Supporting information for

Cu^{I}-Catalyzed Asymmetric [3+2] Cycloaddition of Azomethine Ylides with Cyclobutenones

Javier Corpas,[a,‡] Alberto Ponce,[a,‡] 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

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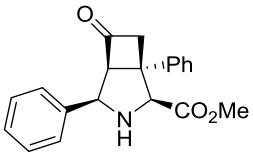
1. General methods

All air- and moisture-sensitive manipulations were carried out in anhydrous solvents and under argon. Toluene, tetrahydrofuran and acetonitrile 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 300 or 500 MHz instrument and calibrated using residual non-deuterated solvent ($CDCl_3$ or benzene-d_6) as internal reference (δ_H=7.26 ppm, δ_C=77.2 ppm for $CDCl_3$ and δ_H=7.16 ppm, δ_C=128.5 ppm for benzene-d_6). HRMS spectra were recorded on a TOF mass spectrometer with electrospray ionization (ES) as the ionization source. The chromatograms of the racemic and enantiomerically enriched cycloadducts were obtained by HPLC or SFC. Arylcyclobutenones **2a, 2b, 2c, 2d,** and **2e** were prepared following the procedure reported in the literature.[1] α-Iminoesters were prepared by condensation of methyl glycinate hydrochloride and the corresponding aldehydes.[2] Due to their lability, all α-iminoesters once isolated were immediately used in the 1,3-dipolar cycloaddition without further purification.

1. Sugimoto, K.; Hayashi, R.; Nemoto, H.; Toyooka, N.; Matsyua, Y. *Org. Lett.*, **2012**, *14*, 3510.
2. a) Cabrera, S.; Arrayás, R. G.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 16394; b) Nájera, C.; Sansano, J. M. *Curr. Org. Chem.* **2003**, *7*, 1105; c) Cooper, D. M.; Grigg, R.; Hargreaves, S.; Kennewell, P.; Redpath, J. *Tetrahedron* **1995**, *51*, 7791.

2. Typical procedure for the asymmetric 1,3-dipolar cycloaddition.

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-3,5a-diphenyl-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3a).



To a solution of $[Cu(CH_3CN)_4]PF_6$ (19.3 mg, 0.052 mmol) and (*R*)-Fesulphos (28.6 mg, 0.062 mmol) in toluene (8 mL), under nitrogen atmosphere, at 0 °C, a solution of α-iminoester **1a** (368.2 mg, 2.08 mmol) in toluene (6.24 mL), KO^{t}Bu (1M in THF) (208 µl, 0.208 mmol) and a solution of 3-phenylcyclobutenone **2a** (150 mg, 1.04 mmol) in toluene (6 mL) were successively added. After 24h at 0 °C, the mixture was diluted with 50 mL of CH_2Cl_2 and filtered through a plug of celite®. The solvent was evaporated under reduced pressure and the residue was purified by silica gel flash chromatography (cyclohexane/EtOAc 6:1) to afford the cycloadduct *endo*-**3a** (282.5 mg, 84%, colorless oil).

$[\alpha]_D^{20}$: +35.8 (c=0.22, $CHCl_3$), 90% *ee*.

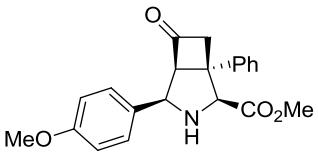
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-ID-3 column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 230.4 nm)]: t_R= 2.584 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3a** and 3.072 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3a**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.46 – 7.30 (m, 10H), 4.73 (d, *J* = 7.3 Hz, 1H), 4.21 (s, 1H), 3.92 (ddd, *J* = 7.2, 3.9, 2.1 Hz, 1H), 3.73 (s, 3H), 3.53 (dd, *J* = 18.4, 2.1 Hz, 1H), 3.43 (dd, *J* = 18.4, 3.9 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.1, 170.7, 142.2, 136.6, 128.7, 128.5, 128.2, 127.4, 127.3, 127.2, 71.3, 65.0, 56.9, 53.6, 52.2, 47.6.

HRMS (ESI+): calcd for $C_{20}H_{20}NO_3$, 322.1443; found, 322.1425 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(4-methoxyphenyl)-4-(oxo)heptahydrocyclobuta[c]-pyrrole-1-carboxylate (*endo*-3b).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1b** (41.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3b** (26.9 mg, 77%, yellow oil).

$[\alpha]_D^{20}$: +44.8 (c=0.22, $CHCl_3$), 98% *ee*.

HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IB column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 230.16 nm): t_R= 81.2 min

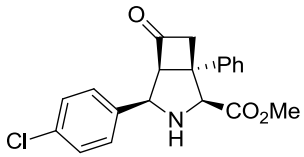
(1*R*, 3*S*, 3*aR*, 5*aS*)-**3b** and 103.1 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.46-7.28 (m, 7H), 6.89 (d, *J* = 8.5 Hz, 2H), 4.69 (d, *J* = 7.2 Hz, 1H), 4.20 (s, 1H), 3.91-3.83 (m, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 3.57-3.48 (m, 1H), 3.42 (dd, *J* = 18.4, 3.8 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.7, 170.9, 159.4, 142.4, 129.0, 128.7, 128.4, 127.5, 127.2, 113.9, 71.4, 64.7, 55.4, 53.6, 52.1, 47.7.

HRMS (ESI+): calcd for $C_{21}H_{22}NO_4$, 352.1549; found, 352.1536 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(4-chlorophenyl)-4(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3c).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1c** (42.3 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3c** (26.9 mg, 84%, white solid).

M.p.: 134-136 °C.

$[\alpha]_D^{20}$: +26.2 (c=0.22, $CHCl_3$), 81% *ee*.

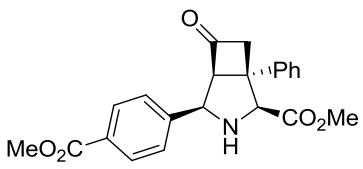
HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IB column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 230.16 nm): t_R= 53.0 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3c** and 61.1 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3c**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.44 – 7.30 (m, 9H), 4.70 (d, *J* = 7.1 Hz, 1H), 4.20 (s, 1H), 3.90 – 3.85 (m, 1H), 3.73 (s, 3H), 3.56-3.48 (m, 1H), 3.48-3.39 (m, 1H), 2.75 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.7, 170.9, 159.4, 142.3, 128.9, 128.7, 128.3, 127.4, 127.1, 113.8, 71.3, 64.7, 55.3, 53.5, 52.1, 47.6.

HRMS (ESI+): calcd for $C_{20}H_{19}NO_3Cl$, 356.1053; found, 356.1052 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(4-methoxycarbonyl)phenyl-4(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3d).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1d** (47.0 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3d** (27.7 mg, 73%, yellow solid).

M.p.: 142-144 °C.

$[\alpha]_D^{20}$: +19.3 (c=0.22, $CHCl_3$), 85% *ee*.

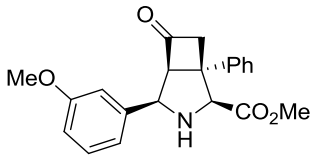
HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IB column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 230.16 nm): t_R= 32.8 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3d** and 35.6 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3d**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.9 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.26 (m, 4H), 7.13 (s, 1H), 4.65 (d, *J* = 7.0 Hz, 1H), 4.09 (s, 1H), 3.85-3.80 (m, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.45-3.36 (m, 1H), 3.32 (dd, *J* = 18.6, 3.3 Hz, 1H), 2.66 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.1, 170.7, 166.9, 142.4, 142.2, 129.8, 129.7, 128.7, 127.4, 127.3, 127.1, 76.0, 71.3, 64.5, 53.8, 52.18, 52.16, 47.4.

HRMS (ESI+): calcd for $C_{22}H_{22}NO_5$, 380.1498; found, 380.1498 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(3-methoxyphenyl)-4(oxo)heptahydrocyclobuta[c]-pyrrole-1-carboxylate (*endo*-3e).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1e** (41.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3e** (27.1 mg, 72%, yellow oil).

$[\alpha]_D^{20}$: +48.6 (c=0.22, $CHCl_3$), 85% *ee.*

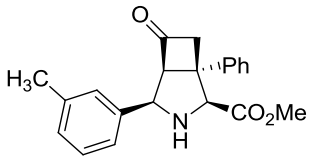
HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IB column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 210.8 nm): t_R= 142.5 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3e** and 215.8 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3e**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.45-7.38 (m, 4H), 7.36-7.24 (m, 2H), 7.04-6.96 (m, 2H), 6.88-6.81 (m, 1H), 4.70 (d, *J* = 7.1 Hz, 1H), 4.19 (s, 1H), 3.93 – 3.86 (m, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 3.59-3.48 (m, 1H), 3.42 (dd, *J* = 18.5, 3.7 Hz, 1H), 2.77 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.3, 170.8, 159.7, 142.3, 138.7, 129.4, 128.7, 127.4, 127.2, 119.4, 113.5, 112.8, 76.6, 71.3, 64.9, 55.3, 53.6, 52.1, 47.5.

HRMS (ESI+): calcd for $C_{21}H_{22}NO_4$, 352.1549; found, 352.1542 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(3-methylphenyl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3f).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1f** (38.2 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3f** (27.9 mg, 84%, colorless oil).

[α]$_D^{20}$: +74.4 (c=0.22, $CHCl_3$), 86% *ee*.

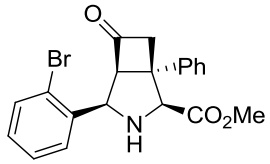
SFC: The enantiomeric excess was determined by SFC using a Chiralpak ID-3 column [CO_2/MeOH 95:5 in 60 min, flow rate 2.0 mL/min (λ = 210.4 nm)]: t_R= 4.996 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3f** and 8.527 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3f**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.21-7.16 (m, 1H), 7.15-7.04 (m, 7H), 7.00 –6.95 (m, 1H), 4.55 (d, *J* = 7.2 Hz, 1H), 4.05 (s, 1H), 3.78-3.73 (m, 1H), 3.59 (s, 3H), 3.38 (dd, *J* = 18.5, 1.9 Hz, 1H), 3.28 (dd, *J* = 18.5, 3.9 Hz, 1H), 2.61 (bs, 1H), 2.22 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.4, 170.9, 142.3, 138.0, 136.9, 128.9, 128.7, 128.3, 127.7, 127.4, 127.2, 124.2, 71.4, 65.0, 53.6, 52.1, 47.6, 29.8, 21.6.

HRMS (ESI+): calcd for $C_{21}H_{22}NO_3$, 336.1594; found, 336.1600 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(2-bromophenyl)-4-(oxo)heptahydrocyclobuta[c]-pyrrole-1-carboxylate (*endo*-3g).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1g** (51.2 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3g** (30.0 mg, 72%, white solid).

M.p.: 150-152 °C.

[α]$_D^{20}$: +70.2 (c=0.22, $CHCl_3$), 92% *ee*.

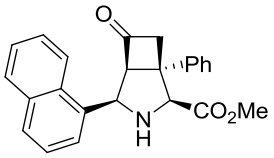
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-ID-3 column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 230.4 nm)]: t_R= 2.411 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3g** and 2.866 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3g**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.57 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.49-7.43 (m, 4H), 7.37 – 7.28 (m, 2H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 4.98 (d, *J* = 6.8 Hz, 1H), 4.21 (s, 1H), 4.18 (ddd, *J* = 6.8, 3.4, 1.9 Hz, 1H), 3.74 (s, 3H), 3.52 (dd, *J* = 18.4, 1.9 Hz, 1H), 3.43 (dd, *J* = 18.4, 3.4 Hz, 1H), 2.62 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.5 , 170.9 , 142.6 , 136.5 , 132.7 , 129.5 , 128.7 , 128.6, 127.6 , 127.2 , 123.2 , 73.1 , 70.8 , 63.6 , 54.0, 52.1 , 46.9.

HRMS (ESI+): calcd for $C_{20}H_{19}NO_3Br$, 400.0548; found, 400.0518 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(1-naphthyl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3h).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1h** (45.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3h** (33.4 mg, 90%, white solid).

M.p.: 108-110 °C.

[α]$_D^{20}$: +23.4 (c=0.22, $CHCl_3$), 97% *ee*.

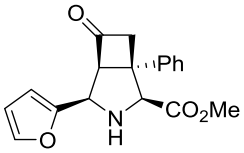
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-ID-3 column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 230.4 nm)]: t_R= 3.597 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3h** and 4.319 (min) (1*S*, 3*R*, 3*aS*, 5*aR*)-**3h**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.01-7.81 (m, 5H), 7.58-7.35 (m, 7H), 7.45-7.34 (m, 7H), 5.43 (d, *J* = 6.9 Hz, 1H), 4.34 (s, 1H), 4.20-4.14 (m, 1H), 3.77 (s, 3H), 3.57 (dd, *J* = 18.4, 2.5 Hz, 1H), 3.44 (dd, *J* = 18.4, 3.9 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.1, 171.0, 142.6, 133.8, 132.7, 130.9, 129.5, 128.8, 128.5, 127.6, 127.3, 126.4, 125.7, 125.6, 124.0, 122.2, 74.9, 70.9, 60.8, 54.0, 52.2, 47.3.

HRMS (ESI+): calcd for $C_{24}H_{22}NO_3$, 372.1600; found, 372.1609 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(furan-2-yl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3i).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1i** (33.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3i** (24.9 mg, 80%, yellow oil).

[α]$_D^{20}$: +18.1 (c=0.22, $CHCl_3$), 88% *ee*.

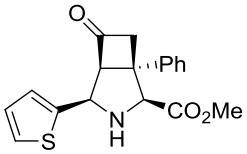
HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IB column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 210.8 nm): t_R= 44.2 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3i** and 57.8 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3i**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.43-7.33 (m, 6H), 6.47-6.34 (m, 2H), 4.74 (d, *J* = 7.3 Hz, 1H), 4.13 (s, 1H), 4.00-3.90 (m, 1H), 3.72 (s, 3H), 3.57-3.47 (m, 1H), 3.47-3.38 (m, 1H), 1.71 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.4, 170.6, 150.3, 142.5, 141.8, 128.8, 127.3, 110.6, 107.8, 71.5, 59.1, 53.2, 52.3, 48.4, 29.8.

HRMS (ESI+): calcd for $C_{18}H_{18}NO_4$, 312.1236; found, 312.1232 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(thiophen-2-yl)-4(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3j).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1j** (36.6 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3j** (24.5 mg, 75%, yellow oil).

$[\alpha]_D^{20}$: +51.0 (c=0.22, $CHCl_3$), 80% *ee*.

