Supporting information for

Catalytic Asymmetric Synthesis of Diazabicyclo[3.1.0]hexanes by 1,3-Dipolar Cycloaddition of Azomethine Ylides with Azirines.

Alba Molina,[a] *Sergio Díaz-Tendero,*[b,c] *Javier Adrio,*[a,b]* *and Juan C. Carretero*[a,b] *

[a]Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain

[b]Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, 28049 Madrid, Spain

Departamento de Química, Facultad de Ciencias, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain

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1. General methods

All anaerobic and moisture-sensitive manipulations were carried out in anhydrous solvents and under nitrogen. Dichloromethane, toluene, and tetrahydrofuran were dried over the PureSolv MD purification system. Melting points were taken in open-end capillary tubes. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (230-400 mesh). Flash column chromatographies were performed using silica gel (230-400 mesh). NMR spectra were recorded on AU-300 MHz instrument and calibrated using residual undeuterated solvent ($CDCl_3$) as internal reference. MS spectra were recorded on a VG *AutoSpec* mass spectrometer. The HPLC chromatograms of the racemic and enantiomerically enriched cycloadducts are also included.

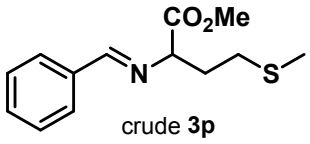
α-Iminoesters (**3a-n**) were prepared by condensation of aminoesters hydrochlorides with the corresponding aldehydes, according to literature procedures.[1] (*E*)-Methyl 2-(benzylideneamino)hept-6-enoate (**3o**) was prepared following the procedure described by Malone and co-workers.[2] Due to their lability all the α-iminoesters once isolated were immediately used in the 1,3-dipolar cycloaddition without further purification. 2*H*-Azirines were prepared following the procedure described by Park and co-workers. [3]

The chromatographic columns were carried out using deactivated silica gel. *Deactivated silica gel preparation*: Et_3N (5 ml) was added to a suspension of 300g of silica gel in cyclohexane, the mixture was stirred for 1h, filtered and dried under reduced pressure on a rotary evaporator.

[1] S. Cabrera, R. Gómez Arrayás, J. C. Carretero, *J. Am. Chem. Soc.* 2005, **127**, 16394.
[2] P. Armstrong, R. Grigg, M. W. Jordan, J. F. Malone, *Tetrahedron* 1985, **41**, 3547.
[3] N. S. Y. Loy, S. Kim, C. M. Park, *Org. Lett*. 2015, **17**, 395.

2. Typical procedure for the synthesis of α-iminoesters

(*E*)-Methyl 2-(benzylideneamino)-4-(methylthio)butanoate (3r)

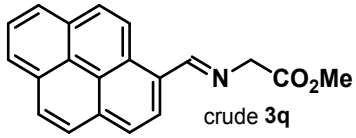


crude **3p**

A suspension of methyl L-methionine methyl ester hydrochloride (0.66 g, 3.3 mmol), $MgSO_4$ (0.66 g) and Et_3N (0.46 mL, 3.3 mmol) in dry dichloromethane (8 mL) was stirred at room temperature for 30 minutes. Benzaldehyde (0.30 mL, 3.0 mmol) in dichloromethane (2 mL) was added and the mixture was stirred 12h at room temperature. Water (10 mL) was added, the organic layer was separated and the aqueous phase was extracted with dichloromethane (15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to afford **3r** (0.78 g, 99%, yellow oil), used without further purification in the next reaction step.

^{1}H NMR (300 MHz, $CDCl_3$) 8.36 (s, 1H), 7.88 – 7.72 (m, 2H), 7.55 – 7.39 (m, 3H), 4.24 (dd, *J* = 8.0, 5.3 Hz, 1H), 3.77 (s, 3H), 2.69 – 2.56 (m, 1H), 2.54 – 2.42 (m, 1H), 2.36 – 2.22 (m, 2H), 2.13 (s, 3H).

(E)-Methyl 2-((pyren-1-ylmethylene)amino)acetate (3s)



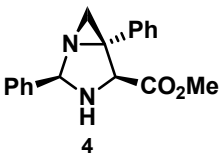
crude **3q**

Following the typical procedure, the reaction of glycine methyl ester hydrochloride (0.52 g, 3.3 mmol), $MgSO_4$ (excess), Et_3N (0.46 mL, 3.3 mmol) and 1-pyrenecarboxaldehyde (0.69 g, 3.0 mmol) in dichloromethane (10 mL) afforded **3s** (0.72 g, 95%, yellow oil).

^{1}H NMR (300 MHz, $CDCl_3$) δ δ 9.34 (s, 1H), 8.91 (d, *J* = 9.3 Hz, 1H), 8.58 (d, *J* = 8.1 Hz, 1H), 8.29 – 8.16 (m, 4H), 8.16 – 7.99 (m, 3H), 4.37 (q, *J* = 6.8 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.70 (s, *J* = 6.8 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

3. Typical procedure for the asymmetric [3+2] cycloaddition of azomethine ylides

(2*R*,4*S*,5*S*) Methyl 2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (4)



4

A suspension of (*R*)-Fesulphos (5.0 mg, 0.011 mmol) and $Cu(CH_3CN)_4PF_6$ (3.7 mg, 0.01 mmol) in DCM (1 mL) under argon atmosphere was stirred for 10 min. A solution of **1a** (23.0 mg, 0.13 mmol) in DCM (1 mL), K^{t}BuO (10 μL, 1 M) and 3-phenyl-2*H*-azirine (11.7 mg, 0.10 mmol) in DCM (1 mL) were successively added. After stirring for 12h at room temperature the mixture was diluted with dichloromethane and filtered over celite®. The crude mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (cyclohexane-EtOAc 10:1) to afford **4** (18.8 mg, 64%, yellow oil).

$[\alpha]_D^{20}$: +30.0 (c = 0.10, $CHCl_3$), 24% *ee*.

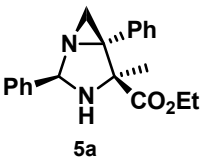
SFC: Chiralpak IA, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 3.4 min (2*R*,4*S*,5*S*)-**4** and 34.4 min (2*S*,4*R*,5*R*)-**4**.

^{1}H NMR (300 MHz, Acetone) δ 7.58 (bd, *J* = 7.5 Hz, 2H), 7.52 (dd, *J* = 6.8, 1.2 Hz, 2H), 7.45 – 7.30 (m, 6H), 5.44 (d, *J* = 10.5 Hz, 1H), 4.24 (d, *J* = 9.5 Hz, 1H), 3.74 (s, 3H), 3.06 (bt, *J* = 9.8 Hz, 1H), 2.09 (s, 1H), 1.84 (s, 1H).

^{13}C NMR (75 MHz, Acetone) δ 172.4, 139.8, 139.5, 129.3, 129.0, 128.9, 128.8, 128.3, 127.6, 81.5, 65.6, 54.0, 52.7, 27.5.

HRMS (ESI+): Calculated for $C_{18}H_{19}N_2O_2$, 295.1441; found, 295.1450 ([M+H], 37).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5a)



5a

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.10 mmol) and **3a** (26.7 mg, 0.13 mmol) afforded after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1) the cycloadduct **5a** (24.4 mg, 76%, yellow oil).

$[\alpha]_D^{20}$: +166.0 (c = 0.10, $CHCl_3$), 95% *ee*.

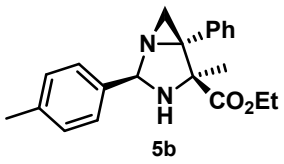
SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 2.9 min (2*R*,4*S*,5*S*)-**5a** and 3.3 min (2*S*,4*R*,5*R*)-**5a**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.56 (m, 2H), 7.49 – 7.30 (m, 8H), 5.60 (d, *J* = 11.8 Hz, 1H), 4.30 (qd, *J* = 7.1, 2.5 Hz, 2H), 3.45 (d, *J* = 11.8 Hz, 1H), 2.04 (s, 1H), 1.76 (s, 1H), 1.36 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 138.1, 137.3, 129.5, 128.6, 128.1, 128.0, 127.7, 126.8, 79.3, 68.2, 62.1, 57.1, 29.1, 21.3, 14.3.

HRMS (ESI+): Calculated for $C_{20}H_{23}N_2O_2$, 323.1754; found, 323.1757 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*p*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5b)



5b

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3b** (28.5 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5b** (26.6 mg, 79%, yellow oil).

$[\alpha]_D^{20}$: +40.0 (c = 0.10, $CHCl_3$), 87% *ee*.

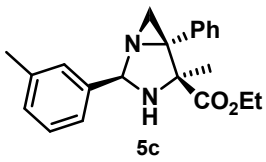
HPLC: Daicel Chiralpak IB, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 8.6 min (2*R*,4*S*,5*S*)-**5b** and 9.8 min (2*S*,4*R*,5*R*)-**5b**.

^{1}H NMR (300 MHz, Acetone) δ 7.53 – 7.40 (m, 4H), 7.37 – 7.26 (m, 3H), 7.21 (d, *J* = 7.9 Hz, 2H), 5.49 (d, *J* = 11.6 Hz, 1H), 4.38 – 4.18 (m, 2H), 3.35 (d, *J* = 11.7 Hz, 1H), 2.33 (s, 3H), 1.99 (s, 1H), 1.56 (s, 1H), 1.33 – 1.24 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 174.0, 138.8, 138.2, 136.7, 130.2, 129.8, 128.5, 128.2, 127.4, 79.6, 68.8, 62.4, 57.4, 29.3, 21.5, 21.1, 14.4.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2$, 337.1910; found, 337.1918 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*m*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5c)



5c

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3c** (28.5 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5c** (24.4 mg, 85%, yellow oil).

$[\alpha]_D^{20}$: +39.2 (c = 0.10, $CHCl_3$), 91% *ee*.

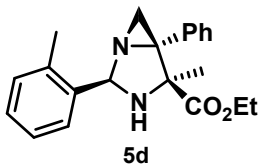
HPLC: Daicel Chiralpak IB, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 7.8 min (2*R*,4*S*,5*S*)-**5c** and 8.8 min (2*S*,4*R*,5*R*)-**5c**.

^{1}H NMR (300 MHz, Acetone) δ 7.56 – 7.46 (m, 2H), 7.40 – 7.24 (m, 6H), 7.16 (d, *J* = 7.4 Hz, 1H), 5.51 (d, *J* = 11.7 Hz, 1H), 4.38 – 4.22 (m, 2H), 3.38 (d, *J* = 11.7 Hz, 1H), 2.36 (s, 3H), 2.00 (s, 1H), 1.59 (s, 1H), 1.36 – 1.18 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 173.9, 139.5, 138.7, 138.6, 130.1, 129.2, 129.0, 128.4, 128.0, 124.3, 79.5, 79.5, 72.2, 68.6, 68.5, 62.3, 57.2, 21.3, 14.3.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2$, 337.1910; found, 337.1925 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*o*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5d)



5d

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3d** (28.5 mg, 0.13 mmol) afforded, after

purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5d** (28.3 mg, 84%, yellow oil).

$[\alpha]_D^{20}$: +82.2 (c = 0.10, $CHCl_3$), 70% *ee*.

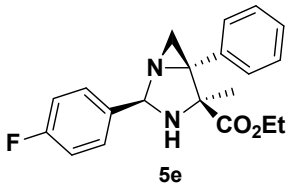
HPLC: Daicel Chiralpak ID, hexane-isopropanol 95-5, flow rate 1 mL/min (λ = 254 nm), t_R: 6.3 min (2*S*,4*R*,5*R*)-**5d** and 7.2 min (2*R*,4*S*,5*S*)-**5d**.

^{1}H NMR (300 MHz, Acetone) δ 7.58 – 7.49 (m, 3H), 7.39 – 7.27 (m, 3H), 7.27 – 7.19 (m, 3H), 5.59 (d, *J* = 11.4 Hz, 1H), 4.43 – 4.16 (m, 2H), 3.32 (d, *J* = 11.3 Hz, 1H), 2.55 (s, 3H), 2.23 (s, 1H), 1.64 (s, 1H), 1.43 – 1.25 (m, 6H).

^{13}C NMR (75 MHz, Acetone) δ 174.1, 138.9, 138.3, 136.9, 131.3, 130.2, 128.7, 128.5, 128.2, 126.4, 125.9, 77.4, 68.7, 62.4, 56.2, 21.4, 19.8, 14.4.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2$, 337.1918; found, 337.1918 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 2-(4-fluorophenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5e)



5e

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3e** (29.0 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5e** (19.0 mg, 55%, white oil).

$[\alpha]_D^{20}$: +58 (c = 0.10, $CHCl_3$), 98% *ee*.

SFC: Chiralpak ID, hexane-isopropanol 97-3, flow rate 2 mL/min (λ = 254 nm), t_R: 5.2 min (2*R*,4*S*,5*S*)-**5e** and (2*S*,4*R*,5*R*)-**5e**.

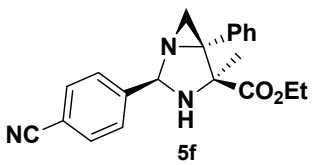
^{1}H NMR (300 MHz, Acetone) δ 7.65 – 7.56 (m, 2H), 7.57 – 7.46 (m, 2H), 7.40 – 7.27 (m, 3H), 7.24 – 7.09 (m, 2H), 5.53 (d, *J* = 11.5 Hz, 1H), 4.36 – 4.22 (m, 2H), 3.37 (d, *J* = 11.5 Hz, 1H), 2.04 (s, 1H), 1.60 (s, 1H), 1.38 – 1.26 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 206.1, 173.9, 163.2 (d, *J* = 244.0 Hz), 135.9 (d, *J* = 3.1 Hz), 130.2, 129.5 (d, *J* = 8.1 Hz), 128.5, 128.2, 115.9 (d, *J* = 21.5 Hz), 79.1, 68.8, 62.4, 57.5, 29.8, 29.4, 21.4, 14.4.

^{19}F NMR (282 MHz, Acetone) δ -116.27.

HRMS (ESI+): Calculated for $C_{20}H_{22}N_2O_2F$, 341.1659; found, 341.1657 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 2-(4-cyanophenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5f)



5f

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3f** (30.0 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5f** (29.9 mg, 86%, white oil).

$[\alpha]_D^{20}$: +130.0 (c = 0.10, $CHCl_3$), 92% *ee*.

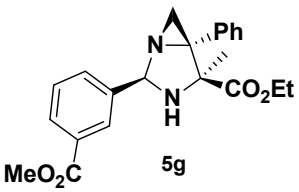
HPLC: Daicel Chiralpak IB, hexane-isopropanol 98-2, flow rate 1 mL/min (λ = 254 nm), t_R: 25.9 min (2*R*,4*S*,5*S*)-**5f** and 35.7 min (2*S*,4*R*,5*R*)-**5f**.

^{1}H NMR (300 MHz, Acetone) δ 7.86 – 7.75 (m, 4H), 7.55 – 7.48 (m, 2H), 7.40 – 7.28 (m, 3H), 5.62 (d, *J* = 11.2 Hz, 1H), 4.42 – 4.15 (m, 2H), 3.45 (d, *J* = 11.2 Hz, 1H), 2.07 (s, 1H), 1.65 (s, 1H), 1.36 – 1.25 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 173.7, 145., 138.4, 133.1, 130.2, 128.7, 128.6, 128.3, 119.2, 112.5, 79.2, 68.8, 62.5, 57.5, 29.8, 21.4, 14.3.

HRMS (ESI+): Calculated for $C_{21}H_{22}N_3O_2$, 348.1706; found, 348.1709 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 2-(3-(methoxycarbonyl)phenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5g)



5g

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3g** (34.2 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 8:1), the cycloadduct **5g** (24.4 mg, 63%, white oil).

$[\alpha]_D^{20}$: +100.0 (c = 0.10, $CHCl_3$), 91% *ee*.

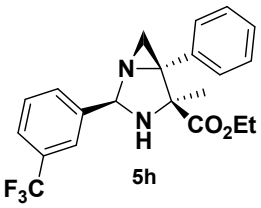
HPLC: Daicel Chiralpak IB, hexane-isopropanol 99-1, flow rate 01 mL/min (λ = 254 nm), t_R: 8.5 min (2*R*,4*S*,5*S*)-**5g** and 11.8 min (2*S*,4*R*,5*R*)-**5g**.

^{1}H NMR (300 MHz, Acetone) δ 8.25 (s, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.62 – 7.51 (m, 3H), 7.44 – 7.26 (m, 3H), 5.63 (d, *J* = 11.2 Hz, 1H), 4.38 – 4.22 (m, 2H), 3.92 (s, 3H), 3.47 (d, *J* = 11.5 Hz, 1H), 2.08 (s, 1H), 1.64 (s, 1H), 1.41 – 1.24 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 173.8, 167.1, 140.3, 138.6, 132.1, 131.3, 130.2, 129.6, 129.6, 128.5, 128.5, 128.3, 79.2, 68.8, 62.4, 57.5, 52.4, 29.8, 29.4, 21.4, 14.4.

HRMS (APCI+): Calculated for $C_{22}H_{25}N_2O_4$, 381.1809; found, 381.1822 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(3-(trifluoromethyl)phenyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5h)



5h

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3h** (29.0 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5h** (21.1 mg, 54%, white oil).

$[\alpha]_D^{20}$: +92.2 (c = 0.10, $CHCl_3$), 96% *ee*.

SFC: Daicel Chiralpak OD, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 9.5 min (2*R*,4*S*,5*S*)-**5h** and 28.9 min (2*S*,4*R*,5*R*)-**5h**.

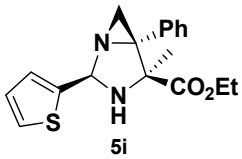
^{1}H NMR (300 MHz, Acetone) δ 7.91 – 7.84 (m, 2H), 7.75 – 7.63 (m, 2H), 7.55 – 7.49 (m, 2H), 7.39 – 7.29 (m, 3H), 5.64 (d, *J* = 11.2 Hz, 1H), 4.36 – 4.23 (m, 2H), 3.47 (d, *J* = 11.3 Hz, 1H), 2.10 (s, 1H), 1.65 (s, 1H), 1.36 – 1.25 (m, 6H).

^{13}C NMR (125 MHz, Acetone) δ 173.7, 141.2, 138.5, 131.5, 130.9 (q, *J* = 32.0 Hz), 130.3, 130.2, 128.6, 128.4, 128.3, 125.4 (q, *J* = 3.8 Hz), 125.3 (q, *J* = 271.5 Hz), 124.3 (q, *J* = 3.9 Hz), 122.1, 79.0, 79.0, 72.3, 68.8, 68.8, 62.4, 57.5, 57.5, 29.8, 21.4, 14.4.

^{19}F NMR (282 MHz, Acetone) δ -63.04.

HRMS (ESI+): Calculated for $C_{21}H_{22}N_2O_2F_3$, 391.1627; found, 391.1621 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(thiophen-2-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5i)



5i

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3i** (27.4 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5i** (28.6 mg, 87%, white oil).

$[\alpha]_D^{20}$: +41.6 (c = 0.10, $CHCl_3$), 90% *ee*.

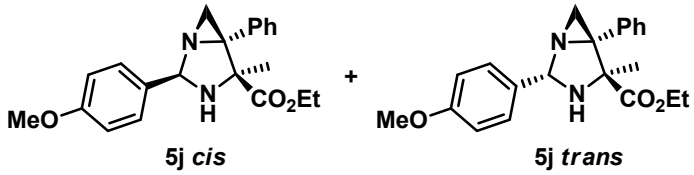
SFC: Chiralpak IA, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 3.2 min (2*S*,4*R*,5*R*)-**5i** and 3.4 min (2*R*,4*S*,5*S*)-**5i**.

^{1}H NMR (300 MHz, Acetone) δ 7.52 – 7.47 (m, 2H), 7.45 (d, *J* = 6.1 Hz, 1H), 7.39 – 7.26 (m, 3H), 7.19 (d, *J* = 2.4 Hz, 1H), 7.05 (dd, *J* = 6.1, 2.4 Hz, 1H), 5.66 (d, *J* = 11.2 Hz, 1H), 4.39 – 4.22 (m, 2H), 3.47 (d, *J* = 11.2 Hz, 1H), 2.17 (s, 1H), 1.61 (s, 1H), 1.34 – 1.28 (m, 3H), 1.27 (s, 3H).

^{13}C NMR (125 MHz, Acetone) δ 173.7, 142.1, 138.4, 130.2, 128.5, 128.3, 127.6, 126.0, 125.8, 76.7, 72.3, 68.9, 68.9, 62.5, 60.8, 21.5, 14.4.

HRMS (ESI+): Calculated for $C_{18}H_{21}N_2O_2S$, 329.1318; found, 329.1323 ([M+H], 100).

(2R,4S,5S)-Ethyl 2-(4-methoxyphenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5j *cis* and 5j *trans*)



5j *cis* + 5j *trans*

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3j** (30.6 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), diasteromer mixture in 2: 1 ratio of **5j *cis*** and **5j *trans*** (18.0 mg, 51%, white oil).

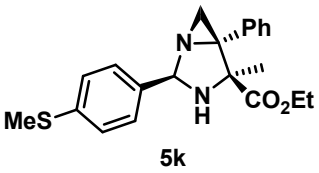
$[\alpha]_D^{20}$: +60 (c = 0.10, $CHCl_3$), 80% ee.

SFC: Chiralpak IC, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 230 nm), t_R: 3.5 min (2S,4R,5R,6S)-**5j** and 3.8 min (2R,4S,5S,6R)-**5j**.

^{1}H NMR (300 MHz, Acetone) δ 7.59 – 7.44 (m, 4H), 7.41 – 7.21 (m, 3H), 7.02 – 6.91 (m, 2H), 5.51-5.49 (m, 1H), 4.43 – 4.17 (m, 2H), 3.83 (s, 3H), 3.35 (d, *J* = 11.2 Hz, 1H), 2.03 (s, 1H), 1.58 (s, 1H), 1.48 – 1.18 (m, 6H).

^{13}C NMR (75 MHz, Acetone) δ 174.5, 174.0, 160.3, 159.8, 138.9, 138.9, 137.6, 131.7, 130.5, 130.2, 129.2, 128.6, 128.5, 128.4, 128.2, 128.0, 114.6, 113.8, 81.2, 79.3, 68.8, 68.8, 62.4, 62.4, 58.5, 57.4, 55.5, 55.4, 33.3, 24.5, 21.5, 14.4.

(2R,4S,5S)-Ethyl 2-(4-methoxyphenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5k)



5k

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3k** (32.6 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5k** (15.0 mg, 41%, white oil).

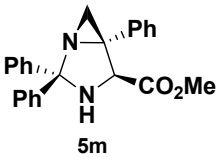
$[\alpha]_D^{20}$: +43 (c = 0.10, $CHCl_3$), 98% ee.

SFC: Chiralpak IC, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 230 nm), t_R: 3.5 min (2S,4R,5R,6S)-**5k** and 3.8 min (2R,4S,5S,6R)-**5k**.

^{1}H NMR (300 MHz, Acetone) δ 7.59 – 7.42 (m, 4H), 7.39 – 7.19 (m, 5H), 5.51 (d, *J* = 11.5 Hz, 1H), 4.43 – 4.16 (m, 2H), 3.36 (d, *J* = 11.4 Hz, 1H), 2.51 (s, 3H), 2.01 (s, 1H), 1.59 (s, 1H), 1.39 – 1.13 (m, 6H).

^{13}C NMR (75 MHz, Acetone) δ 173.9, 139.2, 138.8, 136.4, 130.2, 128.5, 128.2, 128.1, 127.0, 79.3, 79.3, 68.8, 68.7, 62.4, 57.5, 57.5, 21.5, 21.44, 15.4, 14.4.

(4S,5S)-Methyl 2,2,5-triphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5m)



5m

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3m** (73.6 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5m** (31.4 mg, 85%, white oil).

$[\alpha]_D^{20}$: +60 (c = 0.10, $CHCl_3$), 67% *ee*.

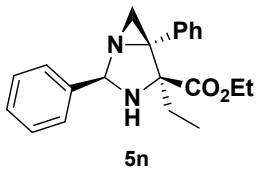
SFC: Daicel Chiralpak ID, hexane-isopropanol 95-5, flow rate 1 mL/min (λ = 254 nm), t_R: 5.1 min (4R, 5S)-**5m** and 5.4 min (4S,5S)-**5m**.

^{1}H NMR (300 MHz, Acetone) δ 8.04 – 7.97 (m, 2H), 7.73 – 7.66 (m, 2H), 7.42 – 7.16 (m, 11H), 3.94 (d, *J* = 10.8 Hz, 1H), 3.75 (s, 3H), 3.53 (d, *J* = 10.8 Hz, 1H), 2.13 (s, 1H), 2.01 (s, 1H).

^{13}C NMR (75 MHz, Acetone) δ 171.3, 149.1, 147.3, 140.2, 129.1, 128.7, 128.1, 127.7, 127.5, 127.4, 126.9, 126.6, 91.9, 65.9, 65.8, 56.0, 50.7, 35.7.

HRMS (ESI+): Calculated for $C_{24}H_{23}N_2O_2$, 371.1754; found, 371.1760 ([M+H], 100).

(2*R*,4*S*,5*S*) Methyl 4-ethyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5n)



5n

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **5n** (28.5 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5n** (21.9 mg, 68%, white oil).

$[\alpha]_D^{20}$: +176 (c = 0.10, $CHCl_3$), 92% *ee*.

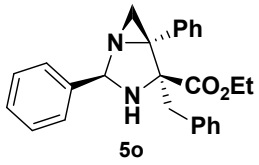
HPLC: Daicel Chiralpak IA, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 6.8 min (2*R*,4*S*,5*S*)-**5n** and 9.2 min (2*S*,4*R*,5*R*)-**5n**.

^{1}H NMR (300 MHz, Acetone) δ 7.62 – 7.55 (m, 2H), 7.54 – 7.46 (m, 2H), 7.45 – 7.27 (m, 6H), 5.49 (d, *J* = 11.9 Hz, 1H), 3.84 (s, 3H), 3.28 (d, *J* = 11.6 Hz, 1H), 1.87 (s, 1H), 1.73 – 1.47 (m, 3H), 0.85 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 173.9, 139.7, 138.7, 130.6, 129.3, 128.7, 128.5, 128.2, 127.4, 79.7, 73.6, 57.3, 52.9, 27.2, 9.5.

HRMS (ESI+): Calculated for $C_{20}H_{23}N_2O_2$, 323.1754; found, 323.1748 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-benzyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5o)



5o

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3o** (36.6 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5o** (27.1 mg, 68%, yellow oil).

$[\alpha]_D^{20}$: +66 (c = 0.10, $CHCl_3$), 89% *ee*.

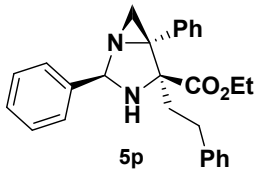
SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 2.3 min (2*S*,4*R*,5*R*)-**5o** and 2.5 min (2*R*,4*S*,5*S*)-**5o**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 2H), 7.60 – 7.52 (m, 2H), 7.42 – 7.33 (m, 6H), 7.31 – 7.15 (m, 5H), 5.75 (d, *J* = 10.0 Hz, 1H), 4.31 – 4.08 (m, 2H), 3.28 (d, *J* = 10.7 Hz, 1H), 3.05 – 2.82 (m, 2H), 1.97 (s, 1H), 1.79 (s, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 172.6, 139.6, 138.5, 138.4, 131.6, 131.1, 129.3, 128.7, 128.5, 128.4, 128.4, 127.5, 127.1, 79.5, 73.7, 62.4, 57.5, 39.4, 28.8, 14.4.

HRMS (ESI+): Calculated for $C_{26}H_{27}N_2O_2$, 399.2067; found, 399.2077 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-phenethyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5p)



Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3p** (38.4 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5p** (23.1 mg, 56%, white oil).

$[\alpha]_D^{20}$: +40.1 (c = 0.10, $CHCl_3$), 92% *ee*.

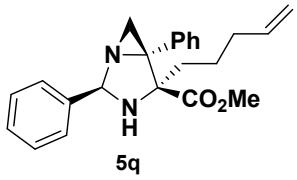
HPLC: Daicel Chiralpak IB, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 8.5 min (2*R*,4*S*,5*S*)-**5p** and 11.8 min (2*S*,4*R*,5*R*)-**5p**.

^{1}H NMR (300 MHz, Acetone) δ 7.73 – 7.65 (m, 2H), 7.52 – 7.25 (m, 10H), 7.23 – 7.11 (m, 3H), 5.64 (d, *J* = 10.4 Hz, 1H), 4.42 – 4.14 (m, 2H), 3.47 (d, *J* = 10.8 Hz, 1H), 3.01 (ddd, *J* = 15.6, 10.5, 5.3 Hz, 1H), 2.48 (ddd, *J* = 13.5, 11.0, 6.0 Hz, 1H), 2.10 – 1.92 (m, 3H), 1.79 (s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) 172.4, 142.2, 138.7, 137.6, 129.8, 128.4, 128.4, 128.2, 127.8, 127.6, 127.3, 126.6, 125.6, 78.9, 71.7, 61.7, 56.5, 54.1, 35.7, 31.3, 13.6.

HRMS (ESI+): Calculated for $C_{27}H_{29}N_2O_2$, 413.2223; found, 413.2220 ([M+H], 100).

(2*R*,4*S*,5*S*) Methyl 4-(pent-4-en-1-yl)-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5q)



Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (23.4 mg, 0.2 mmol) and (*E*)-methyl 2-(benzylideneamino)hept-6-enoate (73.6 mg, 0.26 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5q** (45.6 mg, 63%, white oil).

$[\alpha]_D^{20}$: +125.9 (c = 0.10, $CHCl_3$), 93% *ee*.

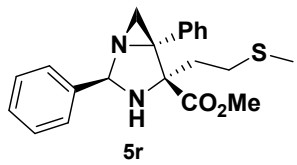
HPLC: Daicel Chiralpak ID, hexane-isopropanol 95-5, flow rate 1 mL/min (λ = 254 nm), t_R: 5.6 min (1S,3R,3aS,6aR)-**5q** and 6.0 min (1R,3S,3aR,6aS)-**5q**.

^{1}H NMR (300 MHz, Acetone) δ 7.61 – 7.54 (m, 2H), 7.53 – 7.46 (m, 2H), 7.45 – 7.38 (m, 2H), 7.38 – 7.27 (m, 4H), 5.82 – 5.65 (m, 1H), 5.50 (d, *J* = 11.7 Hz, 1H), 5.03 – 4.80 (m, 2H), 3.84 (s, 3H), 3.32 (d, *J* = 11.9 Hz, 1H), 1.97 (q, *J* = 6.8 Hz, 1H), 1.87 (s, 1H), 1.81 – 1.52 (m, 2H), 1.25 – 1.07 (m, 1H).

^{13}C NMR (75 MHz, Acetone) δ 174.0, 139.6, 139.5, 138.6, 130.61, 129.3, 128.7, 128.5, 128.2, 127.4, 114.8, 79.7, 72.9, 57.3, 52.9, 34.4, 33.7, 29.1, 25.2.

HRMS (APCI+): Calculated for $C_{23}H_{27}N_2O_2$, 363.2067; found, 363.2066 ([M+H], 100).

(2R,4S,5S)-Ethyl 4-(2-(methylthio)ethyl)-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5r)



5r

Following the typical procedure, the reaction of 3-phenyl-2*H*-azirine (11.7 mg, 0.1 mmol) and **3r** (32.7 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5r** (16.0 mg, 44%, white oil).

$[\alpha]_D^{20}$: +204.0 (c = 0.10, $CHCl_3$), 30% *ee*.

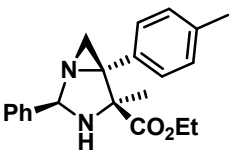
HPLC: Chiralpak ID, hexane-isopropanol 95-5, flow rate 1 mL/min (λ = 254 nm), t_R: 8.4 min (2*S*,4*R*,5*R*)-**5r** and 9.3 min (2*R*,4*S*,5*S*)-**5r**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.53 (m, 2H), 7.49 – 7.31 (m, 8H), 5.53 (d, *J* = 11.6 Hz, 1H), 3.83 (s, 3H), 3.33 (d, *J* = 11.7 Hz, 1H), 2.75 (ddd, *J* = 12.6, 9.7, 5.0 Hz, 1H), 2.36 (ddd, *J* = 12.7, 10.2, 6.4 Hz, 1H), 2.01 (s, 3H), 1.99 – 1.87 (m, 3H), 1.73 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 137.9, 136.7, 129.6, 128.5, 128.0, 128.0, 128.0, 126.7, 79.2, 57.0, 52.6, 33.1, 30.0, 28.8, 15.7.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2S$, 369.1631; found, 369.1646 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-2-phenyl-5-(*p*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5s)



5s

Following the typical procedure, the reaction of 3-(*p*-tolyl)-2H-azirine (19.7 mg, 0.15 mmol) and **3a** (41.1 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5s** (47.9 mg, 95%, brown oil).

$[\alpha]_D^{20}$: +280.0 (c = 0.10, $CHCl_3$), 99% *ee*.

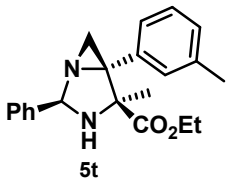
SFC: Daicel Chiralpak OD, hexane-isopropanol 99-1, flow rate 1 mL/min (λ = 254 nm), t_R: 10.7 min (2*S*,4*R*,5*R*)-**5s** and 13.4 min (2*R*,4*S*,5*S*)-**5s**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 – 7.60 (m, 2H), 7.48 – 7.33 (m, 5H), 7.18 (d, *J* = 7.9 Hz, 2H), 5.62 (s, 1H), 4.33 (m, 2H), 3.47 (bs, 1H), 2.40 (s, 3H), 2.05 (s, 1H), 1.76 (s, 1H), 1.39 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 174.0, 139.8, 137.7, 135.8, 130.2, 129.2, 129.2, 128.6, 127.5, 79.7, 68.8, 62.4, 57.2, 29.4, 21.5, 21.2, 14.4.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2$, 337.1910; found, 337.1906 ([M+H], 65).

(2*R*,4*S*,5*S*) Ethyl 4-methyl-2-phenyl-5-(*m*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5t)



5t

Following the typical procedure, the reaction of 3-(*m*-tolyl)-2H-azirine (19.7 mg, 0.15 mmol) and **3a** (41.1 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5t** (38.8 mg, 77%, yellow oil).

$[\alpha]_D^{20}$: +115.0 (c = 0.10, $CHCl_3$), 91% *ee*.

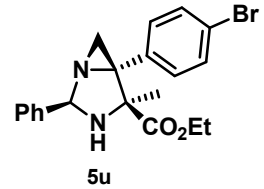
SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 1.7 min (2*S*,4*R*,5*R*)-**5t** and 1.8 min (2*R*,4*S*,5*S*)-**5t**.

^{1}H NMR (300 MHz, Acetone) δ 7.57 (dd, *J* = 7.4, 0.7 Hz, 2H), 7.46 – 7.27 (m, 5H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 5.54 (d, *J* = 11.7 Hz, 1H), 4.52 – 4.15 (m, 2H), 3.39 (d, *J* = 11.6 Hz, 1H), 2.34 (s, 3H), 1.99 (s, 1H), 1.58 (s, 1H), 1.41 – 1.22 (m, 6H).

^{13}C NMR (75 MHz, Acetone) δ 174.0, 139.7, 138.7, 137.9, 130.8, 129.2, 128.9, 128.6, 128.4, 127.5, 127.3, 79.7, 68.7, 62.4, 57.5, 29.4, 21.4, 21.4, 14.4.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_2$, 337.1910; found, 337.1902 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 5-(4-bromophenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5u)



5u

Following the typical procedure, the reaction of 3-(*p*-Bromobencene)-2*H*-azirine (39.9 mg, 0.20 mmol) and **3a** (53.4 mg, 0.26 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5u** (66.0 mg, 82%, yellow oil).

$[\alpha]_D^{20}$: +332.0 (c = 0.10, $CHCl_3$), 97% *ee*.

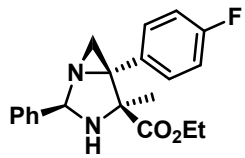
SFC: Daicel Chiralpak OD, hexane-isopropanol 97-3, flow rate 1 mL/min (λ = 254 nm), t_R: 7.1 min (2*R*,4*S*,5*S*)-**5u** and 8.6 min (2*S*,4*R*,5*R*)-**5u**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 2H), 7.49 – 7.44 (m, *J* = 8.4 Hz, 2H), 7.43 – 7.32 (m, 5H), 5.56 (d, *J* = 10.4 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.42 (d, *J* = 10.9 Hz, 1H), 2.02 (s, 1H), 1.71 (s, 1H), 1.33 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 137.9, 136.5, 131.2, 131.1, 128.6, 128.2, 126.8, 121.8, 79.2, 68.1, 62.1, 56.4, 29.1, 21.3, 14.3.

