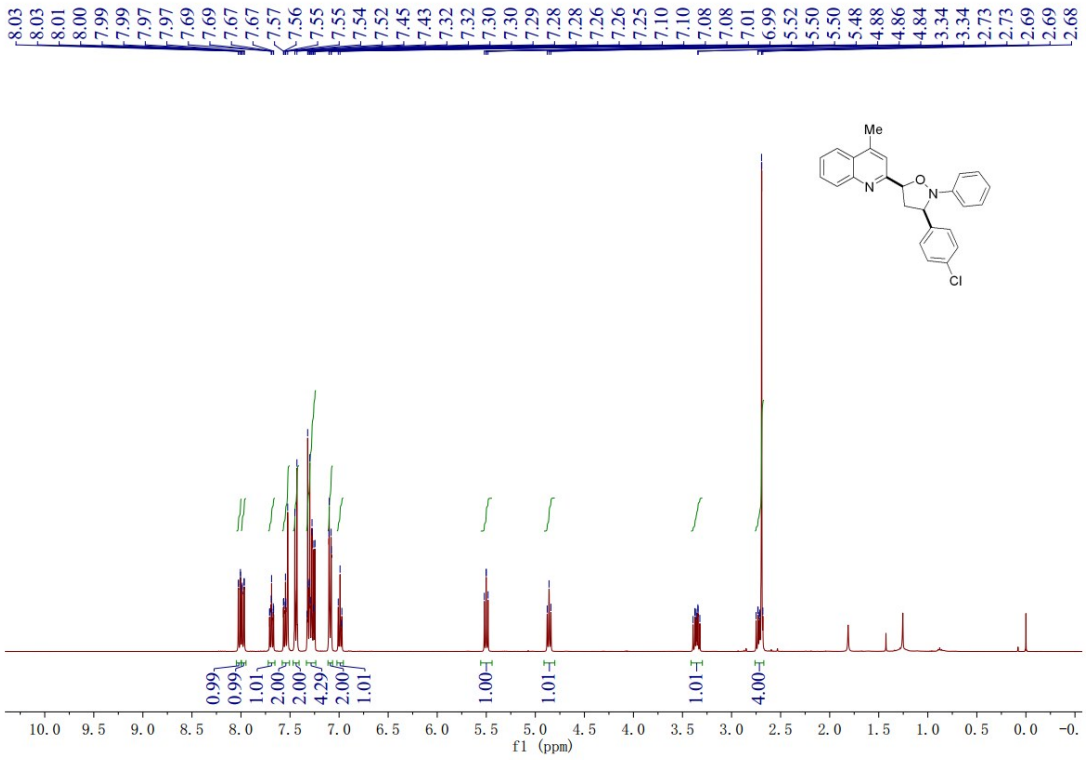


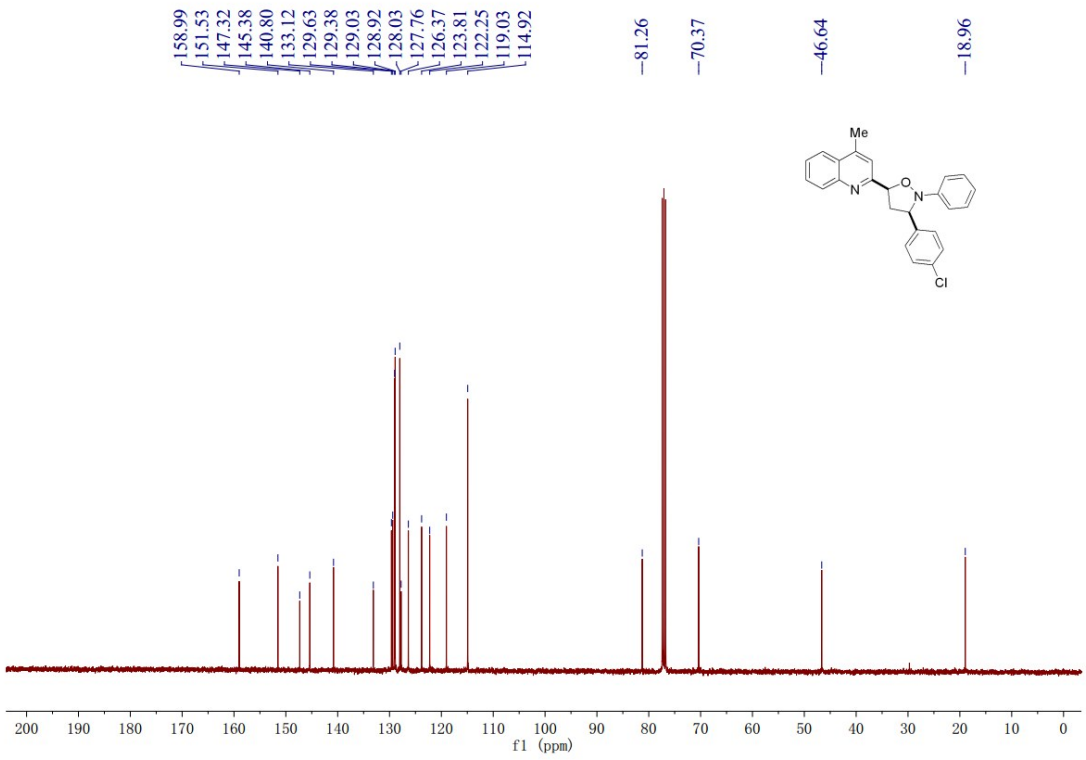
3-(4-Chlorophenyl)-5-(6-chloroquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4k)