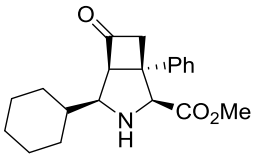
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 230.4 nm)]: t_R= 4.578 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3j** and 6.07 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3j**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.33-7.27 (m, 2H), 7.25-7.17 (m, 2H), 7.16-7.12 (m, 2H), 7.02 (d, *J* = 3.6 Hz, 1H), 6.89 (dd, *J* = 5.0, 3.6 Hz, 1H), 4.85 (d, *J* = 7.2 Hz, 1H), 4.06 (s, 1H), 3.82 (ddd, *J* = 7.1, 3.7, 1.6 Hz, 1H), 3.60 (s, 3H), 3.41 (dd, *J* = 18.6, 1.6 Hz, 1H), 3.32 (dd, *J* = 18.6, 3.7 Hz, 1H), 2.82 (bs, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.8, 170.5, 142.0, 140.2, 128.9, 128.8, 127.4, 127.3, 127.0, 126.0, 125.3, 125.0, 71.4, 61.1, 53.6, 52.2, 48.2, 29.9.

HRMS (ESI+): calcd for $C_{18}H_{18}NO_3S$, 328.1007; found, 328.0991 ([M+H], 100).

(1*S*, 3*S*, 3*aS*, 5*aR*)-Methyl-3-cyclohexyl-5a-phenyl-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3k).



Following the typical procedure, the reaction of 3-phenylcyclobutenone **2a** (14.4mg, 0.1 mmol) and **1k** (36.6 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3k** (20.9 mg, 64%, colorless oil).

$[\alpha]_D^{20}$: +60.1 (c=0.22, $CHCl_3$), 72% *ee*.

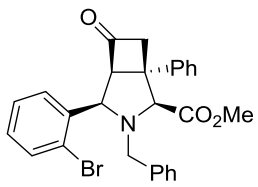
HPLC: The enantiomeric excess was determined by HPLC using a Daicel Chiralpak IA column, *n*-hexane/isopropanol 95:5, flow rate 0.7 mL/min (λ = 210.8 nm): t_R= 19.7 min (1*R*, 3*R*, 3*aR*, 5*aS*)-**3k** and 21.8 min (1*S*, 3*S*, 3*aS*, 5*aR*)-**3k**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.42-7.35 (m, 2H), 7.32-7.27 (m, 3H), 4.00 (s, 1H), 3.81 (ddd, *J* = 7.3, 3.3, 1.4 Hz, 1H), 3.68 (s, 3H), 3.42-3.34 (m, 1H), 3.30 (dd, *J* = 18.6, 1.4 Hz, 1H), 3.20 (dd, *J* = 9.9, 7.1 Hz, 1H), 2.33 (bs, 1H), 2.07-1.93 (m, 2H), 1.77-1.63 (m, 3H), 1.39-1.00 (m, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 207.0, 171.2, 142.7, 128.7, 127.2, 127.1, 75.2, 71.9, 68.2, 52.9, 52.1, 48.0, 39.8, 31.6, 30.8, 26.4, 25.8, 25.7.

HRMS (ESI+): calcd for $C_{20}H_{26}NO_3$, 328.1913; found, 328.1907 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-5a-phenyl-3-(2-bromophenyl)-2-N-(benzyl)-4-(oxo)-heptahydro-cyclobuta[c]pyrrole-1-carboxylate (N-benzyl derivative of *endo*-3g).



To a solution of *endo*-**3g** (116.1 mg, 0.36 mmol) in THF (15.0 mL) at room temperature, was added successively K_2CO_3 (80 mg, 0.58 mmol) and benzyl bromide (56 μL, 0.47 mmol). The mixture was stirred at 40 ºC for 12 h and then was cooled to room temperature. After that, water was added (10.0 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 x 8 mL). The resulting organic phase was washed with brine (2 x 8 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (cyclohexane-EtOAc 3:1), to afford the N-benzyl derivative (142.8 mg, 95%, white solid).

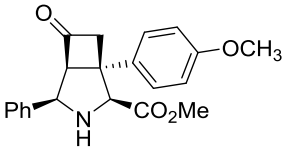
M.p.: 158-160 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.66-7.60 (m, 1H), 7.46-7.33 (m, 3H), 7.32-7.25 (m, 4H), 7.24-7.15 (m, 3H), 6.98 (dd, *J* = 7.0, 2.6 Hz, 1H), 4.45 (d, *J* = 7.7 Hz, 1H), 4.05-3.97 (m, 2H), 3.94 (d, *J* = 14.4 Hz, 1H), 3.70 (d, *J* = 14.4 Hz, 1H), 3.60 (s, 3H), 3.59 (s, 1H), 3.26 (dd, *J* = 18.8, 5.3 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.0, 170.9, 142.0, 134.8, 133.2, 133.0, 130.5, 130.1, 129.6, 128.8, 128.4, 127.8, 127.7, 127.3, 127.1, 124.1, 74.4, 71.8, 67.2, 53.9, 53.8, 51.9, 46.7.

HRMS (ESI+): calcd for $C_{27}H_{25}BrNO_3$, 490.1018; found, 490.1442 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-3-phenyl-5a-(4-methoxyphenyl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3l).



Following the typical procedure, the reaction of 3-(4-methoxyphenyl)cyclobutenone **2b** (17.4 mg, 0.1 mmol) and **1a** (35.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3l** (28.1 mg, 80%, white solid).

M.p.: 134-136 °C.

[α]$_D^{20}$: +22.7 (c=0.22, $CHCl_3$), 90% *ee*.

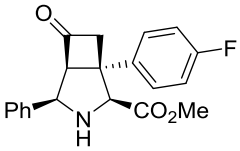
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 230.4 nm)]: t_R= 5.1 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3l** and 6.085 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3l**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.45-7.29 (m, 7H), 6.97-6.92 (m, 2H), 4.71 (d, *J* = 7.3 Hz, 1H), 4.17 (s, 1H), 3.90-3.86 (m, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 3.50 (dd, *J* = 18.4, 2.3 Hz, 1H), 3.38 (dd, *J* = 18.4, 4.2 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.4, 170.9, 158.6, 137.0, 134.1, 128.5, 128.4, 128.0, 127.0, 114.0, 71.3, 64.8, 55.3, 53.6, 53.4, 52.0, 47.0.

HRMS (ESI+): calcd for $C_{21}H_{21}NO_4$, 352.1549; found, 352.1538 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-3-phenyl-5a-(4-fluorophenyl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3m).



Following the typical procedure, the reaction of 3-(4-fluorophenyl)cyclobutenone **2c** (16.2 mg, 0.1 mmol) and **1a** (35.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3m** (24.4 mg, 72%, yellow solid).

M.p.: 150-152 °C.

[α]$_D^{20}$: +12.6 (c=0.22, $CHCl_3$), 90% *ee*.

SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 3.989 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3m** and 4.917 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3m**.

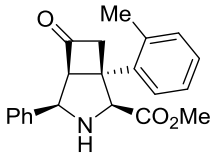
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.43-7.31 (m, 7H), 7.10 (t, *J* = 8.6 Hz, 2H), 4.71 (d, *J* = 7.3 Hz, 1H), 4.16 (s, 1H), 3.87 (ddd, *J* = 7.3, 4.3, 2.5 Hz, 1H), 3.74 (s, 3H), 3.53 (dd, *J* = 18.4, 2.5 Hz, 1H), 3.38 (dd, *J* = 18.4, 4.3 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.0, 170.8, 162.0 (d, *J* = 246.6 Hz), 138.1 (d, *J* = 3.3 Hz), 137.0, 129.2 (d, *J* = 8.1 Hz), 128.5, 128.2, 127.1, 115.6 (d, *J* = 21.5 Hz), 76.5, 71.4, 65.0, 53.9, 52.2, 47.1.

^{19}F-NMR (75 MHz, $CDCl_3$): δ -115.4.

HRMS (ESI+): calcd for $C_{20}H_{18}FNO_3$, 340.1349; found, 340.1356 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-3-phenyl-5a-(2-methylphenyl)-4-(oxo)heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-3n).



Following the typical procedure, the reaction of 3-(2-methylphenyl)cyclobutenone **2d** (15.8 mg, 0.1 mmol) and **1a** (35.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-3**n** (23.1 mg, 69%, white solid).

M.p.: 172-174 °C.

$[\alpha]_D^{20}$: +33.0 (c=0.22, $CHCl_3$), 92% *ee*.

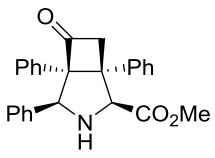
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 4.564 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**3n** and 5.654 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**3n**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.37-7.13 (m, 9H), 4.77 (d, *J* = 7.1 Hz, 1H), 4.10 (s, 1H), 4.06-3.98 (m, 1H), 3.63-3.54 (m, 4H), 3.37 (dd, *J* = 18.4, 4.5 Hz, 1H), 2.31 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.1, 171.4, 139.0, 137.0, 136.0, 132.3, 129.3, 128.5, 128.1, 127.7, 127.1, 126.4, 75.0, 70.0, 64.4, 53.8, 52.1, 49.2, 21.4.

HRMS (ESI+): calcd for $C_{21}H_{21}NO_3$, 336.1600; found, 336.1586 ([M+H], 100).

(1*S*, 3*S*, 3*aS*, 5*aS*)-Methyl-3,3a,5a-triphenyl-4-(oxo)heptahydrocyclobuta[c]-pyrrole-1-carboxylate (*endo*-3o).



Following the typical procedure, the reaction of 2,3-diphenylcyclobutenone **2e** (22.0 mg, 0.1 mmol) and **1a** (35.4 mg, 0.2 mmol) afforded, after purification by silica gel flash chromatography (cyclohexane/EtOAc 6:1), the cycloadduct *endo*-**3o** (22.3 mg, 64%, white solid).

M.p.: 152-154 °C.

$[\alpha]_D^{20}$: +30.3 (c=0.22, $CHCl_3$), 84% *ee*.

SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 4.475 min

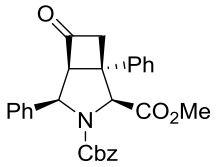
(1*S*, 3*S*, 3*aS*, 5*aS*)-**3o** and 4.745 min (1*R*, 3*R*, 3*aR*, 5*aR*)-**3o**.

^{1}H-NMR (300 MHz, Benzene-d_6): δ 7.12-7.06 (m, 3H), 7.04-6.84 (m, 12H), 4.51 (s, 1H), 4.13 (s, 1H), 3.90 (d, *J* = 18.9 Hz, 1H), 3.30 (s, 3H), 3.22 (d, *J* = 18.9 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 207.8, 171.2, 139.9, 136.3, 135.8, 128.3, 128.1, 128.0 (bs), 127.9, 127.8, 127.2, 126.9, 126.6, 86.6, 73.3, 65.7, 55.1, 52.8, 52.5.

HRMS (ESI+): calcd for $C_{26}H_{23}NO_3$, 398.1756; found, 398.1751 ([M+H], 100).

(1*S*, 3*R*, 3*aS*, 5*aR*)-Methyl-3, 5a-diphenyl-2-N-(benzyloxycarbonyl)-4-(oxo)-heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-7).



To a solution of *endo*-**3a** (125 mg, 0.39 mmol) in THF (16.0 mL) at room temperature, K_2CO_3 (95.8 mg, 0.69 mmol) and benzyl chloroformate (66 μL, 0.46 mmol) were successively added. The reaction was stirred at room temperature for 12 hours and the mixture was quenched with H_2O (10.0 mL). Then the aqueous phase was extracted with CH_2Cl_2 (3 x 8 mL) and the resulting organic phase was washed with brine (20 mL), dried over $MgSO_4$ and concentrated under reduce pressure. The residue was purified by silica gel flash chromatography (CH_2Cl_2/TBME (*tert*-butyl methyl ether) 80:1) to afford the compound *endo*-**7** (158 mg, 89%, orange solid).

M.p.: 168-170 °C.

$[\alpha]_D^{20}$: +41.7 (c=0.22, $CHCl_3$), 90 % *ee*.

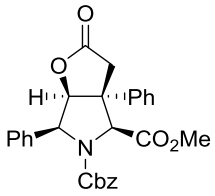
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 4.475 min (1*R*, 3*S*, 3*aR*, 5*aS*)-**7** and 5.682 min (1*S*, 3*R*, 3*aS*, 5*aR*)-**7**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.4 Hz, 2H), 7.46 – 7.27 (m, 9H), 7.21 – 7.13 (m, 2H), 6.93-6.84 (m, 2H), 5.44 (d, *J* = 10.5 Hz, 1H), 4.96 (s, 2H), 4.83 (s, 1H), 4.27 (ddd, *J* = 10.5, 5.2, 2.4 Hz, 1H), 3.75 (s, 3H), 3.60 (dd, *J* = 18.1, 2.4 Hz, 1H), 3.27 (dd, *J* = 18.1, 5.2 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 200.6, 170.9, 155.1, 142.6, 138.2, 135.7, 129.2, 128.7, 128.4, 128.0, 127.8, 127.7, 127.6, 126.3, 126.2, 75.0, 72.2, 67.8, 65.6, 55.3, 52.6, 48.2.

HRMS (ESI+): calcd for $C_{28}H_{26}NO_5$, 456.1811; found, 456.1808 ([M+H], 100).

5-Benzyl 4-methyl (3*aR*, 4*S*, 6*S*, 6*aS*)-2-oxo-3a,6-diphenylhexahydro-5*H*-furo[2,3-c]pyrrole-4,5-dicarboxylate (*endo*-8).



To a solution of *endo*-**7** (80.0 mg, 0.18 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C *m*-chloroperbenzoic acid (≤77 % purity, 151.9 mg, 0.88 mmol) was added. The mixture was stirred at room temperature for 24 h and CH_2Cl_2 (5.0 mL) and a solution of saturated Na_2SO_3 (5.0 mL) were added. The organic phase was sequentially washed with a saturated solution of $NaHCO_3$ (5 x 10 mL), H_2O (2 x 10 mL) and brine (2 x 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (cyclohexane-EtOAc 4:1), to afford the lactone *endo*-**8** (59.7 mg, 72 %, white solid).

M.p.: 178-180 °C.

$[\alpha]_D^{20}$: + 22.4 (c=0.22, $CHCl_3$), 90 % *ee*.

SFC: The enantiomeric excess was determined by SFC using a Chiralpak-ID column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 5.390 min (3*aS*, 4*R*, 6*R*, 6*aR*)-**8** and 5.615 min (3*aR*, 4*S*, 6*S*, 6*aS*)-**8**.