HRMS (ESI+): Calculated for $C_{20}H_{22}N_2O_2Br$, 401.0859; found, 401.0862 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 5-(4-fluorophenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5v)



5v

Following the typical procedure, the reaction of 3-(*p*-Fluorobencene)-2*H*- azirine (20.2 mg, 0.15 mmol) and **3a** (41.1 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5v** (57.0 mg, 84%, white oil).

$[\alpha]_D^{20}$: +232 (c = 0.10, $CHCl_3$), 92% *ee*.

SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 210 nm), t_R: 1.7 min (2*S*,4*R*,5*R*)-**5v** and 2.0 min (2*R*,4*S*,5*S*)-**5v**.

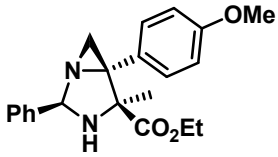
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.54 (m, 2H), 7.51 – 7.31 (m, 5H), 7.06 – 6.95 (m, 2H), 5.57 (s, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.41 (s, 1H), 2.02 (s, *J* = 25.8 Hz, 1H), 1.71 (s, *J* = 20.7 Hz, 1H), 1.45 – 1.21 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 162.3 (d, *J* = 246.2 Hz), 138.0, 133.0 (d, *J* = 3.2 Hz), 131.0 (d, *J* = 8.1 Hz), 128.6, 128.1, 126.8, 114.8 (d, *J* = 21.5 Hz), 79.2, 68.2, 62.0, 56.3, 29.1, 21.3, 14.3.

^{19}F NMR (282 MHz, $CDCl_3$): δ -114.32.

HRMS (ESI+): Calculated for $C_{20}H_{22}N_2O_2F$, 341.1659 ; found, 341.1667 ([M+H], 100).

(2*R*,4*S*,5*S*) Ethyl 5-(4-methoxyphenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5w)



5w

Following the typical procedure, the reaction of *N*-methylmaleimide (11.1 mg, 0.10 mmol) and **3a** (36.8 mg, 0.13 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **5w** (12.3 mg, 35%, brown oil).

$[\alpha]_D^{20}$: +96 (c = 0.10, $CHCl_3$), 90% *ee*.

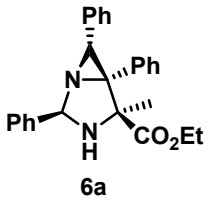
HPLC: Daicel Chiralpak AS-H, hexane-isopropanol 80-20, flow rate 0.7 mL/min (λ = 230 nm), t_R: 30.0 min (1S,3R,3aS,6aR)-**5w** and 36.4 min (1R,3S,3aR,6aS)- **5w**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.48 (m, 1H), 7.48 – 7.43 (m, 1H), 7.33 – 7.27 (m, 2H), 4.89 (d, J = 8.2 Hz, 1H), 4.12 (d, J = 6.7 Hz, 1H), 3.93 (s, 3H), 3.72 (t, J = 8.0 Hz, 1H), 3.62 (t, J = 7.3 Hz, 1H), 2.89 (s, 3H), 2.51 (t, J = 6.9 Hz, 2H), 1.73 – 1.46 (m, 4H), 1.01 (t, J = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 174.1, 160.0, 139.8, 131.4, 130.6, 129.2, 128.6, 127.5, 113.9, 79.6, 68.9, 62.4, 56.9, 55.5, 29.4, 21.5, 14.4.

HRMS (ESI+): Calculated for $C_{21}H_{25}N_2O_3$, 353.1859; found, 353.1860 ([M+H], 100).

(2R,4S,5S,6R) Ethyl 4-methyl-2,5,6-triphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6a)



6a

Following the typical procedure, the reaction of 2,3-diphenyl-2*H*-azirine (29.0 mg, 0.15 mmol) and **3a** (41.1 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct **6a** (22.1 mg, 37%, white oil).

$[\alpha]_D^{20}$: +41 (c = 0.10, $CHCl_3$), 97% ee.

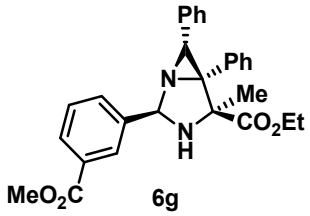
SFC: Daicel Chiralpak OD, hexane-isopropanol 99.2-0.8, flow rate 1 mL/min (λ = 254 nm), t_R: 7.3 min (2R,4S,5S,6R)-**6a** and 8.7 min (2S,4R,5R,6S)-**6a**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 6.7, 1.3 Hz, 2H), 7.43 – 7.28 (m, 5H), 7.22 – 7.12 (m, 2H), 7.13 – 6.95 (m, 6H), 5.77 (d, *J* = 12.0 Hz, 1H), 4.44 – 4.22 (m, 2H), 3.60 (d, *J* = 11.9 Hz, 1H), 3.27 (s, 1H), 1.46 – 1.23 (m, 6H).

^{13}C NMR (75 MHz, Acetone) δ 173.9, 139.7, 137.4, 135.0, 129.3, 128.7, 128.4, 128.0, 127.5, 127.3, 80.8, 70.3, 65.2, 62.6, 40.9, 22.2, 14.5.

HRMS (ESI+): Calculated for $C_{26}H_{27}N_2O_2$, 399.2067; found, 399.2061 ([M+H], 100).

(2R,4S,5S,6R)-Ethyl 2-(3-(methoxycarbonyl)phenyl)-4-methyl-5,6-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6g)



6g

Following the typical procedure, the reaction of 2,3-diphenyl-2*H*-azirine (29.0 mg, 0.15 mmol) and **3g** (52.66 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct *endo*-**2h** (21.2 mg, 37%, white oil).

$[\alpha]_D^{20}$: +62 (c = 0.10, $CHCl_3$), ≥98% ee.

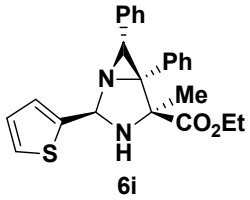
SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 254 nm), t_R: 7.3 min (2R,4S,5S,6R)-**6g.**

^{1}H NMR (300 MHz, Acetone) δ 8.25 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.37 – 7.24 (m, *J* = 8.6, 7.1 Hz, 2H), 7.19 – 7.12 (m, *J* = 7.1 Hz, 2H), 7.11 – 6.98 (m, 6H), 5.82 (d, *J* = 10.6 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 3.66 (d, *J* = 10.8 Hz, 1H), 3.41 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.30 (s, 3H).

^{13}C NMR (75 MHz, Acetone) δ 173.8, 166.9, 140.2, 137.2, 134.8, 132.0, 131.3, 129.6, 128.67, 128.4, 128.4, 128.1, 127.3, 80.2, 70.3, 65.2, 62.6, 52.4, 40.9, 22.1, 14.5.

HRMS (ESI+): Calculated for $C_{28}H_{29}N_2O_4$, 457.2121; found, 457.2105 ([M+H], 100).

(2R,4S,5S,6R)-Ethyl 4-methyl-5,6-diphenyl-2-(thiophen-2-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6i)



6i

Following the typical procedure, the reaction of 2,3-diphenyl-2*H*-azirine (29.0 mg, 0.15 mmol) and **3i** (42.26 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct *endo*-**2h** (17.6 mg, 29%, white oil).

$[\alpha]_D^{20}$: +35 (c = 0.10, $CHCl_3$), 71% ee.

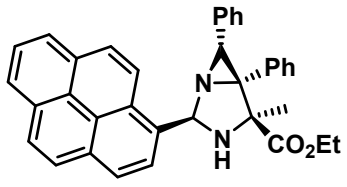
SFC: Chiralpak IB, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 230 nm), t_R: 2.8 min (2R,4S,5S,6R)-**6i** and 2.9 min (2S,4R,5R,6S)-**6i**.

^{1}H NMR (300 MHz, Acetone) δ 7.77 – 7.60 (m, 1H), 7.38 (ddd, *J* = 5.0, 2.4, 1.2 Hz, 1H), 7.34 – 7.22 (m, 1H), 7.21 – 7.12 (m, 2H), 7.11 – 6.98 (m, 7H), 6.95 – 6.82 (m, 1H), 5.86 (d, *J* = 11.0 Hz, 1H), 4.48 – 4.26 (m, 2H), 3.67 (d, *J* = 11.0 Hz, 1H), 3.50 (d, *J* = 1.9 Hz, 1H), 1.40 – 1.31 (m, 3H), 1.25 (d, *J* = 2.2 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 173.4, 141.6, 136.8, 134.4, 128.2, 128.1, 127.9, 127.8, 127.4, 127.1, 125.9, 125.7, 77.3, 70.3, 65.2, 62.4, 41.0, 21.9, 14.2.

HRMS (ESI+): Calculated for $C_{24}H_{25}N_2O_2$, 405.1631; found, 405.1622 ([M+H], 100).

(2R,4S,5S,6R) Ethyl 4-methyl-5,6-diphenyl-2-(pyren-1-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6s)



6s

Following the typical procedure, the reaction of 2,3-diphenyl-2*H*-azirine (29.0 mg, 0.15 mmol) and **3q** (65.9 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 15:1), the cycloadduct **6q** (35.2 mg, 45%, white oil).

$[\alpha]_D^{20}$: +101 (c = 0.10, $CHCl_3$), 93% ee.

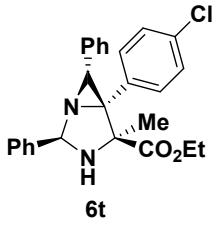
SFC: Chiralpak ID, CO_2/MeOH from 95-5 to 60-40 in 8 min, flow rate 2 mL/min (λ = 230 nm), t_R: 4.2 min (2S,4R,5R,6S)-**6q** and 5.0 min (2R,4S,5S,6R)-**6q**.

^{1}H NMR (300 MHz, Acetone) δ 9.00 (d, *J* = 9.3 Hz, 1H), 8.42 – 8.22 (m, 4H), 8.19 – 8.02 (m, *J* = 15.5, 7.6 Hz, 4H), 7.98 – 7.83 (m, 1H), 7.50 – 7.30 (m, 1H), 7.26 – 7.14 (m, 3H), 7.13 – 6.88 (m, 5H), 6.58 (d, *J* = 11.1 Hz, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 3.85 (d, *J* = 11.2 Hz, 1H), 3.72 (s, 1H), 1.49 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 173.9, 137.4, 135.1, 132.6, 132.5, 132.2, 132.1, 131.8, 130.2, 128.6, 128.5, 128.4, 128.2, 128.1, 127.4, 127.1, 126.2, 126.1, 125.6, 125.5, 125.3, 124.6, 79.2, 70.7, 64.5, 62.5, 41.8, 22.4, 14.5.

HRMS (ESI+): Calculated for $C_{36}H_{27}N_2O_2$, 523.2380; found, 523.2363 ([M+H], 100).

(2R,4S,5S,6R)-Ethyl 5-(4-chlorophenyl)-4-methyl-2,6-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6t)



6t

Following the typical procedure, the reaction of 3-(4-chlorophenyl)-2-phenyl-2H-azirine (34.1 mg, 0.15 mmol) and **3q** (41.0 mg, 0.20 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane-EtOAc 10:1), the cycloadduct *endo*-**2h** (25.3 mg, 39%, white oil).

$[\alpha]_D^{20}$: +57 (c = 0.10, $CHCl_3$), 53% ee.

SFC: Daicel Chiralpak ID, hexane-isopropanol 95-5-0.8, flow rate 1 mL/min (λ = 254 nm), t_R: 2.7 min (2R,4S,5S,6R)-**6r** and 2.8 min(2S,4R,5R,6S)-**6r**.

^{1}H NMR (300 MHz, Acetone) δ 7.65 – 7.46 (m, 2H), 7.44 – 7.23 (m, 5H), 7.06 (dt, *J* = 7.9, 2.8 Hz, 7H), 5.77 (d, *J* = 11.4 Hz, 1H), 4.57 – 4.21 (m, 2H), 3.61 (d, *J* = 11.5 Hz, 1H), 3.37 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.30 (s, 3H).

^{13}C NMR (75 MHz, Acetone) δ 173.7, 139.4, 137.0, 134.1, 133.4, 132.6, 131.4, 130.3, 129.9, 129.6, 129.3, 128.7, 128.5, 128.4, 127.5, 127.4, 80.6, 70.2, 64.4, 62.7, 40.9, 22.2, 14.5.

HRMS (ESI+): Calculated for $C_{26}H_{27}N_2O_2$, 433.1677; found, 433.1672 ([M+H], 100).

4. Preparation of racemic products for HPLC analysis.

The racemic pyrrolidines were prepared according to the general procedure, but using dppf as ligand. The samples for HPLC analysis were dissolved in isopropyl alcohol and used as quickly as possible to minimize the formation of decomposition products.

5. Mechanistic studies

In order to shed light to the mechanism of the epimerization of the adduct **4** during the silica gel chromatographic purification process, we performed several experiments. First, the adduct **4** was dissolved in $CDCl_3$ and stirred in the present of SiO_2 (10% in weight) in a NMR tube, after 5 min. a new set of signals corresponding to a new diastereomer can be observed by ^{1}H-NMR (Spectrum B, Figure 1). This mixture was analyzed by nOe experiments (Figure 2), after irradiation of the sample at H^1 (original isomer A), an important nOe correlation was observed between H^1 and H^2 (1.83%) which is in agreement with a *cis* configuration. On the contrary, the irradiation at the $H^{1'}$ (new isomer B) does not show any correlation between that hydrogen atom and $H^{2'}$, which would indicate the *trans* configuration of this adduct.

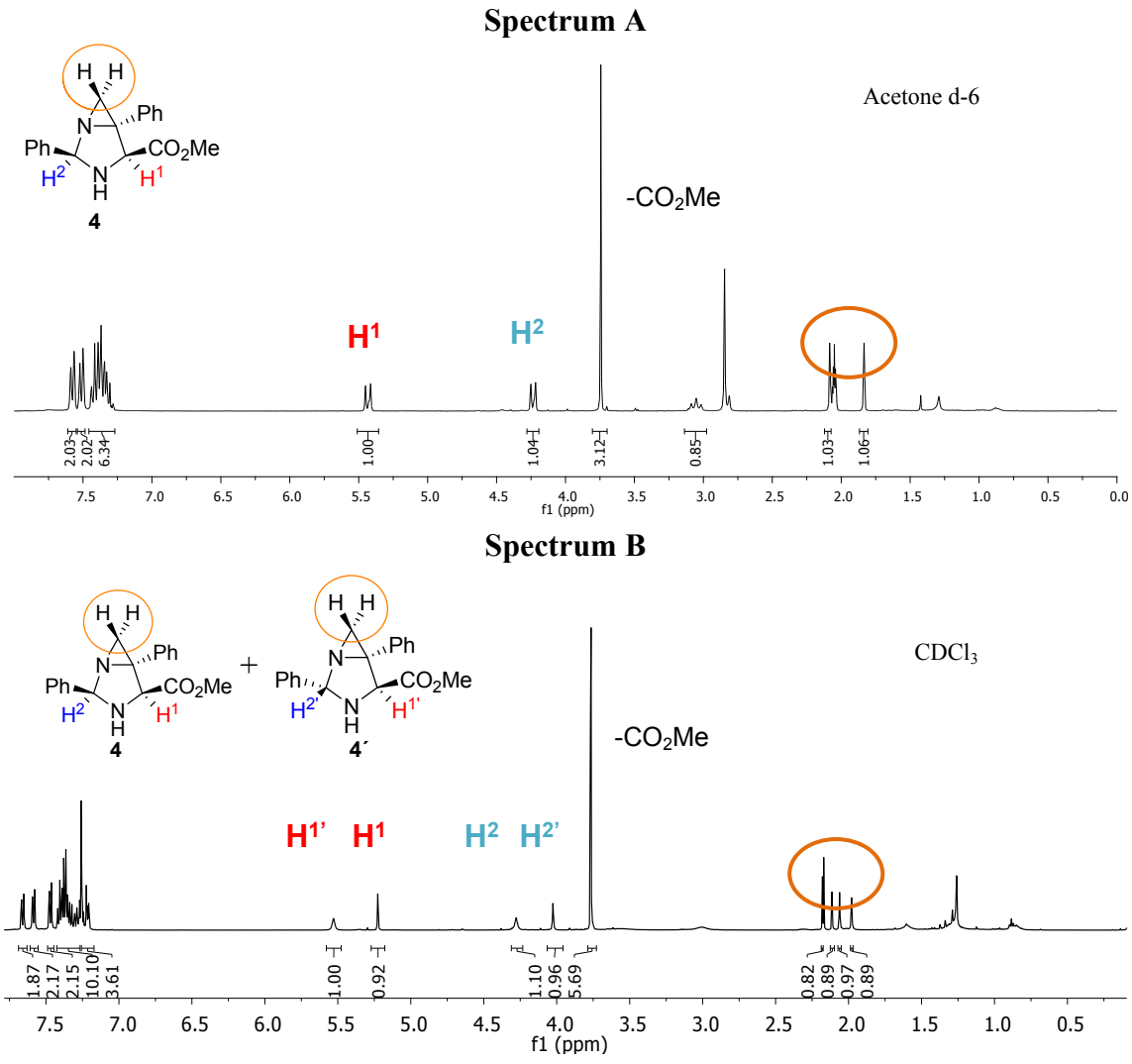


Figure 1

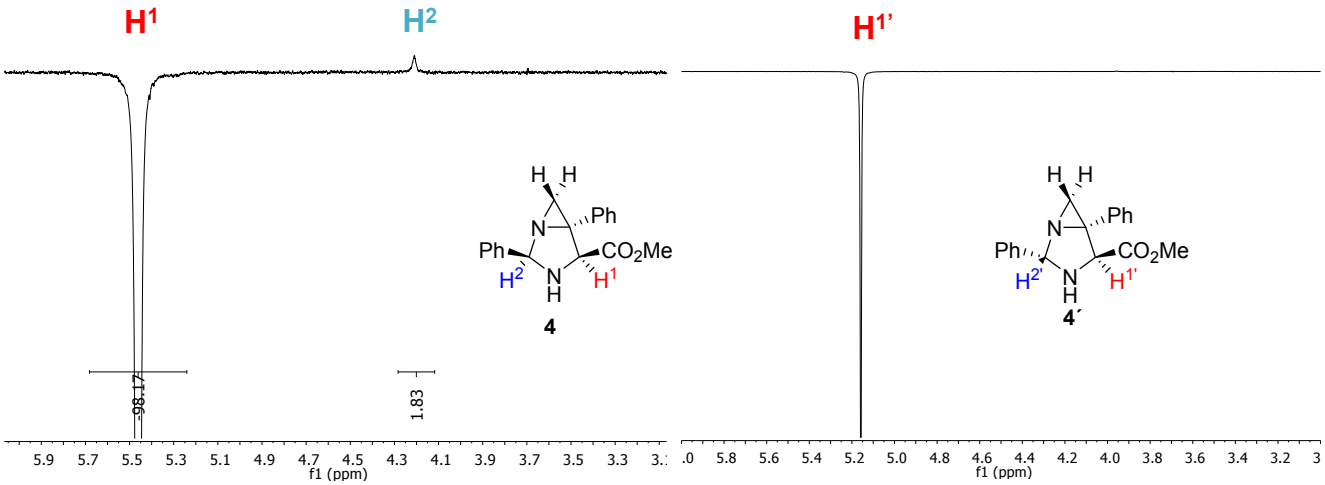
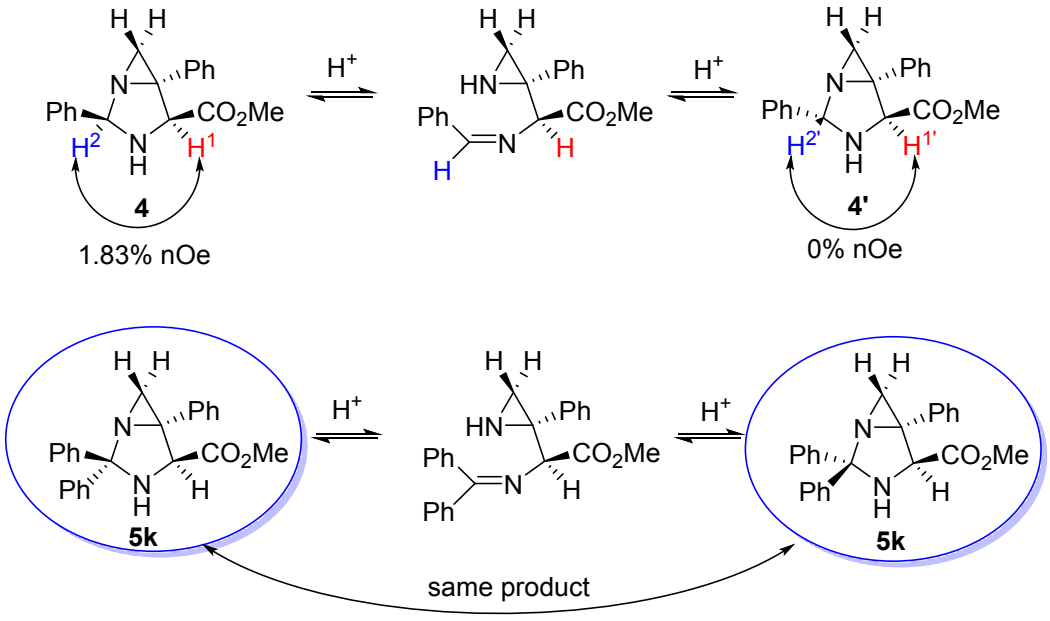


Figure 2

The same procedure was carried out using the adduct **5k** with a diphenyl substitution at C-2. In this case, when the adduct was stirred in the present of SiO_2 (10% in weight) in a NMR tube no alteration on the ^{1}H-NMR spectrum was observed. These results suggest that the observed epimerization at C-2 position in adduct **4** could take place likely by an acid catalyzed ring opening/ring closing procedure via the imine intermediate[4] (Figure 3). In the case of the C-2 diphenyl disubstituted adduct **5k** this opening/ring closing reaction would lead to the same product. In accordance with this mechanistic hypothesis formation of benzaldehyde was observed by ^{1}H-NMR when adduct **4** was treated with wet trifluoroacetic acid.



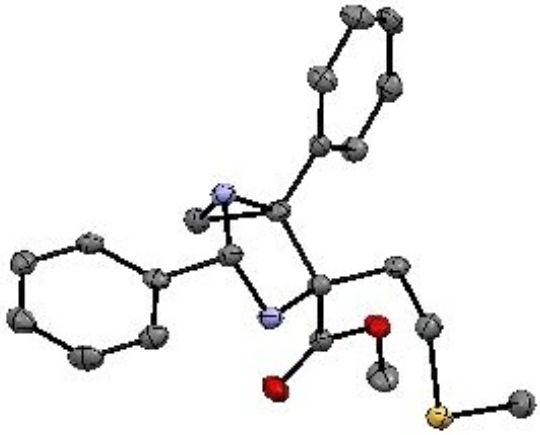
[4] L. Lázár, A. Göblyös, F. Evanics, C. Bernath. and F. Fülöp, *Tetrahedron*, 1998, **54**, 13639.

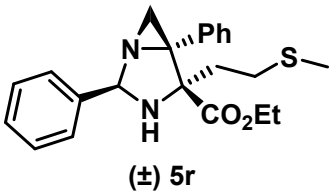
Figure 3

6. Stereochemical assignment

The relative configuration of **5p** and **6q** was unequivocally established by X-ray crystal structure analysis.

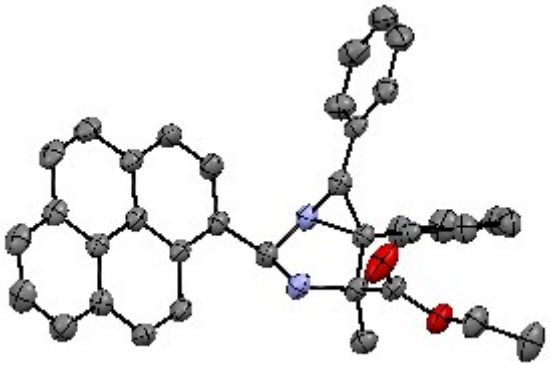
X Ray Structure of 5r

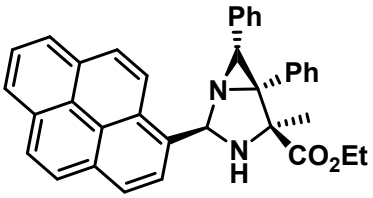




(±) 5r

X Ray Structure of 6s





(±) 6s

Figure 4

7. Experimentally and simulated Electronic Circular Dichroism spectra

Quantum Chemistry calculations have been performed using the Gaussian16 software package[5]. Geometry optimization has been computed using the density functional theory, in particular with the B3LYP functional[6,7,8,9] in combination with the 6-31+g(d) basis set. Electronic circular dichroism (ECD) spectrum was computed using the previously optimized geometry and with the long-range-corrected CAM-B3LYP functional[10] and the same basis set. To mimic the experimental conditions, both in the geometry optimization and in the circular dichroism we included solvent effects (dichloromethane) throught the Polarizable Continuum Model (PCM) using the integral equation formalism variant (IEFPCM).[11,12] Figure 5 shows the experimental and simulated ECD spectra together with the optimized geometry of **6s**; several views with different orientations are shown. The comparison shows that the experimentally measured ECD spectra verify that the synthetized species corresponds to (2R,4S,5S,6R)- isomer.

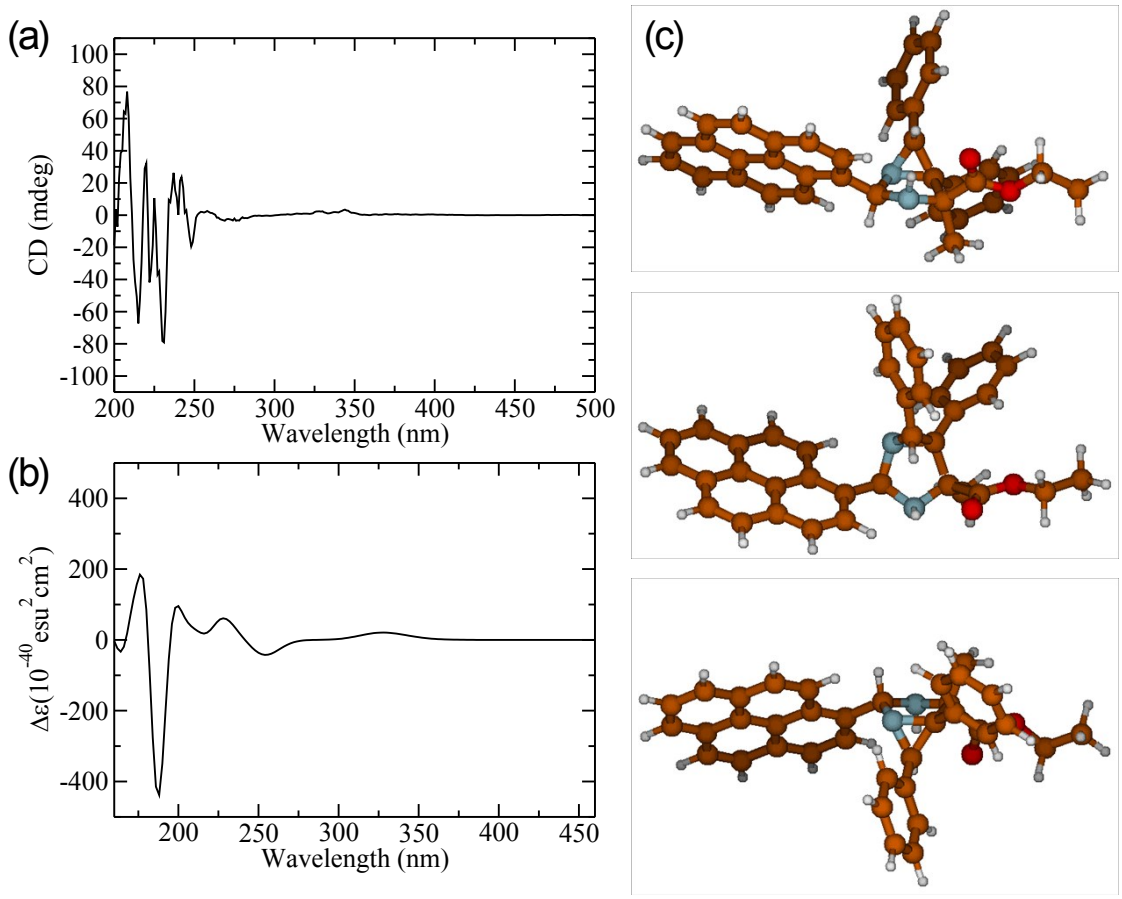


Figure 5. (a) Experimentally measured Electronic Circular Dichroism spectra, (b) Simulated Electronic Circular Dichroism spectra, (c) several orientations of (2R,4S,5S,6R)- **6s** isomer used in the simulation of the spectra.

9. HPLC Charts.

[5] M. J. Frisch et al., Gaussian 16, Revision C.01, Gaussian, Inc., Wallingford CT, (2019).
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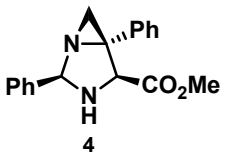
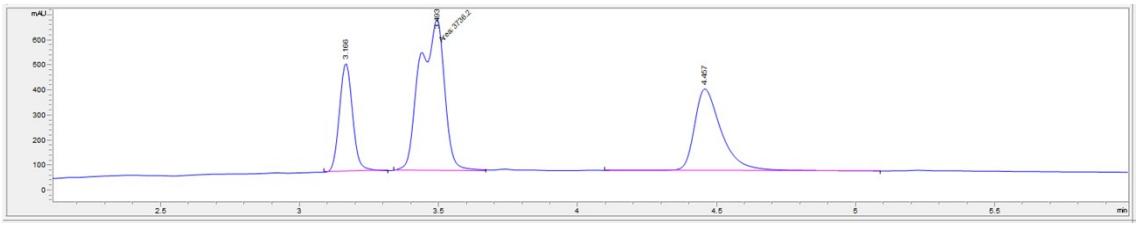
[12] J. Tomasi, B. Mennucci, and R. Cammi, *Chem. Rev.* 2005, **105**, 2999.



4

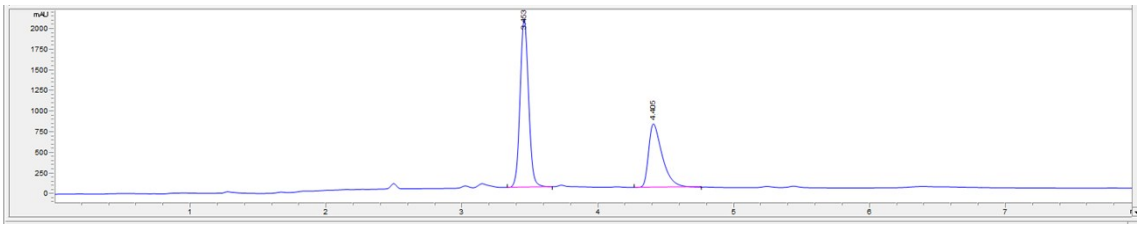
(±)-**4**

Mixure of diastereoisomers *cis* and *trans*

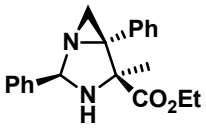


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.166	BB	1443	435.3	0.0507	19.517	0.896
2	3.493	MM	3736.2	610.4	0.102	50.533	1.987
3	4.457	BB	2214.4	328	0.1008	29.950	0.586

(+)-4; 24% *ee*

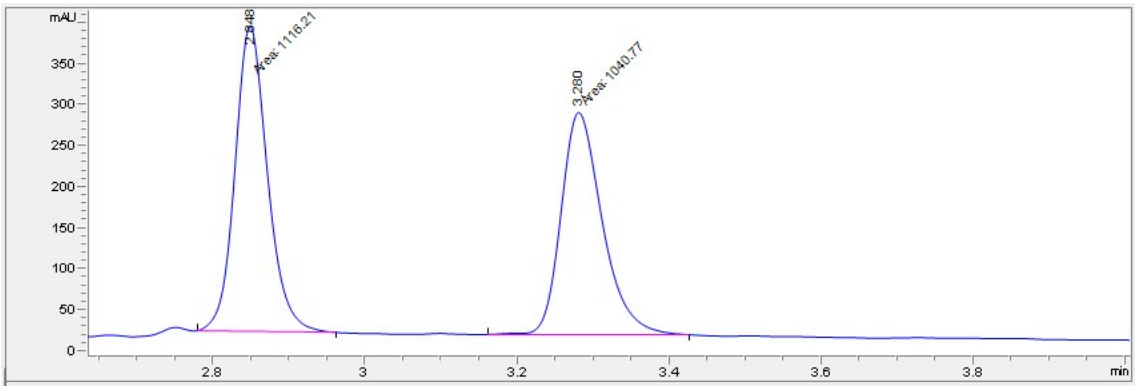


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.453	BB	8862.9	2046.1	0.0665	62.244	0.87
2	4.405	BB	5376	771.2	0.1053	37.756	0.507



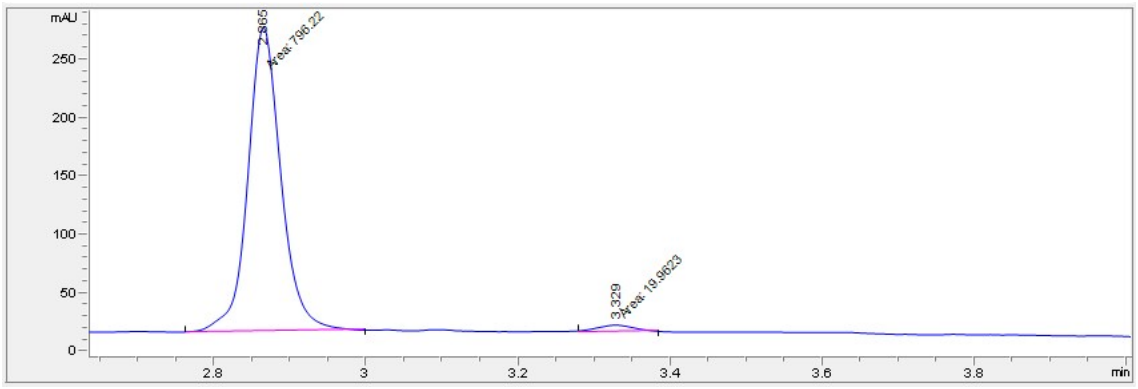
5a

(±)-**5a**

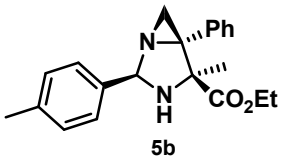


#	Time	Area	Height	Width	Area%	Symmetry
1	2.848	1116.2	374.3	0.0497	51.749	0.835
2	3.28	1040.8	272.4	0.0637	48.251	0.734

(+)-**5a**; 97% *ee*



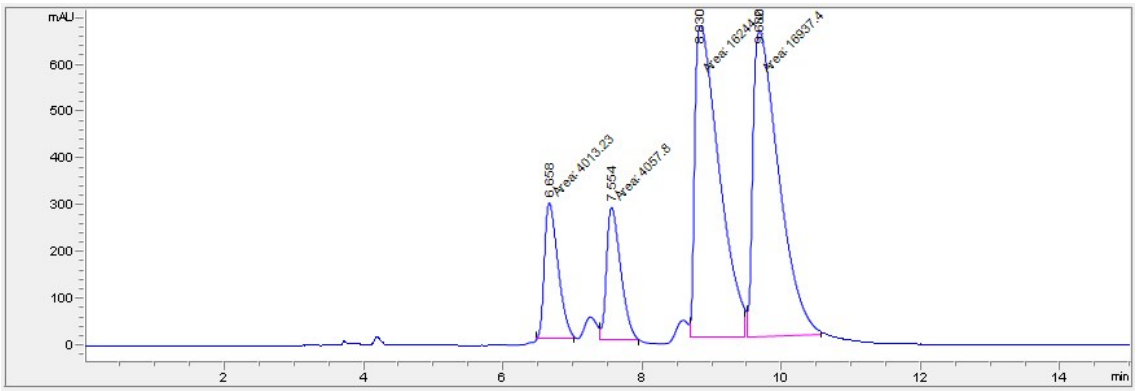
#	Time	Area	Height	Width	Area%	Symmetry
1	2.865	796.2	261.5	0.0507	97.554	0.87
2	3.329	20	5.8	0.0573	2.446	1.1