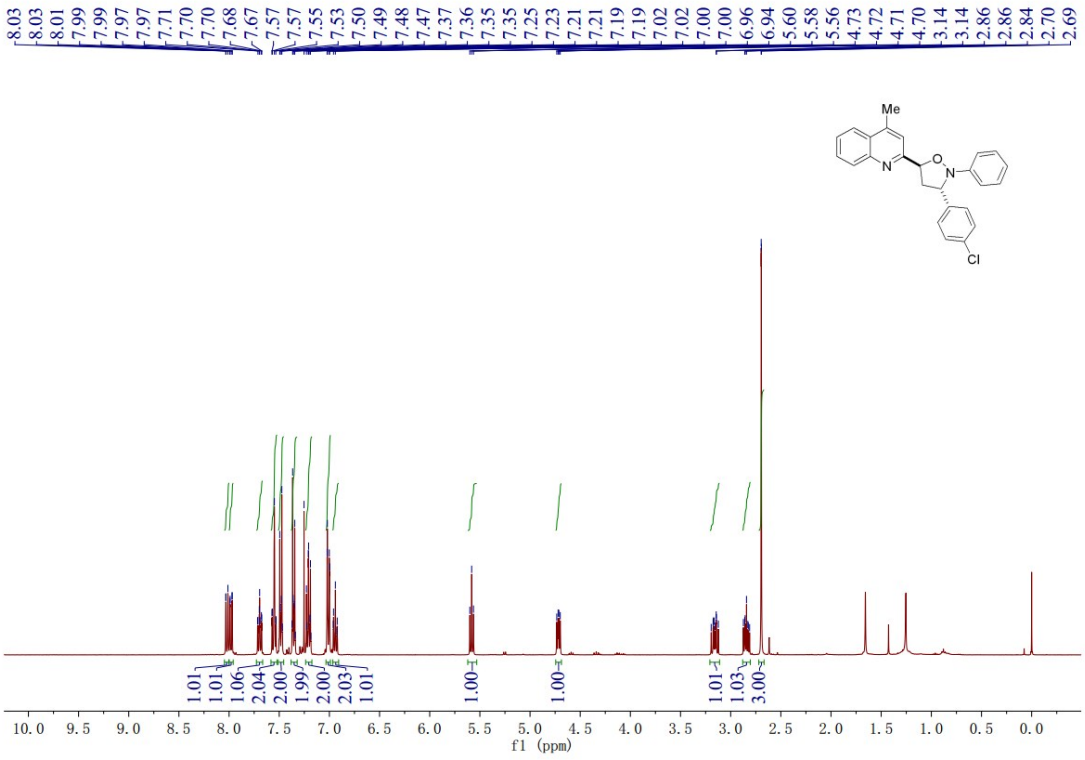


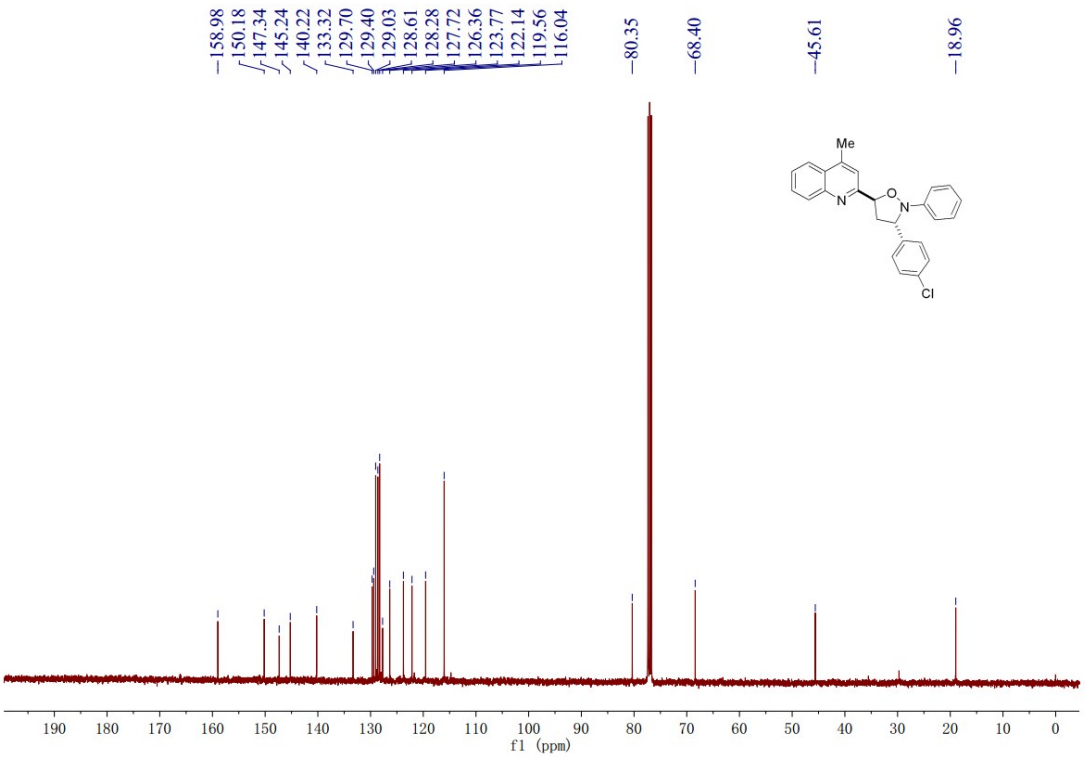
3-(4-Chlorophenyl)-5-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4l)