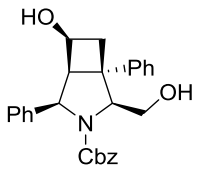
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.65 –7.57 (m, 2H), 7.49 – 7.29 (m, 10H), 7.25-7.18 (m, 3H), 5.46 (d, *J* = 5.9 Hz, 1H), 5.26 (d, *J* = 5.9 Hz, 1H), 5.01 (d, *J* = 10.4 Hz, 2H), 4.97 (s, 1H), 3.86 (s, 3H), 3.18 (d, *J* = 18.0 Hz, 1H), 2.90 (d, *J* = 18.0 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 172.5 170.5, 141.0, 135.7, 135.6, 129.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.5, 125.3, 88.1, 70.0, 67.9, 66.0, 56.3, 53.0, 39.1.

HRMS (ESI+): calcd for $C_{28}H_{26}NO_6$, 472.1760; found, 472.1774 ([M+H], 100).

IR (KBr, cm^{-1}): 1708, 1755, 1794.

(1*S*, 3*R*, 3a*S*, 4*S*, 5a*R*)-4-hydroxy-1-hydroxymethyl-3, 5a-diphenyl-2-N-(benzyloxycarbonyl)-heptahydrocyclobuta[c]pyrrole (*endo*-9).



To a solution of *endo*-**7** (134.4 mg, 0.295 mmol) in THF (1.5 mL) a 1 M solution of lithium aluminum hydride in THF (0.885 mL, 0.885 mmol) was added dropwise at -78 °C. The mixture was stirred at -78 °C for 4 h and then warmed to room temperature and stirred for 12 hours until completion. Ethyl acetate (3.5 mL) was added, the mixture was stirred for one hour and a saturated solution of aqueous ammonium chloride (5 mL) was added. The organic phase was separated, washed with water (10 mL) and brine (10 mL), dried with $MgSO_4$, filtered and evaporated at reduced pressure. After purification by flash chromatography (cyclohexane/EtOAc 3:1) diol *endo*-**9** was obtained as white solid (112.7 mg, 89%).

M.p.: 172-174 °C.

$[\alpha]_D^{20}$: + 36.5 (c=0.22, $CHCl_3$), 90 % *ee*.

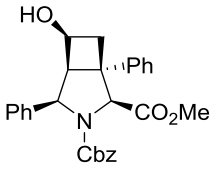
SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 6.484 min (1*S*, 3*R*, 3a*S*, 4*S*, 5a*R*)-**9** and 7.726 min (1*R*, 3*S*, 3a*R*, 4*R*, 5a*S*)-**9**.

^{1}H-NMR (300 MHz, Benzene-d_6): δ 7.25 (d, *J* = 7.4 Hz, 2H), 7.13-7.04 (m, 5H), 7.02-6.92 (m, 6H), 6.73-6.66 (m, 2H), 5.28 (d, *J* = 10.4 Hz, 1H), 4.93 (d, *J* = 12.6 Hz, 1H), 4.82 (d, *J* = 12.6 Hz, 1H), 4.24 (dd, *J* = 11.7, 6.3 Hz, 1H), 4.13 (dd, *J* = 11.7, 3.0 Hz, 1H), 4.08 (dd, *J* = 6.3, 3.0 Hz, 1H), 3.80 (q, *J* = 7.8 Hz, 1H), 3.08 (ddd, *J* = 10.4, 6.8, 3.9 Hz, 1H), 2.80 (d, *J* = 8.7 Hz, 1H), 2.41 (ddd, *J* = 12.1, 8.0, 3.9 Hz, 1H), 2.29 (dd, *J* = 12.1, 8.0 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 157.9, 143.7, 140.2, 135.7, 129.3, 129.0, 128.4, 128.0, 127.9, 127.5, 127.1, 126.3, 126.2, 73.6, 68.0, 65.3, 65.2, 63.9, 55.5, 50.4, 37.2.

HRMS (ESI+): calcd for $C_{27}H_{25}NO_4$, 430.2018 and 452.1838; found, 430.2012 ([M+H], 17), 452.1812 ([M+Na], 100).

(1*S*, 3*R*, 3a*S*, 4*S*, 5a*R*)-Methyl-3, 5a-diphenyl-2-N-(benzyloxycarbonyl)-4-hydroxy-heptahydrocyclobuta[c]pyrrole-1-carboxylate (*endo*-10).



To a solution of *endo*-**7** (150.0 mg, 0.329 mmol) in MeOH (5.0 mL) at room temperature $NaBH_4$ (18.7 mg, 0.49 mmol) was added and the mixture was stirred for 2 h. Then a saturated solution of NH_4Cl (5.0 mL) was added and the resulting aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL). The organic phase was washed successively with a saturated solution of $NaHCO_3$ (2 x 5 mL), H_2O (2 x 5mL) and brine (5.0 mL). The resulting organic solution was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (cyclohexane/EtOAc 1:1), to afford the alcohol *endo*-**10** (98.7 mg, 65%, white solid).

M.p.: 154-156 °C.

$[\alpha]_D^{20}$: + 57.8 (c=0.22, $CHCl_3$), 90 % *ee*.

SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 210.4 nm)]: t_R= 5.281 min (1*R*, 3*S*, 3a*R*, 4*R*, 5a*S*)-**10** and 6.656 min (1*S*, 3*R*, 3a*S*, 4*S*, 5a*R*)-**10**.

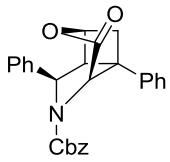
^{1}H-NMR (300 MHz, C_6D_6): δ 7.85 (d, *J*=7.5 Hz, 2H), 7.53-7.22 (m, 11H), 7.10-6.93 (m, 2H), 5.75 (d, *J* = 10.3 Hz, 1H), 5.07 (s, 2H), 4.56 (s, 1H), 4.10-3.95 (m, 1H), 3.92 – 3.82

(m, 1H), 3.79 (s, 3H), 2.87– 2.65 (m, 2H), 1.16 (d, *J* = 11.4 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.1, 155.1, 143.0, 139.7, 136.0, 129.2, 128.9, 128.4, 128.0, 127.9, 127.5, 127.3, 126.9, 126.3, 72.1, 67.6, 65.2, 64.6, 56.9, 52.3, 50.3, 39.2.

HRMS (ESI+): calcd for $C_{28}H_{28}NO_5$, 458.1967; found, 458.1922 ([M+H], 100).

(1*R*, 3*S*, 6*S*, 8*R*, 9*S*)-Benzyl-5-oxo-1,8-diphenyl-4-oxa-7-azatricycle[4.3.0.0^{3,9}]-nonane-7-carboxylate (*endo*-11).



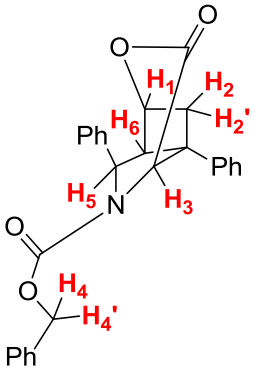
To a solution of PPh_3AuCl (3.25 mg, 0.0066 mmol) and AgOTf (1.69 mg, 0.0066 mmol) in toluene (1.0 mL) at room temperature a suspension of alcohol *endo*-**10** (30.0 mg, 0.066 mmol) in toluene (1.5 mL) was added. Then, the mixture was stirred at 110 °C for 30 minutes and Et_3N (0.1 mL), AcOEt (5.0 mL) and H_2O (5.0 mL) were succesively added. The aqueous phase was extracted with CH_2Cl_2 (3 x 3mL) and the resulting organic phase was washed with H_2O (2 x 5 mL) and brine (2 x 5mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (cyclohexane/EtOAc 4:1), to afford the lactone **11** (27.8 mg, 99%, white solid).

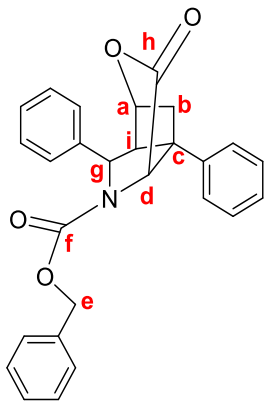
M.p.: 148-150 °C.

[α]$_D^{20}$: + 48.2 (c=0.22, $CHCl_3$), 90 % *ee*.

SFC: The enantiomeric excess was determined by SFC using a Chiralpak-IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, 2.0 mL/min (λ = 240.4 nm)]: t_R= 5.315 min (1*R*, 3*S*, 6*S*, 8*R*, 9*S*)-**11** and 6.424 min (1*S*, 3*R*, 6*R*, 8*S*, 9*R*)-**11**

^{1}H-NMR, **COSY** (300 MHz, $CDCl_3$, 1:0.63 mixture of rotamers. The asterisk * denotes the signal of the minor rotamer): δ 7.40-7.13 (m, 15 H), 5,63 (d, *J*=6.5 Hz, 1H, H_5), 5,51* (d, *J*=6.3 Hz, 1H, H_5), 5, 42* (d, *J*=1.5 Hz, 1H, H_3), 5, 30 (d, *J*=1.4Hz, 1H, H_3), 5, 29* (d, *J*=12.5 Hz, 2H, H_4/$H_{4'}$), 5.09 (d, *J*=12.5 Hz, 2H, H_4/$H_{4'}$), 4.72 (t, *J*=4.1 Hz, 1H, H_1), 4.69* (t, *J*= 4.2 Hz, 1 H, H_1), 3.68 (m, 1H, H_6), 3.61* (m, 1H, H_6), 2.59 (dd, *J*= 12.0, 4.2 Hz, H_2/$H_{2'}$), 2.40 (dd, *J*=11.9, 4.7 Hz, 1H, H_2/$H_{2'}$.





^{13}C-NMR, **DEPT-135**, **HMQC**, **HMBC** (75 MHz, $CDCl_3$, 1:0.63 mixture of rotamers. The asterisk * denotes the signal of the minor rotamer):[3] δ 166.8 (1C, C_h), 154.3 (1C, C_f), 154.1* (1C, C_f), 139.3 (1C, CH_{ar}), 139.1* (1C, CH_{ar}), 137.0* (1C, CH_{ar}), 136.2 (1C, CH_{ar}), 135.8 (1C, CH_{ar}), 135.7* (1C, CH_{ar}), 129.2 (3C, CH, CH_{ar}), 128.7 (CH_{ar}), 128.6* (CH_{ar}), 128.5 (2C, CH_{ar}), 128.3* (CH_{ar}), 127.9* (CH_{ar}), 127.6*, 127.5* (2C, CH, CH_{ar}), 127.3 (2C, CH, CH_{ar}), 125.3* (CH_{ar}), 125.24* (CH_{ar}), 125.3 (2C, CH, CH_{ar}), 125.0* (2C, CH, CH_{ar}), 75.74* (1C, CH, C_a), 75.7 (1C, CH, C_a), 69.45 (1C, CH, C_d), 68.9* (1C, CH, C_d), 67.7 (1C, CH_2, C_e), 67.6* (1C, CH_2, C_e), 62.3* (1C, CH, C_g), 62.2 (1C, CH, C_g), 60.3 (1C, CH, C_i), 56.5* (1C, CH, C_i), 55.1 (1C, C_c), 54.5* (1C, C_c), 36.3 (1C, CH_2, C_b), 36.4* (1C, CH_2, C_b).

HRMS (ESI+): calcd for $C_{27}H_{24}NO_4$, 426.1705; found, 426.1532 ([M+H], 100).

3. Preparation of racemic products for HPLC analysis.

The racemic pyrrolidines were prepared according to the general procedure, but using (±)-Binap as ligand. The samples for HPLC analysis were dissolved in isopropyl alcohol for the determination of enantiomeric excess in the case of HPLC and dichloromethane for SFC, and used as quickly as possible to minimize the formation of decomposition products.

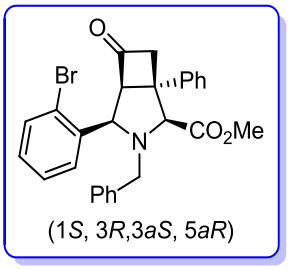
4. Regiochemical and stereochemical assignment

The relative and absolute configuration of *endo*-**3g** was unequivocally established by X-ray crystal structure analysis of its N-benzyl derivative.

CCDC 1828413 contains the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk

3. Some aromatic carbons could not be assigned from the collected spectroscopic data due to the complexity of the spectrum around 125.0-140.0 ppm. These signals are indicated as CH_{ar}.

Figure S1: X-Ray Structure of the N-benzyl derivative of *endo*-**3g**



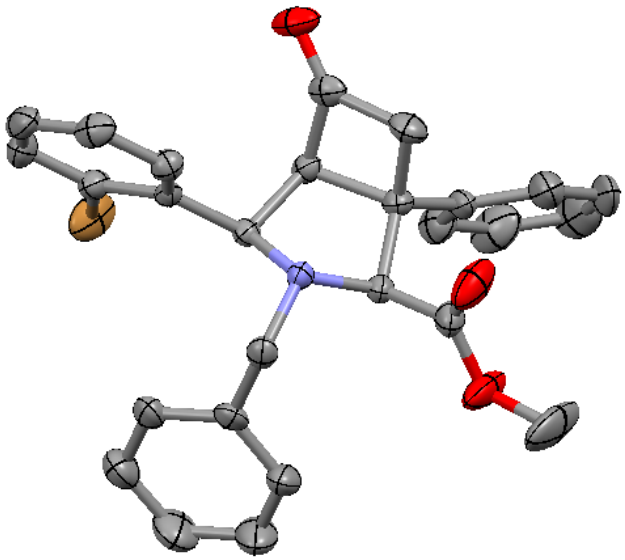


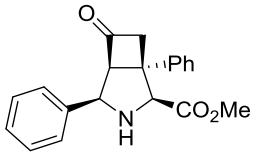
Table S1. Crystal data of 7 (Hydrogen atoms removed for clarity).