5b

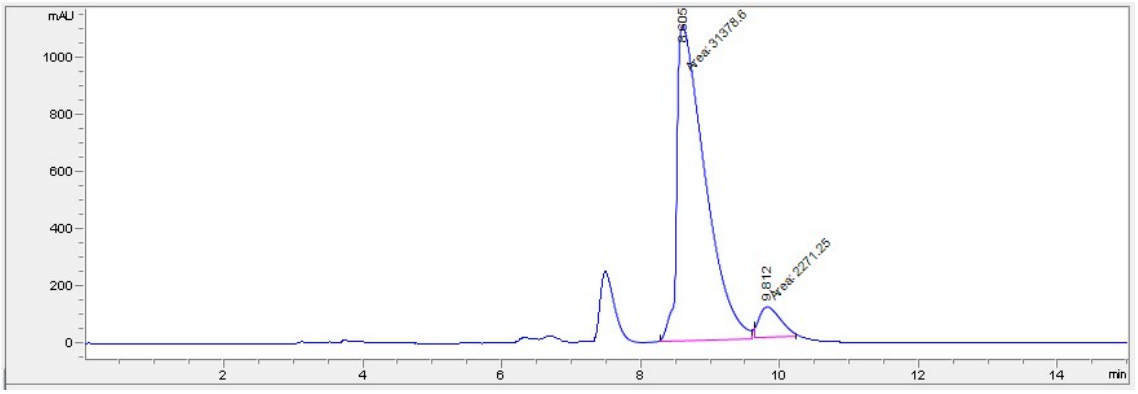
(±)-**5b**

Mixure of diastereoisomers *cis* and *trans*

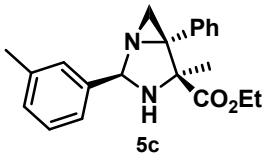


#	Time	Area	Height	Width	Area%	Symmetry
1	6.658	4013.2	291.6	0.2293	9.728	0.531
2	7.554	4057.8	284.7	0.2375	9.836	0.54
3	8.83	16244.3	665	0.4071	39.378	0.285
4	9.68	16937.4	656.4	0.4301	41.058	0.331

(+)-5b; 87% *ee*



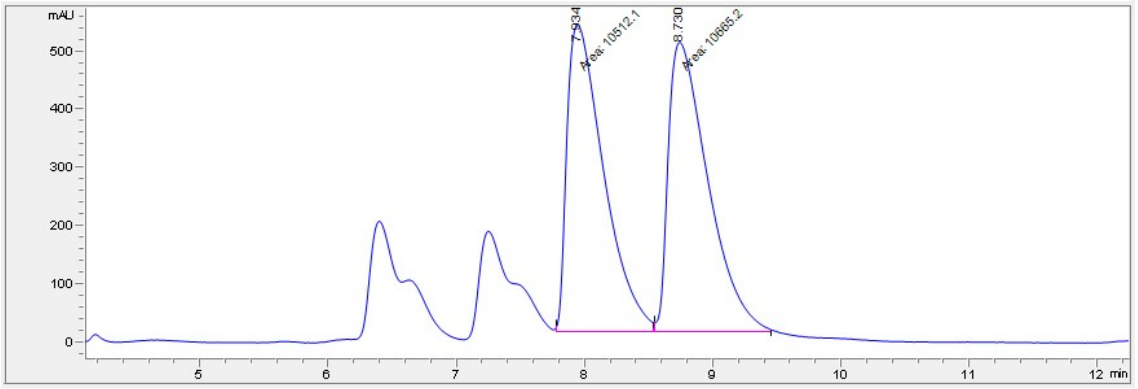
#	Time	Area	Height	Width	Area%	Symmetry
1	8.605	31378.6	1104.4	0.4735	93.250	0.285
2	9.812	2271.3	106.4	0.3559	6.750	0.577



5c

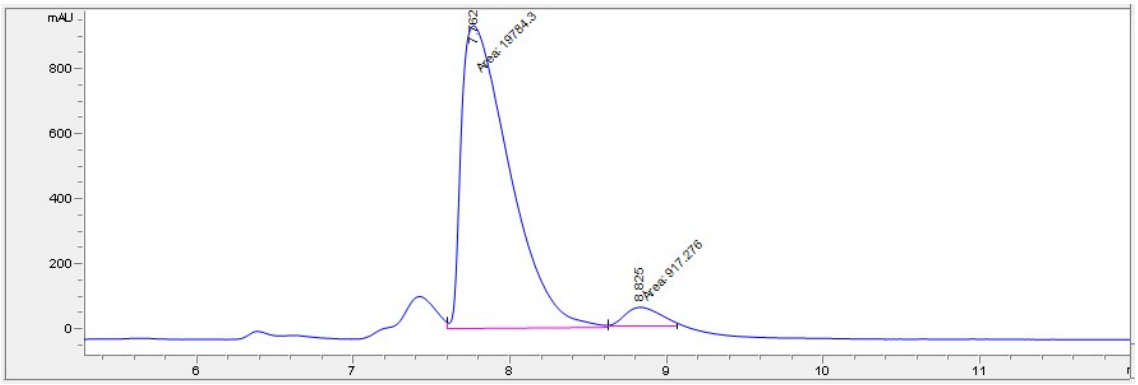
(±)-**5c**

Mixure of diastereoisomers *cis* and *trans*

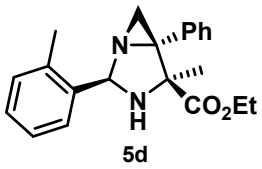


#	Time	Area	Height	Width	Area%	Symmetry
1	7.934	10512.1	527.2	0.3323	49.638	0.382
2	8.73	10665.2	497.8	0.3571	50.362	0.387

(+)-5c; 91% *ee*

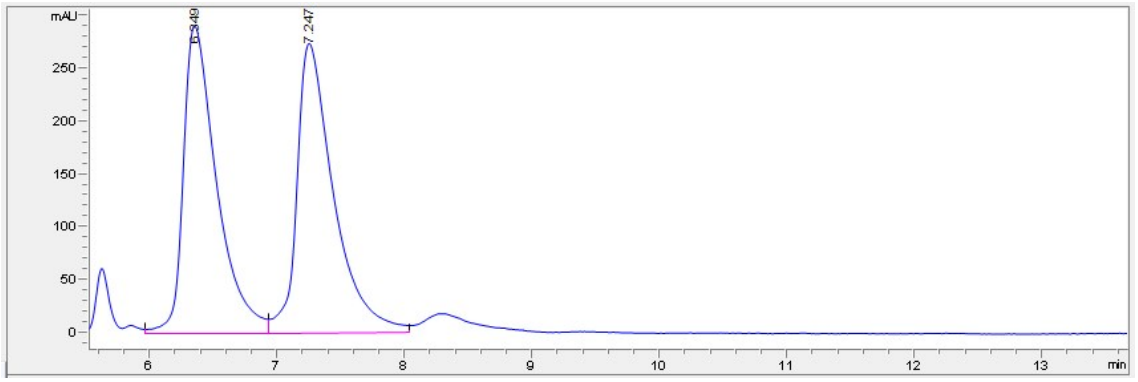


#	Time	Area	Height	Width	Area%	Symmetry
1	7.762	19784.3	927.9	0.3554	95.569	0.336
2	8.825	917.3	58.1	0.263	4.431	0.738



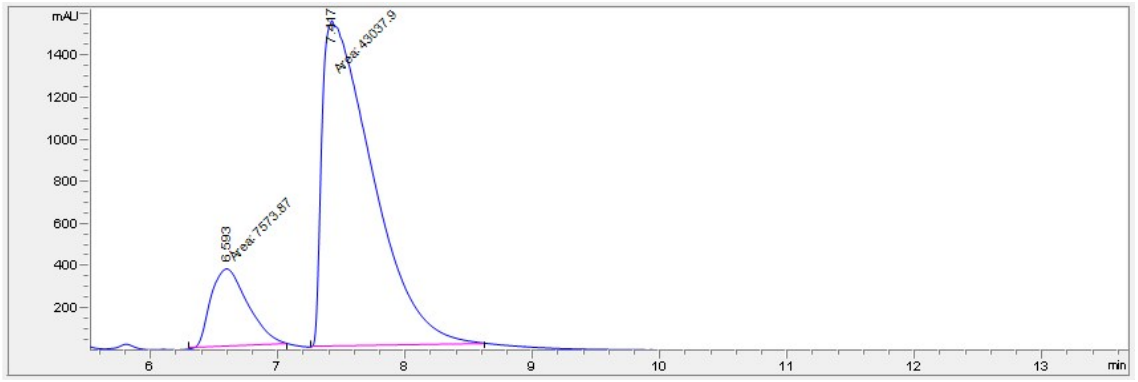
5d

(±)-**5d**

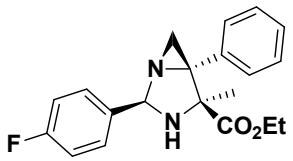


#	Time	Area	Height	Width	Area%	Symmetry
1	6.349	5338.4	292.3	0.2701	48.960	0.49
2	7.247	5565.1	275.9	0.2894	51.040	0.479

(+)-5d; 70% *ee*

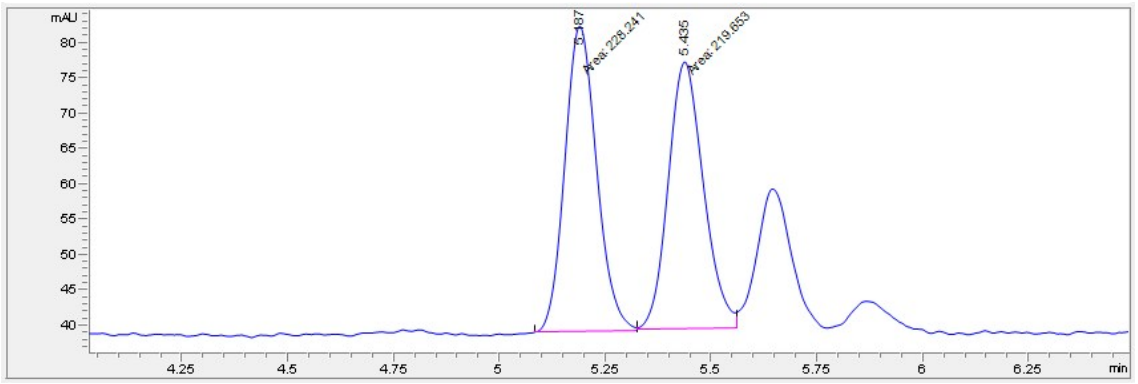


#	Time	Area	Height	Width	Area%	Symmetry
1	6.593	7573.9	372.3	0.339	14.965	0.731
2	7.417	43037.9	1552.8	0.4619	85.035	0.235



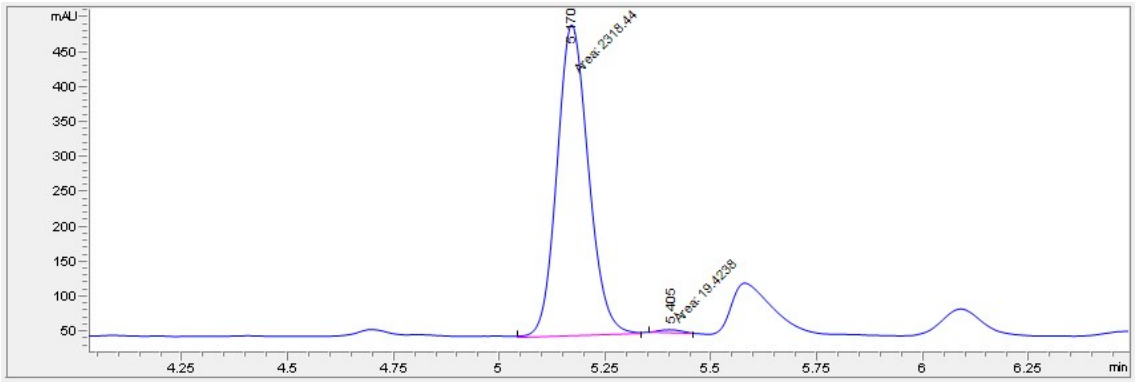
5e

(±)-**5e**

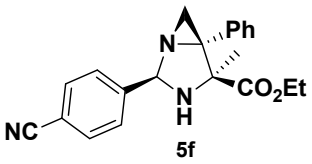


#	Time	Area	Height	Width	Area%	Symmetry
1	5.187	228.2	43.3	0.0878	50.959	0.855
2	5.435	219.7	37.8	0.0968	49.041	0.856

(+)-5e; 98% *ee*

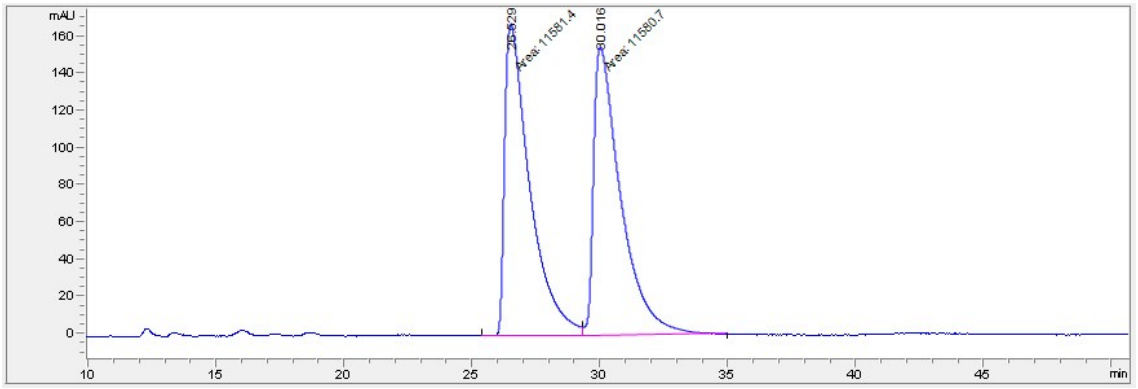


#	Time	Area	Height	Width	Area%	Symmetry
1	5.17	2318.4	446.8	0.0865	99.169	0.858
2	5.405	19.4	4.8	0.0669	0.831	0.702



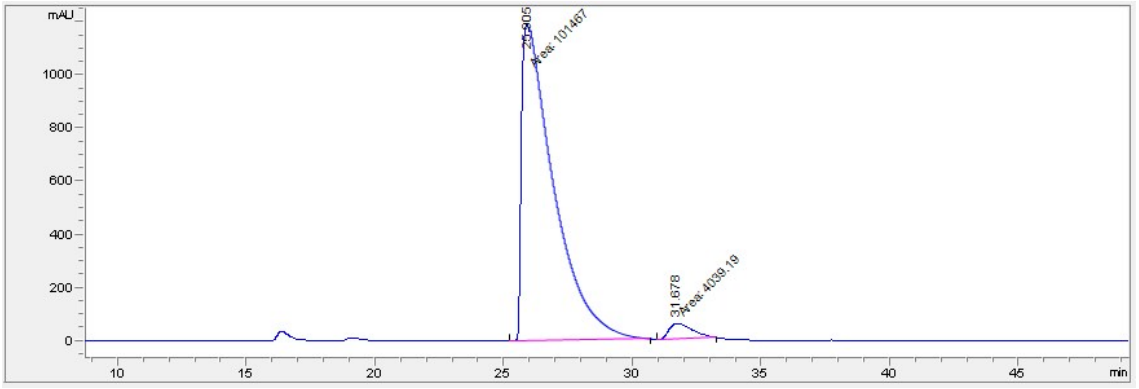
5f

(±)-**5f**

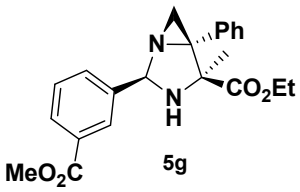


#	Time	Area	Height	Width	Area%	Symmetry
1	26.529	11581.4	167.7	1.1508	50.001	0.323
2	30.016	11580.7	155	1.2451	49.999	0.307

(+)-5f; 92% *ee*

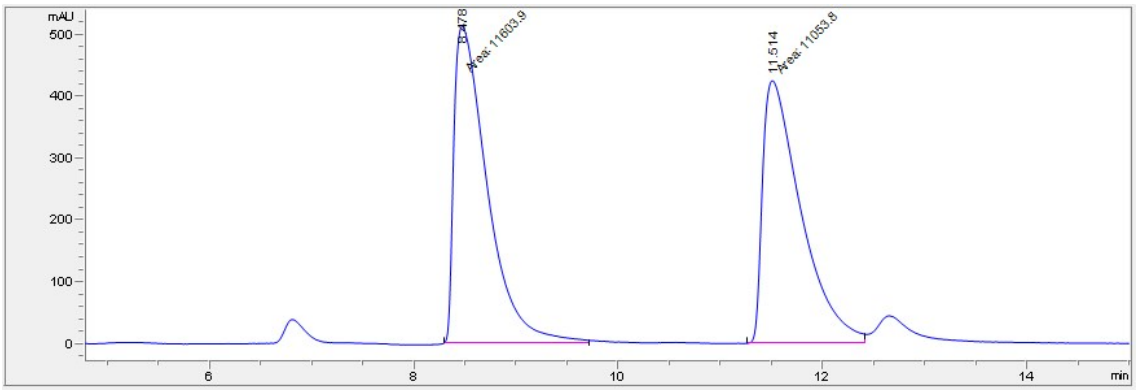


#	Time	Area	Height	Width	Area%	Symmetry
1	25.905	101467.1	1196.8	1.413	96.172	0.206
2	31.678	4039.2	61.6	1.0931	3.828	0.494



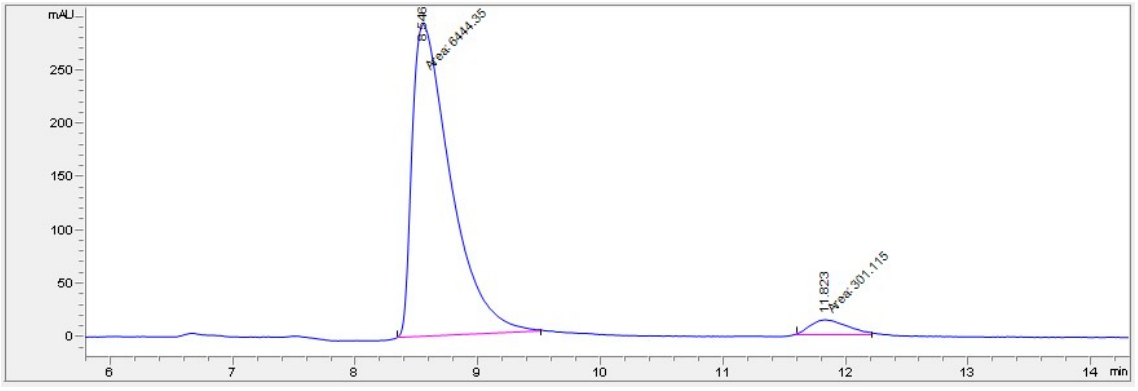
5g

(±)-**5g**

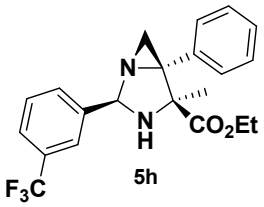


#	Time	Area	Height	Width	Area%	Symmetry
1	8.478	11603.9	511.7	0.378	51.214	0.334
2	11.514	11053.8	423.6	0.435	48.786	0.325

(+)-5g; 91% *ee*

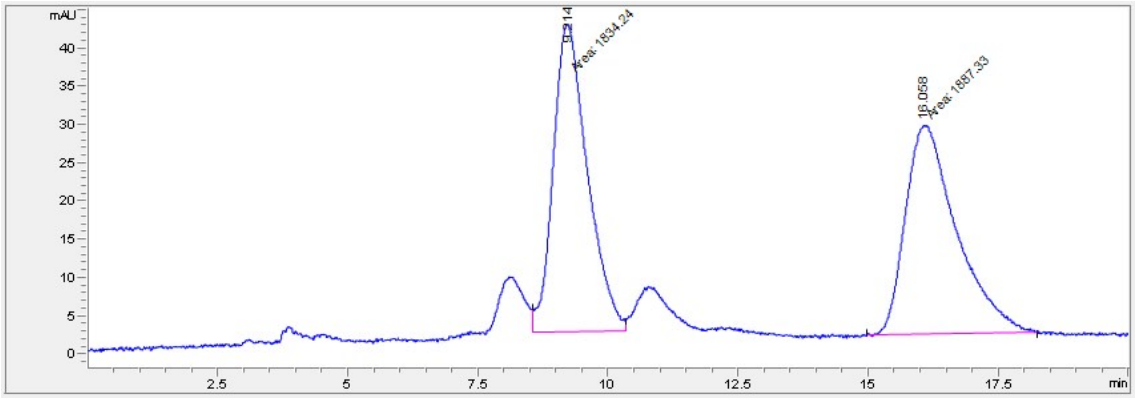


#	Time	Area	Height	Width	Area%	Symmetry
1	8.546	6444.3	293	0.3665	95.536	0.385
2	11.823	301.1	14.2	0.3539	4.464	0.652



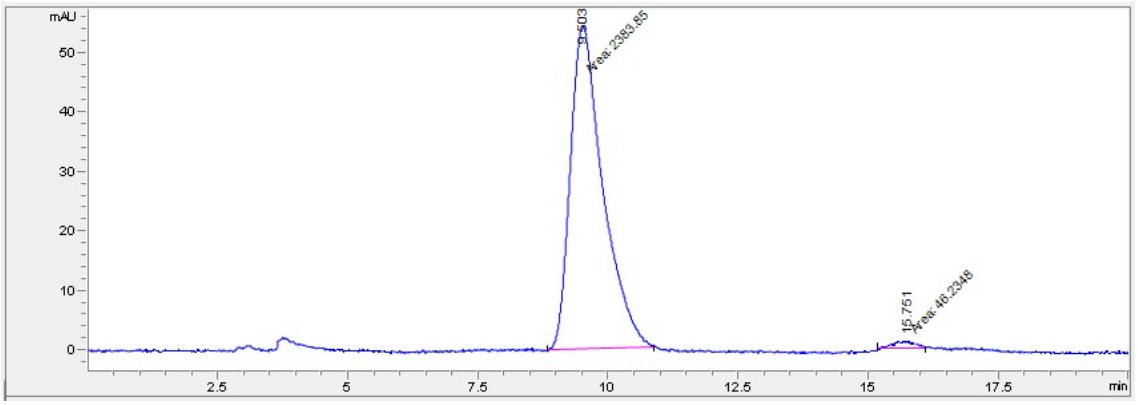
5h

(±)-**5h**

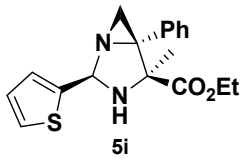


#	Time	Area	Height	Width	Area%	Symmetry
1	9.214	1834.2	40.2	0.7604	49.287	0.727
2	16.058	1887.3	27.4	1.1499	50.713	0.568

(+)-5h; 96% *ee*



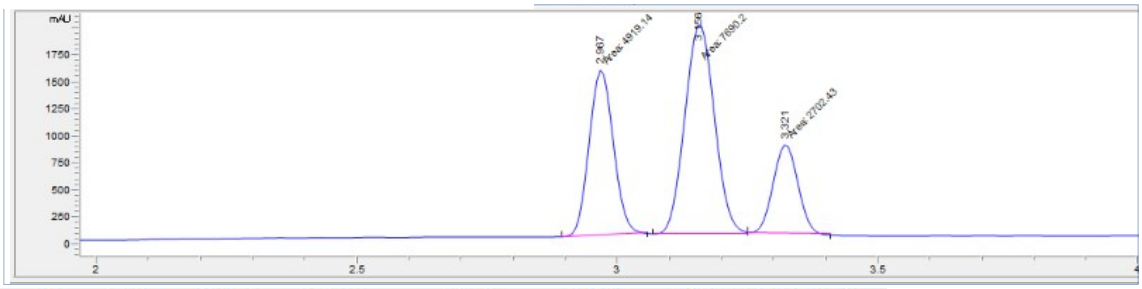
#	Time	Area	Height	Width	Area%	Symmetry
1	9.503	2383.9	54.4	0.7298	98.097	0.616
2	15.751	46.2	1.4	0.5546	1.903	1.612



5i

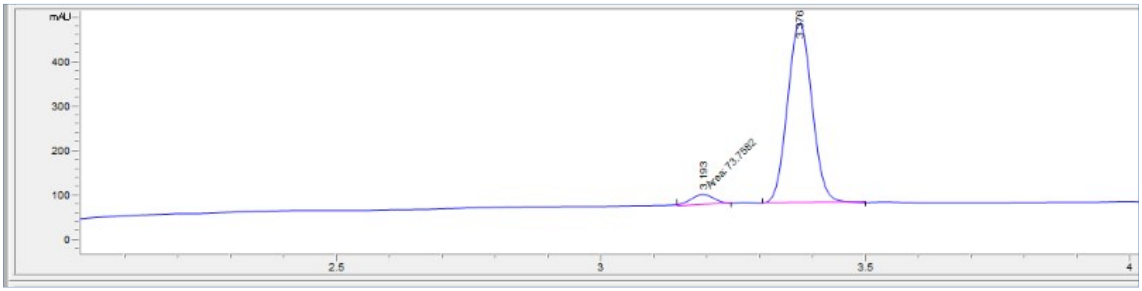
(±)-**5i**

Mixure of diastereoisomers *cis* and *trans*

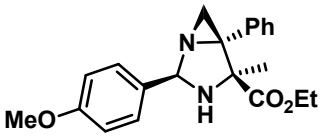


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.967	MM	4919.1	1535.6	0.0534	32.127	0.938
2	3.156	MM	7690.2	1953.1	0.0656	50.224	0.958
3	3.321	MM	2702.4	825.6	0.0546	17.649	0.953

(+)-**5i**; ≥99% *ee*



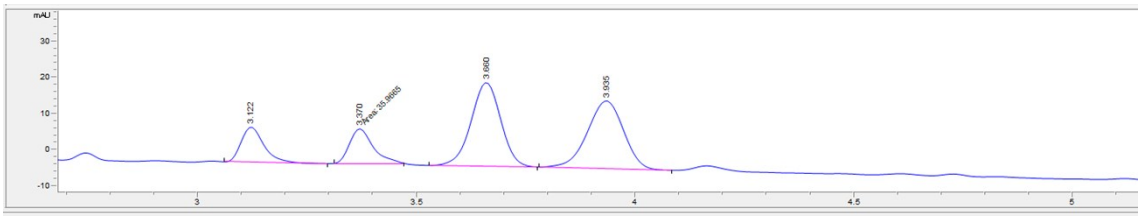
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.193	MM	73.8	23.5	0.0522	5.332	1.052
2	3.376	BB	1309.6	407.6	0.0495	94.668	0.932



5j

(±)-**5j**

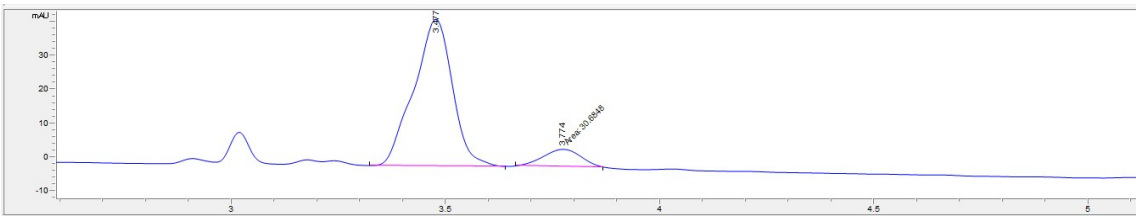
Mixure of diastereoisomers *cis* and *trans*



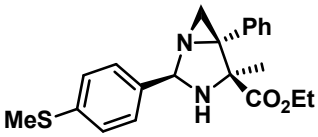
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.122	BB	34.9	9.7	0.0562	12.157	0.723
2	3.37	MM	36	9.6	0.0625	12.516	0.727
3	3.66	BB	109	23	0.0732	37.934	1.026
4	3.935	BB	107.4	18.6	0.0913	37.393	1.068

(+)-5j; 80% *ee*

Mixure of diastereoisomers *cis* and *trans*

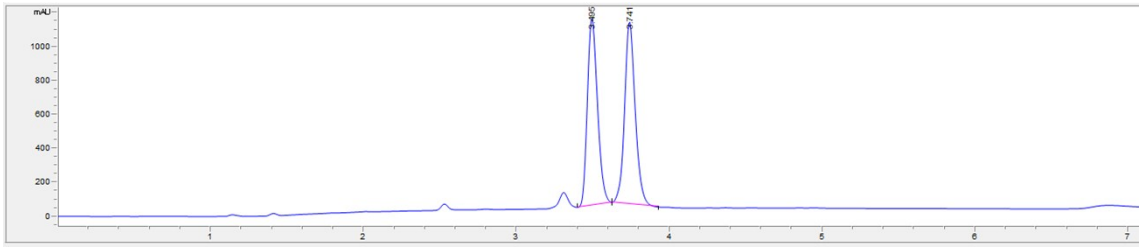


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.477	BB	270.4	43.3	0.0908	89.809	1.271
2	3.774	MM	30.7	5.1	0.1007	10.191	1.014



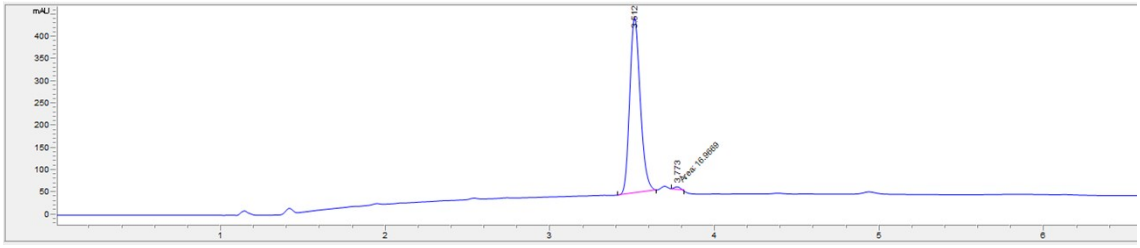
5k

(±)-**5k**

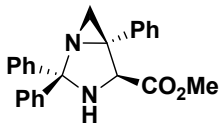


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.495	BB	5070.3	1106.9	0.0714	49.208	0.76
2	3.741	BB	5233.5	1080.7	0.0725	50.792	0.814

(+)-5k; 98% *ee*

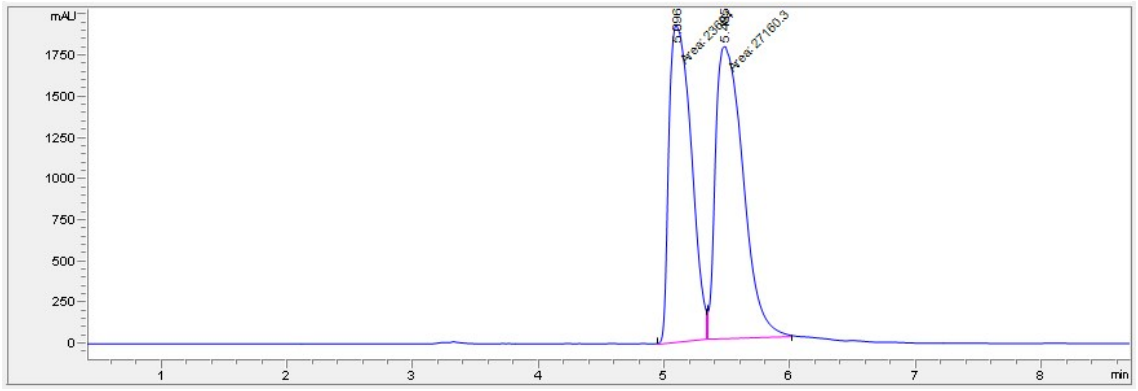


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.512	BB	1756.4	397	0.0676	99.043	0.802
2	3.773	MM	17	6.7	0.0421	0.957	0.693



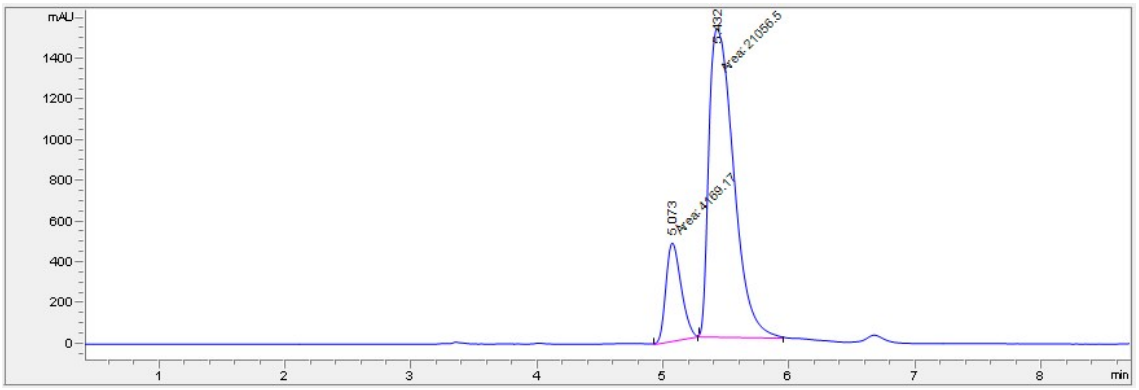
5m

(±)-**5m**

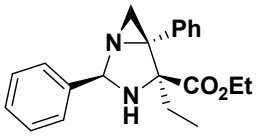


#	Time	Area	Height	Width	Area%	Symmetry
1	5.096	23694	1929.4	0.2047	46.592	0.49
2	5.485	27160.3	1774.1	0.2551	53.408	0.511

(+)-5m; 67% *ee*



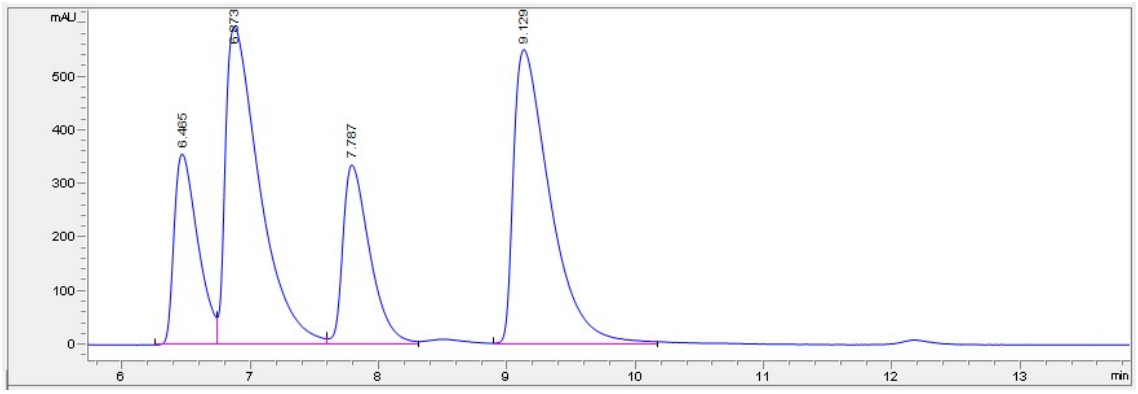
#	Time	Area	Height	Width	Area%	Symmetry
1	5.073	4169.2	489.2	0.142	16.528	0.713
2	5.432	21056.5	1532.5	0.229	83.472	0.511



5n

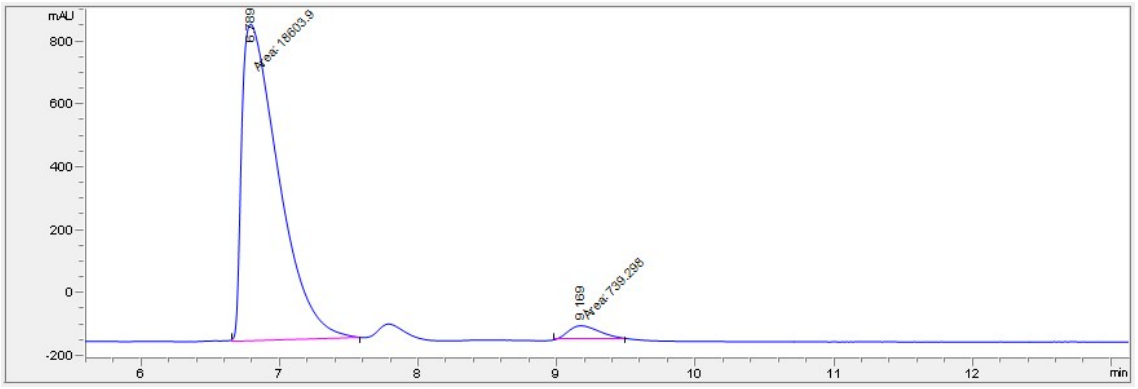
(±)-**5n**

Mixure of diastereoisomers *cis* and *trans*

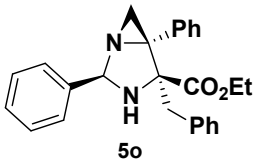


#	Time	Area	Height	Width	Area%	Symmetry
1	6.465	4606.4	357.4	0.1974	14.515	0.486
2	6.873	11093.2	594.5	0.2707	34.956	0.33
3	7.787	4977	337	0.2243	15.683	0.466
4	9.129	11058	552.5	0.2875	34.845	0.361