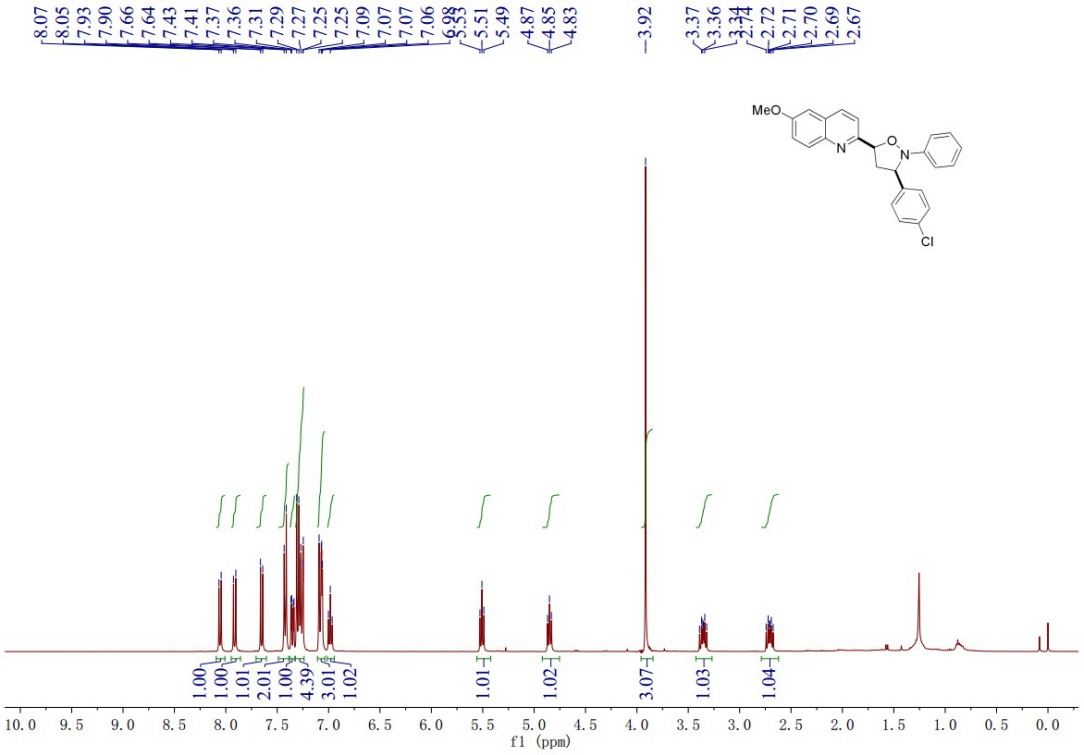


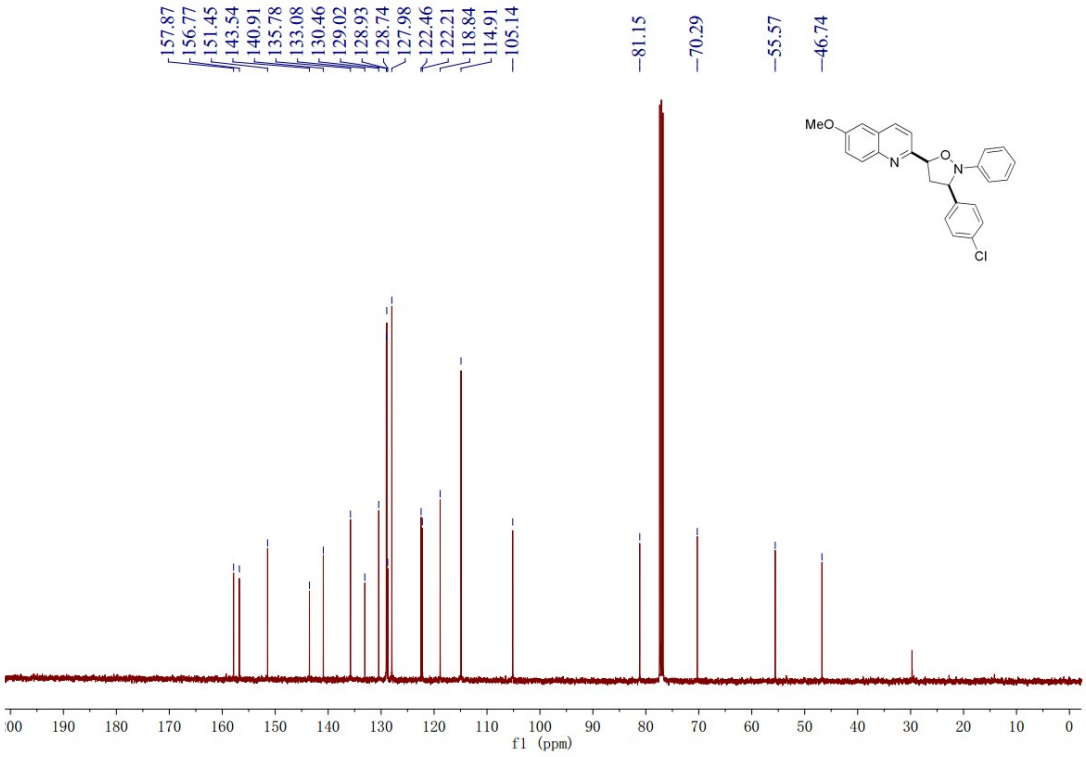
3-(4-Chlorophenyl)-5-(4-methylquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4l)



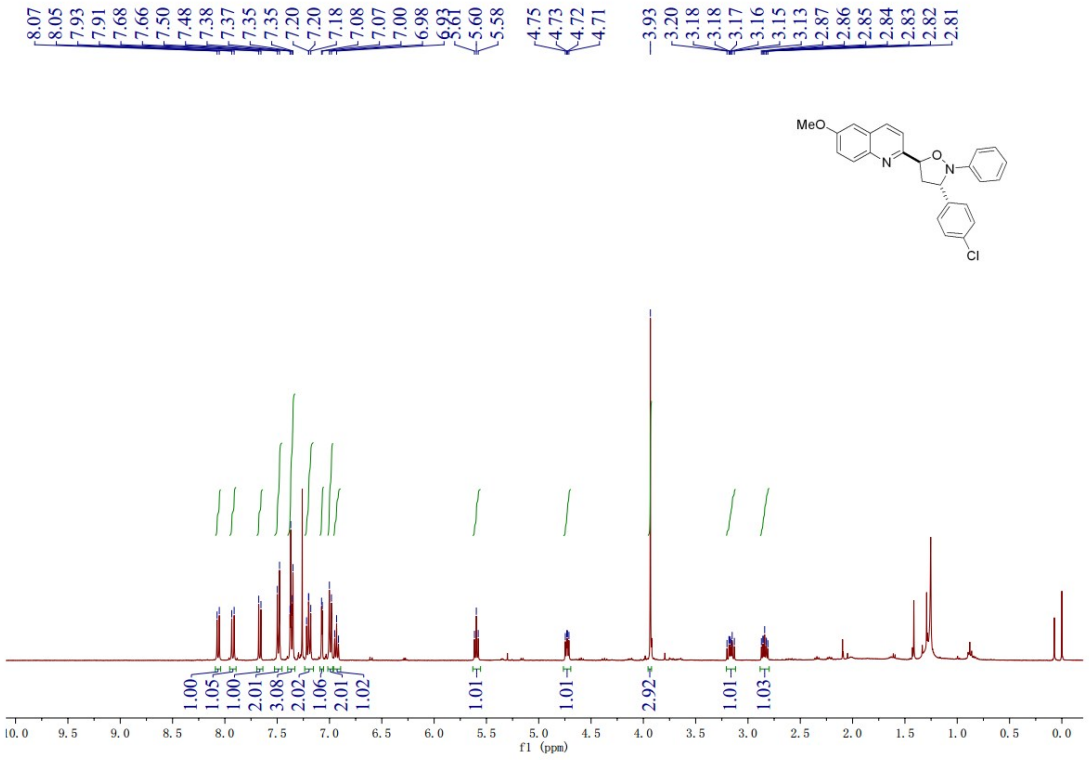


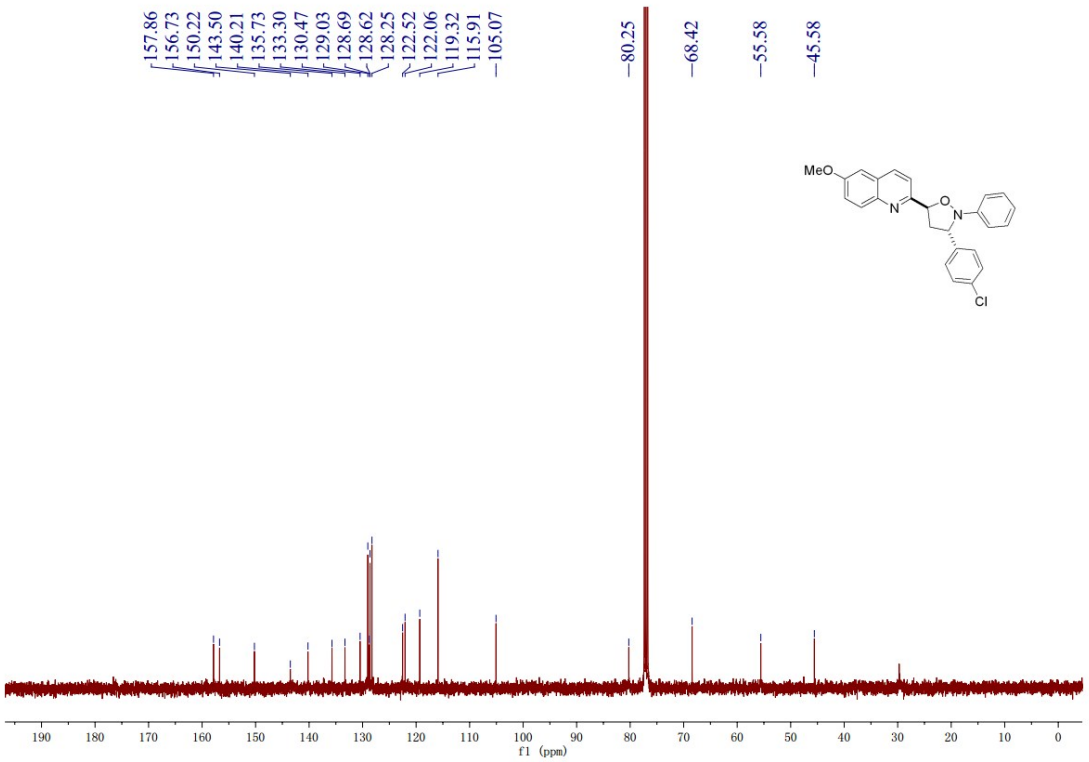
3-(4-Chlorophenyl)-5-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*cis*-4m)