Chemical formula	$C_{27}H_{24}BrNO_3$	
Formula weight	490.38 g/mol	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal size	0.076 x 0.191 x 0.427 mm	
Crystal habit	clear colourless prismatic	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.3574(3) Å	α = 90°
	b = 17.3491(9) Å	β = 90°
	c = 18.2869(9) Å	γ = 90°
Volume	2334.22(19) $Å^3$	
Z	4	
Density (calculated)	1.395 g/cm^3	
Absorption coefficient	1.789 mm^{-1}	
F(000)	1008	

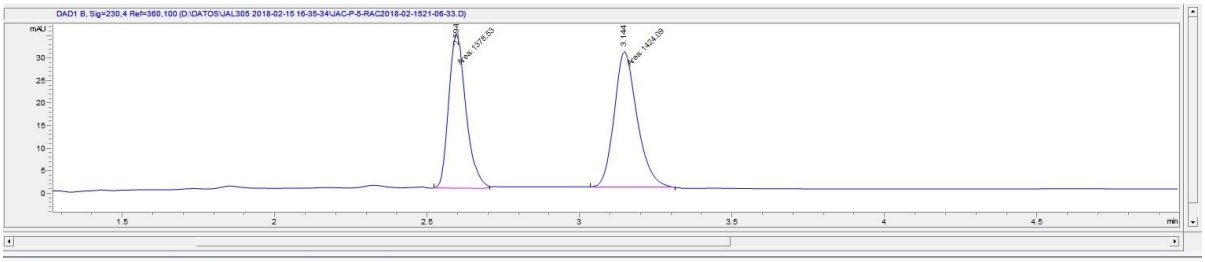
Table S2. Data collection and structure refinement

Diffractometer	Bruker APEX-II CCD
Theta range for data collection	2.23 to 25.35°
Index ranges	-7<=h<=8, -20<=k<=20, -22<=l<=2
Reflections collected	21048
Independent reflections	4274 [R(int) = 0.0597]
Coverage of independent reflections	100.0%
Absorption correction	multi-scan
Max. and min. transmission	0.8760 and 0.5150
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4274 / 0 / 290
Goodness-of-fit on F^2	1.012
Final R indices	3399 data; I>2σ(I): R1 = 0.0361, wR2 = 0.0684
	all data: R1 = 0.0561, wR2 = 0.0746
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0313P)^2+0.3686P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	-0.0(0)
Largest diff. peak and hole	0.294 and -0.349 eÅ^{-3}
R.M.S. deviation from mean	0.051 eÅ^{-3}

5. HPLC charts.

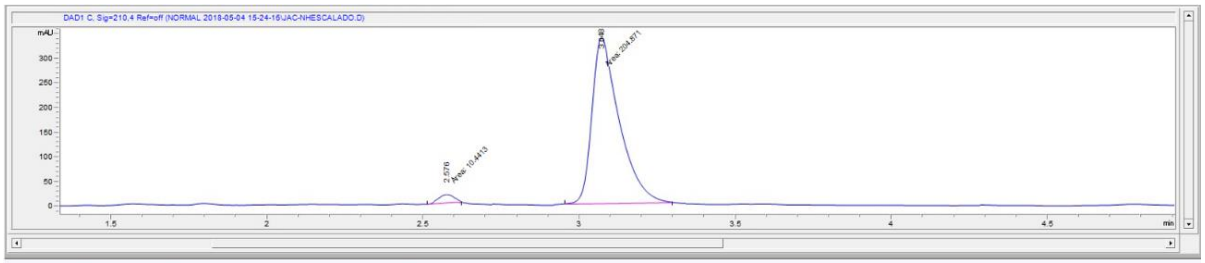


endo-**3a**



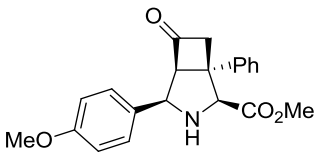
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.594	MM	1378.5	34.2	0.0642	49.187	0.784
2	3.144	MM	1424.1	30.5	0.0912	50.813	0.847

Figure S2: (±)-*endo*-**3a**

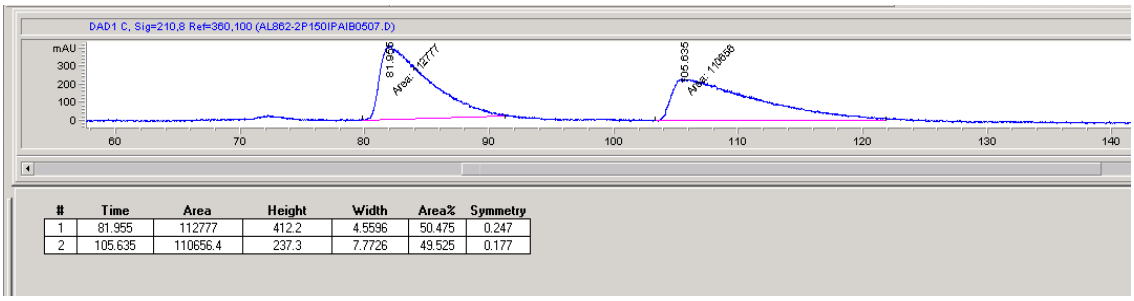


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.576	MM	10.4	4.6	0.0375	4.849	1.023
2	3.048	MM	204.9	19.8	0.1724	95.151	1.292

Figure S3: (+)-*endo*-**3a**; 90% *ee*

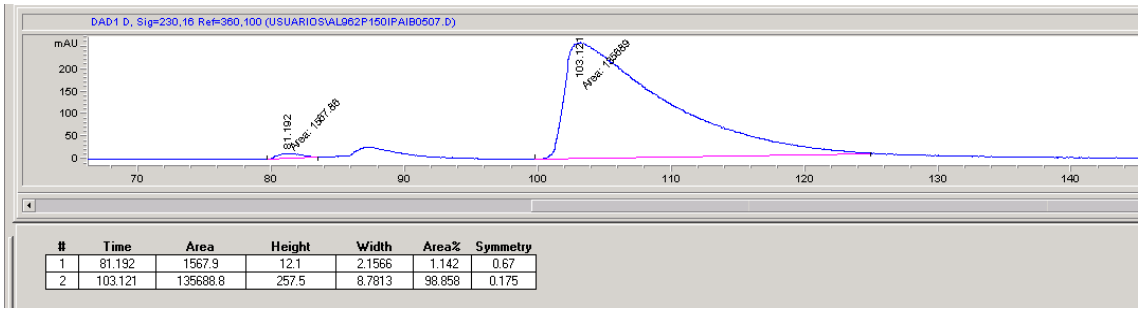


endo-**3b**



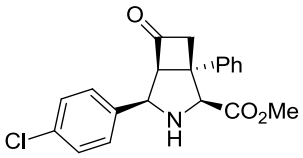
#	Time	Area	Height	Width	Area%	Symmetry
1	81.955	112777	412.2	4.5596	50.475	0.247
2	105.635	110656.4	237.3	7.7726	49.525	0.177

Figure S4: (±)-*endo*-**3b**

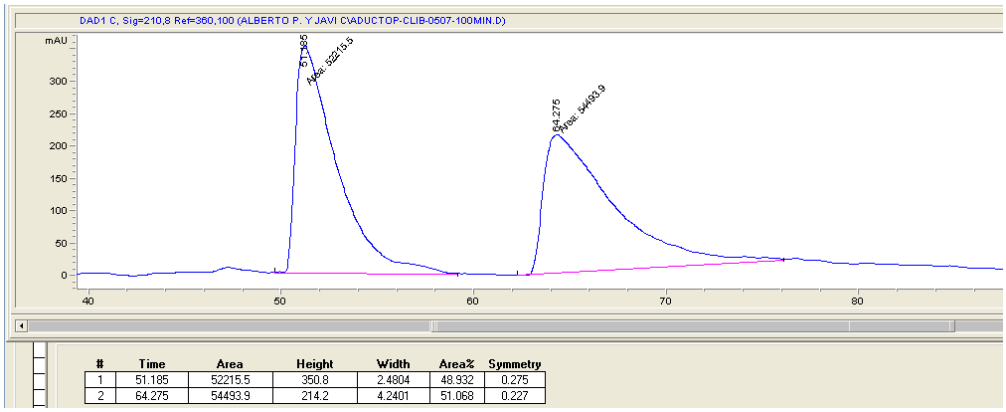


#	Time	Area	Height	Width	Area%	Symmetry
1	81.192	1567.9	12.1	2.1566	1.142	0.67
2	103.121	135688.8	257.5	8.7813	98.858	0.175

Figure S5: (+)-*endo*-**3b**; 98% *ee*

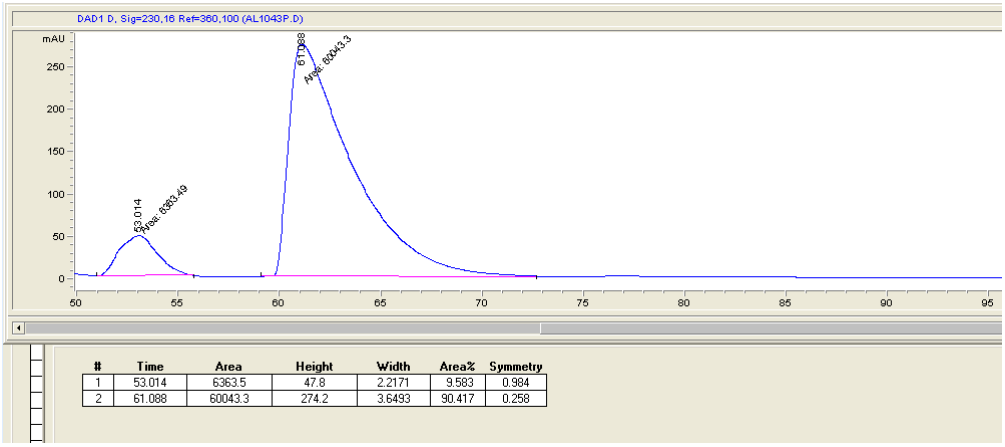


endo-**3c**



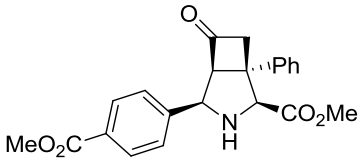
#	Time	Area	Height	Width	Area%	Symmetry
1	51.185	52215.5	350.8	2.4804	48.932	0.275
2	64.275	54493.9	214.2	4.2401	51.068	0.227

Figure S6: (±)-*endo*-**3c**

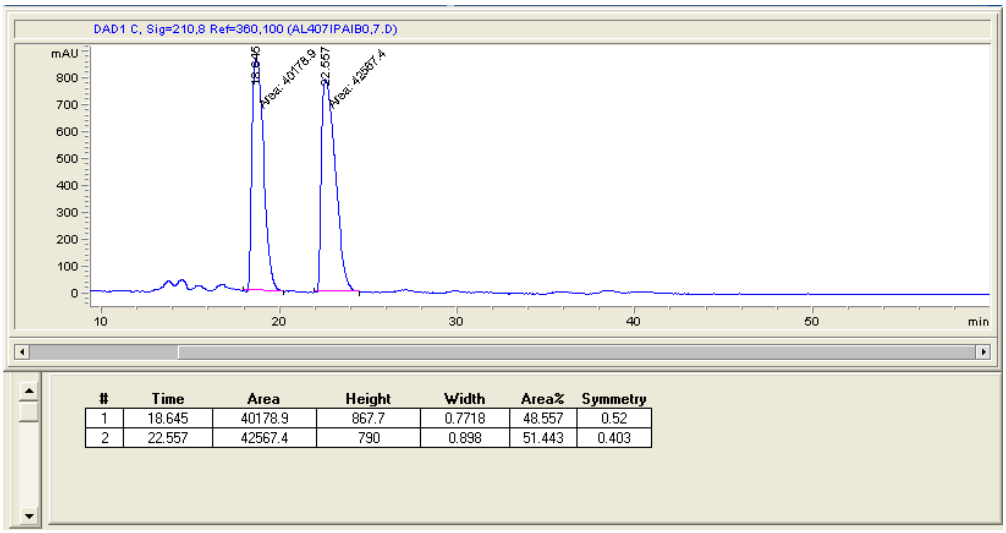


#	Time	Area	Height	Width	Area%	Symmetry
1	53.014	6363.5	47.8	2.2171	9.583	0.984
2	61.088	60043.3	274.2	3.6493	90.417	0.258

Figure S7: (+)-*endo*-**3c**; 81% *ee*

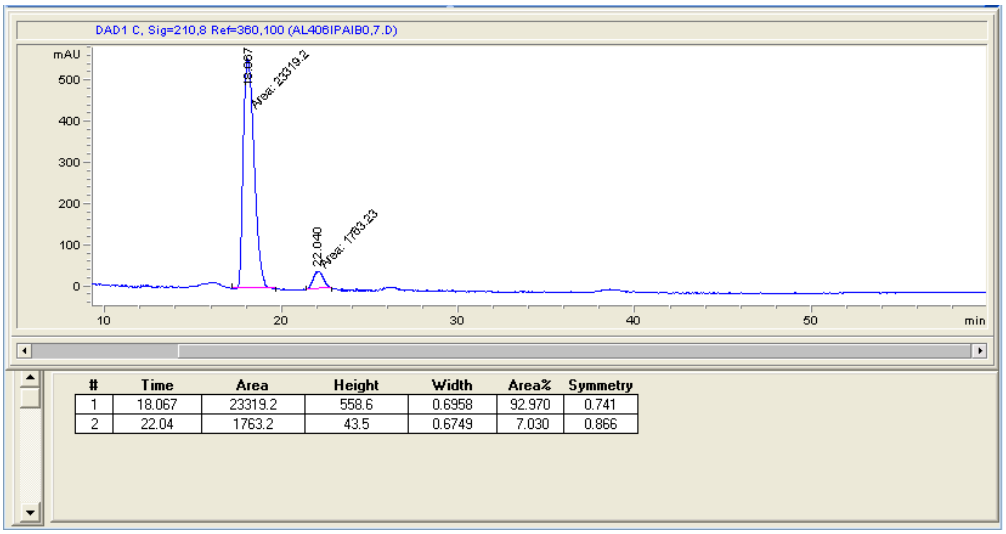


endo-**3d**



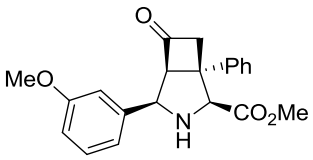
#	Time	Area	Height	Width	Area%	Symmetry
1	18.645	40178.9	867.7	0.7718	48.557	0.52
2	22.557	42567.4	790	0.898	51.443	0.403