(+)-5n; 92% *ee*

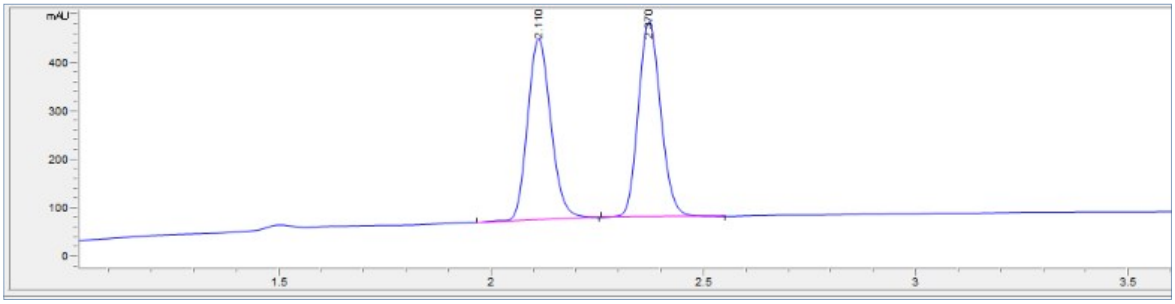


#	Time	Area	Height	Width	Area%	Symmetry
1	6.789	18603.9	1005	0.3085	96.178	0.311
2	9.169	739.3	44.7	0.2754	3.822	0.613



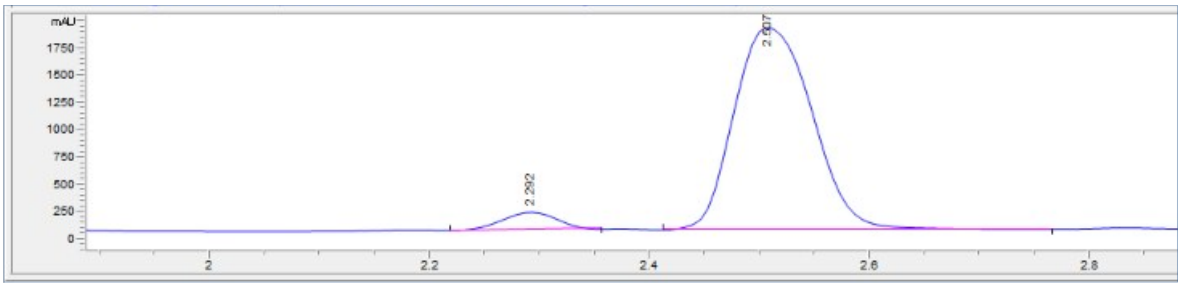
5o

(±)-**5o**

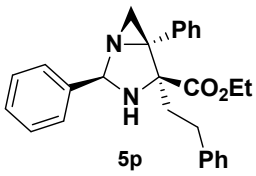


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.11	BB	1423.4	375.4	0.0602	49.014	0.849
2	2.37	BB	1480.7	404.6	0.0567	50.986	0.844

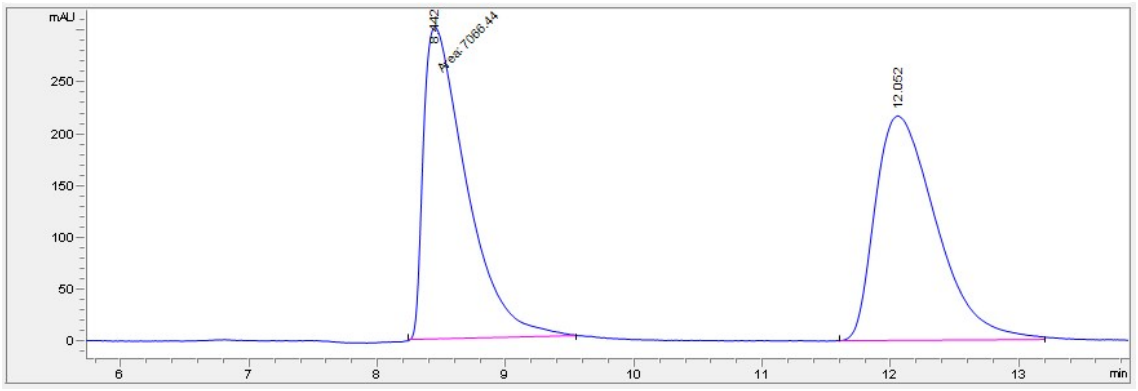
(+)-5o; 65% *ee*



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.292	BB	550.2	160.1	0.0541	5.656	1.073
2	2.507	BB	9176.7	1864.5	0.0814	94.344	0.745

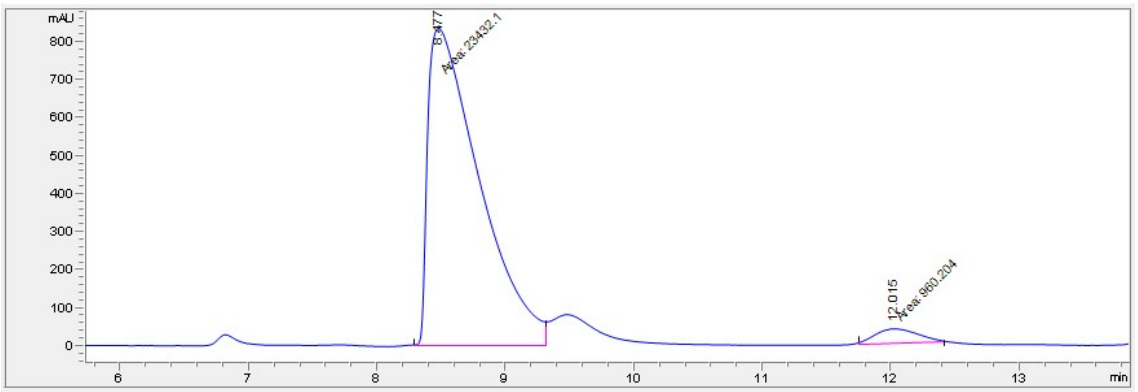


(±)-**5p**

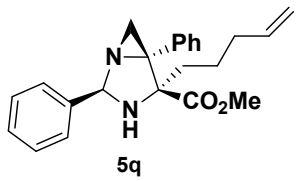


#	Time	Area	Height	Width	Area%	Symmetry
1	8.442	7066.4	303.1	0.3886	49.341	0.344
2	12.052	7255.2	218	0.4403	50.659	0.538

(+)-5p; 92% *ee*

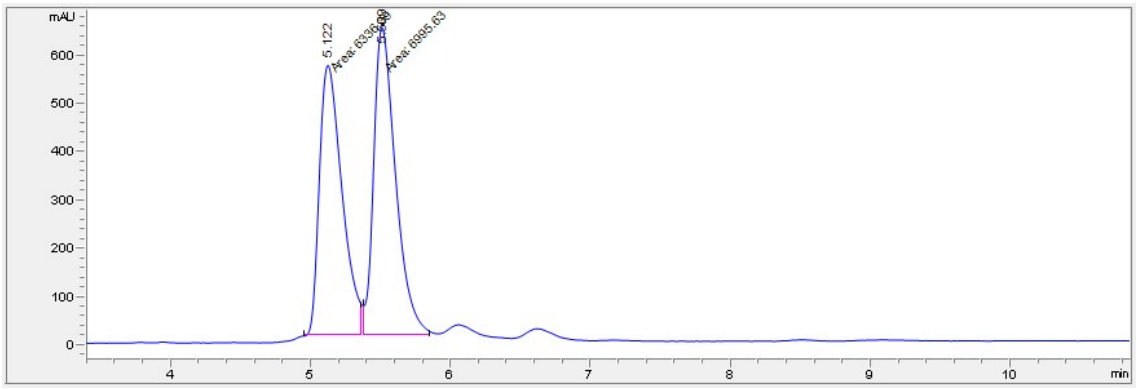


#	Time	Area	Height	Width	Area%	Symmetry
1	8.477	23432.1	840.1	0.4649	96.064	0.257
2	12.015	960.2	39.7	0.4028	3.936	0.679



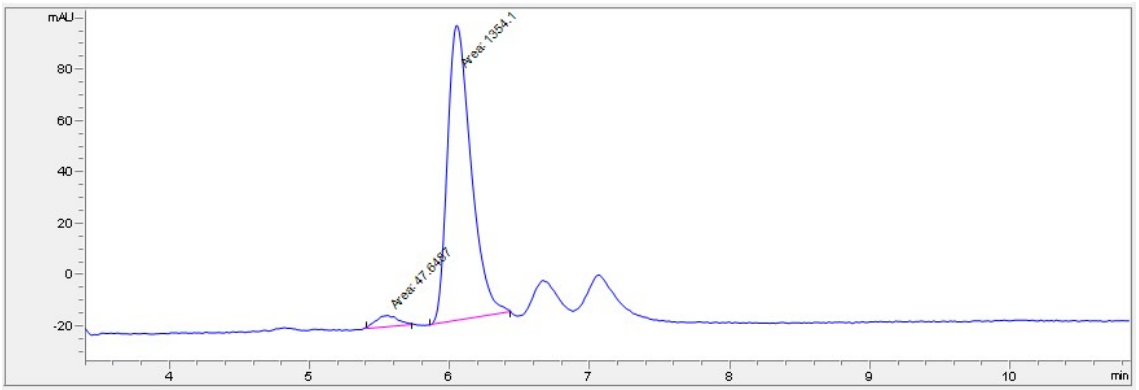
5q

(±)-**5q**

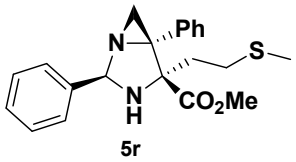


#	Time	Area	Height	Width	Area%	Symmetry
1	5.122	6336.4	563.1	0.1875	47.528	0.587
2	5.509	6995.6	641.4	0.1818	52.472	0.586

(+)-5q; 93% *ee*

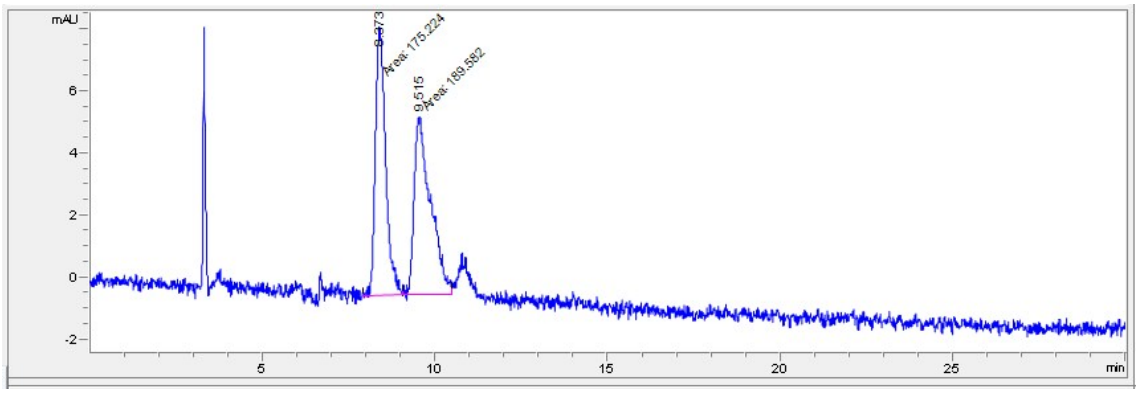


#	Time	Area	Height	Width	Area%	Symmetry
1	5.556	47.6	4.3	0.1832	3.399	1.142
2	6.05	1354.1	114.7	0.1968	96.601	0.63



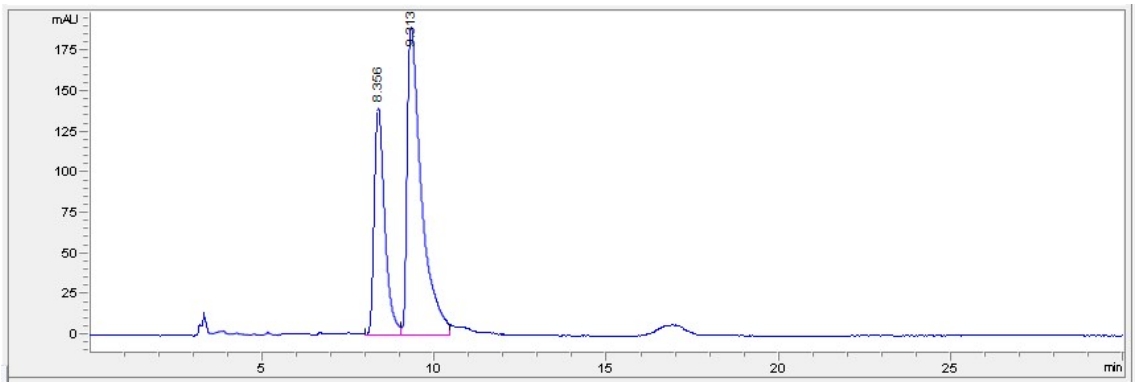
5r

(±)-**5r**

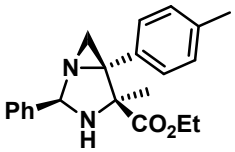


#	Time	Area	Height	Width	Area%	Symmetry
1	8.373	175.2	8.6	0.3388	48.032	0.636
2	9.515	189.6	5.7	0.5559	51.968	0.402

(+)-5r; 30% *ee*

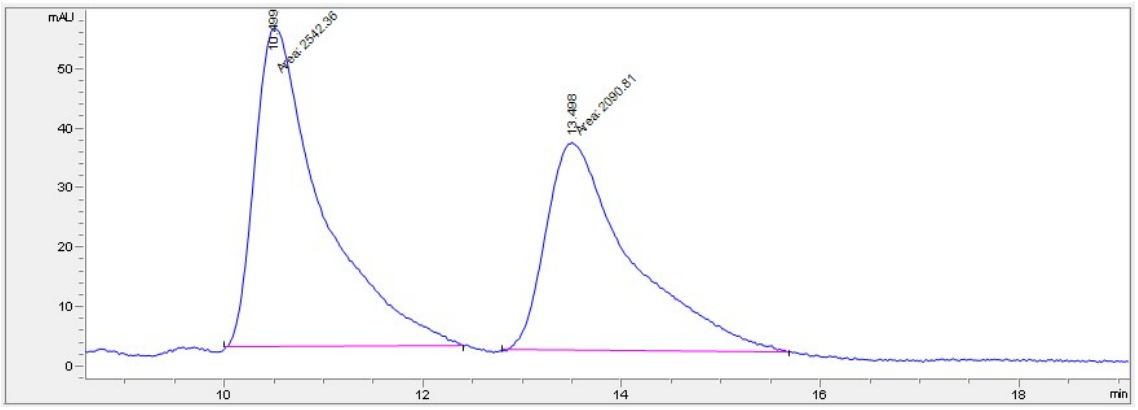


#	Time	Area	Height	Width	Area%	Symmetry
1	8.356	2957.9	140.2	0.3102	34.811	0.554
2	9.313	5539	190.1	0.387	65.189	0.361



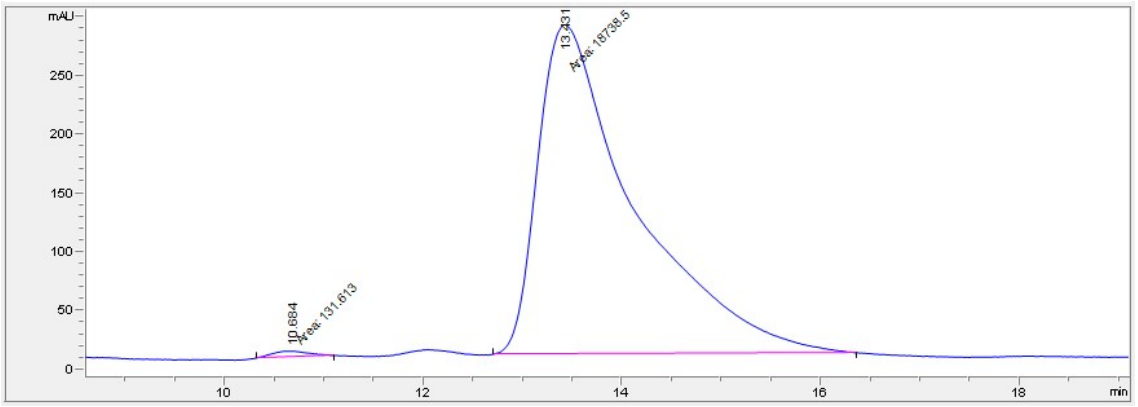
5s

(±)-**5s**

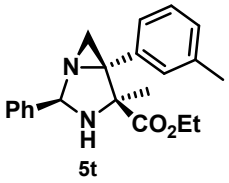


#	Time	Area	Height	Width	Area%	Symmetry
1	10.499	2542.4	53.8	0.7873	54.873	0.4
2	13.498	2090.8	35.2	0.9909	45.127	0.433

(+)-5s; 99% *ee*

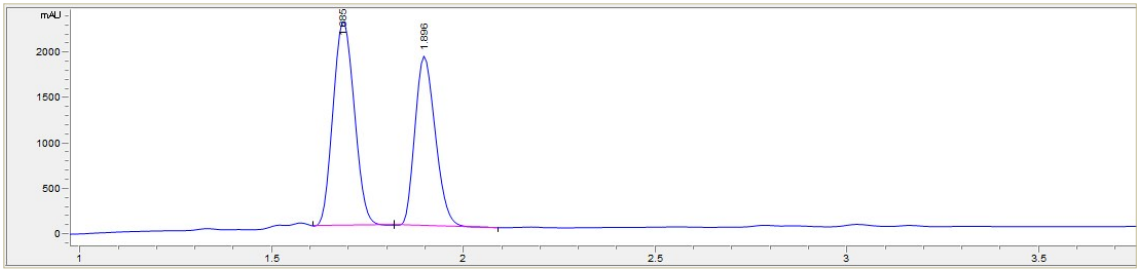


#	Time	Area	Height	Width	Area%	Symmetry
1	10.684	131.6	5	0.4412	0.697	1.521
2	13.431	18738.5	278.5	1.1215	99.303	0.388



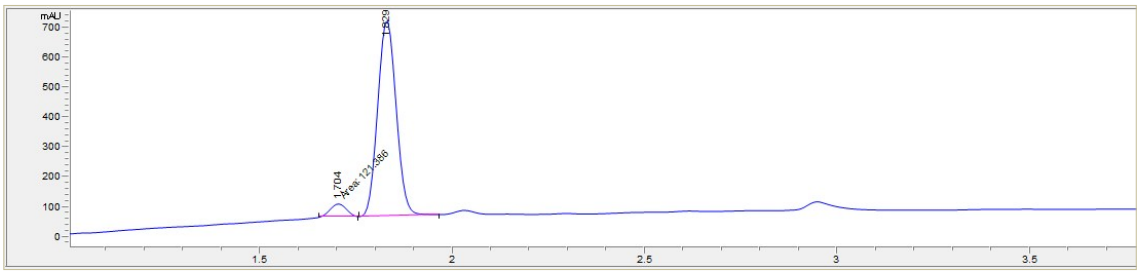
5t

(±)-**5t**

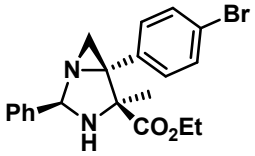


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	1.685	BB	8762.9	2270.9	0.061	55.726	0.866
2	1.896	BB	6962	1879.5	0.0572	44.274	0.765

(+)-5t; 77% *ee*

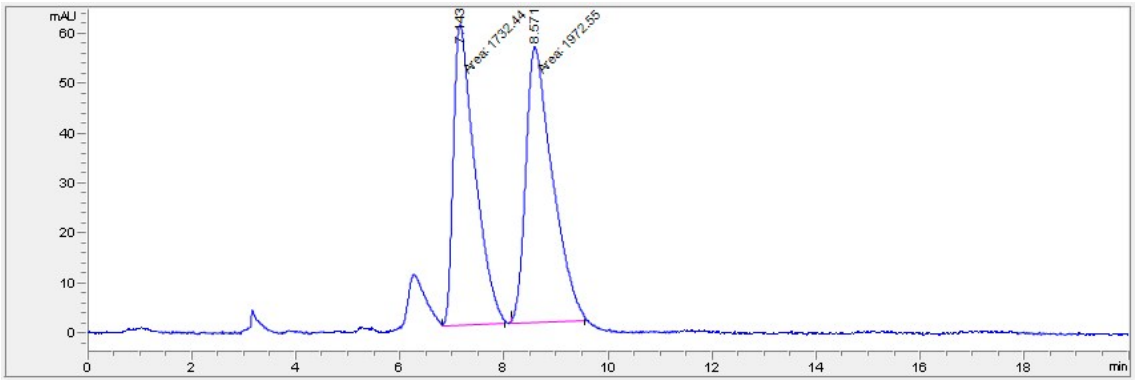


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	1.704	MM	121.4	42.3	0.0479	5.284	0.908
2	1.829	BB	2175.8	655.1	0.0507	94.716	0.918



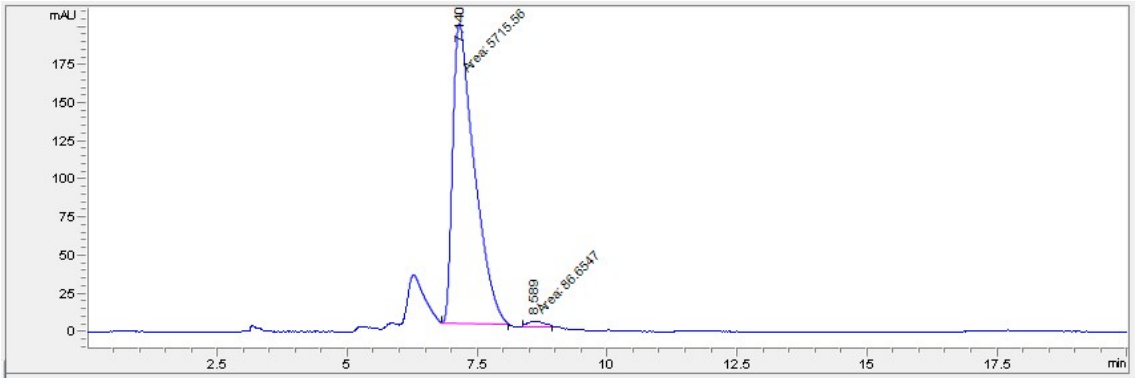
5u

(±)-**5u**

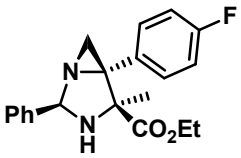


#	Time	Area	Height	Width	Area%	Symmetry
1	7.143	1670	59.2	0.4705	46.462	0.445
2	8.571	1924.3	54.5	0.5885	53.538	0.468

(+)-5u; 97% *ee*

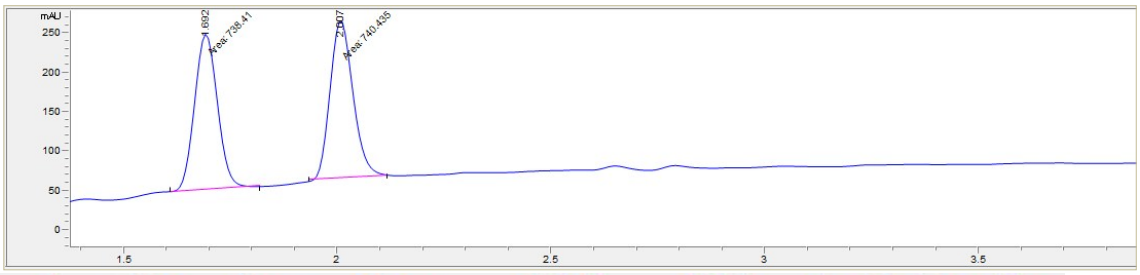


#	Time	Area	Height	Width	Area%	Symmetry
1	7.14	5715.6	196.5	0.4849	98.507	0.429
2	8.589	86.7	3.9	0.3727	1.493	0.727



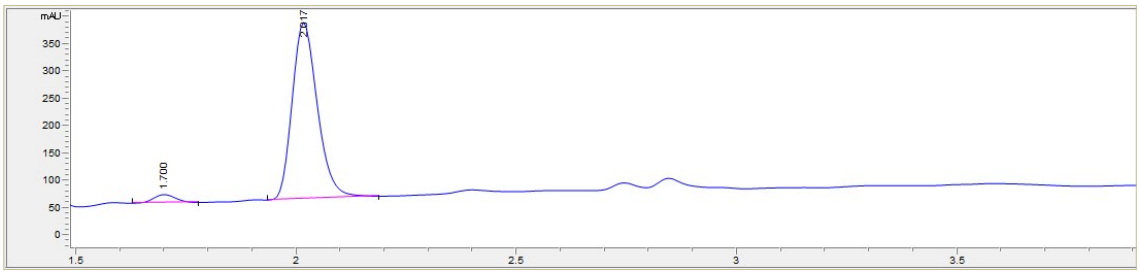
5v

(±)-**5v**

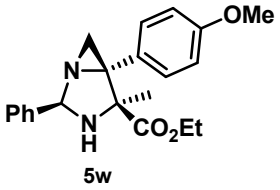


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	1.692	MM	738.4	198.5	0.062	49.932	0.935
2	2.007	MM	740.4	201	0.0614	50.068	0.835

(+)-5v; 92% *ee*

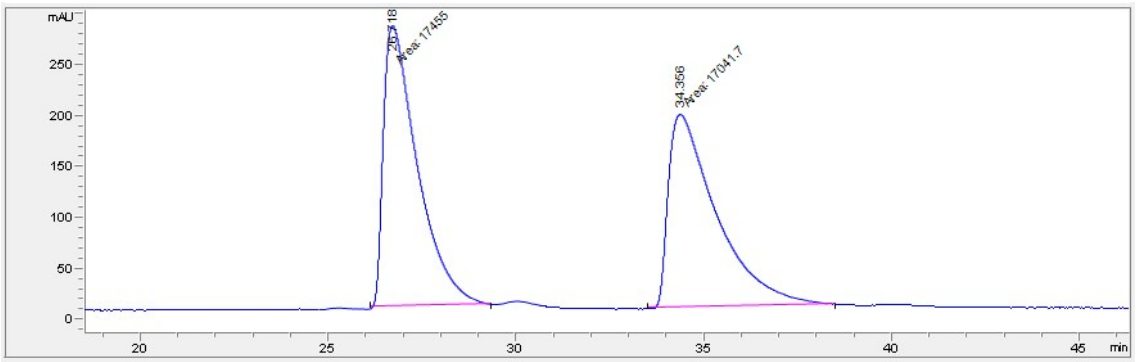


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	1.7	BB	52.9	15.3	0.0544	3.942	0.877
2	2.017	BB	1288.4	324.2	0.0604	96.058	0.761



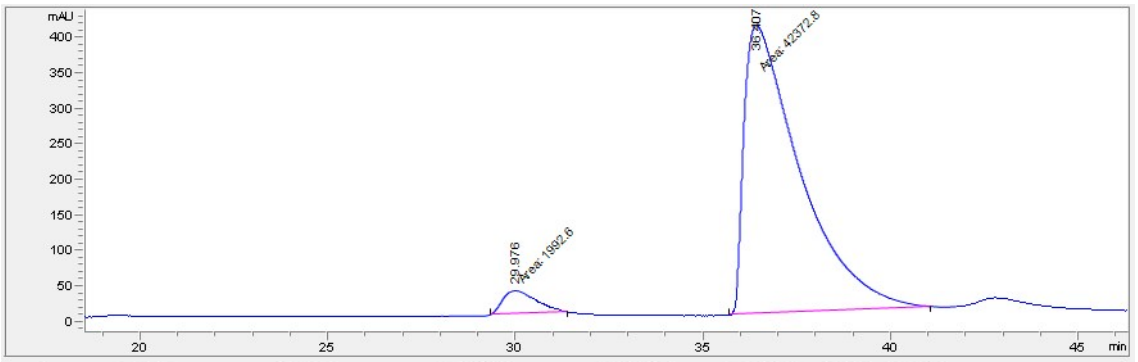
5w

(±)-**5w**

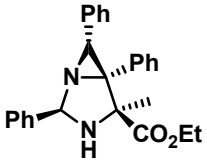


#	Time	Area	Height	Width	Area%	Symmetry
1	26.718	17455	276.4	1.0525	50.599	0.38
2	34.356	17041.7	190.4	1.492	49.401	0.3

(+)-5w; 90% *ee*

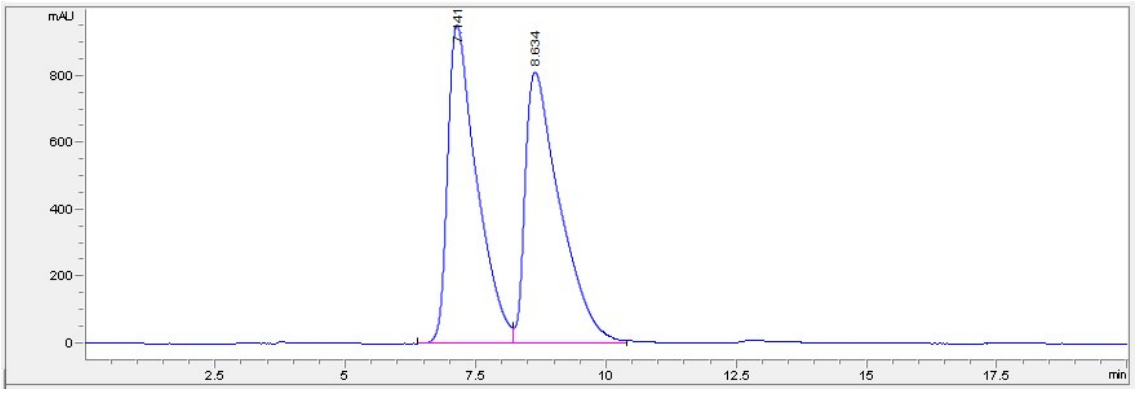


#	Time	Area	Height	Width	Area%	Symmetry
1	29.976	1992.6	33.3	0.9964	4.491	0.61
2	36.407	42372.8	408	1.731	95.509	0.262



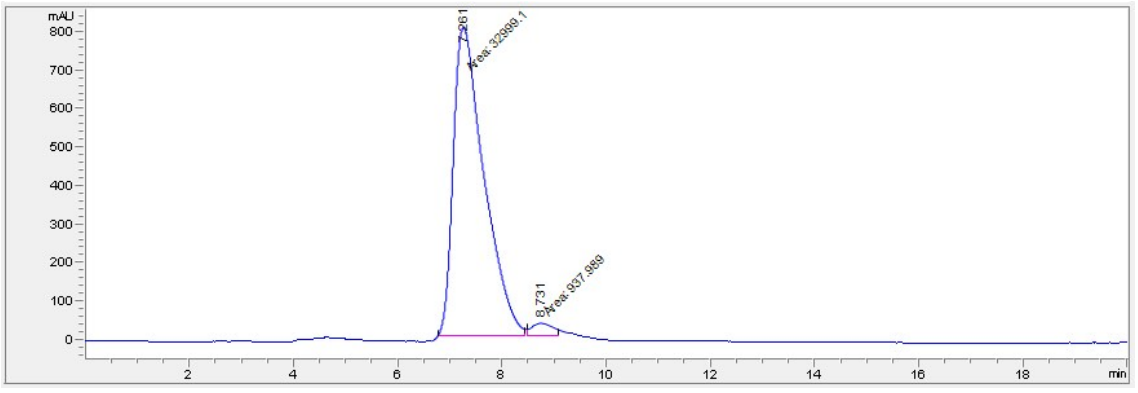
6a

(±)-**6a**

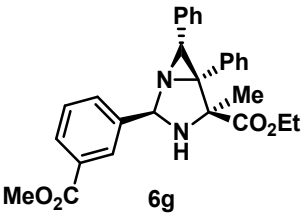


#	Time	Area	Height	Width	Area%	Symmetry
1	7.141	37095.1	952.2	0.5175	49.536	0.452
2	8.634	37789.3	811.5	0.5663	50.464	0.375

(+)-6a; 94% *ee*

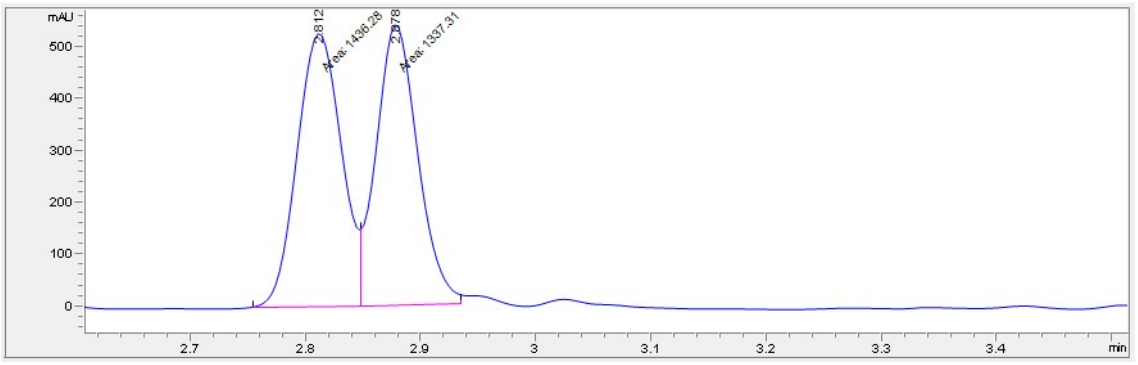


#	Time	Area	Height	Width	Area%	Symmetry
1	7.261	32999.1	806.1	0.6822	97.236	0.483
2	8.731	938	32.9	0.4757	2.764	0.7



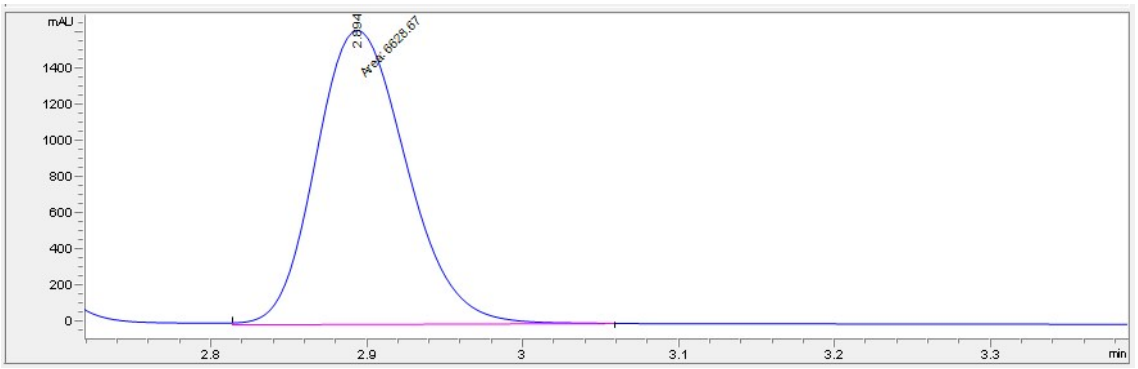
6g

(±)-**6g**

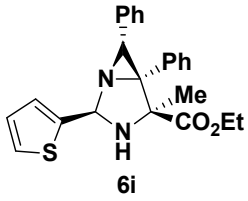


#	Time	Area	Height	Width	Area%	Symmetry
1	2.812	1436.3	529.4	0.0452	51.784	0.941
2	2.878	1337.3	542.8	0.0411	48.216	0.819