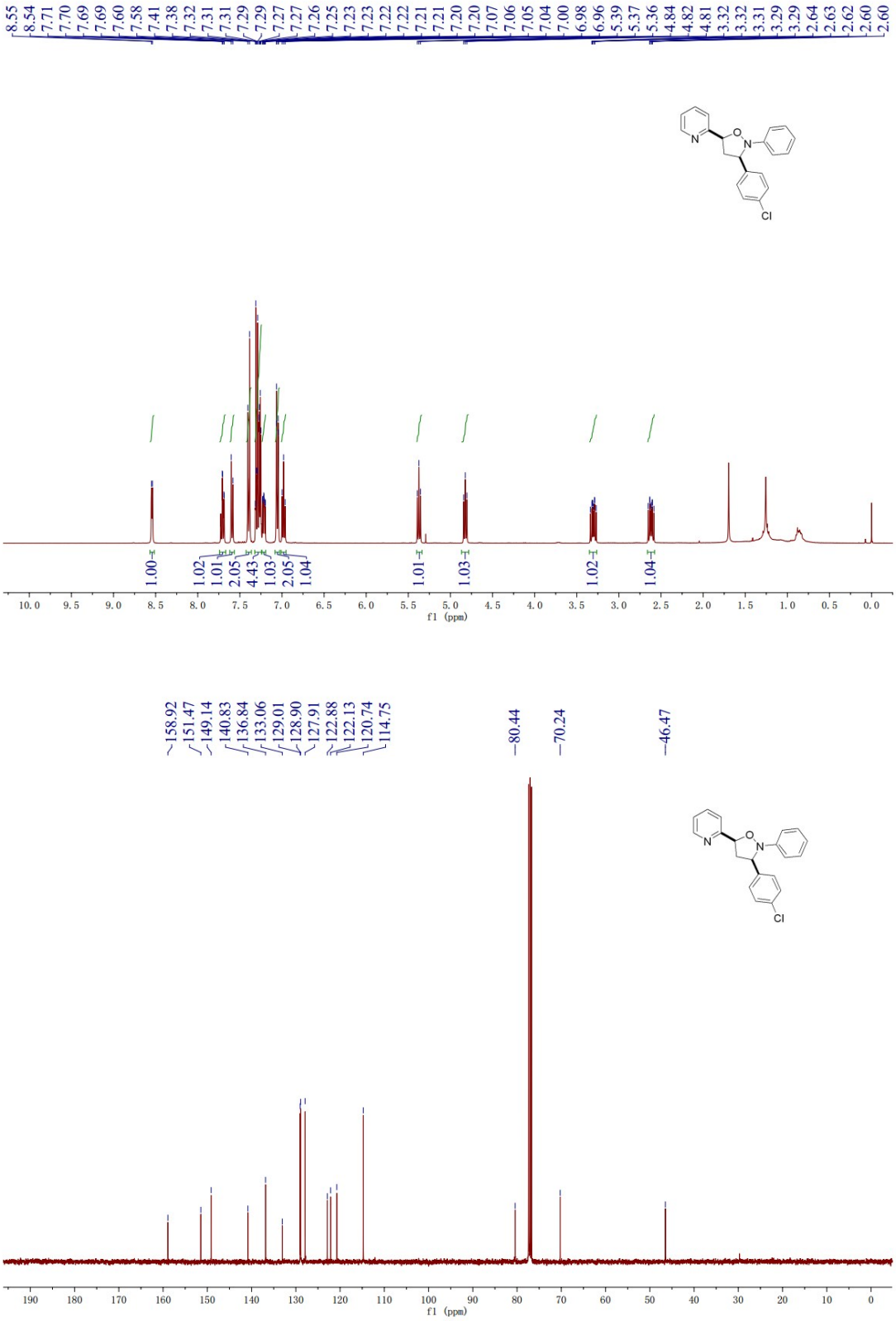


3-(4-Chlorophenyl)-5-(6-methoxyquinolin-2-yl)-2-phenylisoxazolidine (*trans*-4m)