Figure S8: (±)-*endo*-**3d**

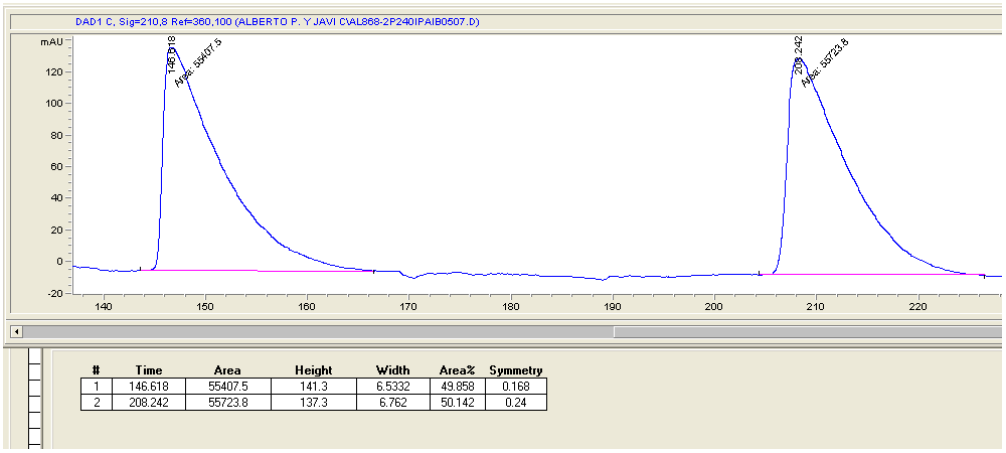


#	Time	Area	Height	Width	Area%	Symmetry
1	18.067	23319.2	558.6	0.6958	92.970	0.741
2	22.04	1763.2	43.5	0.6749	7.030	0.866

Figure S9: (+)-*endo*-**3d**; 85% *ee*

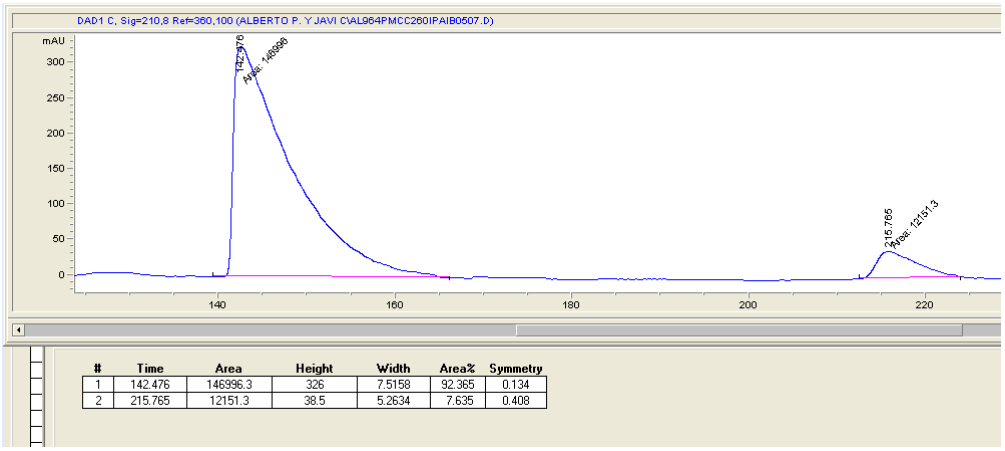


endo-**3e**



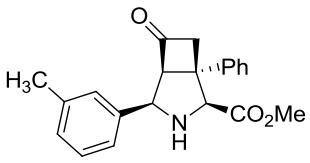
#	Time	Area	Height	Width	Area%	Symmetry
1	146.618	55407.5	141.3	6.5332	49.858	0.168
2	208.242	55723.8	137.3	6.762	50.142	0.24

Figure S10: (±)-*endo*-**3e**

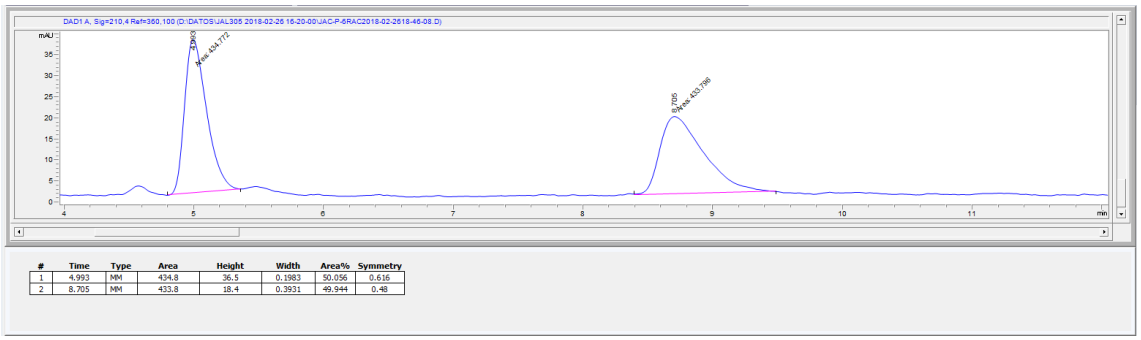


#	Time	Area	Height	Width	Area%	Symmetry
1	142.476	146996.3	326	7.5158	92.365	0.134
2	215.765	12151.3	38.5	5.2634	7.635	0.408

Figure S11: (+)-*endo*-**3e**; 85% *ee*

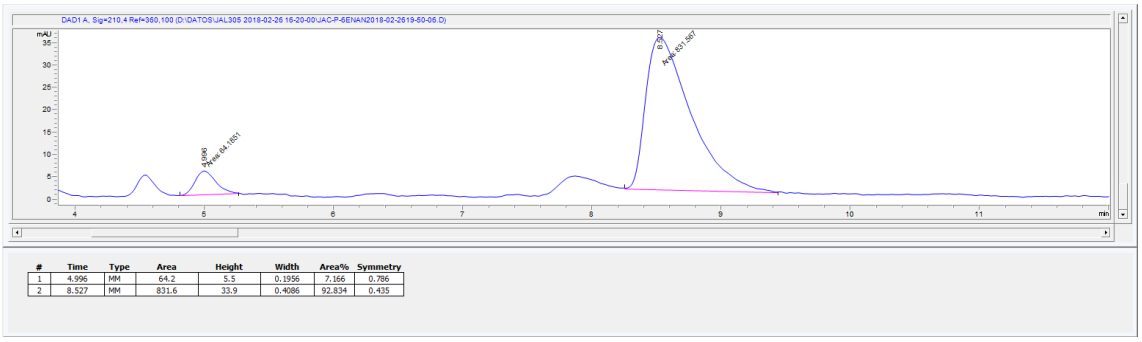


endo-**3f**



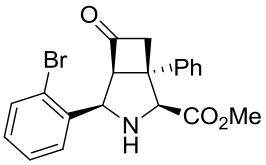
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.993	MM	434.8	36.5	0.1983	50.056	0.616
2	8.705	MM	433.8	18.4	0.3931	49.944	0.48

Figure S12: (±)-*endo*-**3f**

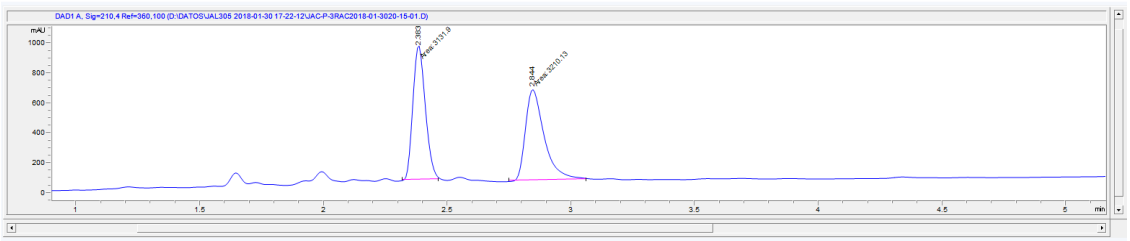


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.996	MM	64.2	5.5	0.1956	7.166	0.786
2	8.527	MM	831.6	33.9	0.4086	92.834	0.435

Figure S13: (+)-*endo*-**3f**; 86% *ee*

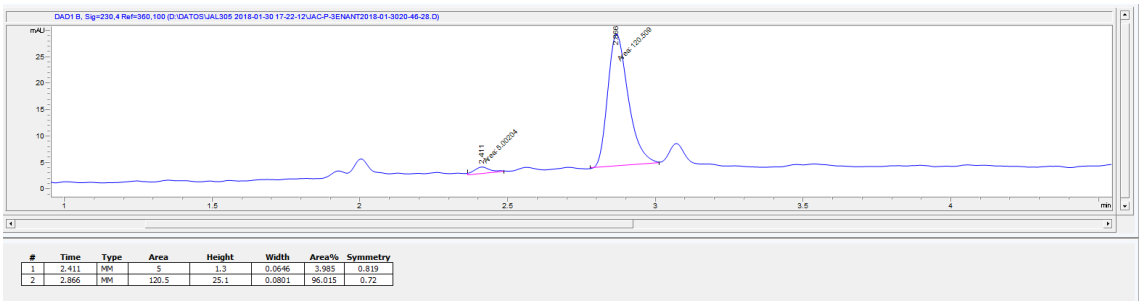


endo-**3g**



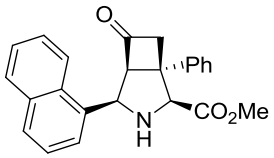
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.383	MM	3131.9	899	0.0581	49.383	0.818
2	2.844	MM	3210.1	606.7	0.0882	50.617	0.604

Figure S14: (±)-*endo*-**3g**

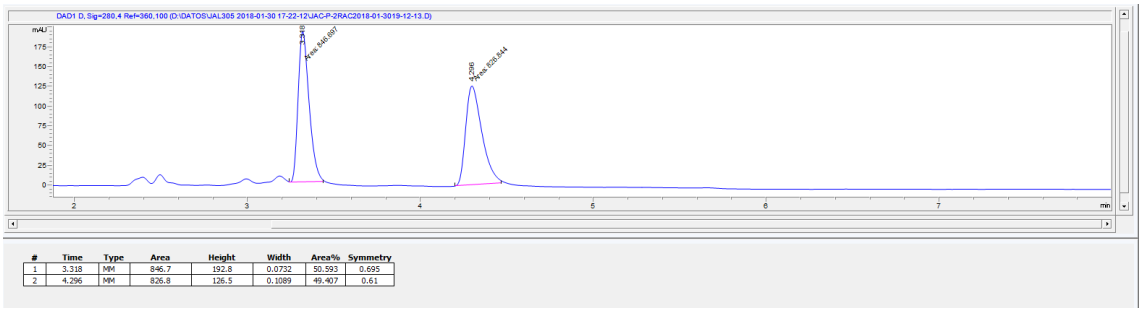


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.411	MM	5	1.3	0.0646	3.985	0.819
2	2.866	MM	120.5	25.1	0.0801	96.015	0.72

Figure S15: (+)-*endo*-**3g**; 92% *ee*

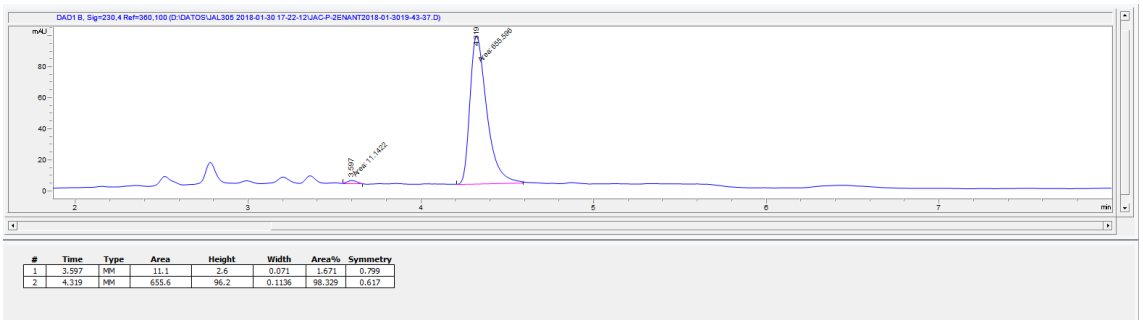


endo-**3h**



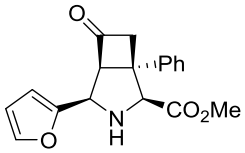
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.318	MM	846.7	192.8	0.0732	50.593	0.695
2	4.296	MM	826.8	126.5	0.1089	49.407	0.61

Figure S16: (±)-*endo*-**3h**

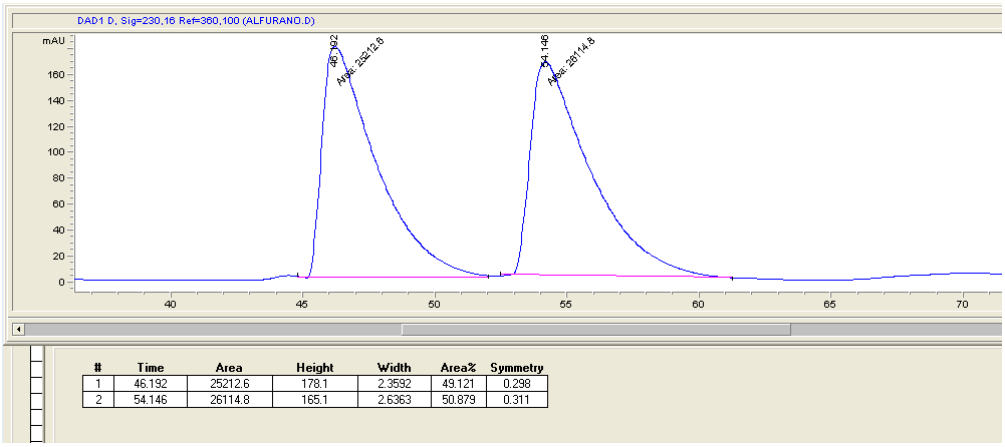


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.597	MM	11.1	2.6	0.071	1.671	0.799
2	4.319	MM	655.6	96.2	0.1136	98.329	0.617