(+)-6a; 94% *ee*

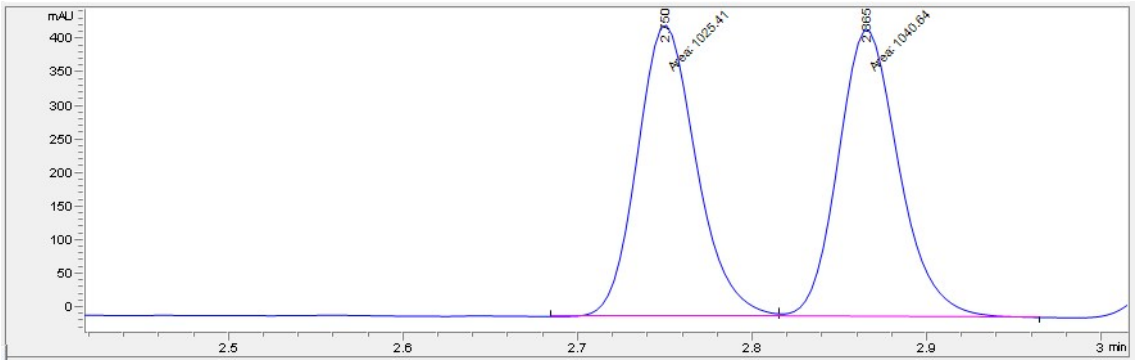


#	Time	Area	Height	Width	Area%	Symmetry
1	2.894	6628.7	1632.2	0.0677	100.000	0.818



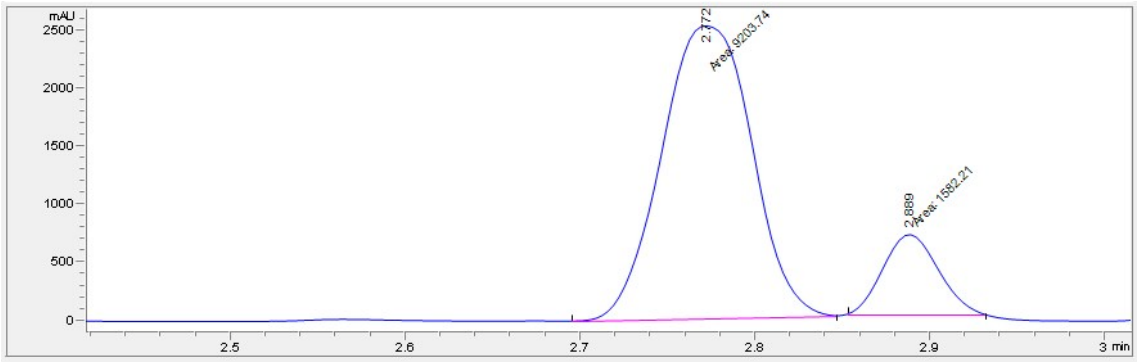
6i

(±)-**6i**

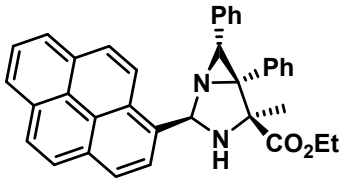


#	Time	Area	Height	Width	Area%	Symmetry
1	2.75	1025.4	436.6	0.0391	49.631	0.852
2	2.865	1040.6	430.2	0.0403	50.369	0.843

(+)-6i; 71% *ee*

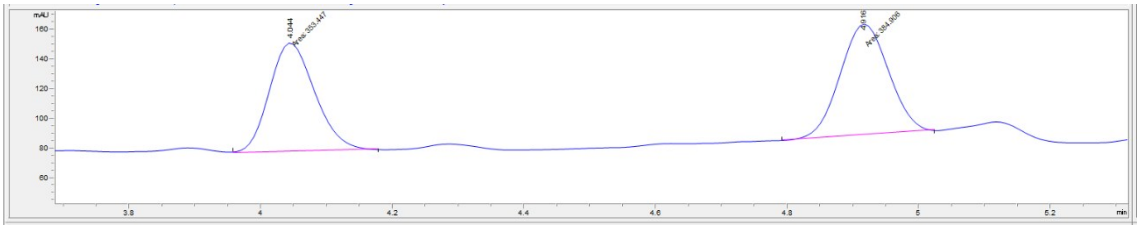


#	Time	Area	Height	Width	Area%	Symmetry
1	2.772	9203.7	2546.7	0.0602	85.331	0.954
2	2.889	1582.2	708	0.0372	14.669	0.886



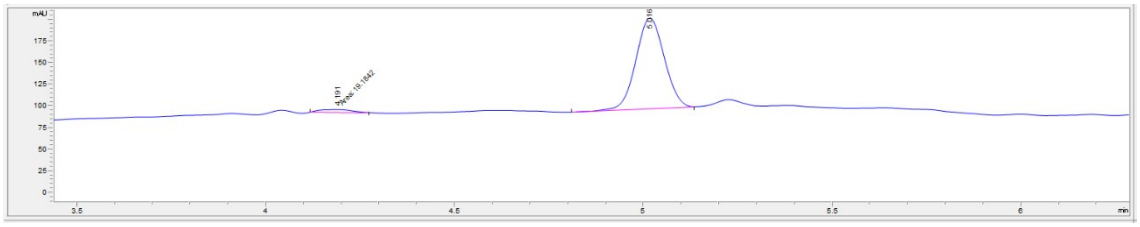
6s

(±)-**6s**

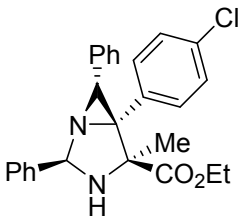


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.044	MM	353.4	73.9	0.0797	47.870	0.812
2	4.916	MM	384.9	75.5	0.085	52.130	0.972

(+)-6s; 93% *ee*

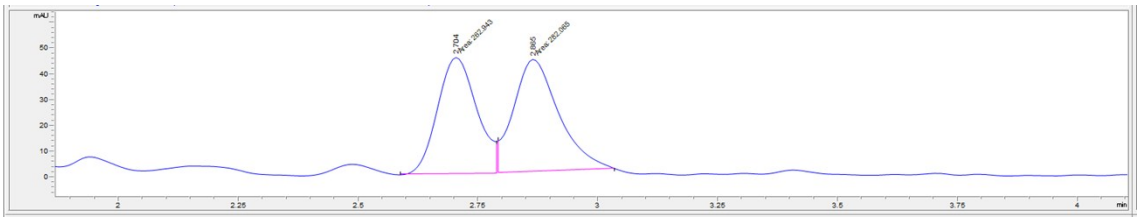


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.191	MM	19.2	3.3	0.0977	3.388	0.895
2	5.016	BB	547	104.9	0.0808	96.612	0.956



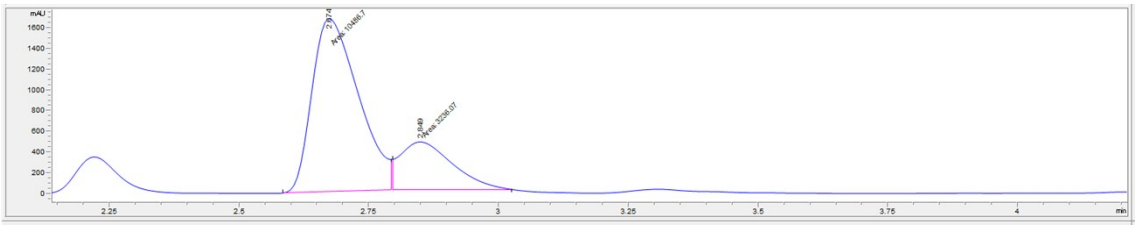
6t

(±)-**6t**



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.704	MM	262.9	45.3	0.0968	48.246	0.847
2	2.865	MM	282.1	43.6	0.1079	51.754	0.728

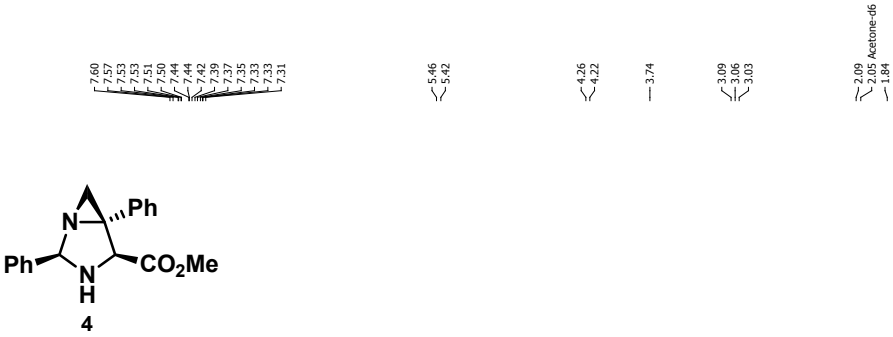
(+)-6t; 53% *ee*



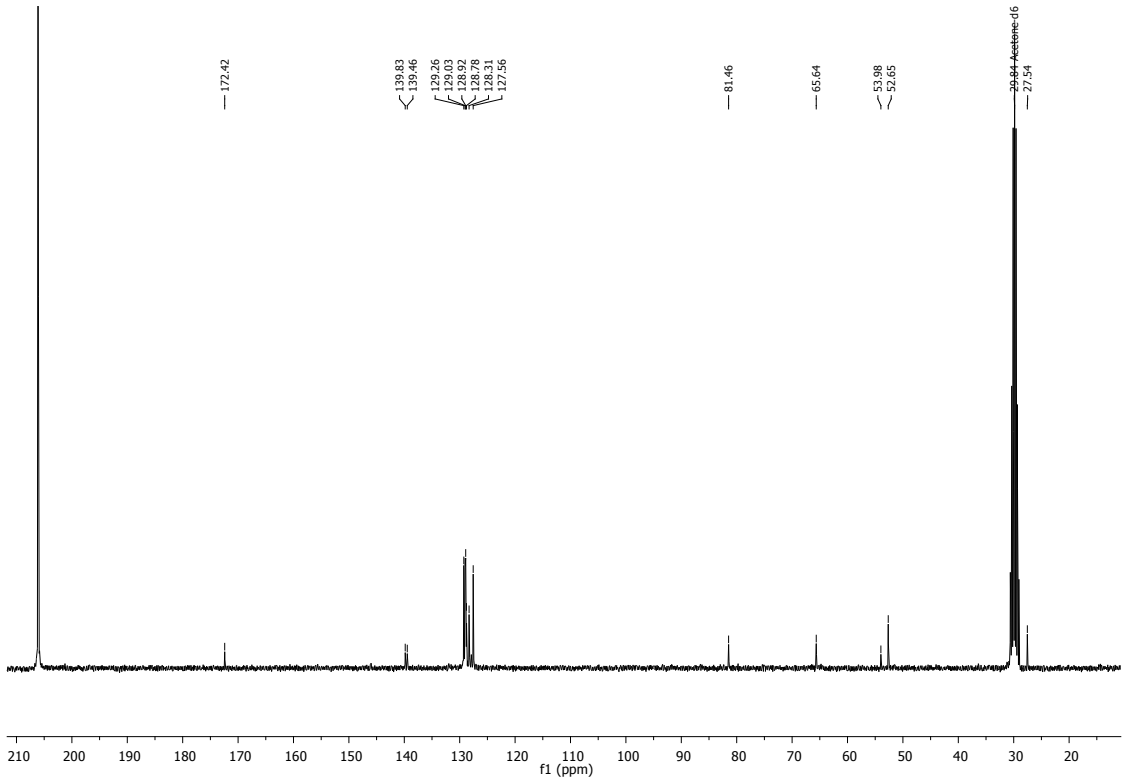
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.674	MM	10486.7	1676.8	0.1042	76.418	0.576
2	2.849	MM	3236.1	464.5	0.1161	23.582	0.553

8. NMR Spectra collection

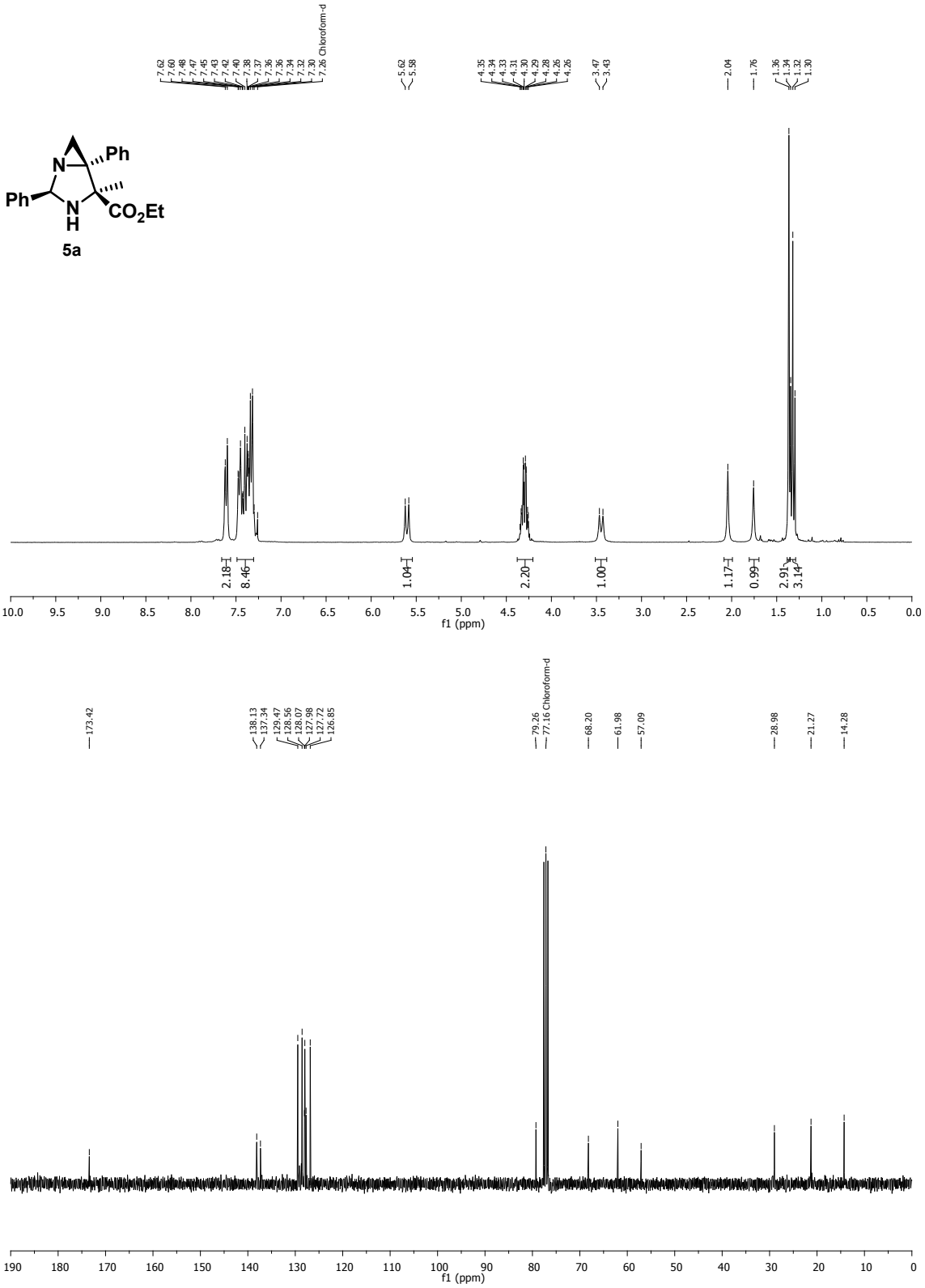
(2*R*,4*S*,5*S*) Methyl 2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (4)



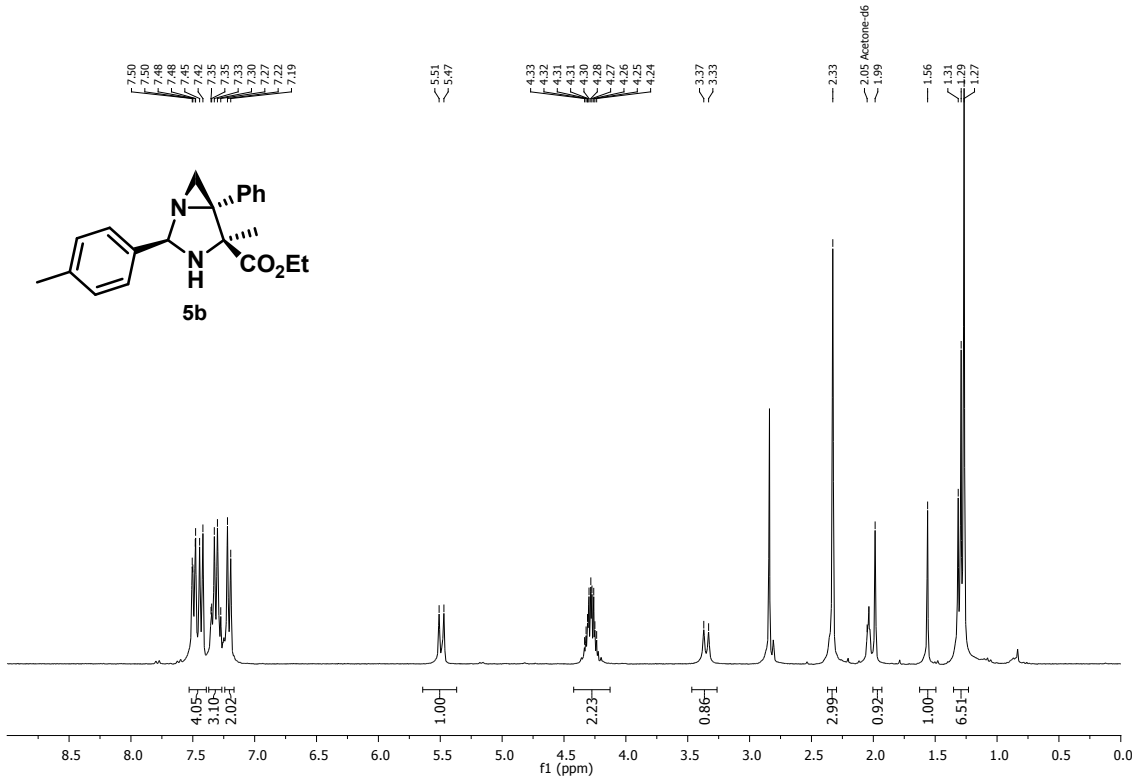
4

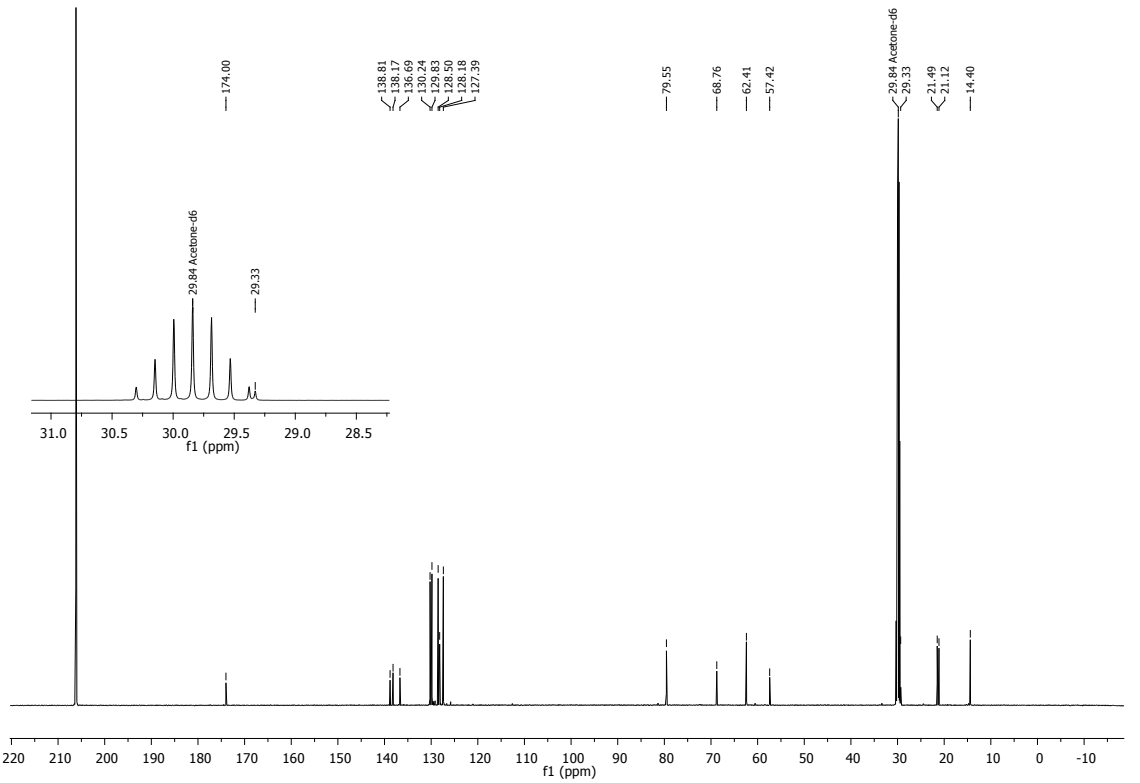


(2*R*,4*S*,5*S*) Ethyl 4-methyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5a)

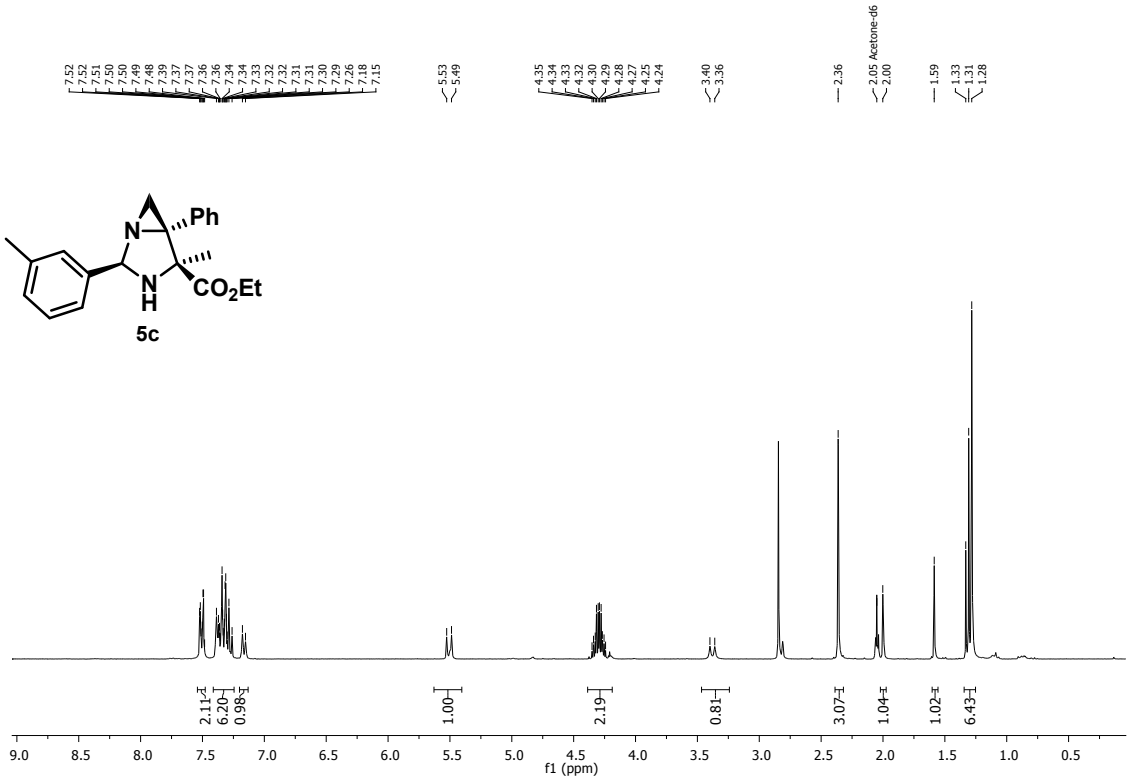


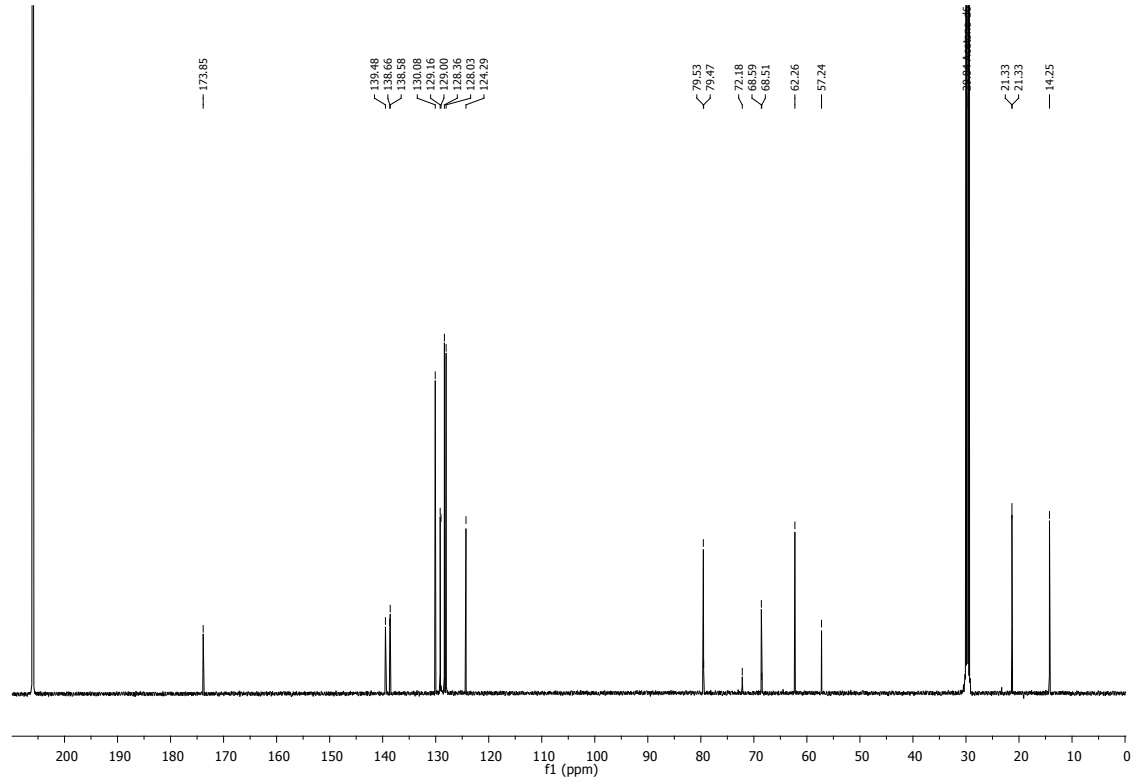
(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*p*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5b)



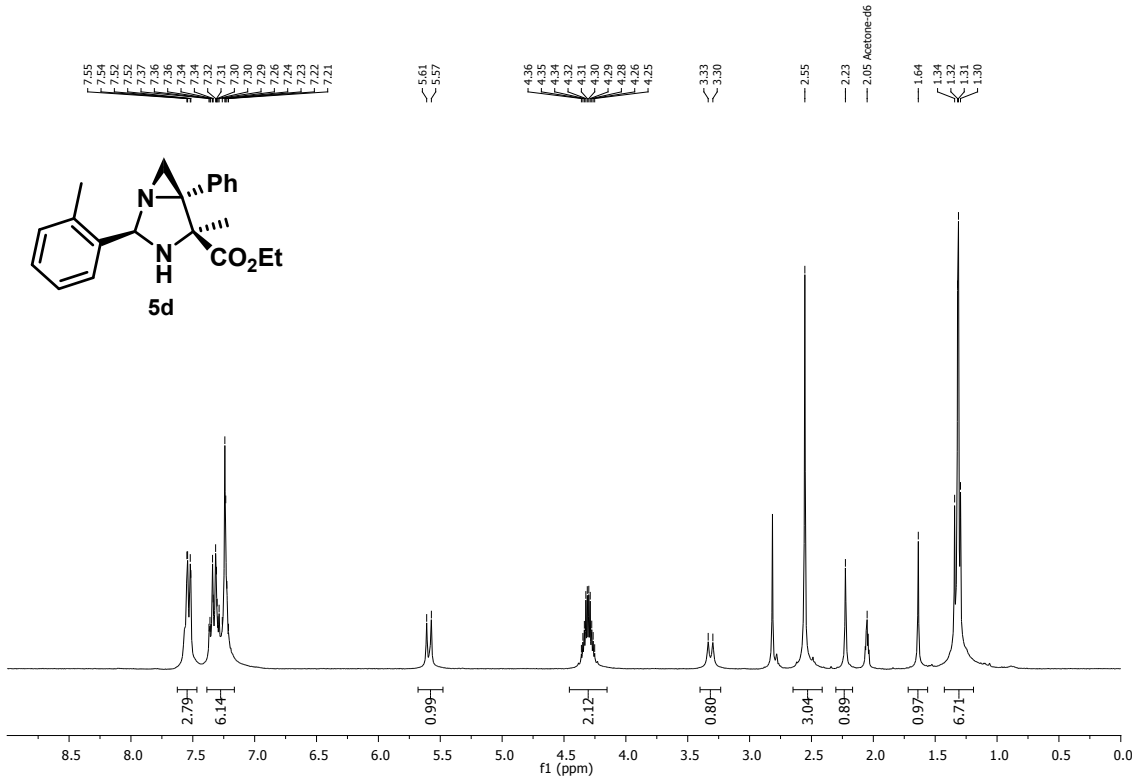


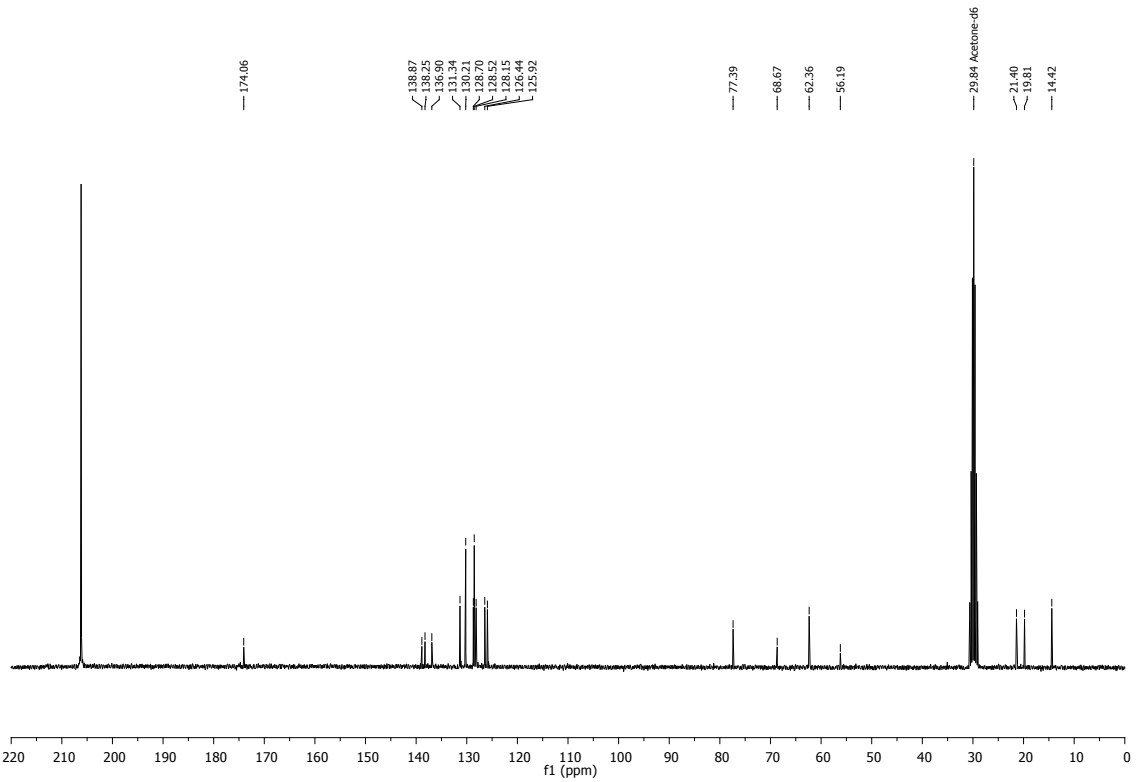
(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*m*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5c)



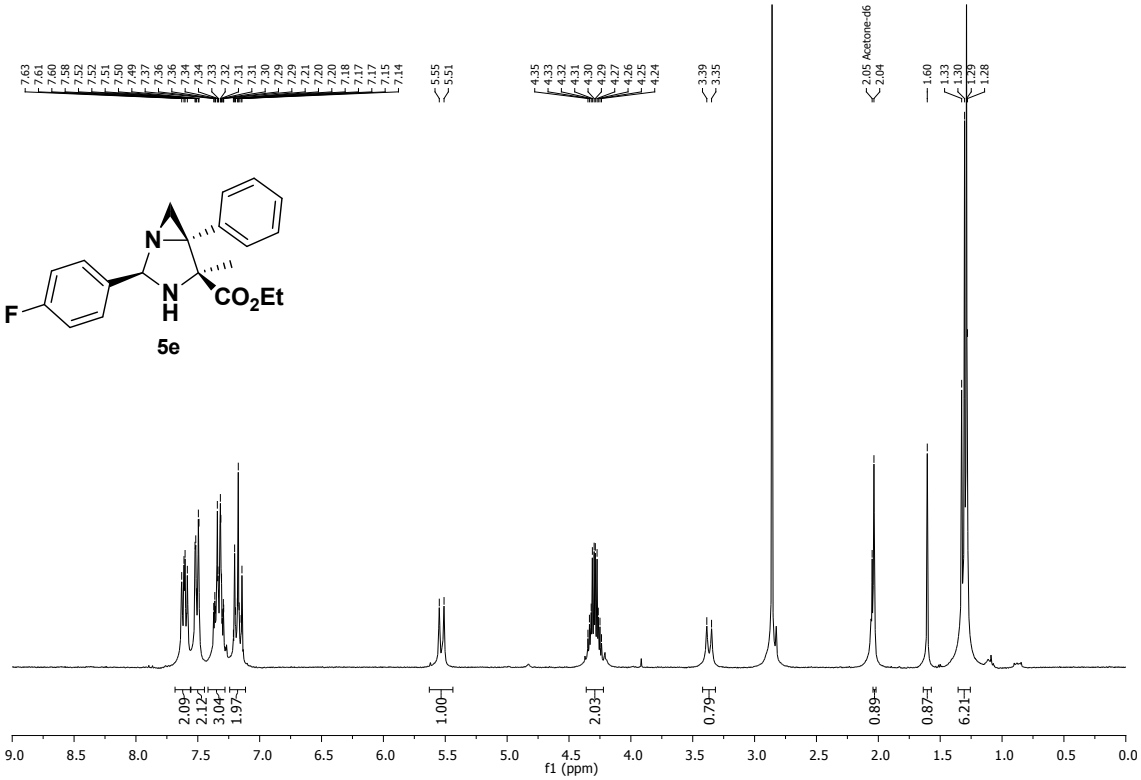


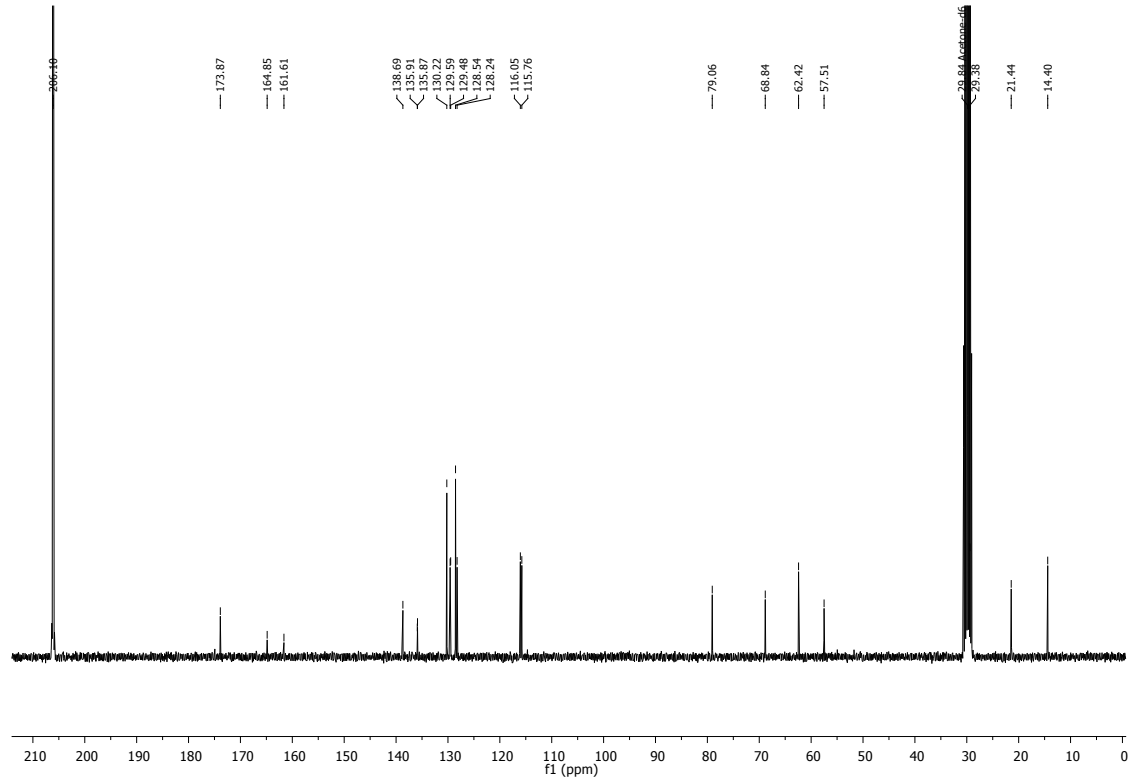
(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(*o*-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5d)