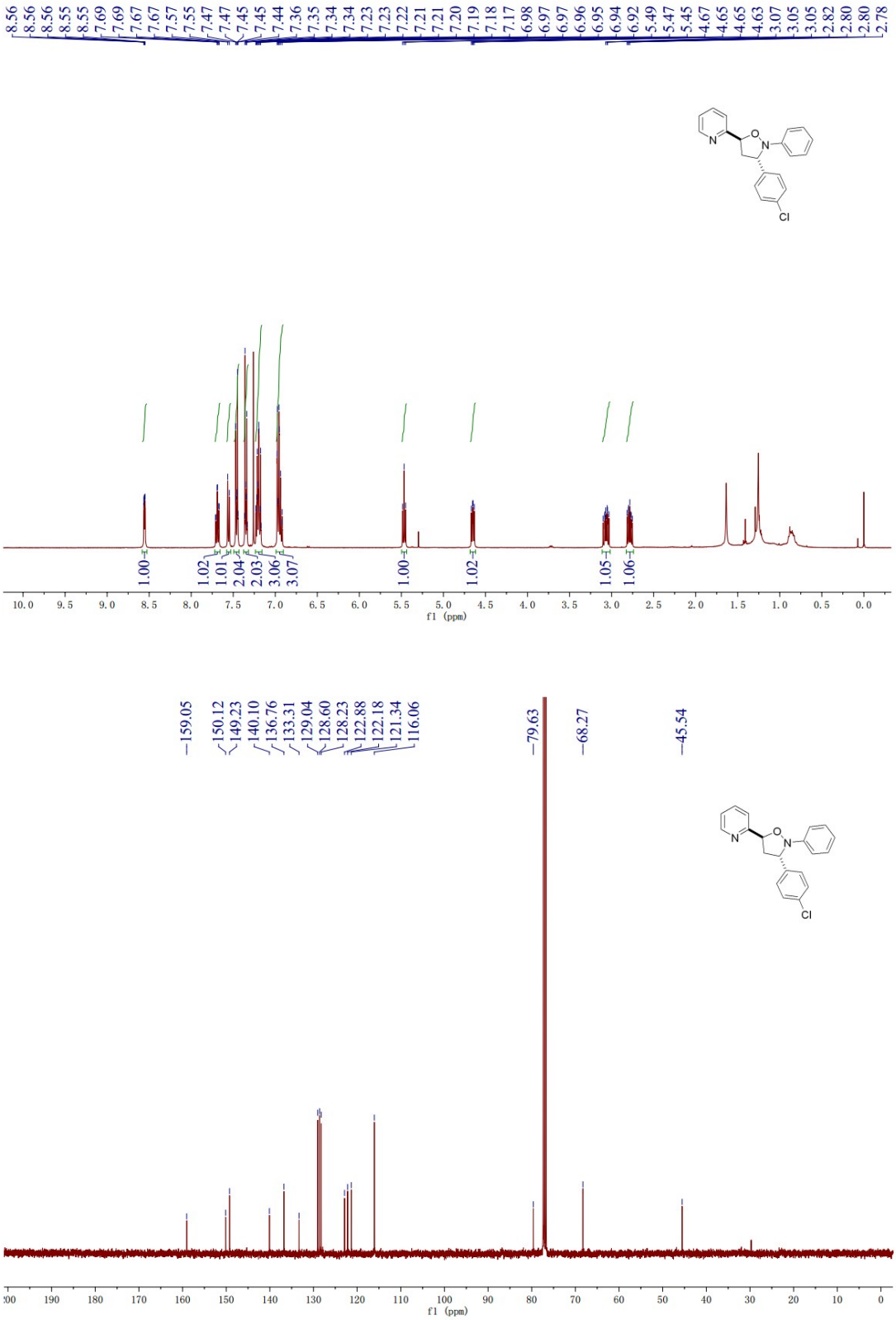




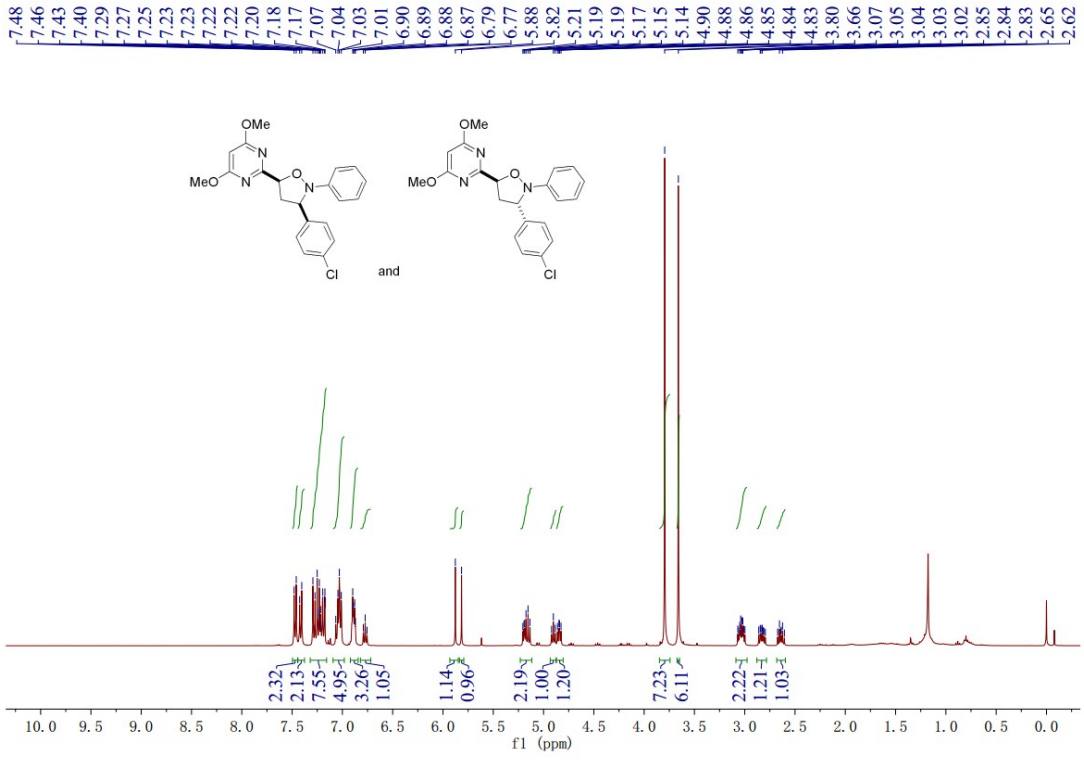
3-(4-Chlorophenyl)-2-phenyl-5-(pyridin-2-yl)isoxazolidine (*cis*-4n)