Figure S17: (+)-*endo*-**3h**; 97% *ee*

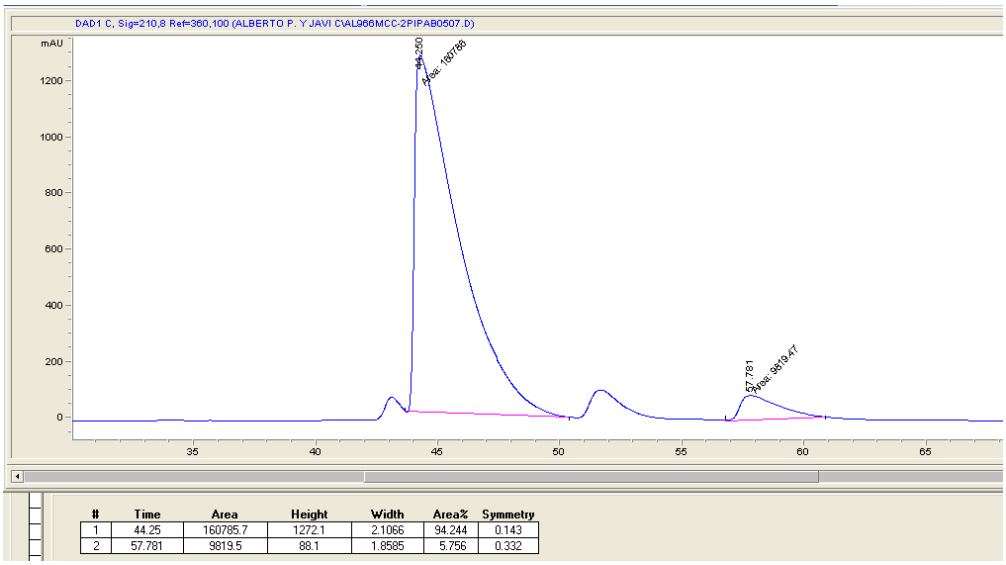


endo-**3i**



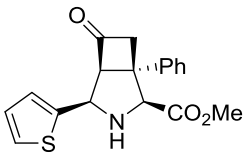
#	Time	Area	Height	Width	Area%	Symmetry
1	46.192	25212.6	178.1	2.3592	49.121	0.298
2	54.146	26114.8	165.1	2.6363	50.879	0.311

Figure S18: (±)-*endo*-**3i**

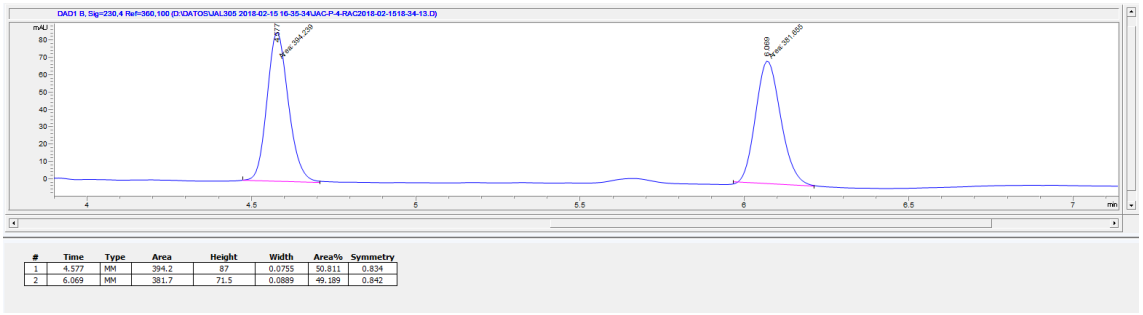


#	Time	Area	Height	Width	Area%	Symmetry
1	44.25	160785.7	1272.1	2.1066	94.244	0.143
2	57.781	9819.5	88.1	1.8585	5.756	0.332

Figure S19: (+)-*endo*-**3i**; 88% *ee*

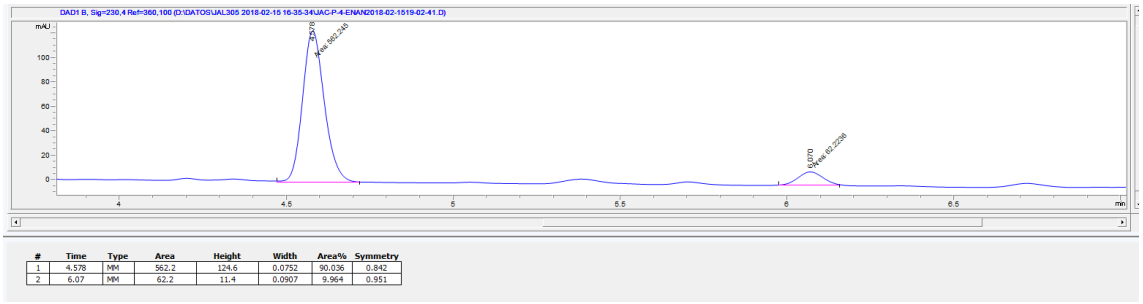


endo-**3j**



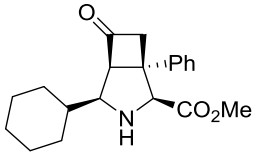
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.577	MM	394.2	87	0.0755	50.811	0.834
2	6.069	MM	381.7	71.5	0.0889	49.189	0.842

Figure S20: (±)-*endo*-**3j**

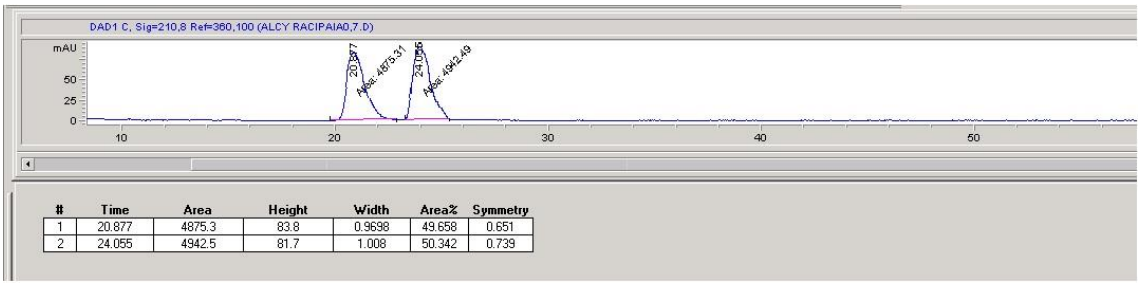


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.578	MM	562.2	124.6	0.0752	90.036	0.842
2	6.07	MM	62.2	11.4	0.0907	9.964	0.951

Figure S21: (+)-*endo*-**3j**; 80% *ee*

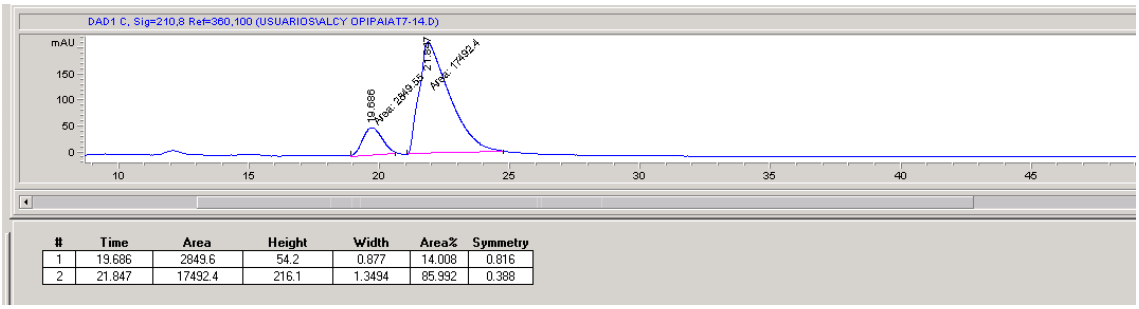


endo-**3k**



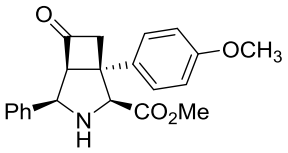
#	Time	Area	Height	Width	Area%	Symmetry
1	20.877	4875.3	83.8	0.9698	49.658	0.651
2	24.055	4942.5	81.7	1.008	50.342	0.739

Figure S22: (±)-*endo*-**3k**

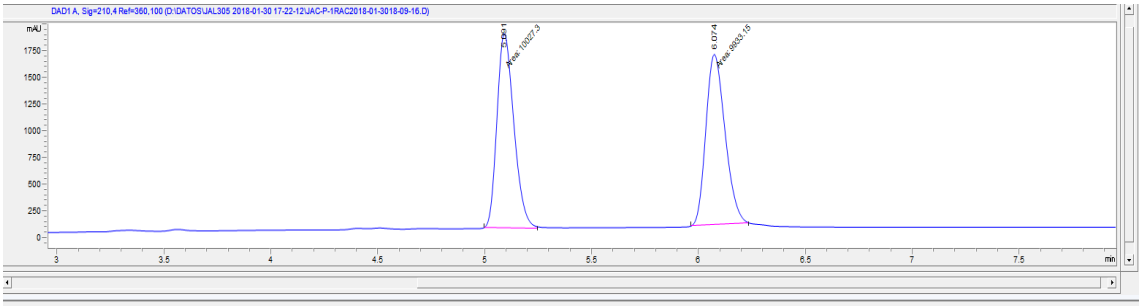


#	Time	Area	Height	Width	Area%	Symmetry
1	19.686	2849.6	54.2	0.877	14.008	0.816
2	21.847	17492.4	216.1	1.3494	85.992	0.388

Figure S23: (+)-*endo*-**3k**; 72% *ee*

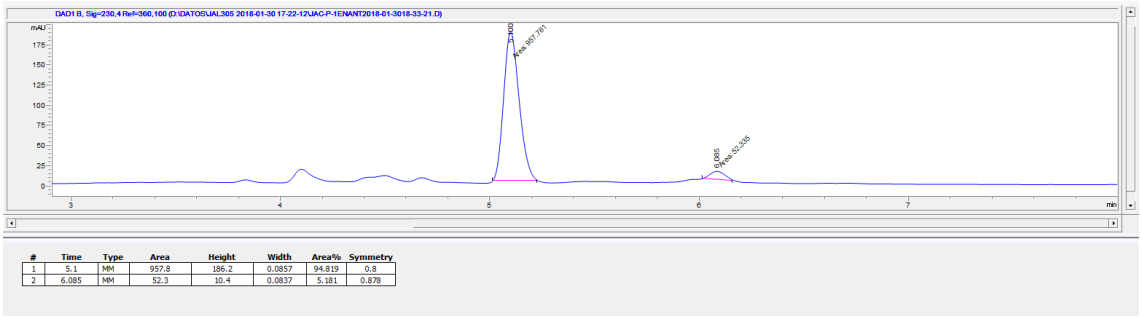


endo-**3l**



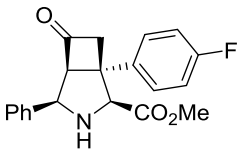
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.091	MM	10027.3	1827.3	0.0915	50.236	0.743
2	6.074	MM	9933.2	1598.1	0.1036	49.764	0.767

Figure S24: (±)-*endo*-**3l**

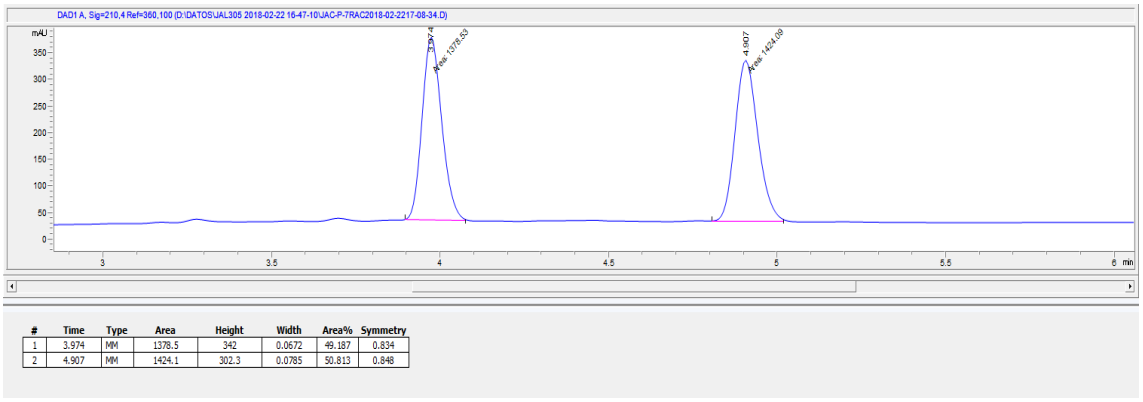


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.1	MM	957.8	186.2	0.0857	94.819	0.8
2	6.085	MM	52.3	10.4	0.0837	5.181	0.878

Figure S25: (+)-*endo*-**3l**; 90% *ee*

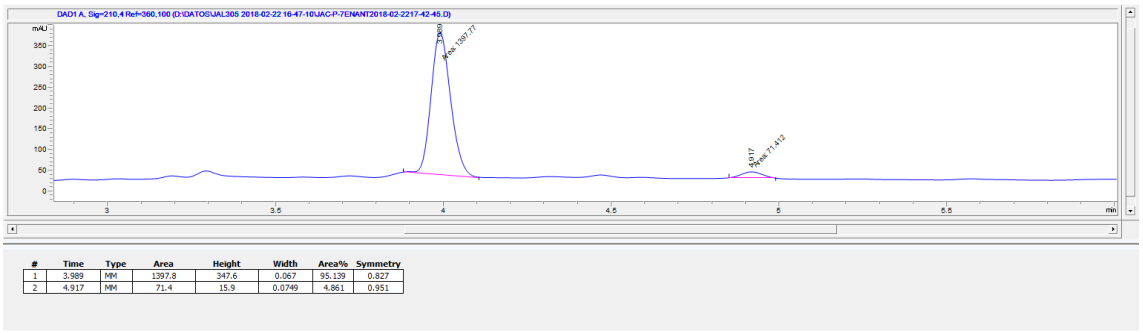


endo-**3m**



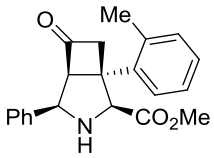
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.974	MM	1378.5	342	0.0672	49.187	0.834
2	4.907	MM	1424.1	302.3	0.0785	50.813	0.848

Figure S26: (±)-*endo*-**3m**

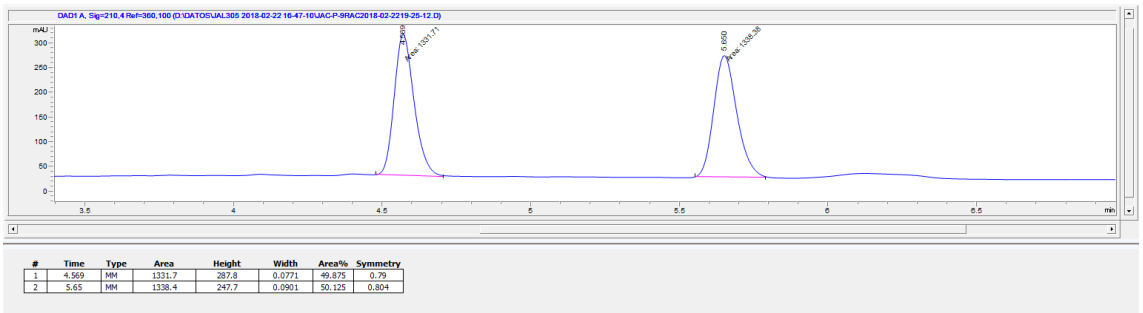


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.989	MM	1397.8	347.6	0.067	95.139	0.827
2	4.917	MM	71.4	15.9	0.0749	4.861	0.951