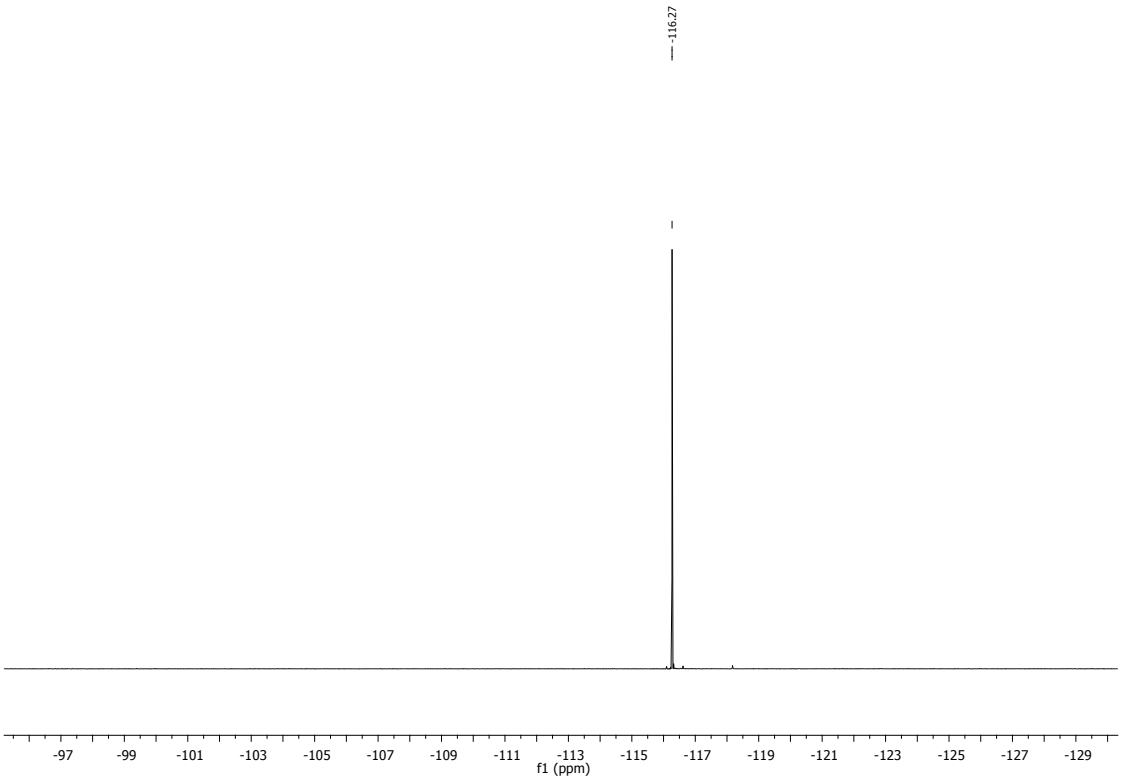




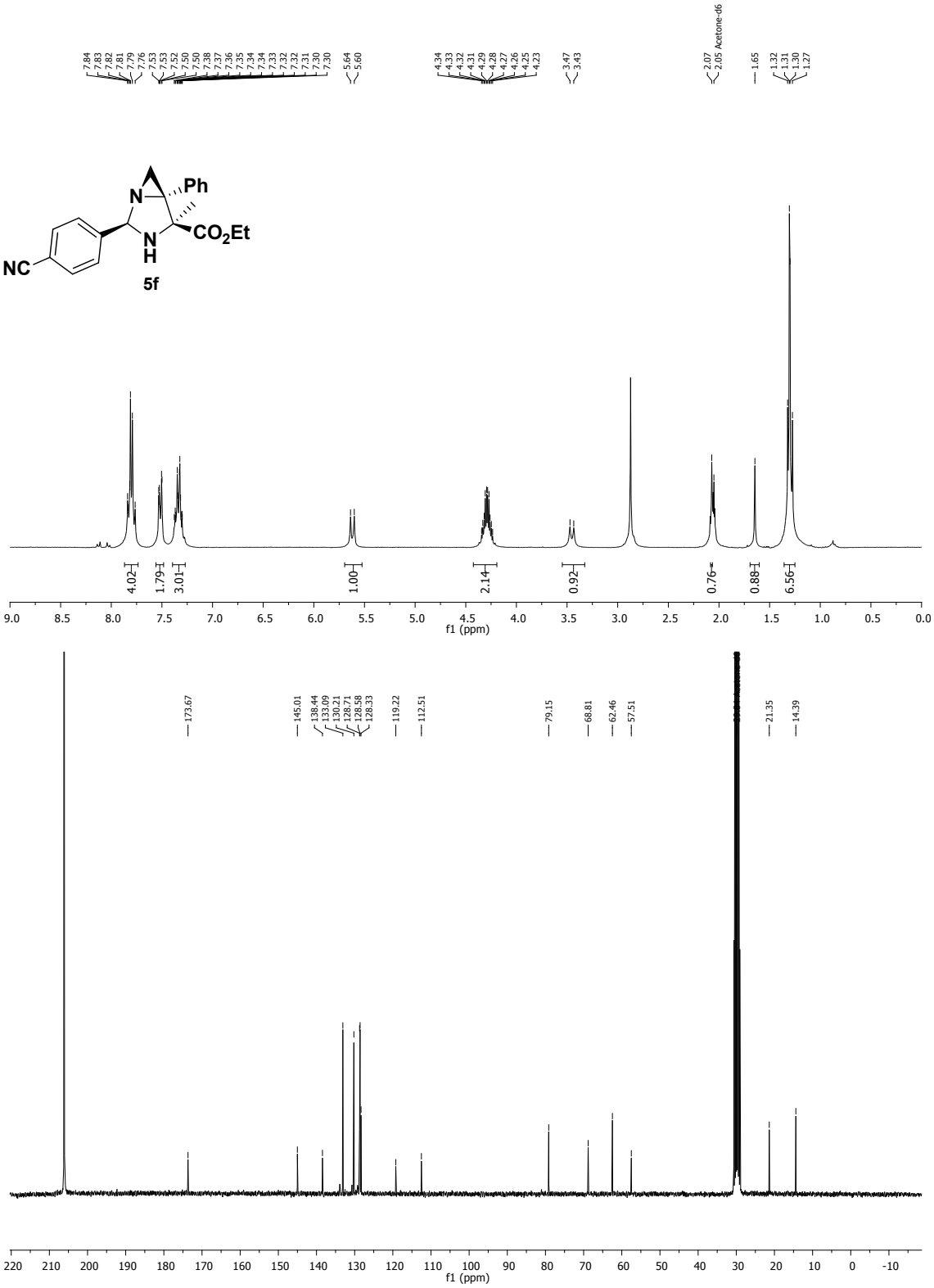
(2*R*,4*S*,5*S*) Ethyl 2-(4-fluorophenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5e)



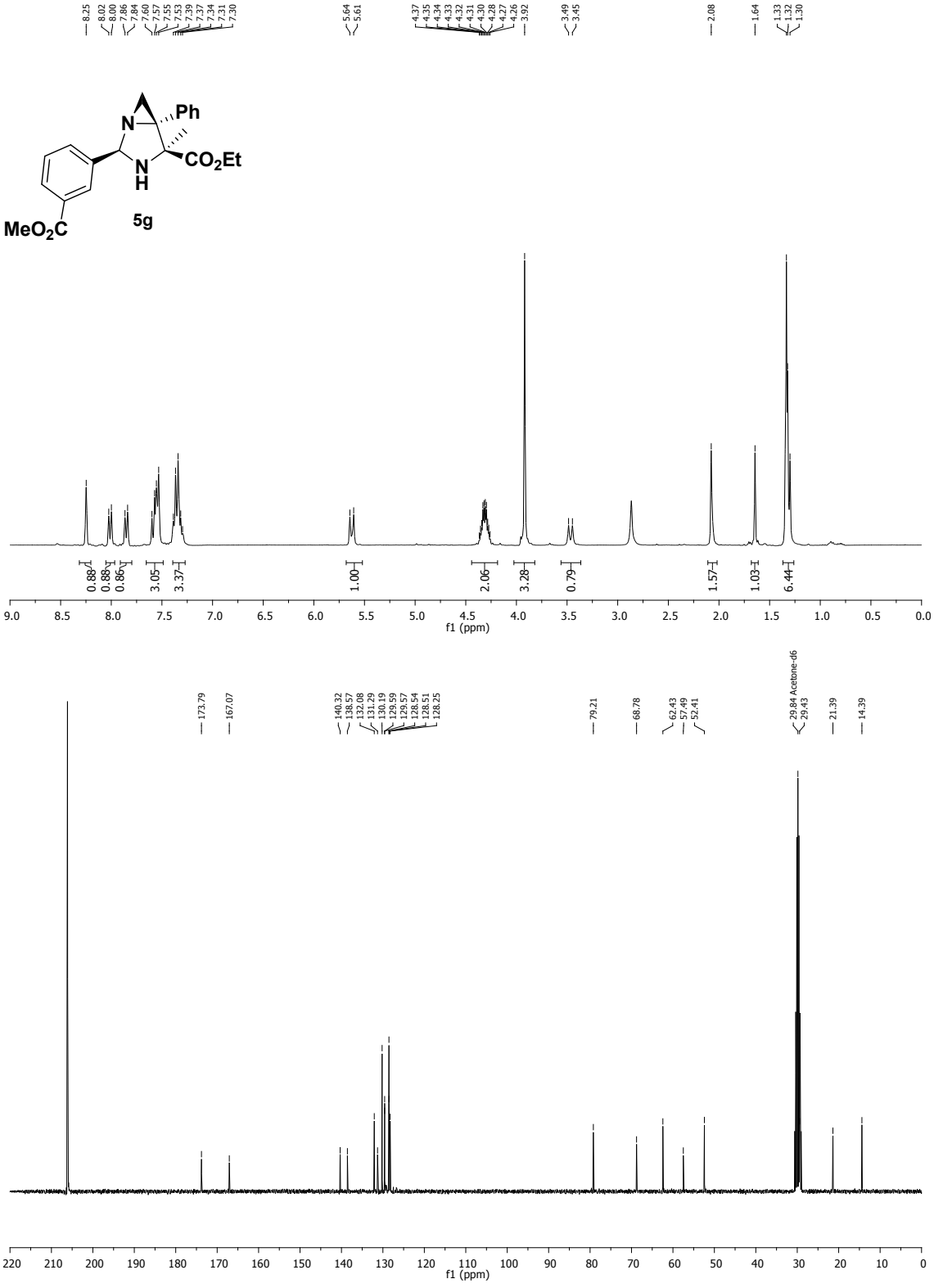



-116.27
-97
-99
-101
-103
-105
-107
-109
-111
-113
-115
-117
-119
-121
-123
-125
-127
-129
f1 (ppm)

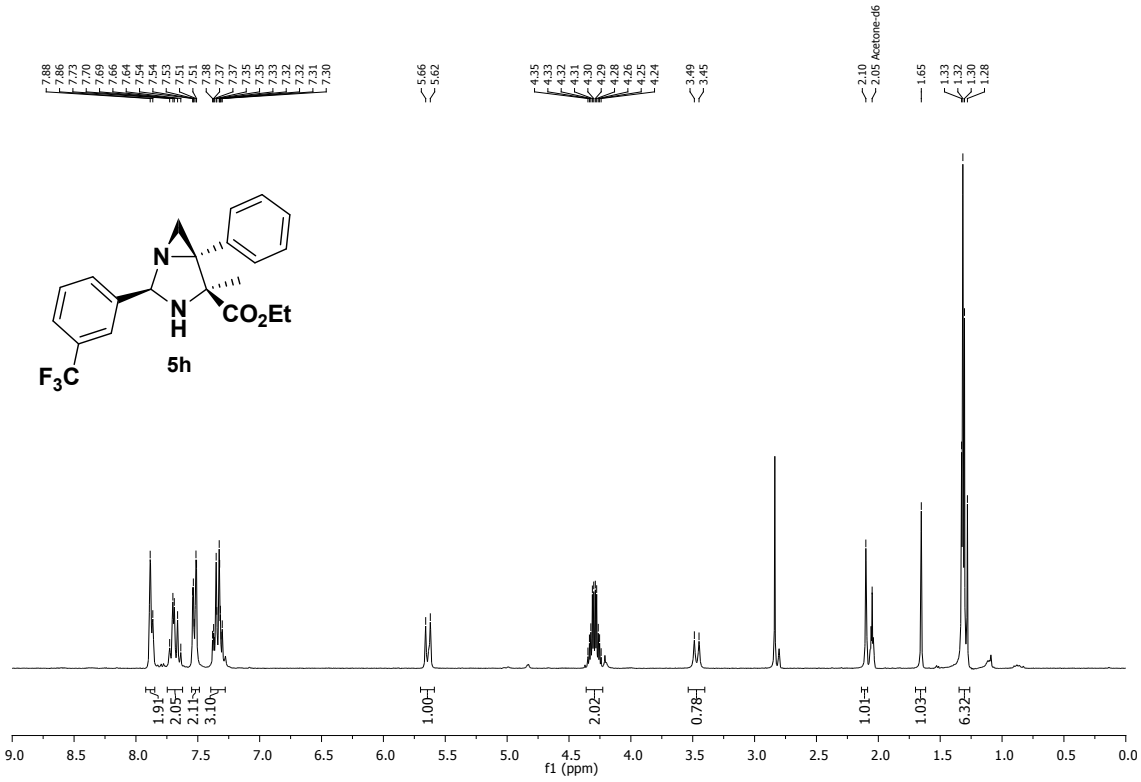
(2*R*,4*S*,5*S*) Ethyl 2-(4-cyanophenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5f)

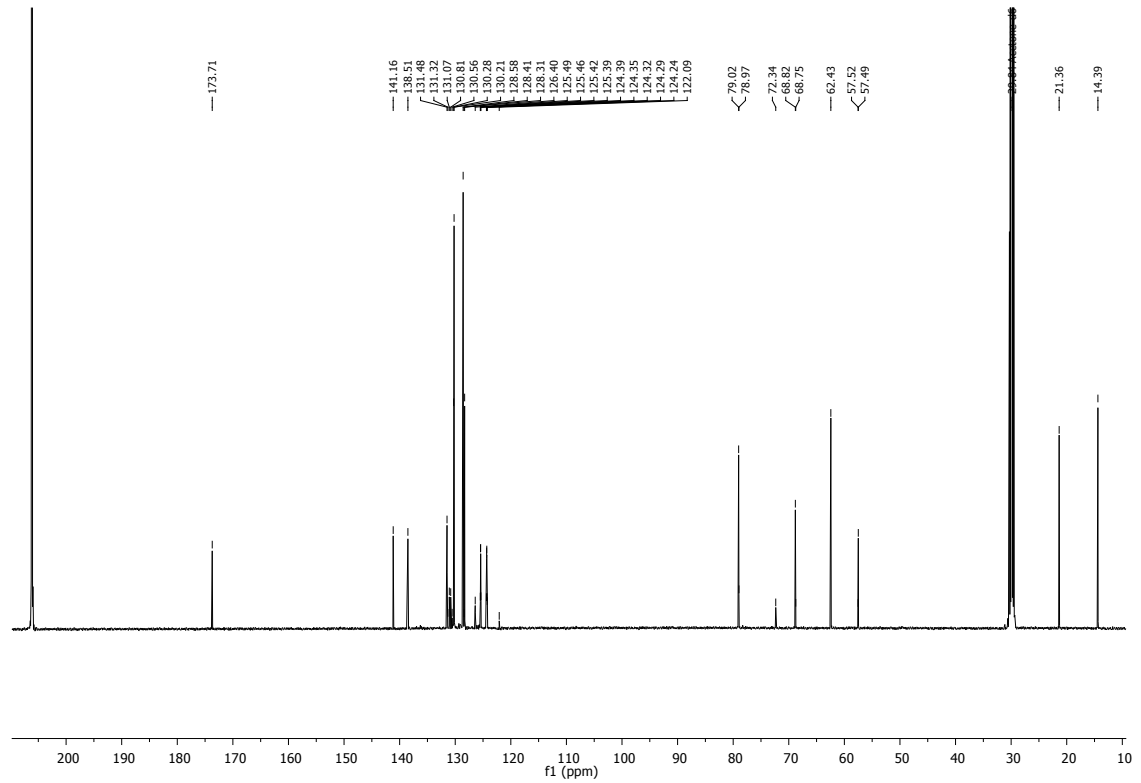


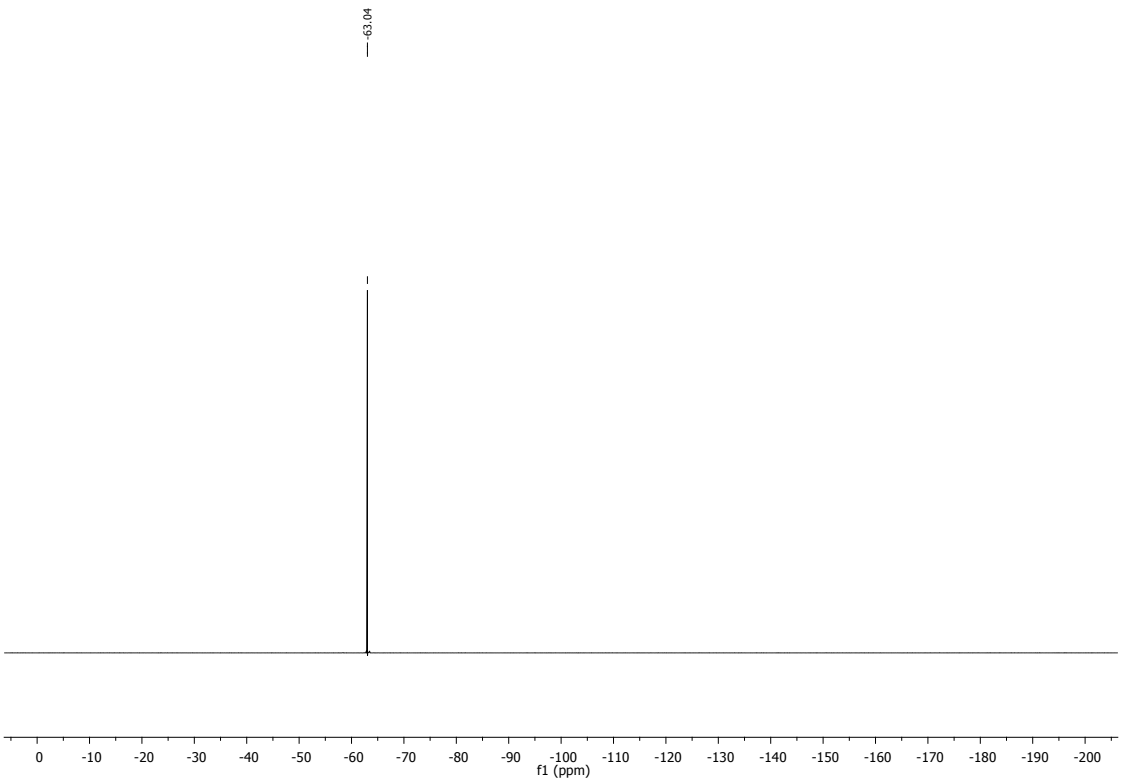
(2*R*,4*S*,5*S*) Ethyl 2-(3-(methoxycarbonyl)phenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5g)



(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(3-(trifluoromethyl)phenyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5h)






-63.04
0
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-60
-70
-80
-90
-100
-110
-120
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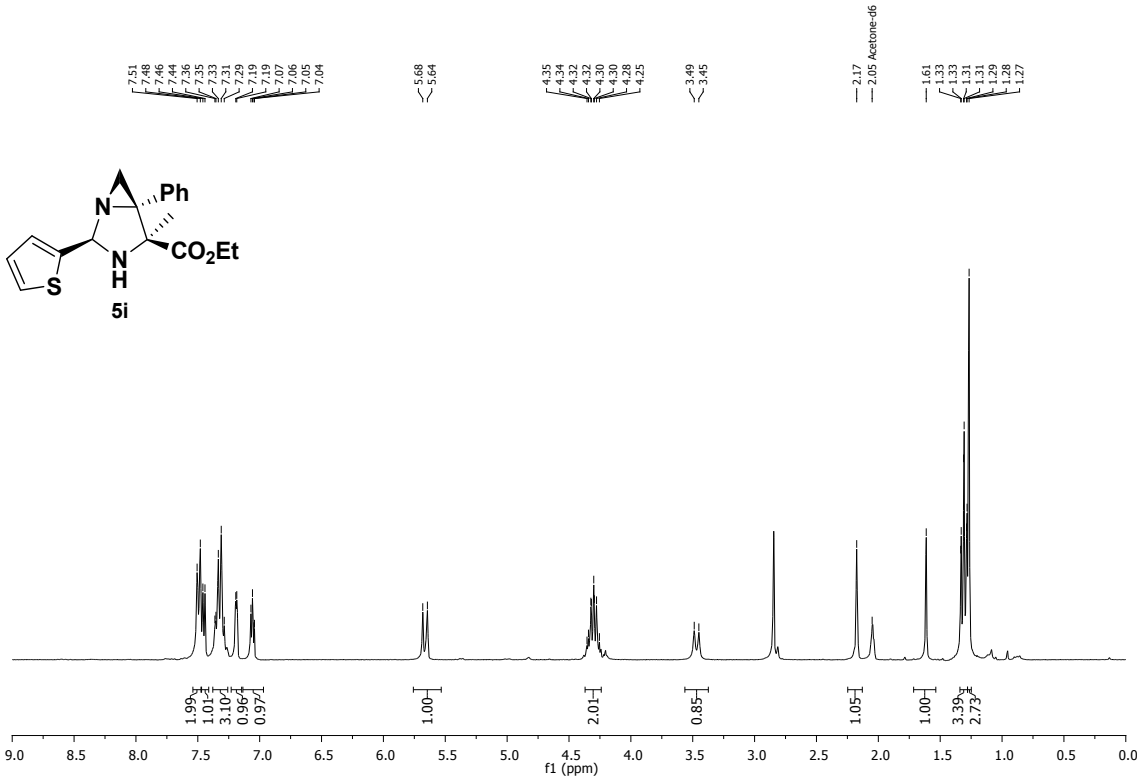
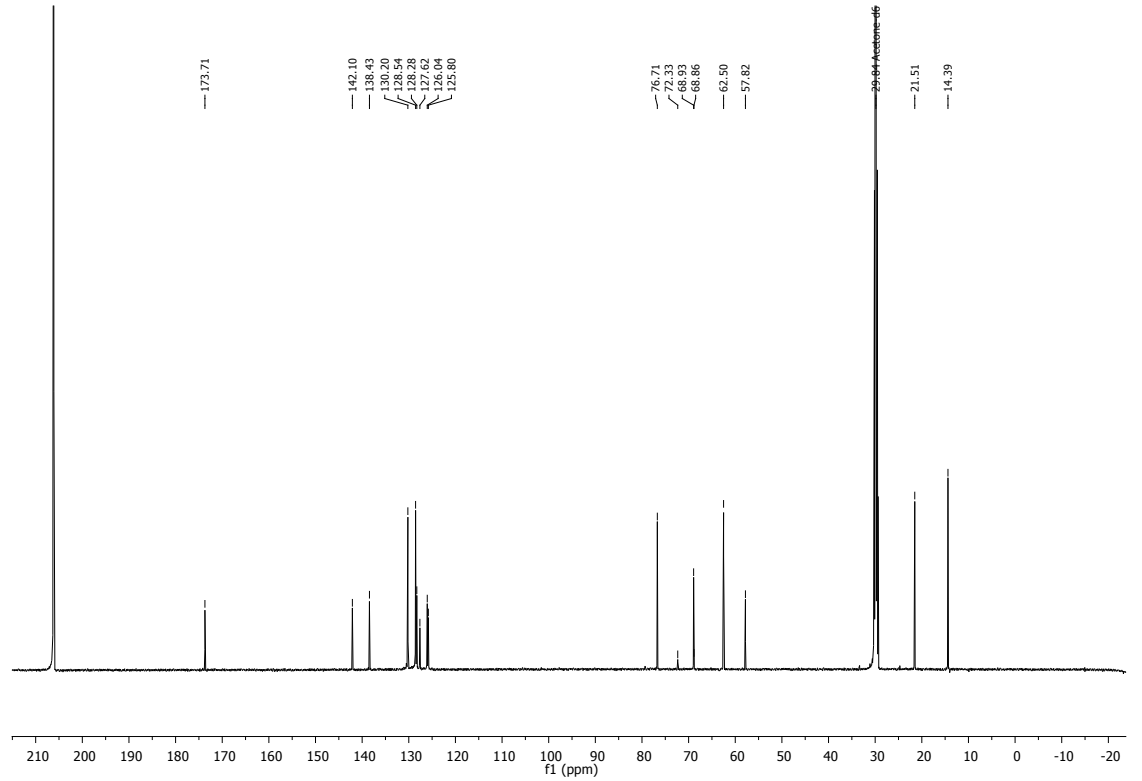
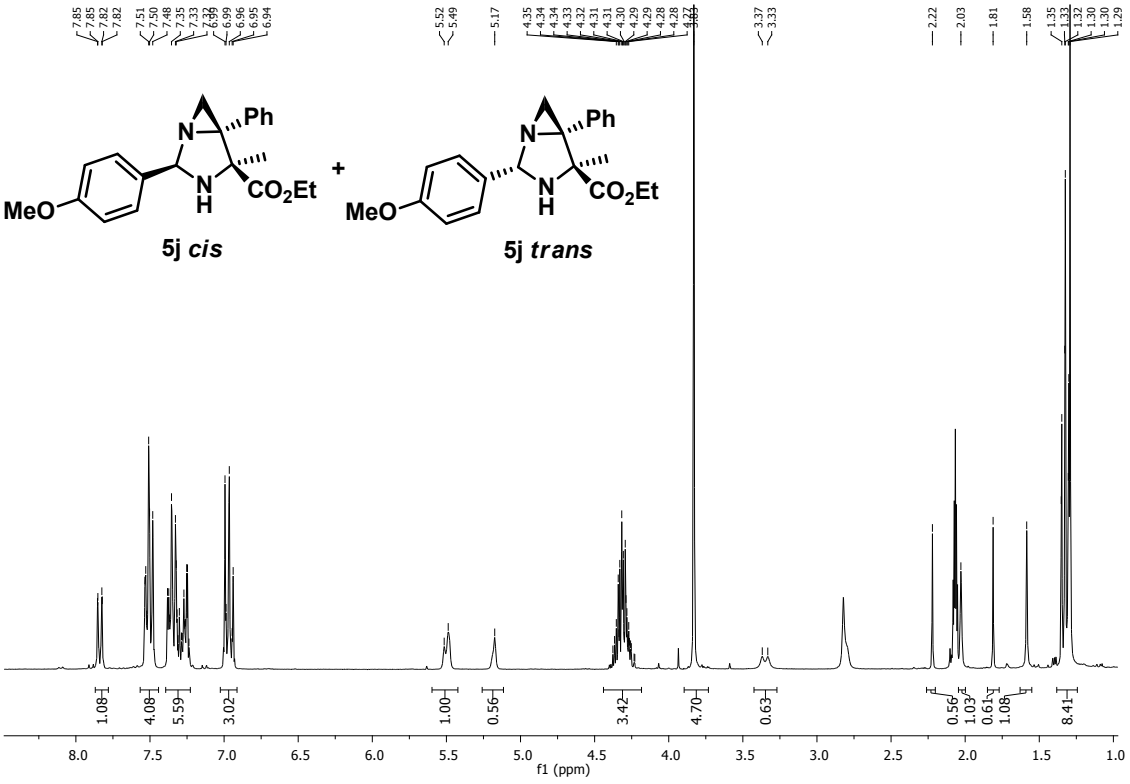
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

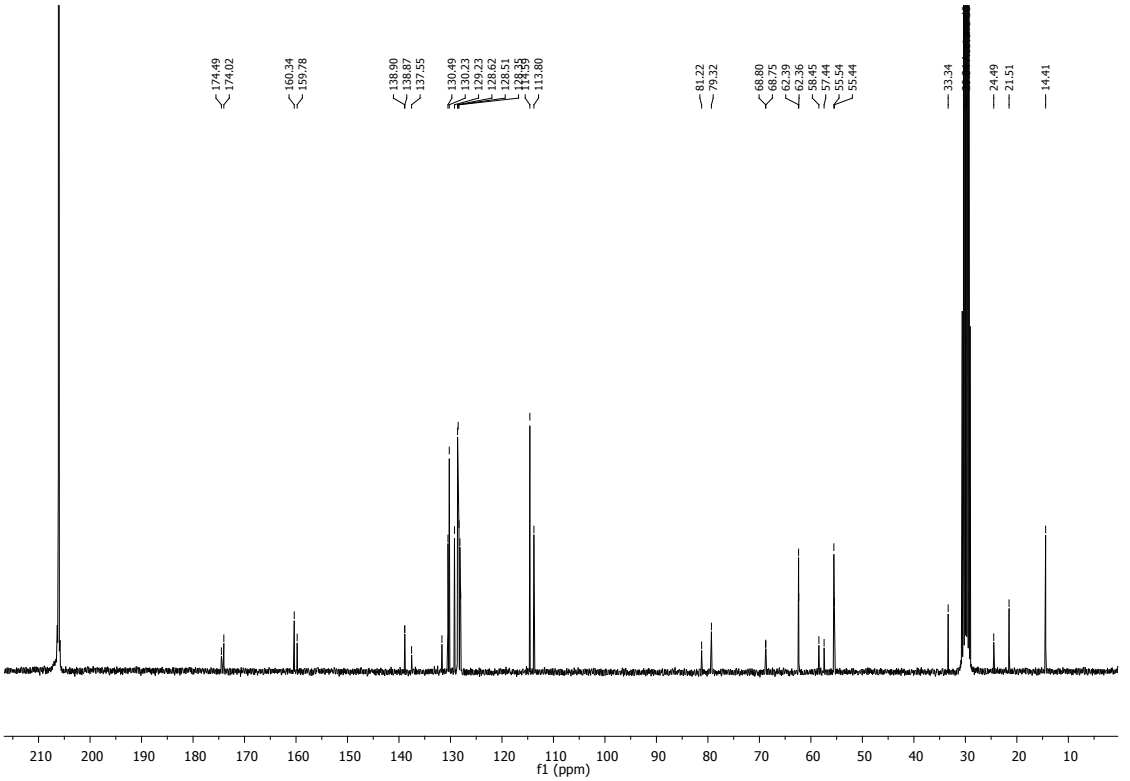
(2*R*,4*S*,5*S*) Ethyl 4-methyl-5-phenyl-2-(thiophen-2-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5i)



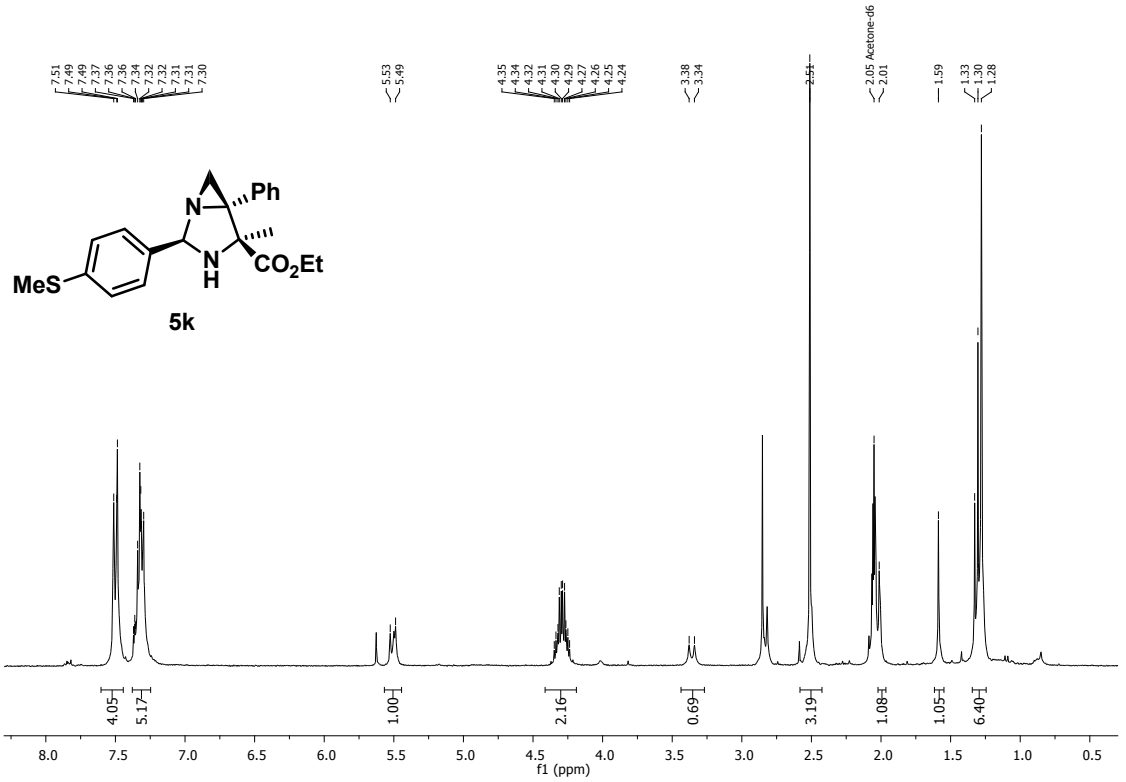


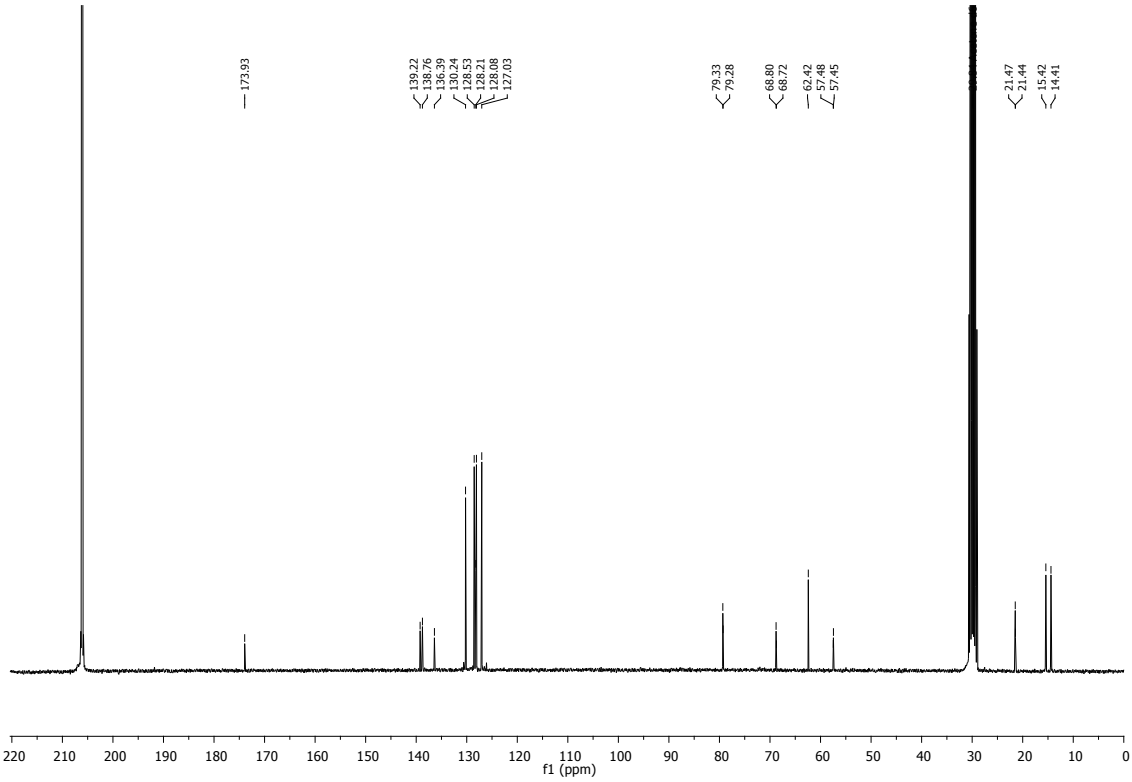
(2R,4S,5S)-Ethyl 2-(4-methoxyphenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5j)



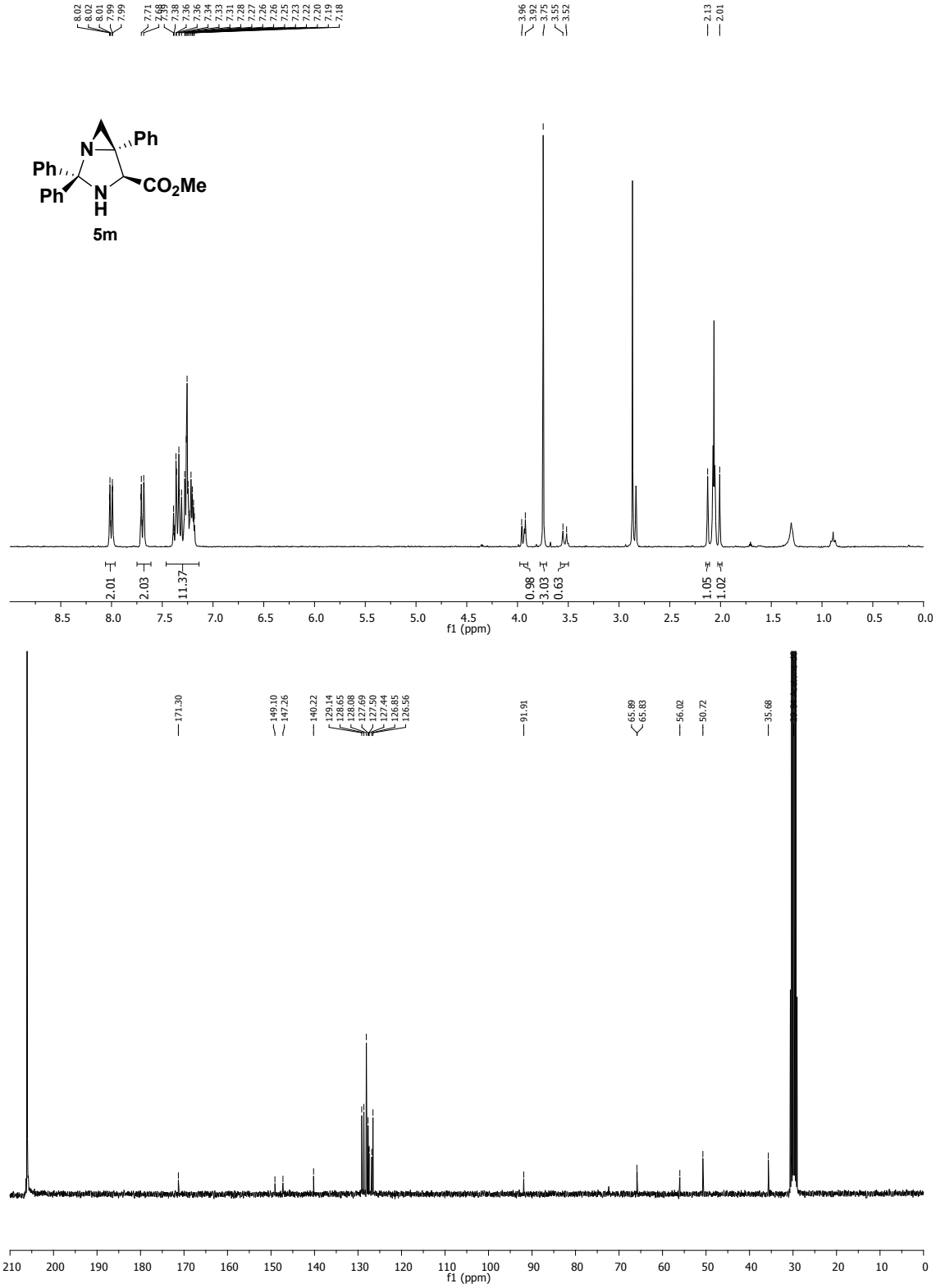


(2R,4S,5S)-Ethyl 2-(4-methoxyphenyl)-4-methyl-5-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5k)