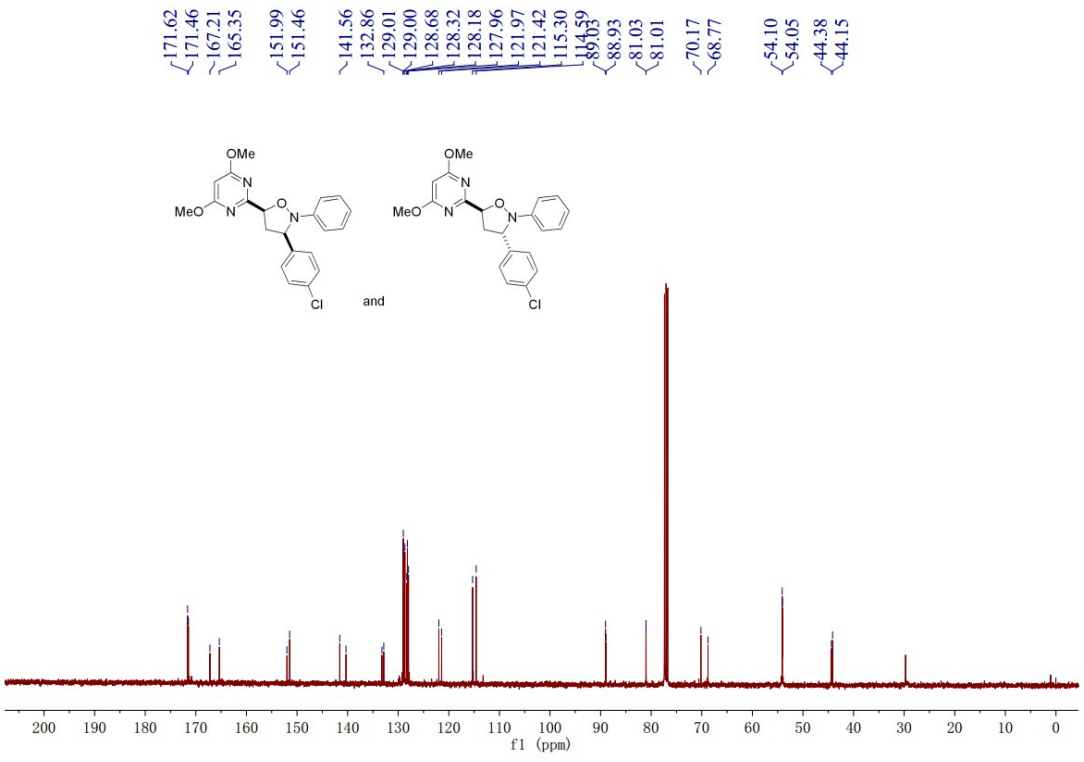


3-(4-Chlorophenyl)-2-phenyl-5-(pyridin-2-yl)isoxazolidine (*trans*-4n)

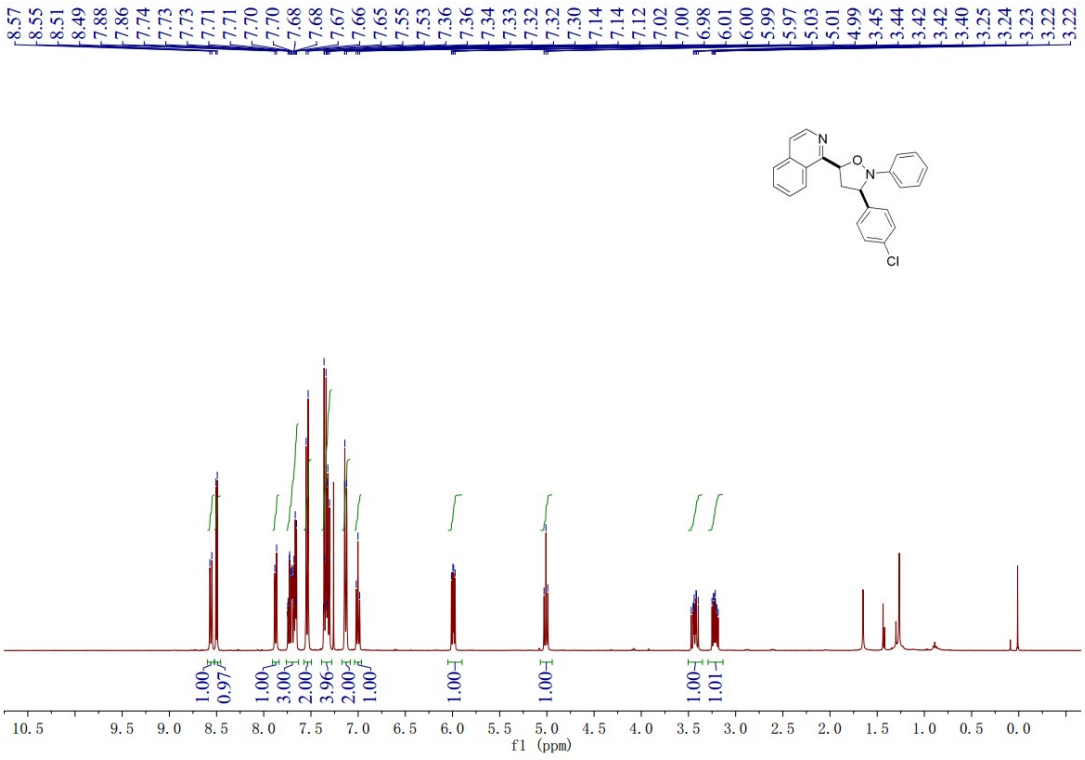


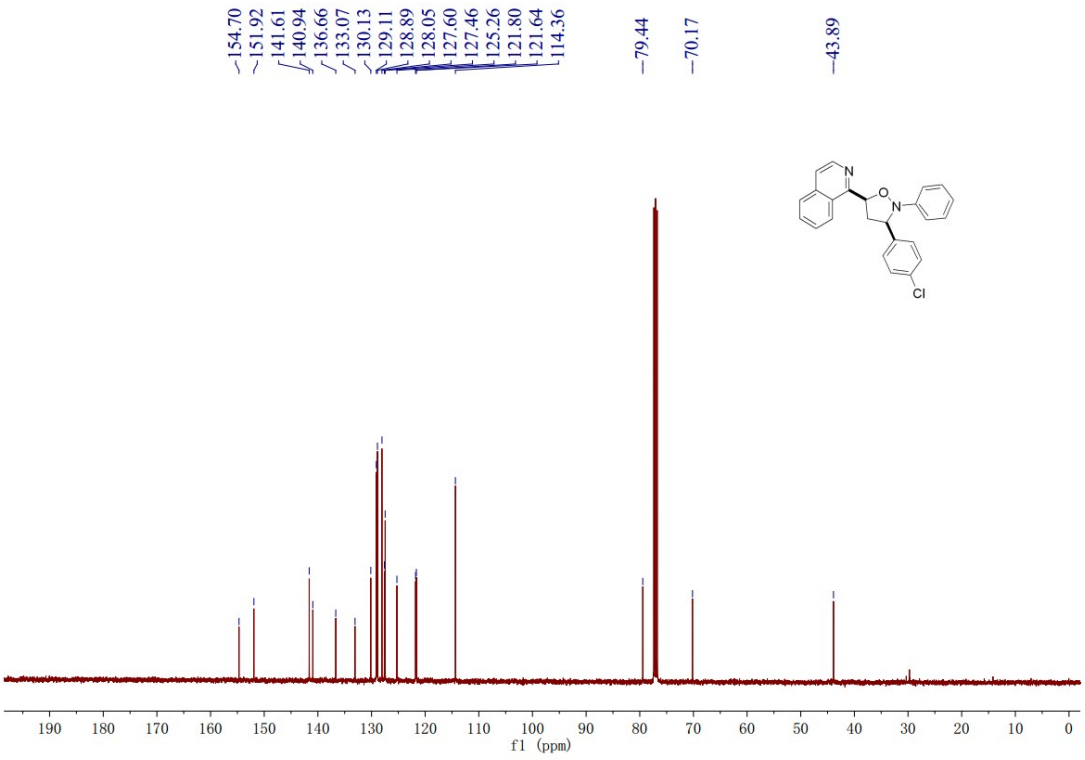
3-(4-Chlorophenyl)-5-(4,6-dimethoxypyrimidin-2-yl)-2-phenylisoxazolidine (*cis*-4o and *trans*-4o)