Figure S27: (+)-*endo*-**3m**; 90% *ee*

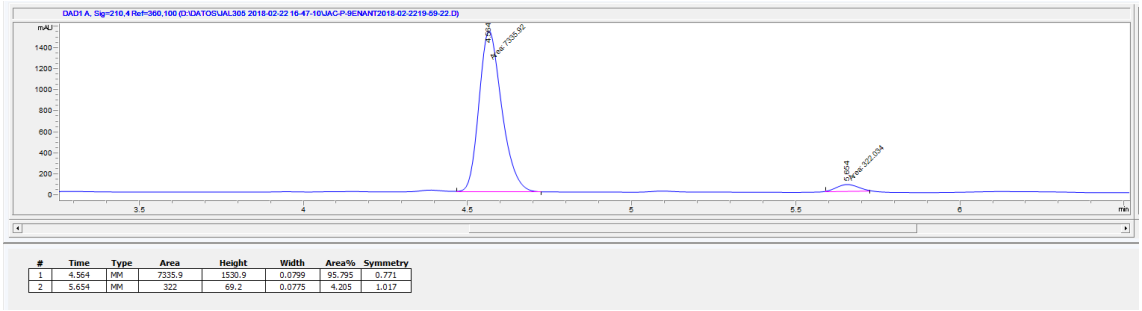


endo-**3n**



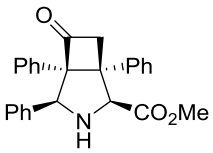
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.569	MM	1331.7	287.8	0.0771	49.875	0.79
2	5.65	MM	1338.4	247.7	0.0901	50.125	0.804

Figure S28: (±)-*endo*-**3n**

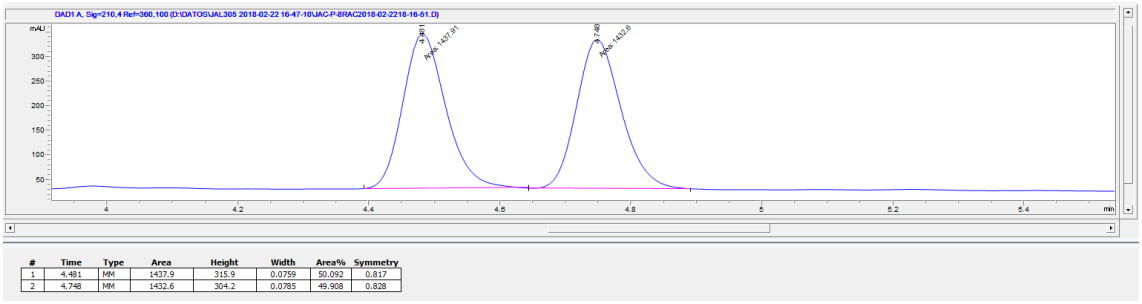


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.564	MM	7335.9	1530.9	0.0799	95.795	0.771
2	5.654	MM	322	69.2	0.0775	4.205	1.017

Figure S29: (+)-*endo*-**3n**; 92% *ee*

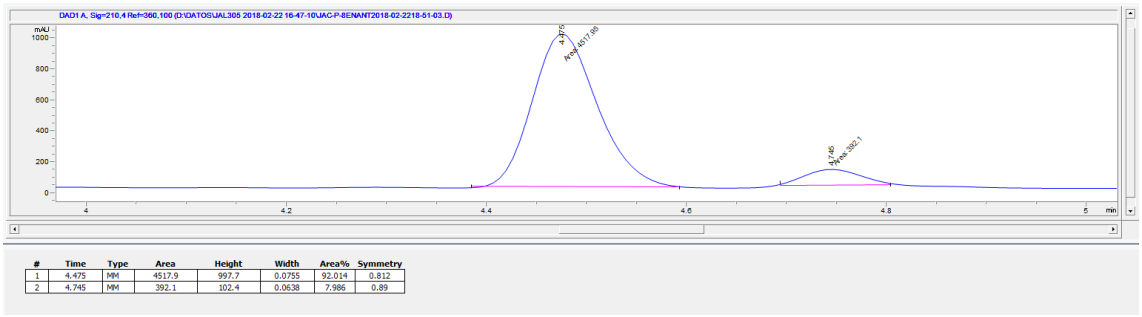


endo-**3o**



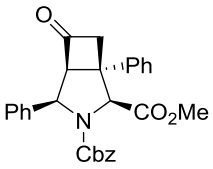
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.481	MM	1437.9	315.9	0.0759	50.092	0.817
2	4.748	MM	1432.6	304.2	0.0785	49.908	0.828

Figure S30: (±)-*endo*-**3o**

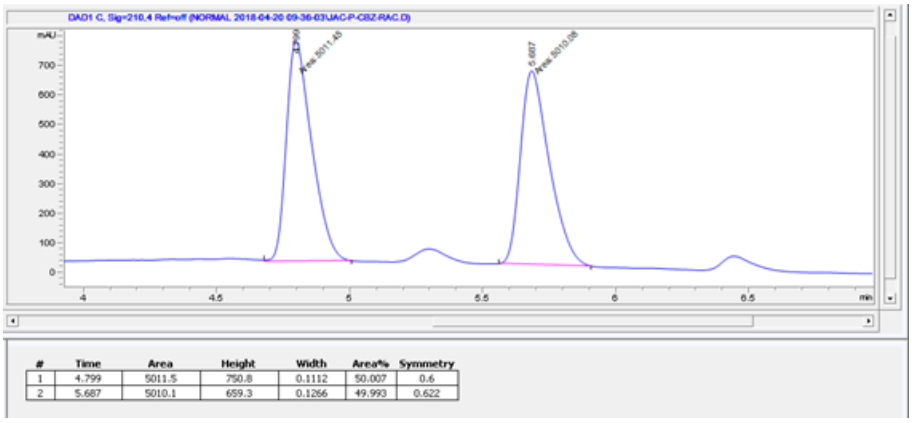


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.475	MM	4517.9	997.7	0.0755	92.014	0.812
2	4.745	MM	392.1	102.4	0.0638	7.986	0.89

Figure S31: (+)-*endo*-**3o**; 84% *ee*

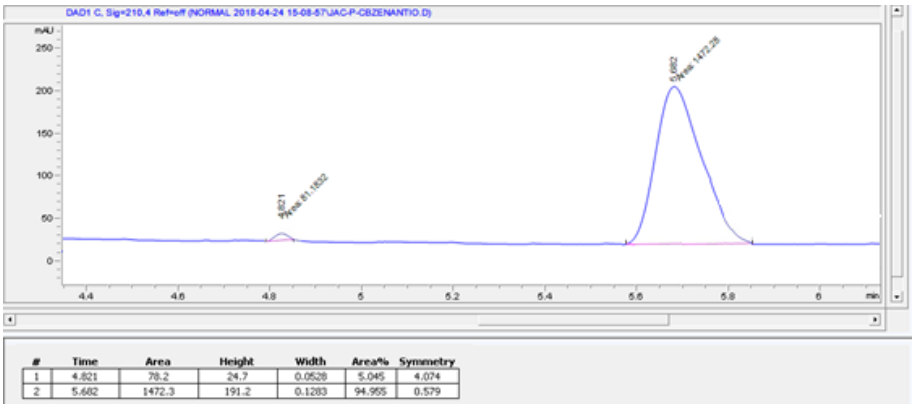


endo-**7**



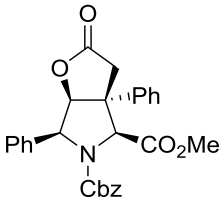
#	Time	Area	Height	Width	Area%	Symmetry
1	4.799	5011.5	750.8	0.1112	50.007	0.6
2	5.687	5010.1	659.3	0.1266	49.993	0.622

Figure S32: (±)-*endo*-**7**



#	Time	Area	Height	Width	Area%	Symmetry
1	4.821	78.2	24.7	0.0528	5.045	4.074
2	5.682	1472.3	191.2	0.1283	94.955	0.579

Figure S33: (+)-*endo*-**7**, 90 % *ee*



endo-**8**

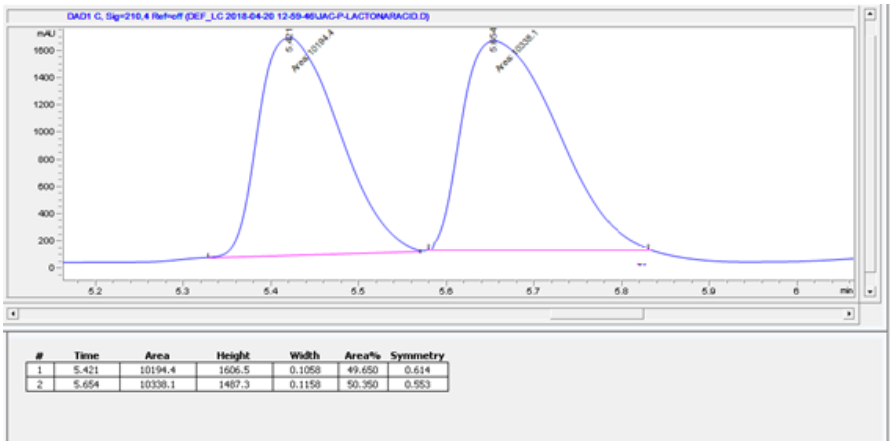


Figure S34: (±)-*endo*-**8**

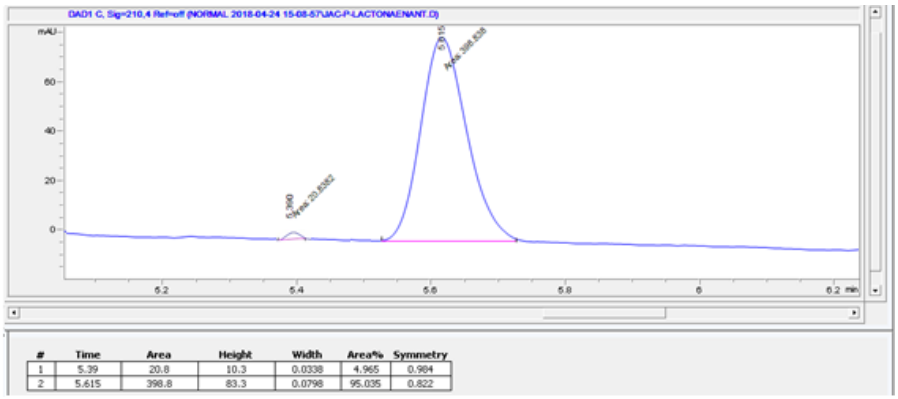
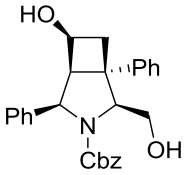


Figure S35: (+)-*endo*-**8**, 90 % *ee*



endo-**9**

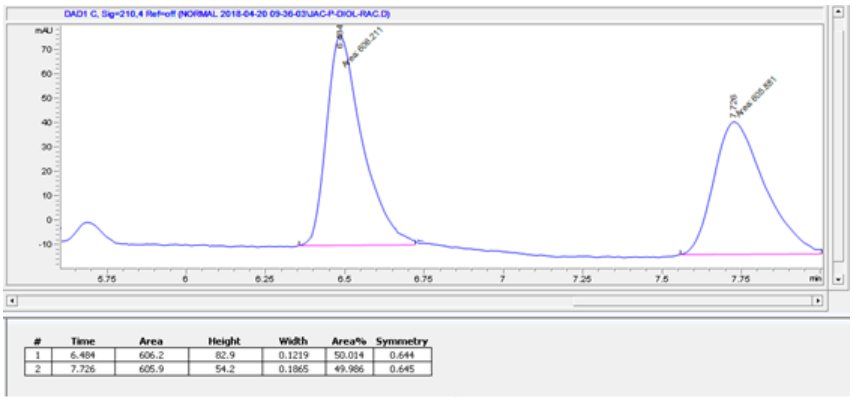


Figure S36: (±)-*endo*-**9**

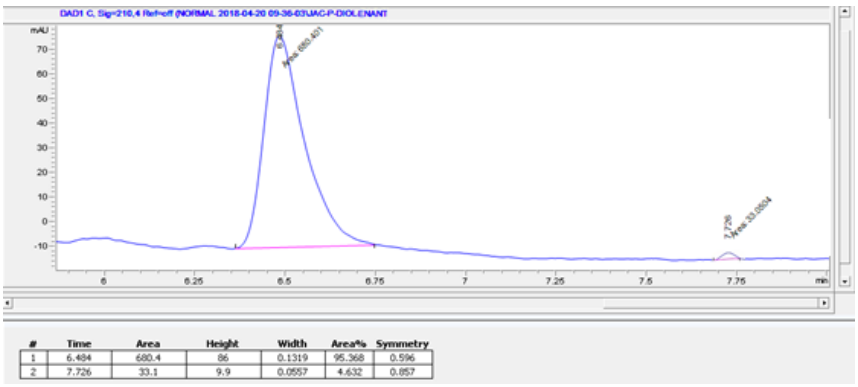
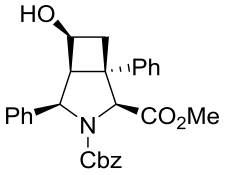