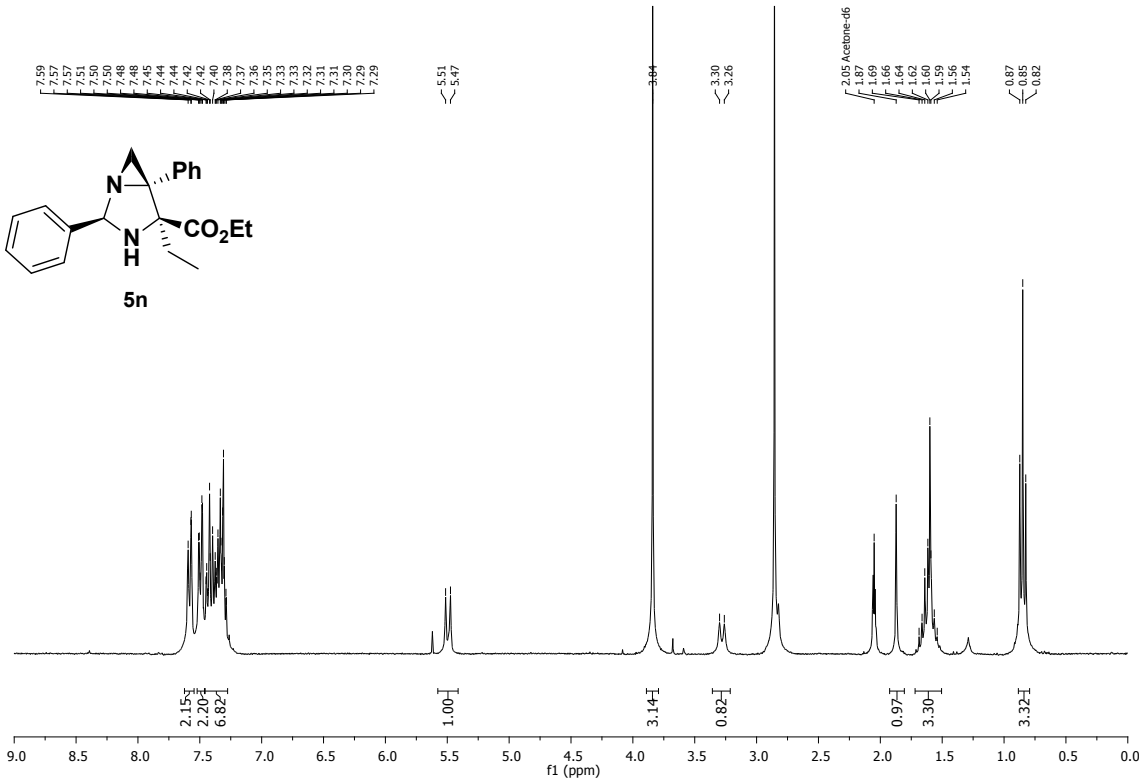


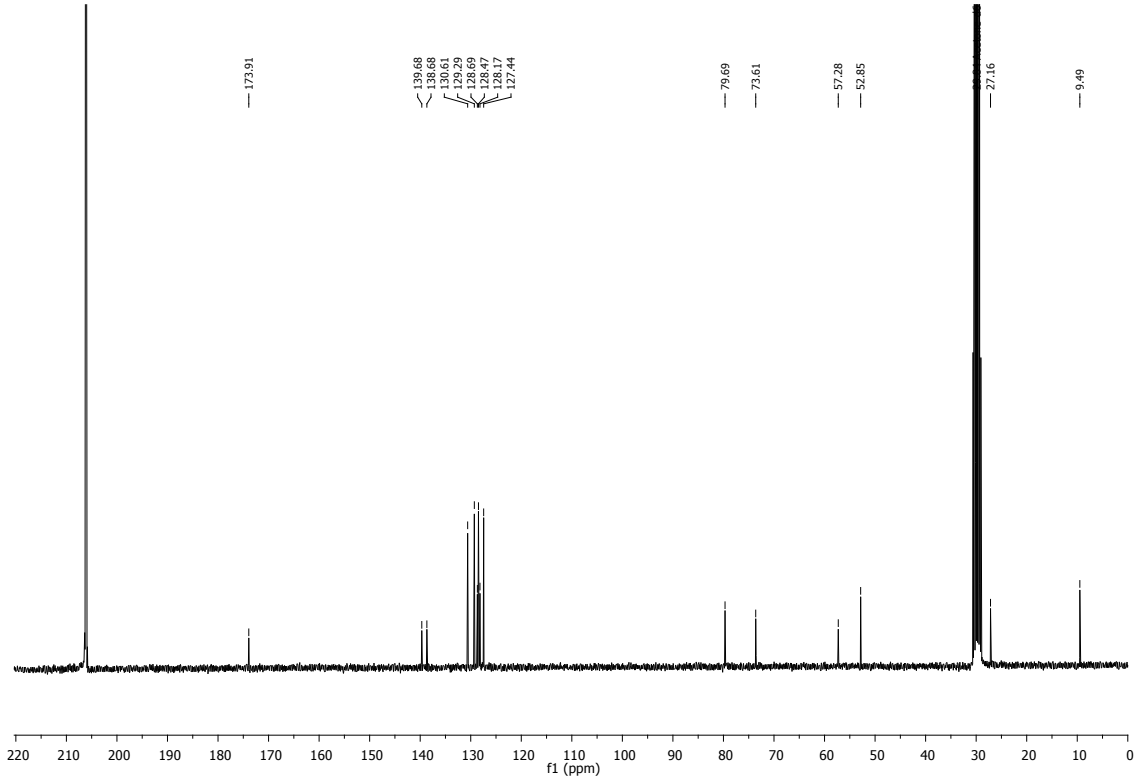


(4S,5S)-Methyl 2,2,5-triphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5m)

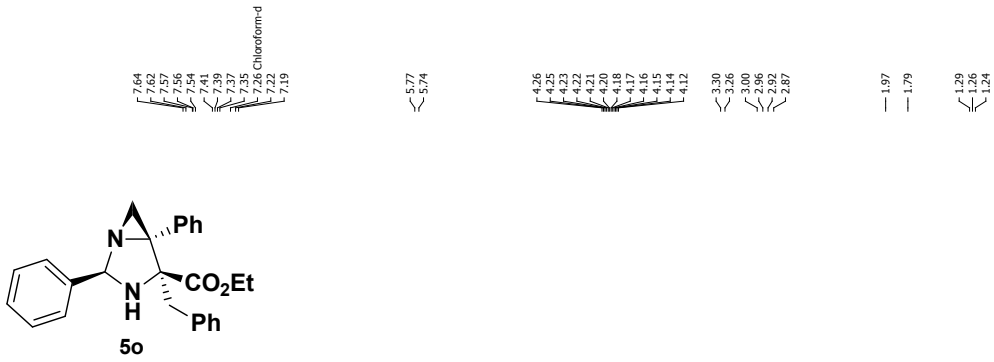


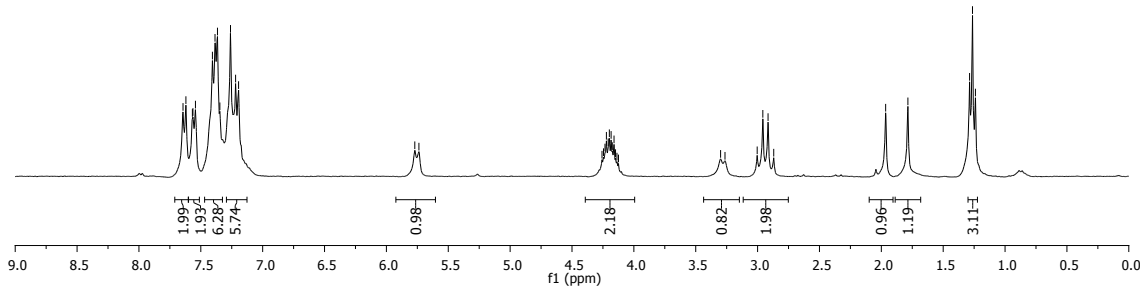
(2*R*,4*S*,5*S*) Methyl 4-ethyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5n)

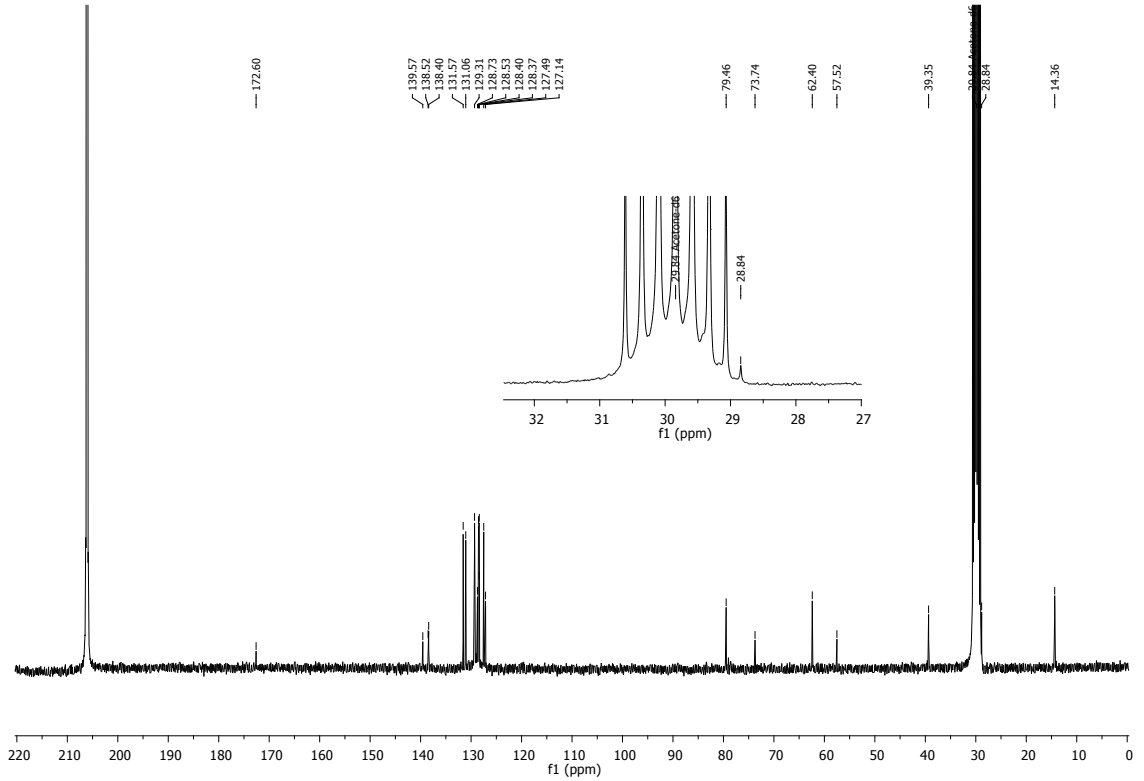




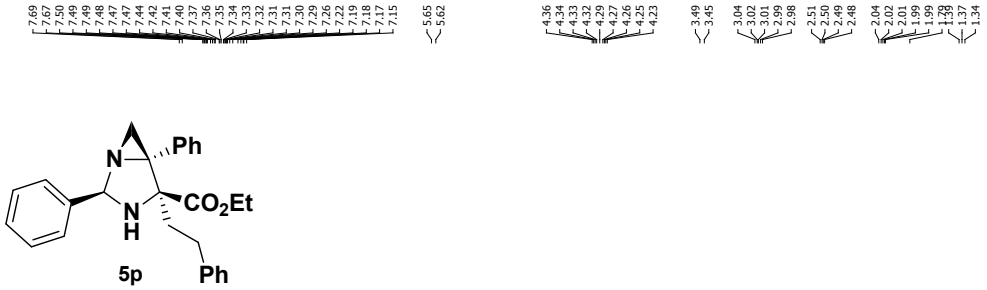
(2*R*,4*S*,5*S*) Eth(2*R*,4*S*,5*S*) Ethyl 4-benzyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5o)

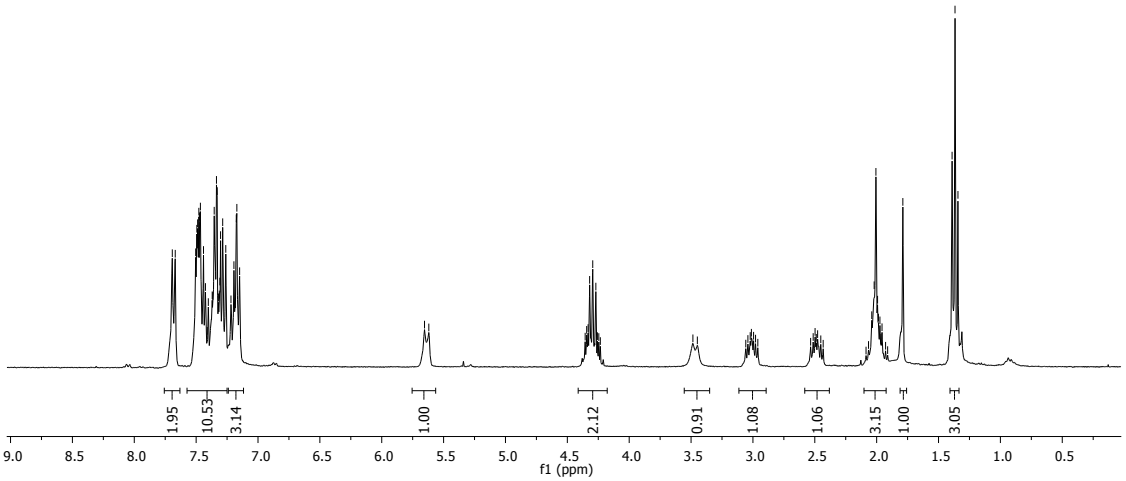


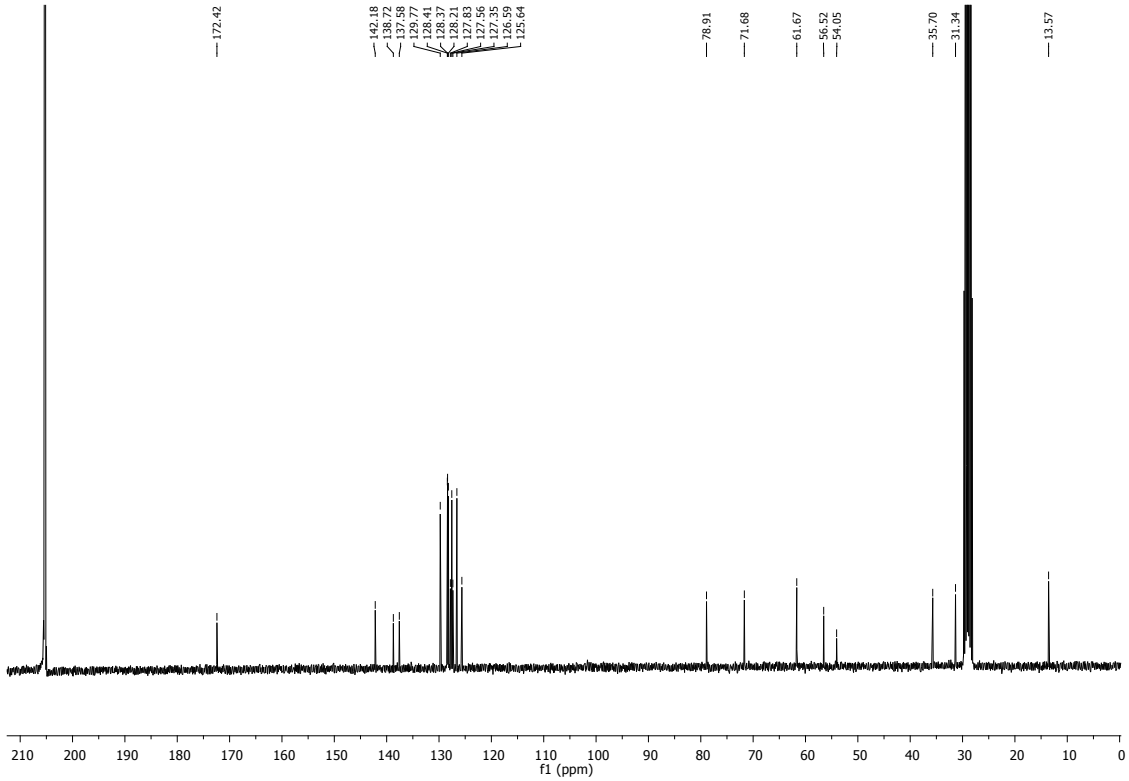




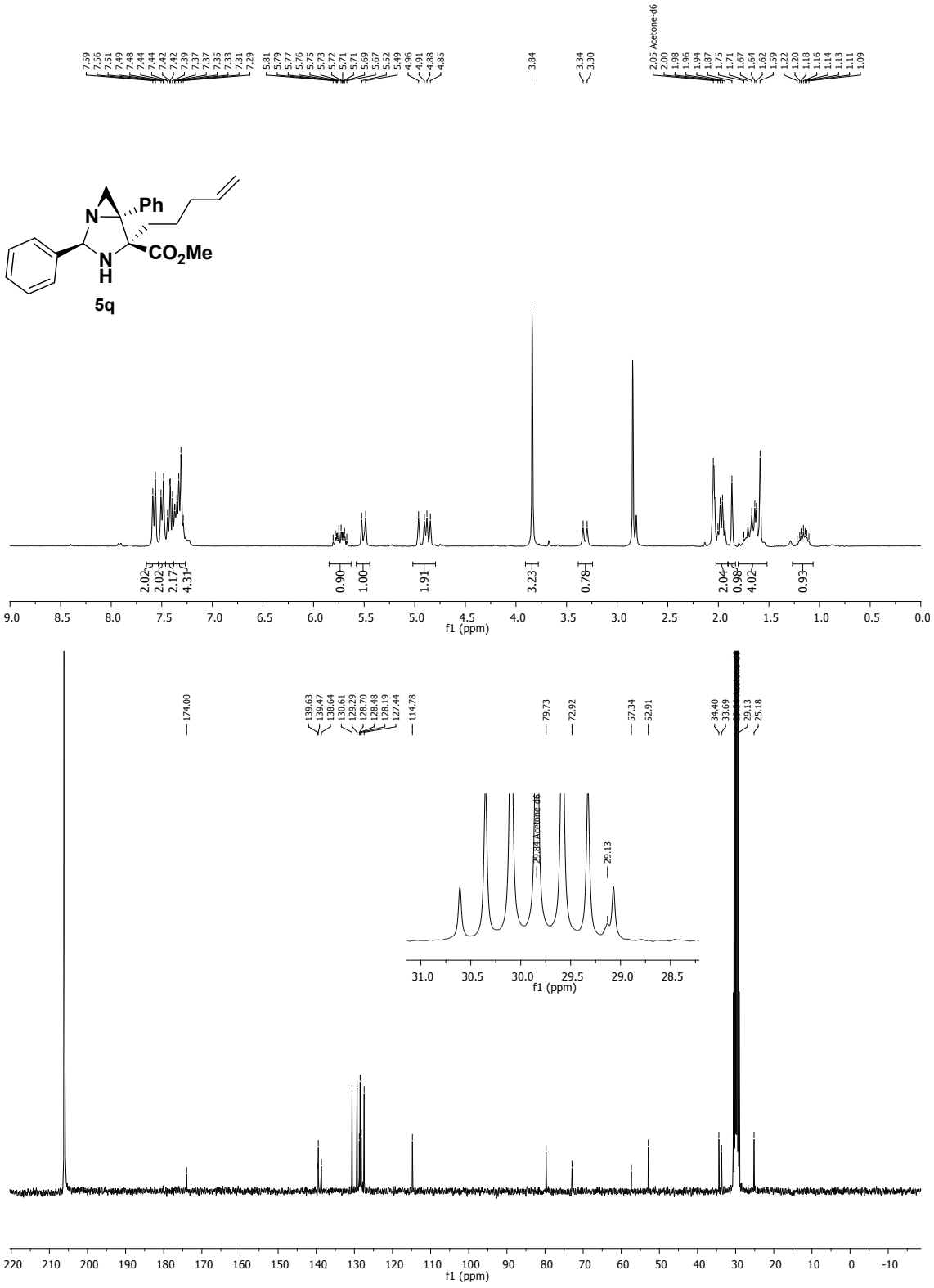
(2*R*,4*S*,5*S*) Ethyl 4-phenethyl-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5p)



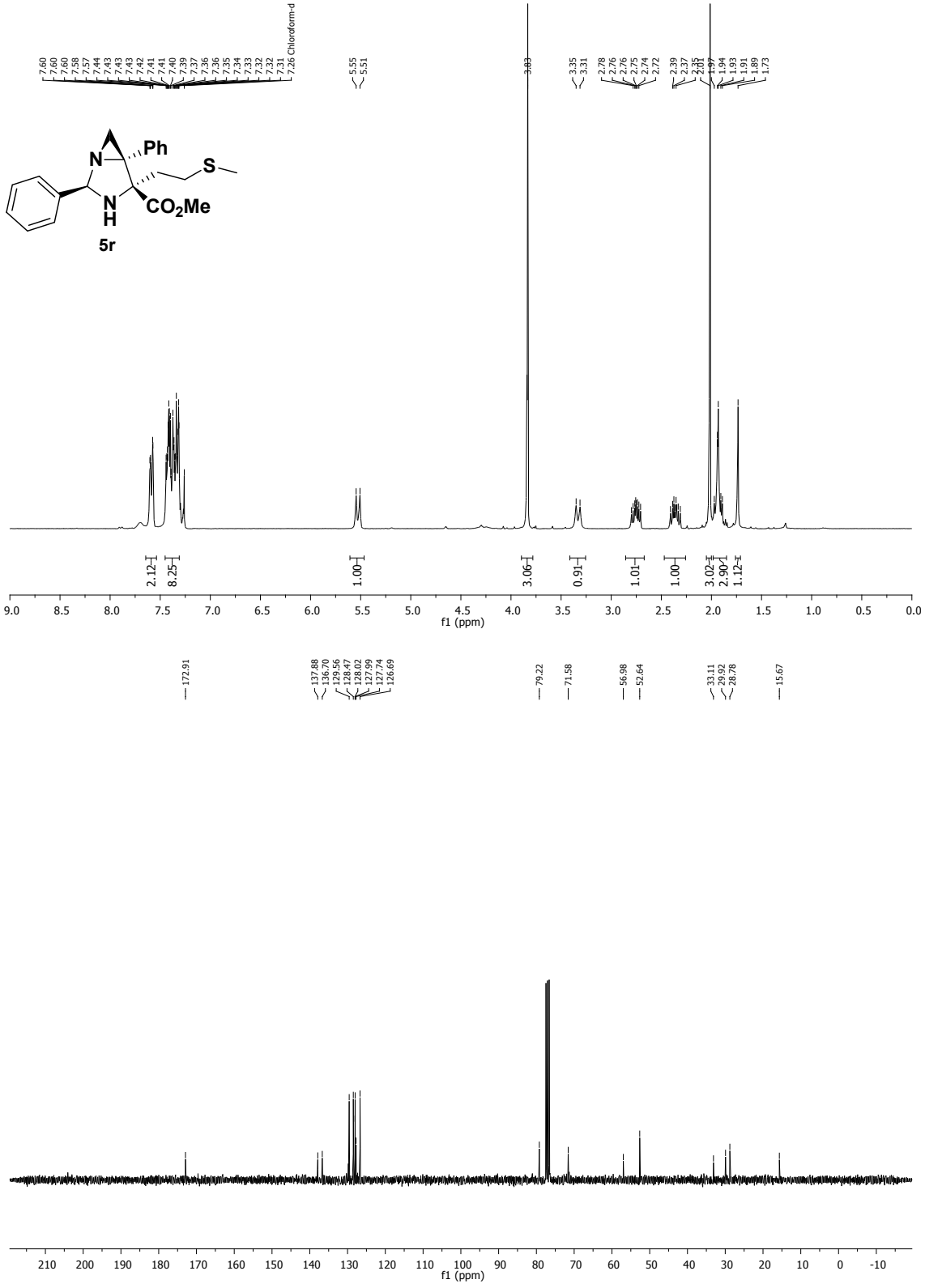




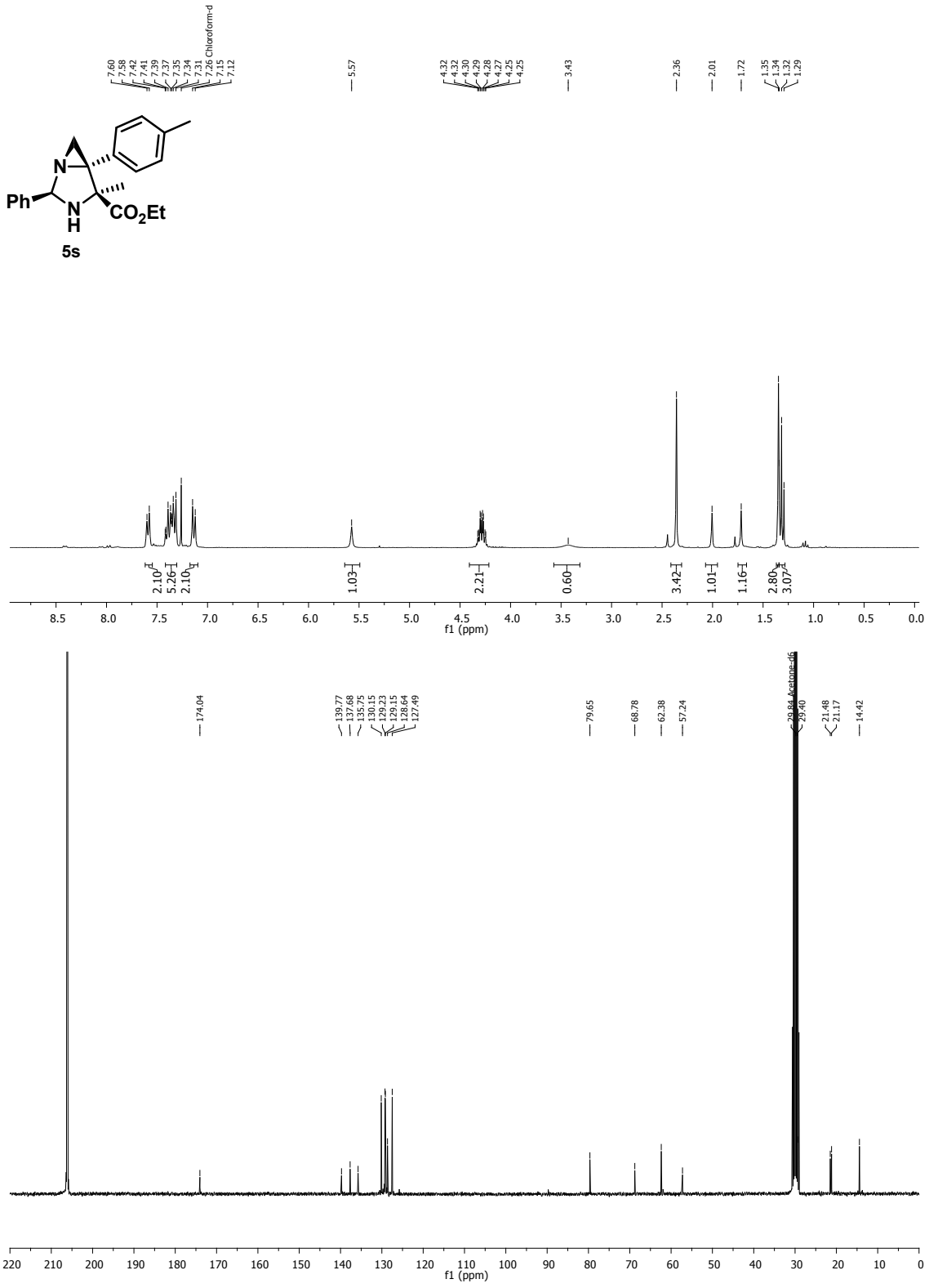
(2*R*,4*S*,5*S*) Methyl 4-(pent-4-en-1-yl)-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5q)



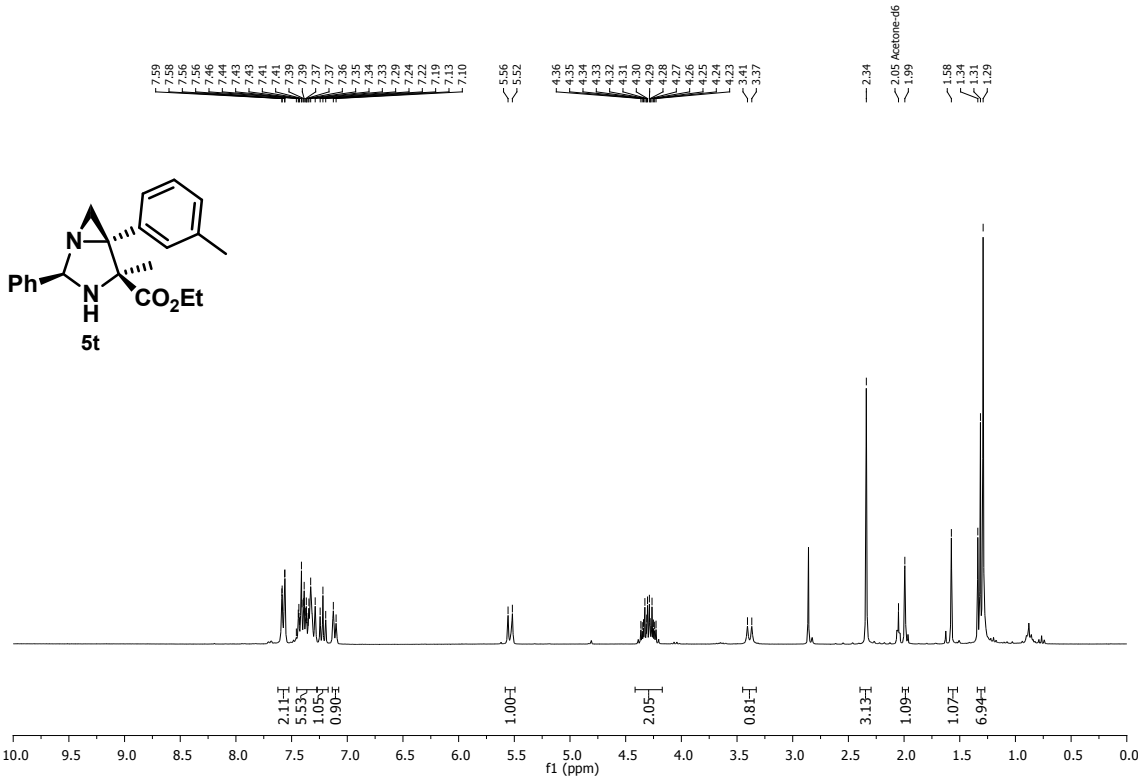
(2R,4S,5S)-Ethyl 4-(2-(methylthio)ethyl)-2,5-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5r)

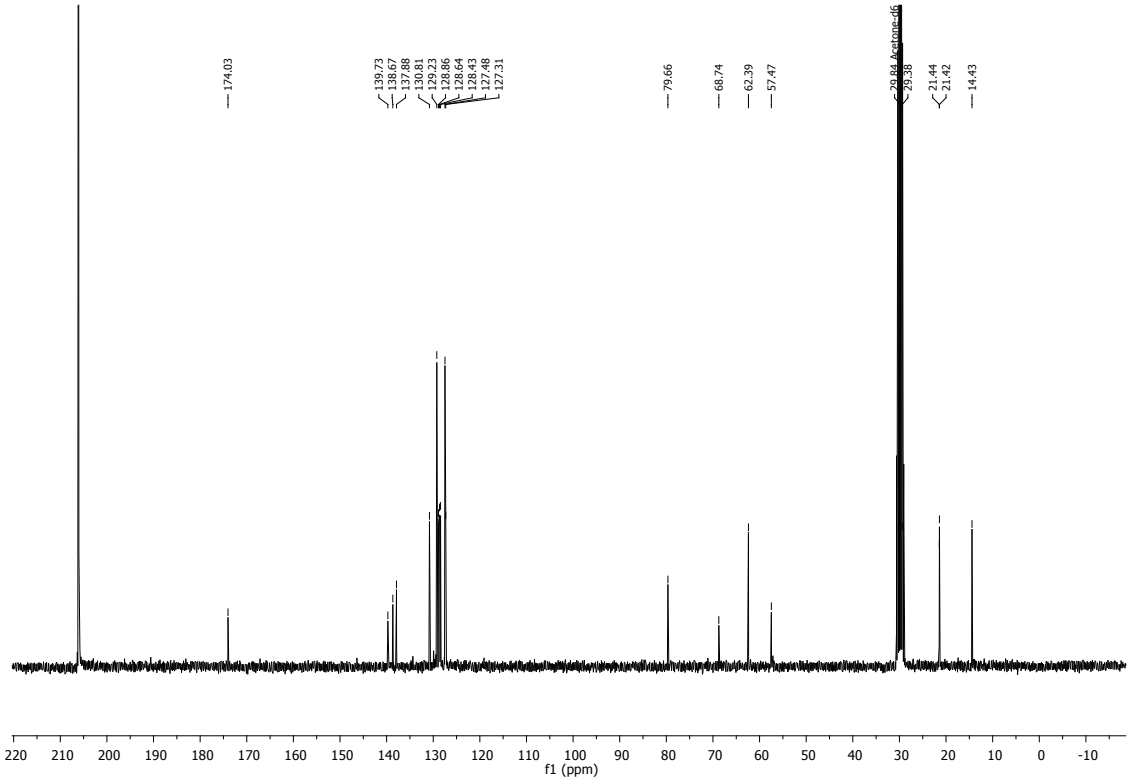


(2*R*,4*S*,5*S*) Ethyl 4-methyl-2-phenyl-5-(p-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5s)