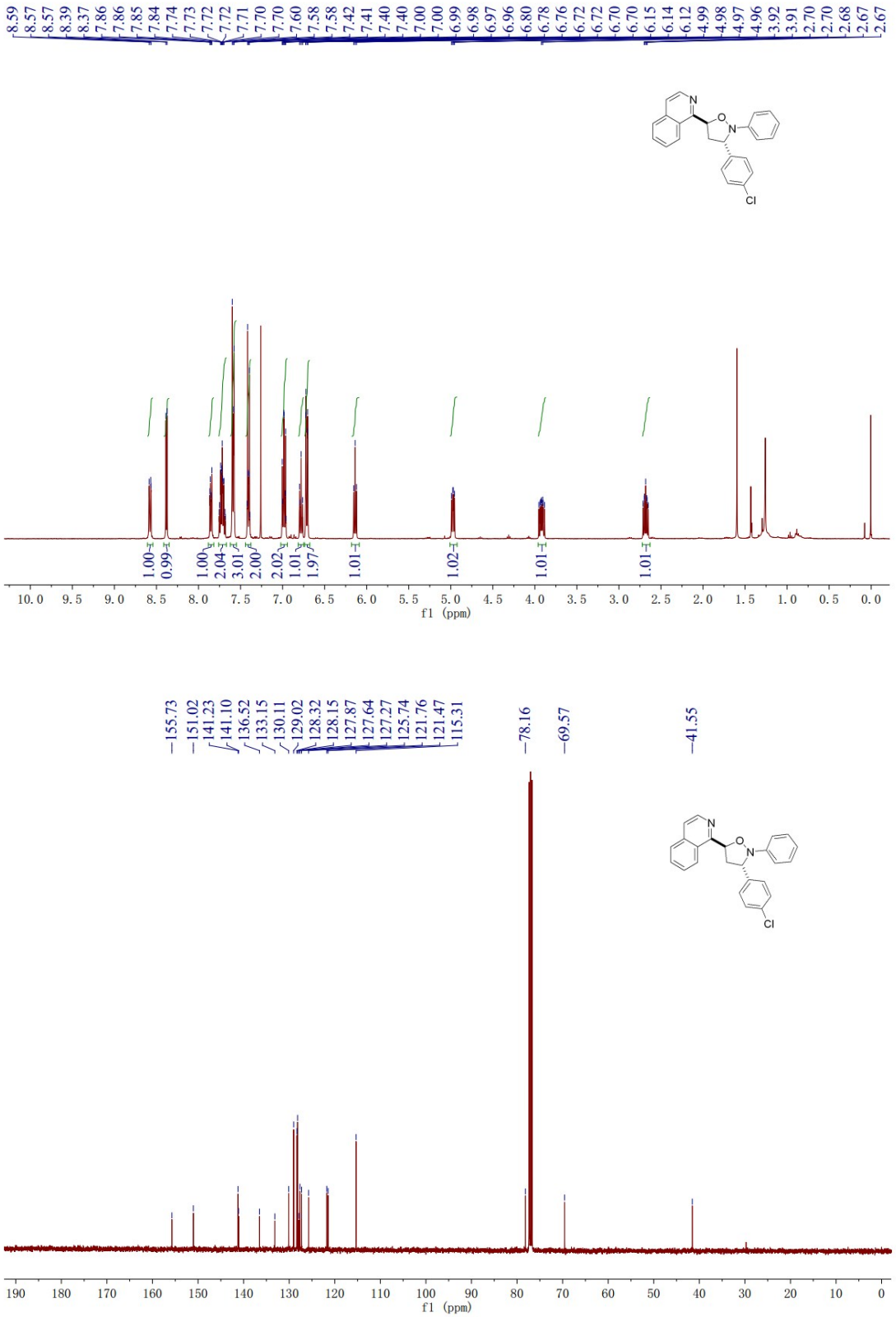


3-(4-Chlorophenyl)-5-(isoquinolin-1-yl)-2-phenylisoxazolidine (*cis*-4p)