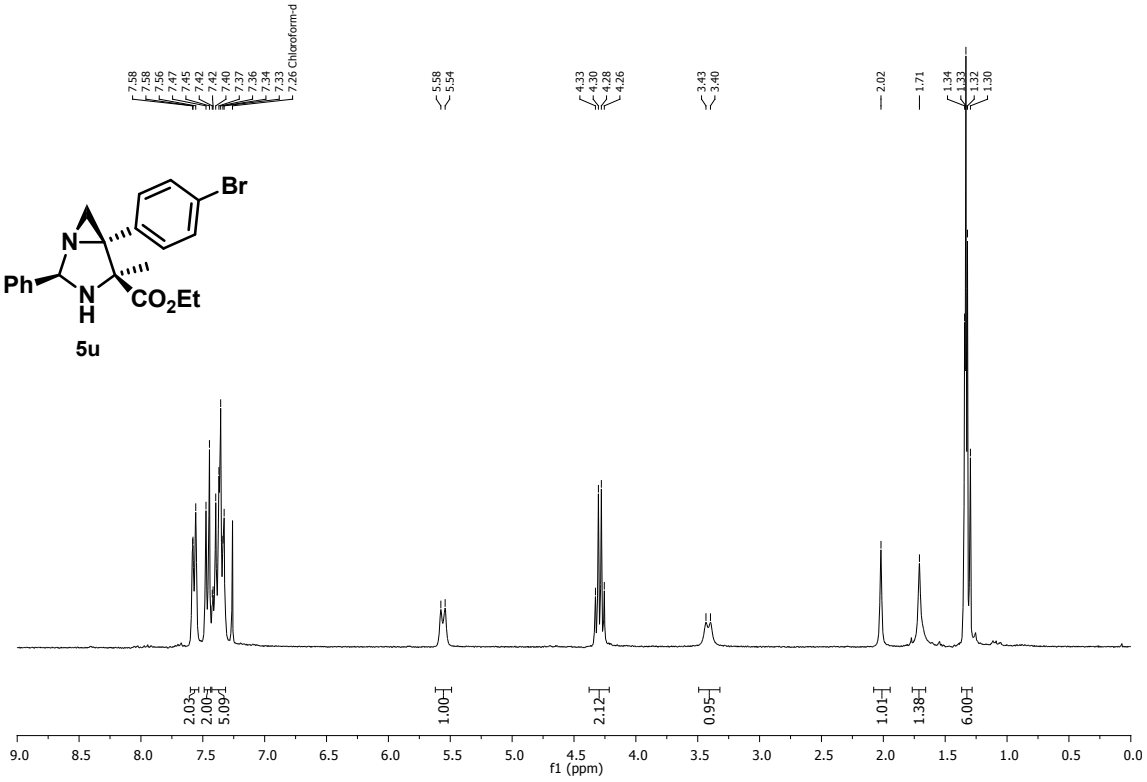


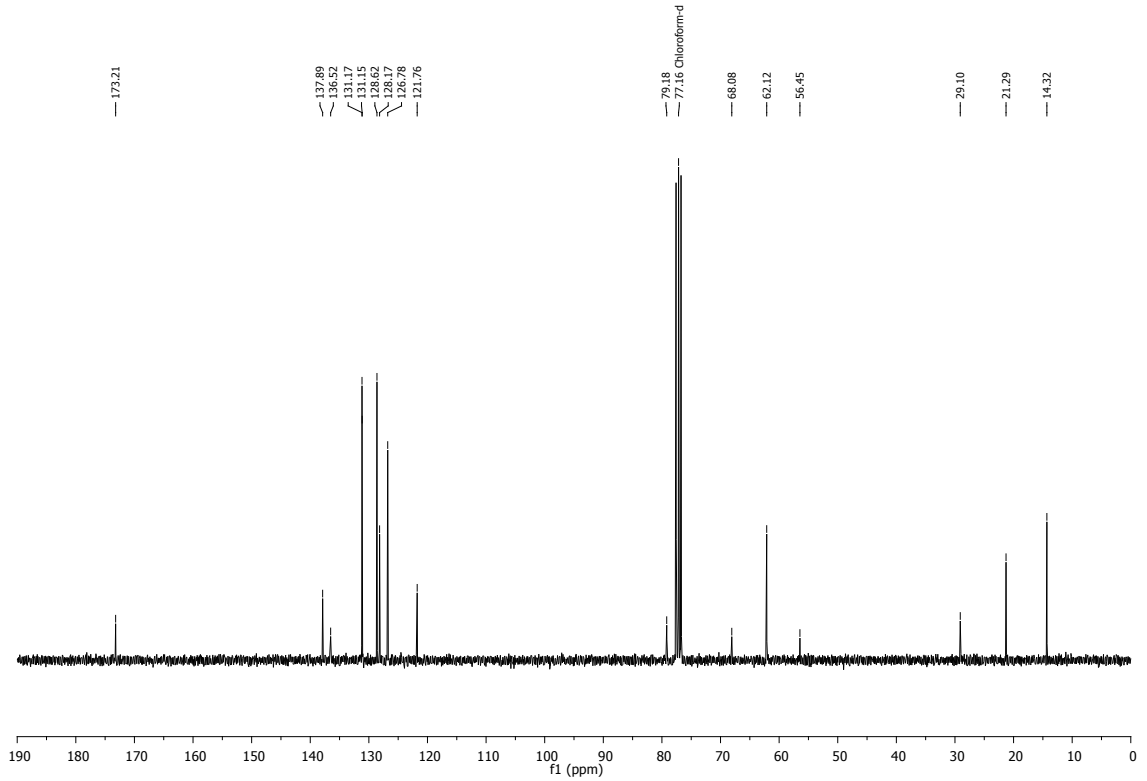
(2*R*,4*S*,5*S*) Ethyl 4-methyl-2-phenyl-5-(m-tolyl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5t)



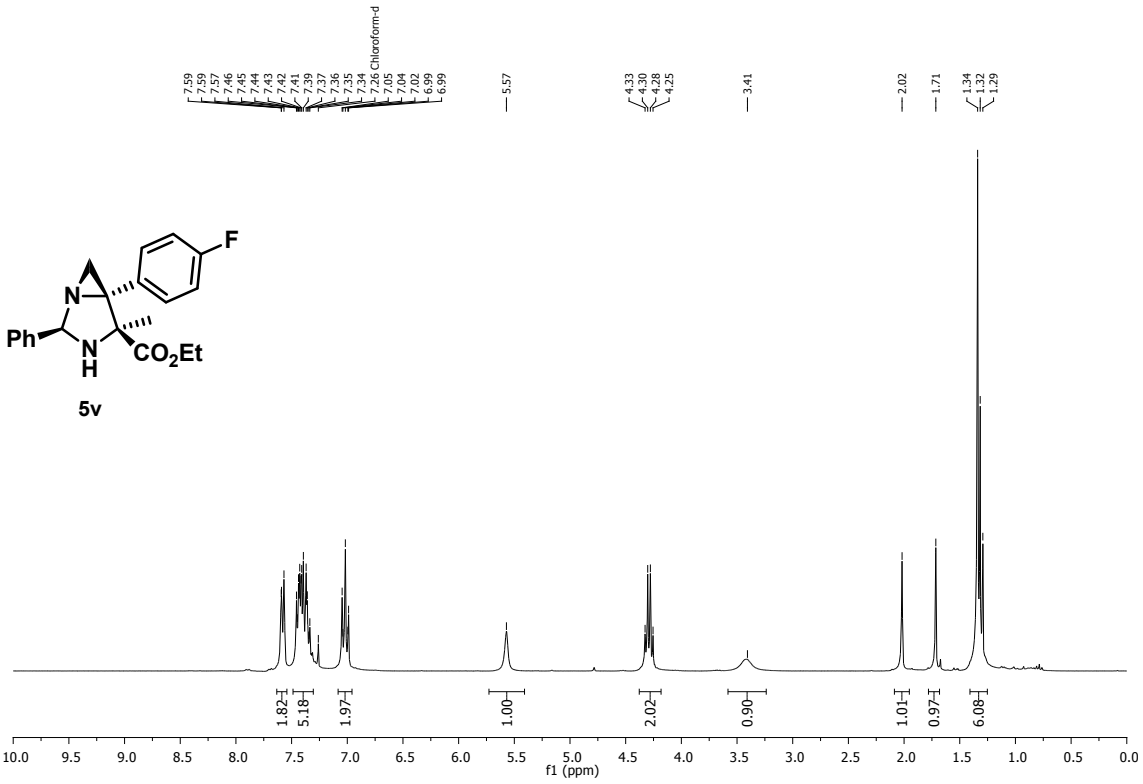


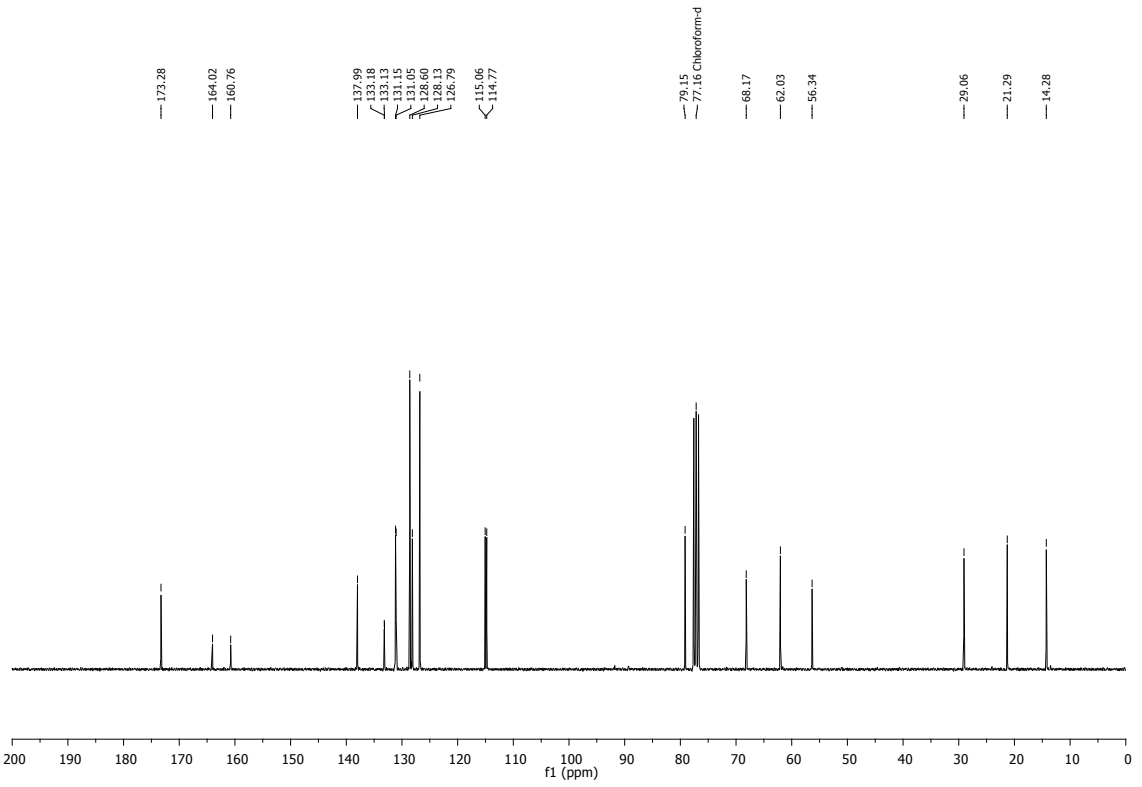
(2*R*,4*S*,5*S*) Ethyl 5-(4-bromophenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5u)

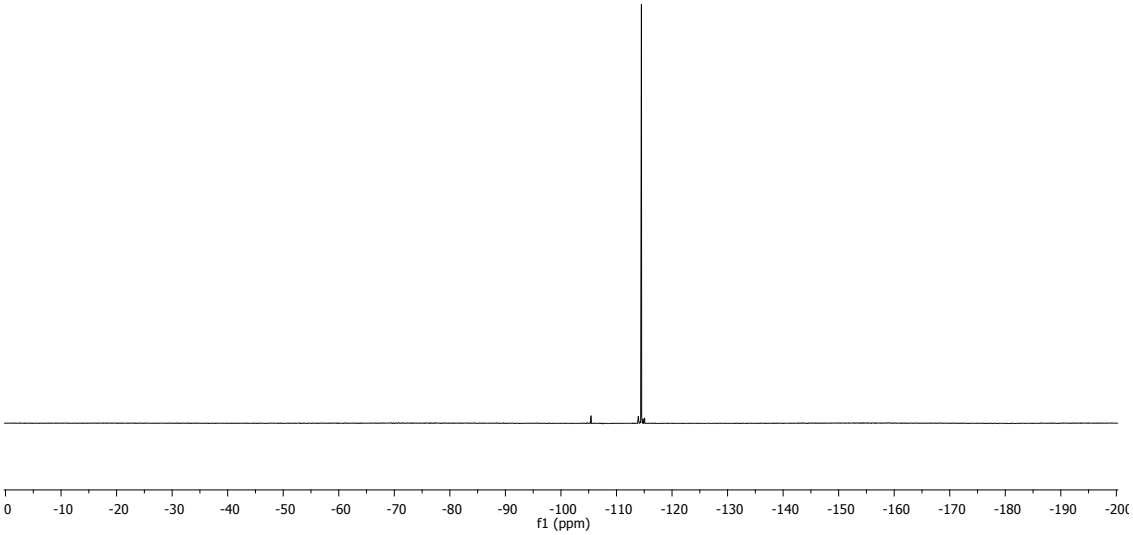




(2*R*,4*S*,5*S*) Ethyl 5-(4-fluorophenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5v)






0
-10
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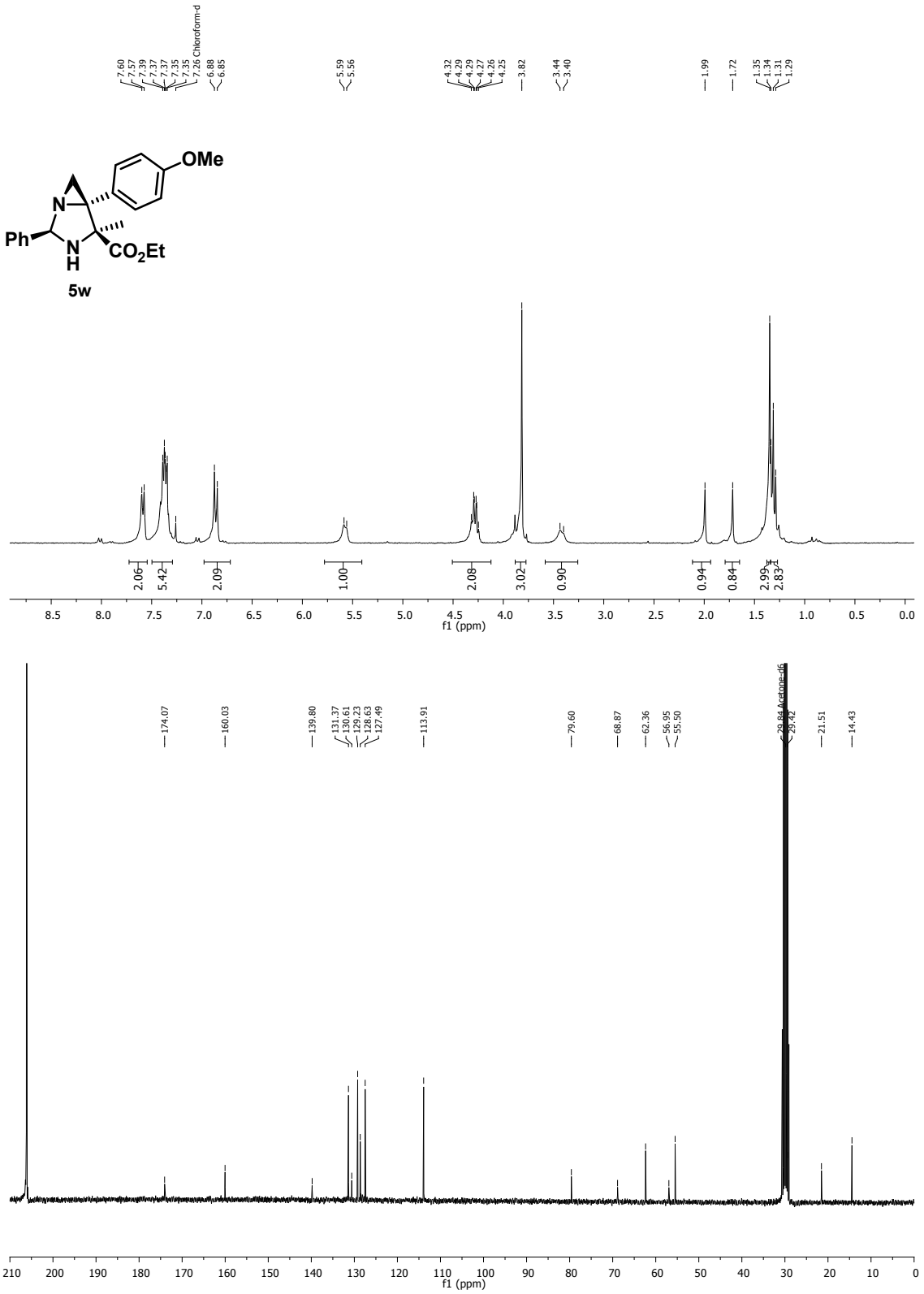
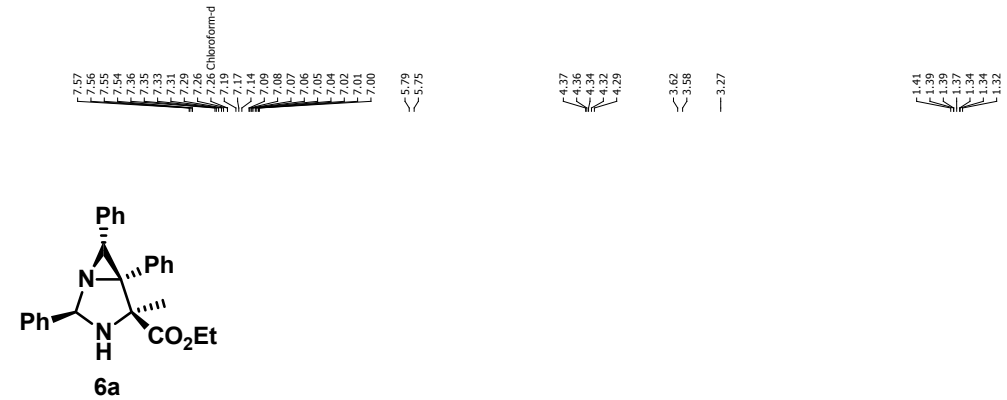
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

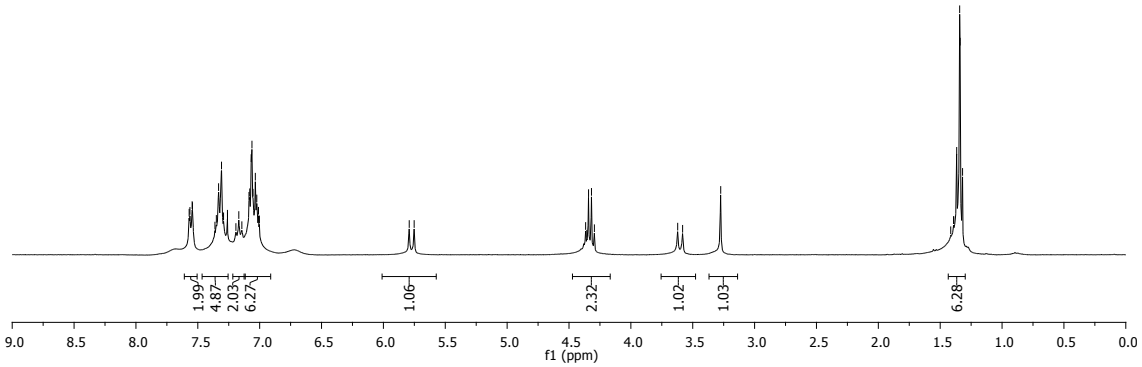
Ethyl 5-(4-methoxyphenyl)-4-methyl-2-phenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (5w)

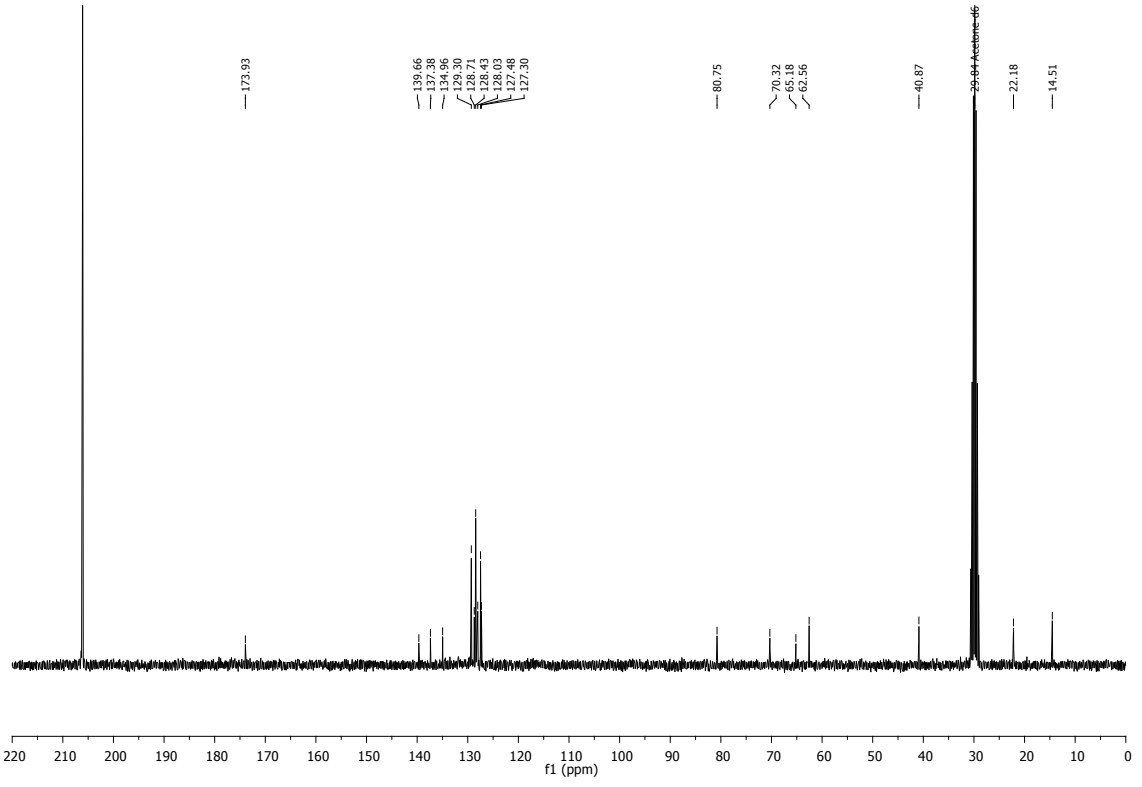


(2R,4S,5S,6R) Ethyl 4-methyl-2,5,6-triphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6a)

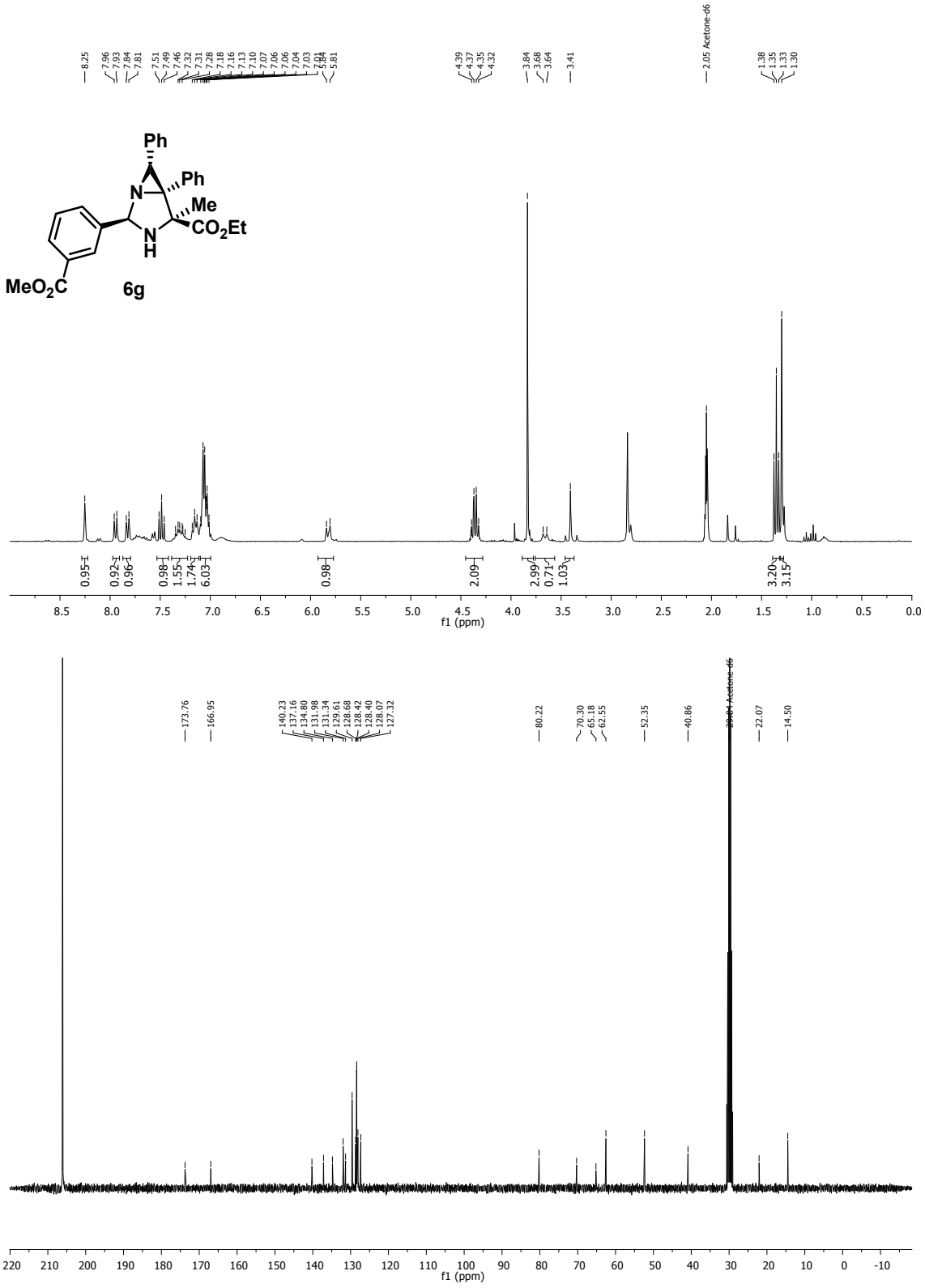


6a

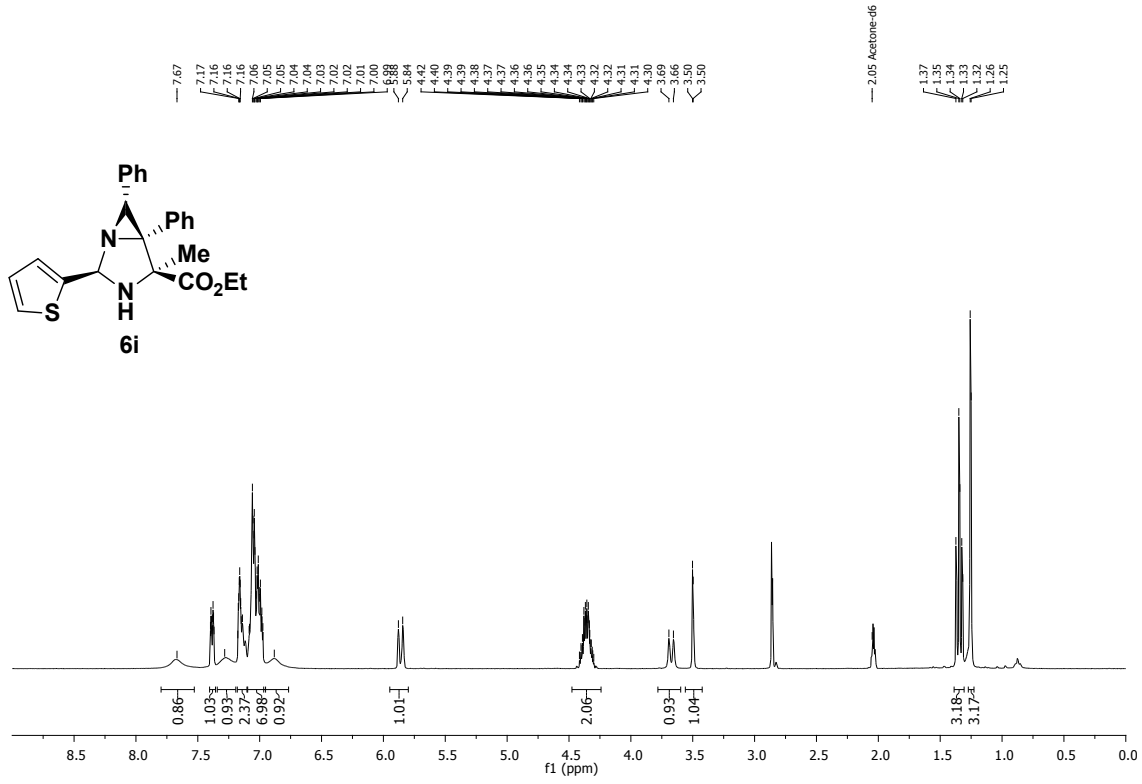


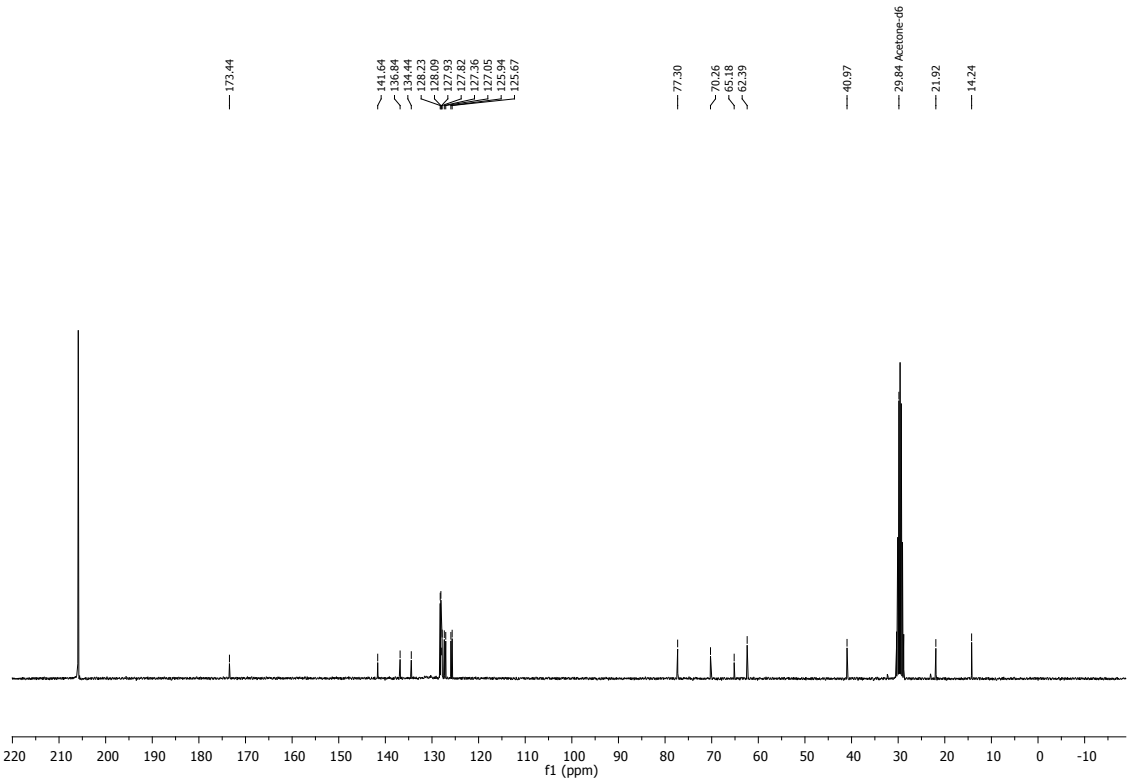


(2R,4S,5S,6R)-Ethyl 2-(3-(methoxycarbonyl)phenyl)-4-methyl-5,6-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6g)

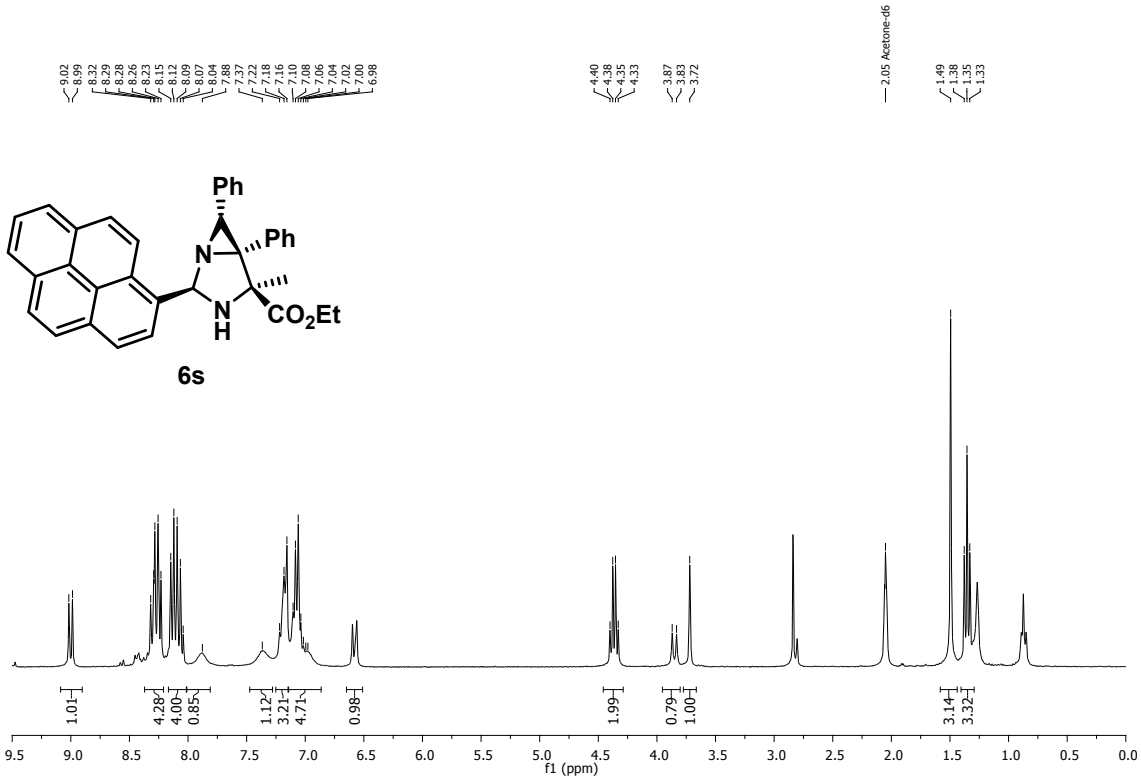


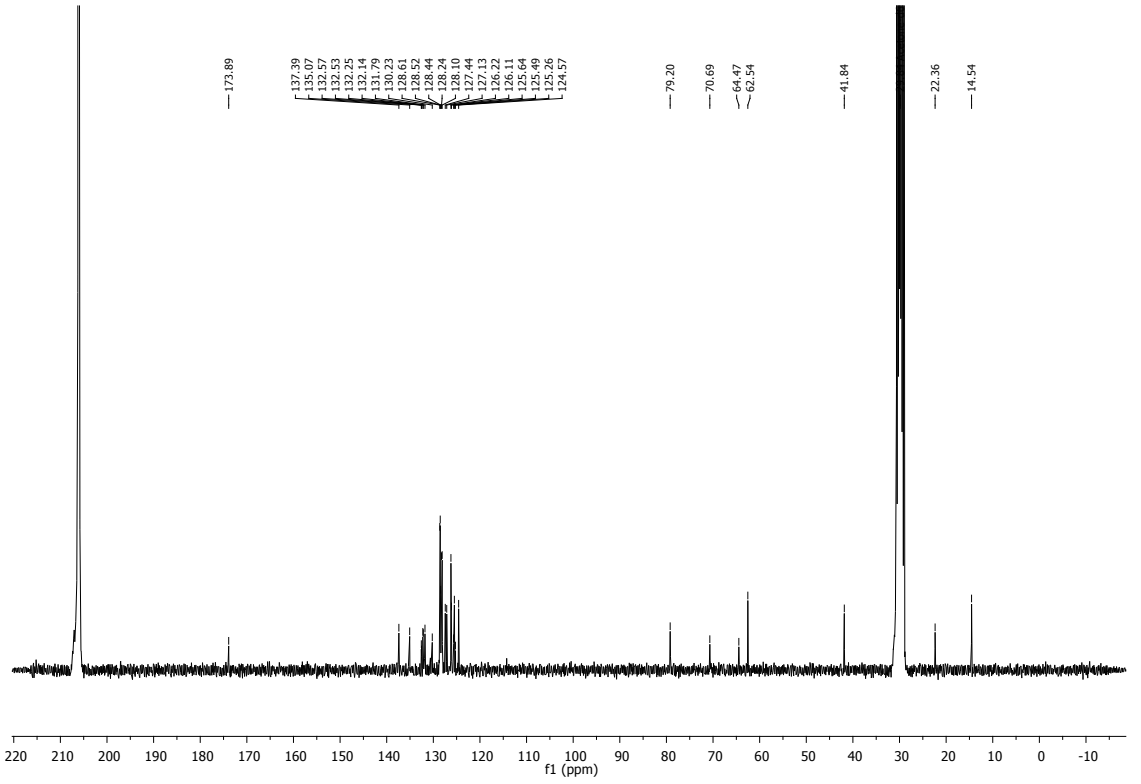
(2R,4S,5S,6R)-Ethyl 4-methyl-5,6-diphenyl-2-(thiophen-2-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6i)





(2R,4S,5S,6R) Ethyl 4-methyl-5,6-diphenyl-2-(pyren-1-yl)-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6s)





(2R,4S,5S,6R)-Ethyl 5-(4-chlorophenyl)-4-methyl-2,6-diphenyl-1,3-diazabicyclo[3.1.0]hexane-4-carboxylate (6t)