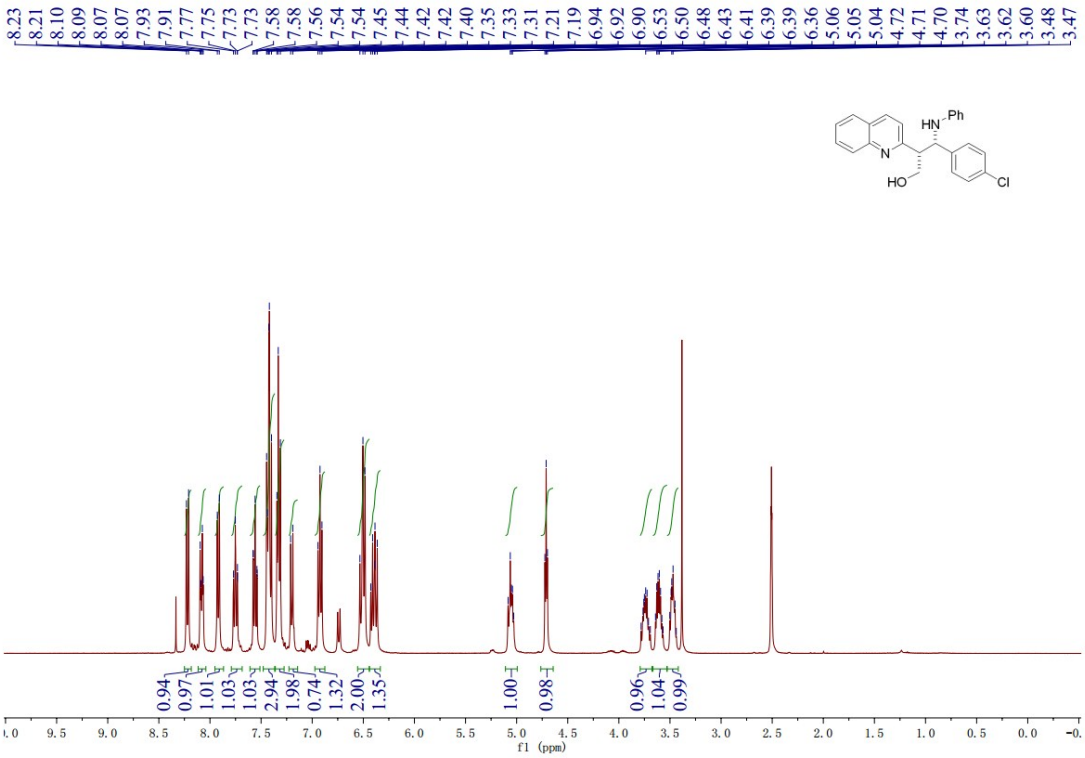


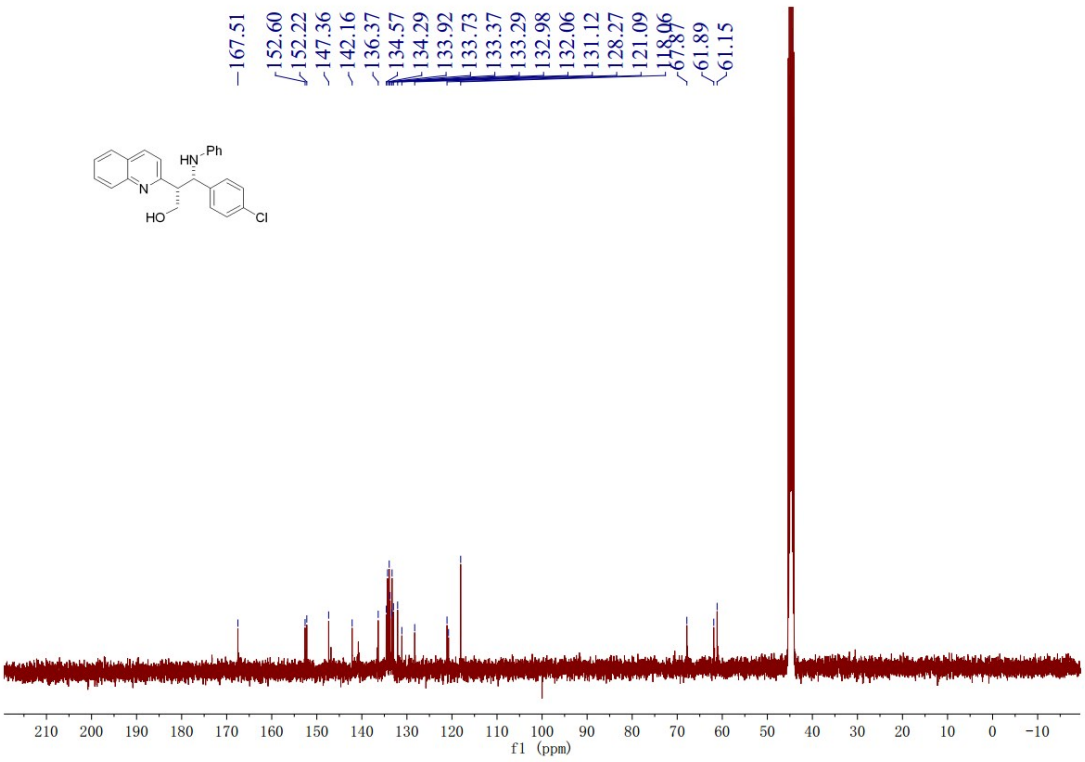


3-(4-Chlorophenyl)-5-(isoquinolin-1-yl)-2-phenylisoxazolidine (*trans*-4p)



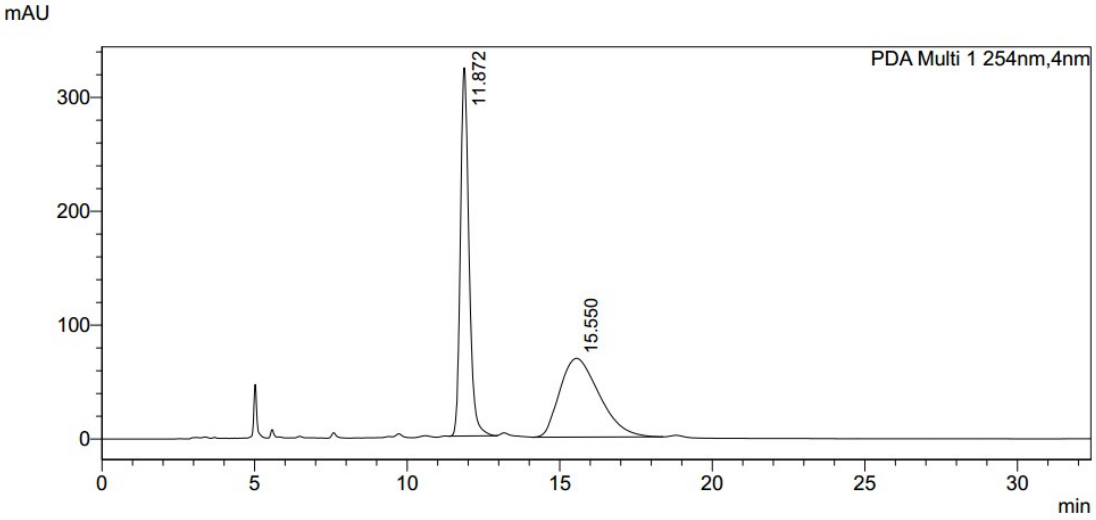
3-(4-Chlorophenyl)-3-(phenylamino)-2-(quinolin-2-yl)propan-1-ol (*cis*-5)





IX. HPLC spectra of the compound *cis*-3x (Table S1, enrty 3)

<Chromatogram>

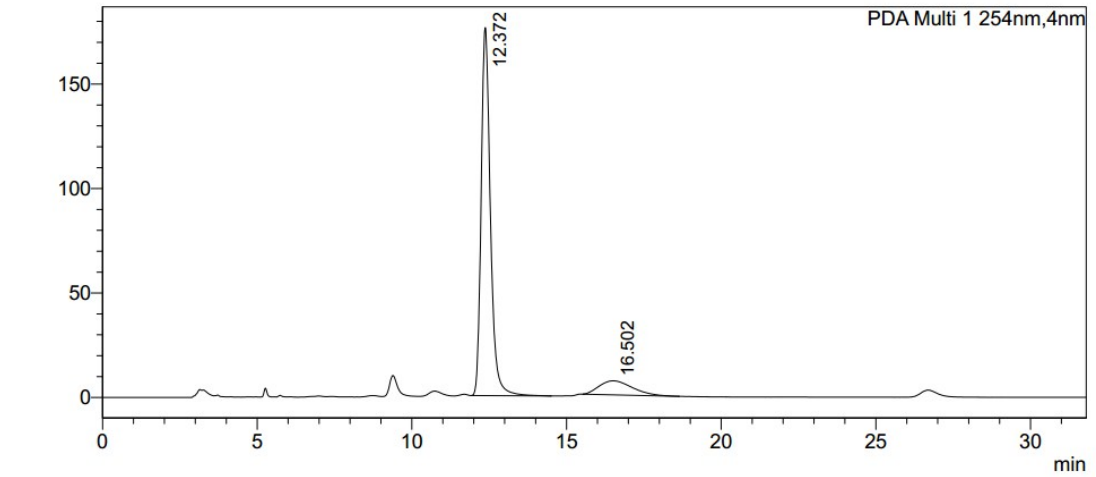


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.872	6340681	323585	50.444	%		RT:11.872
2	15.550	6228939	69187	49.556	%		RT:15.550
Total		12569620	392771				

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.372	3667272	176243	87.967	%		RT:12.372
2	16.502	501626	6709	12.033	%		RT:16.502
Total		4168898	182952				