Figure S37: (+)-*endo*-**9**, 90 % *ee*



endo-**10**

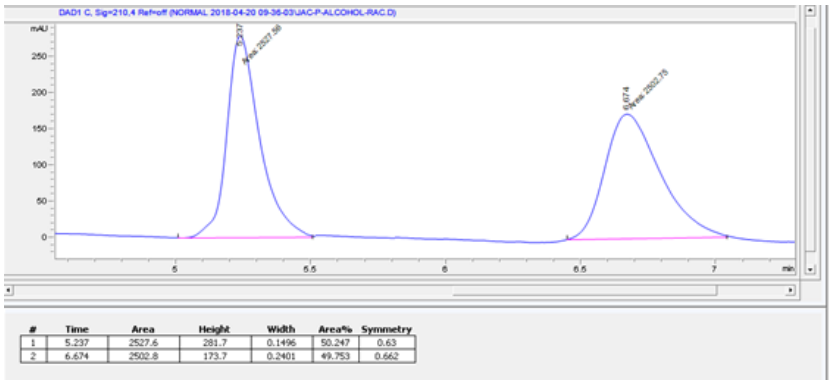


Figure S38: (±)-*endo*-**10**

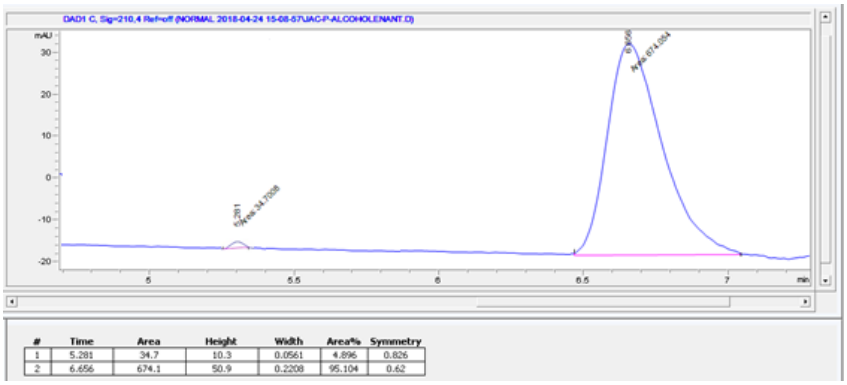
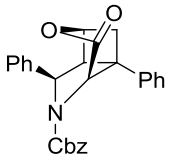


Figure S39: (+)-*endo*-**10**, 90 % *ee*



endo-**11**

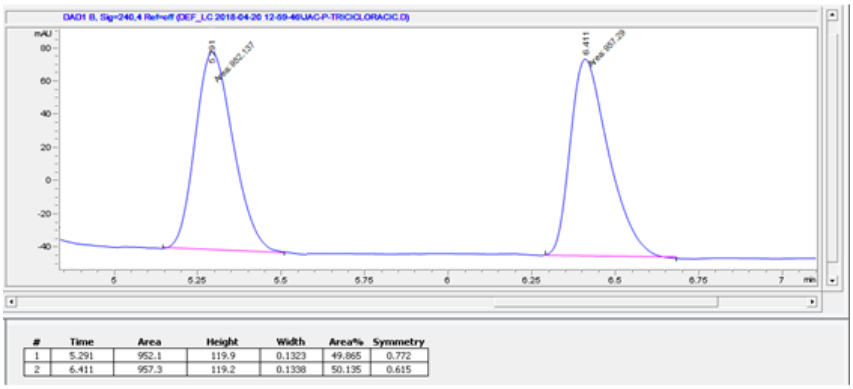


Figure S40: (±)-*endo*-**11**

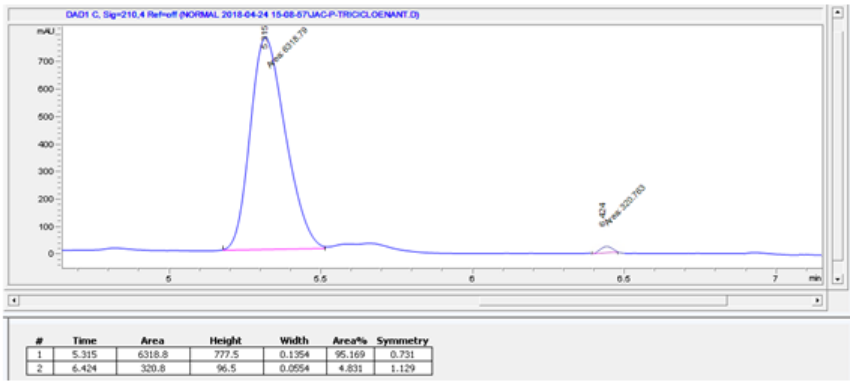
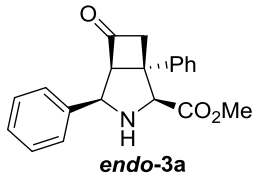
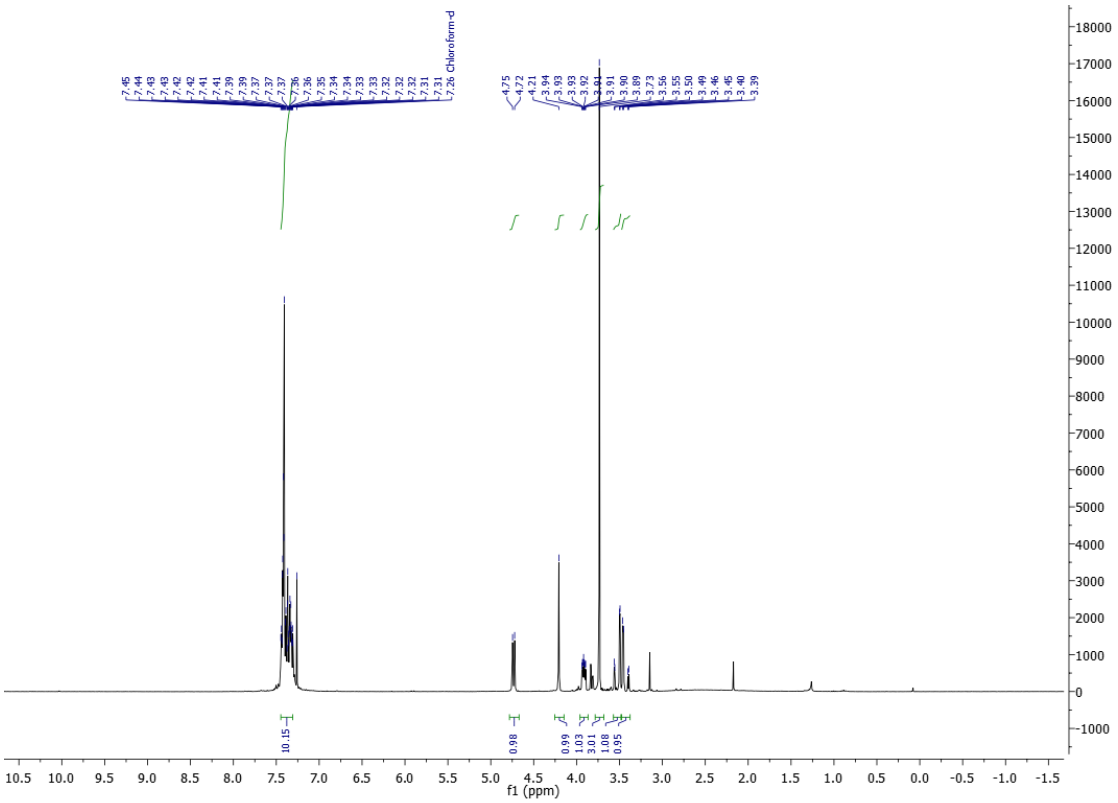


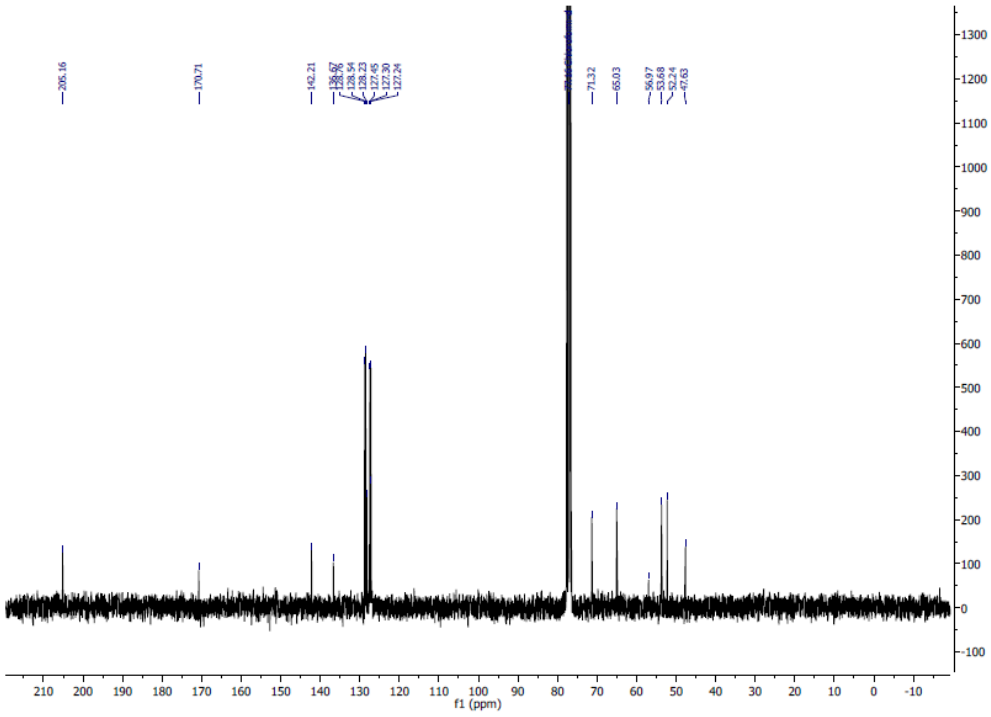
Figure S41: (+)-*endo*-**11**, 90 % *ee*

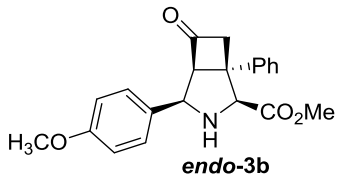
6. NMR spectra collection



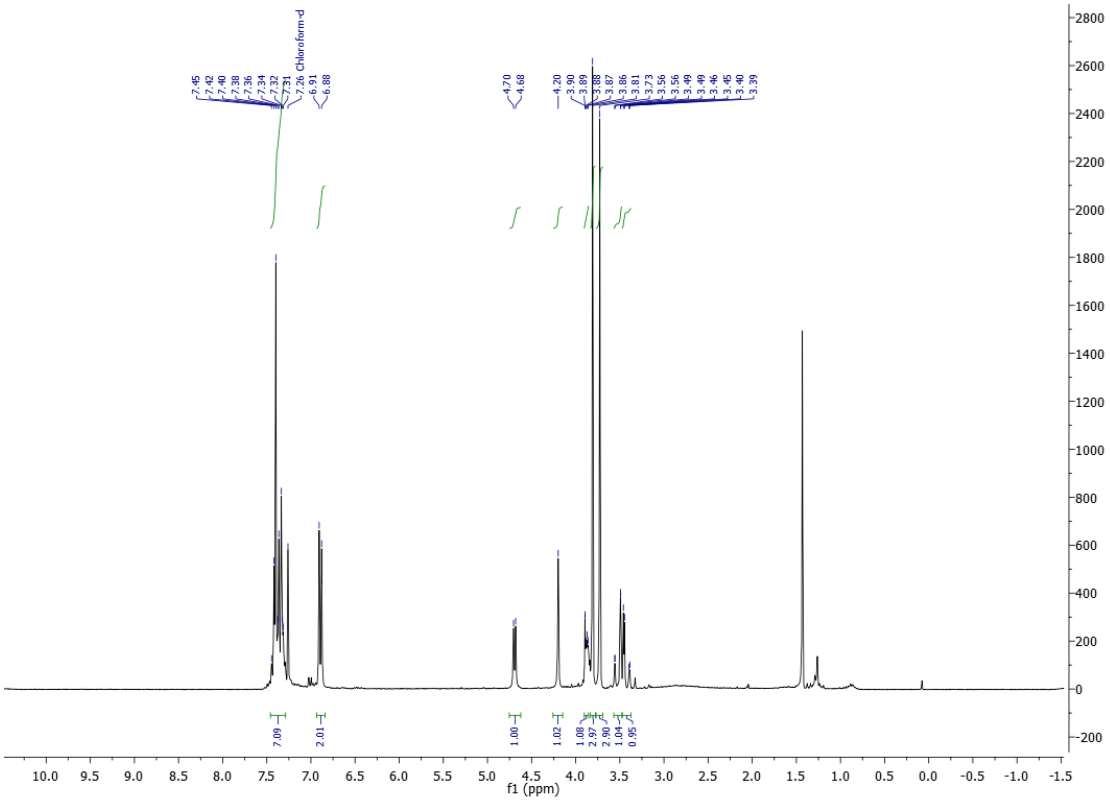
***endo*-3a**

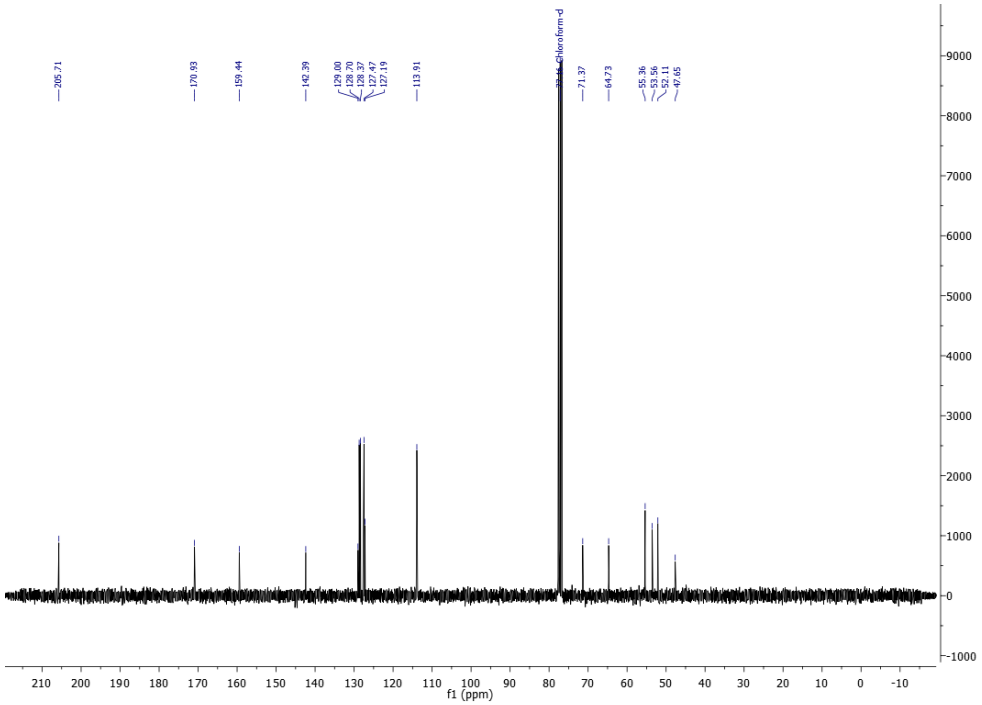




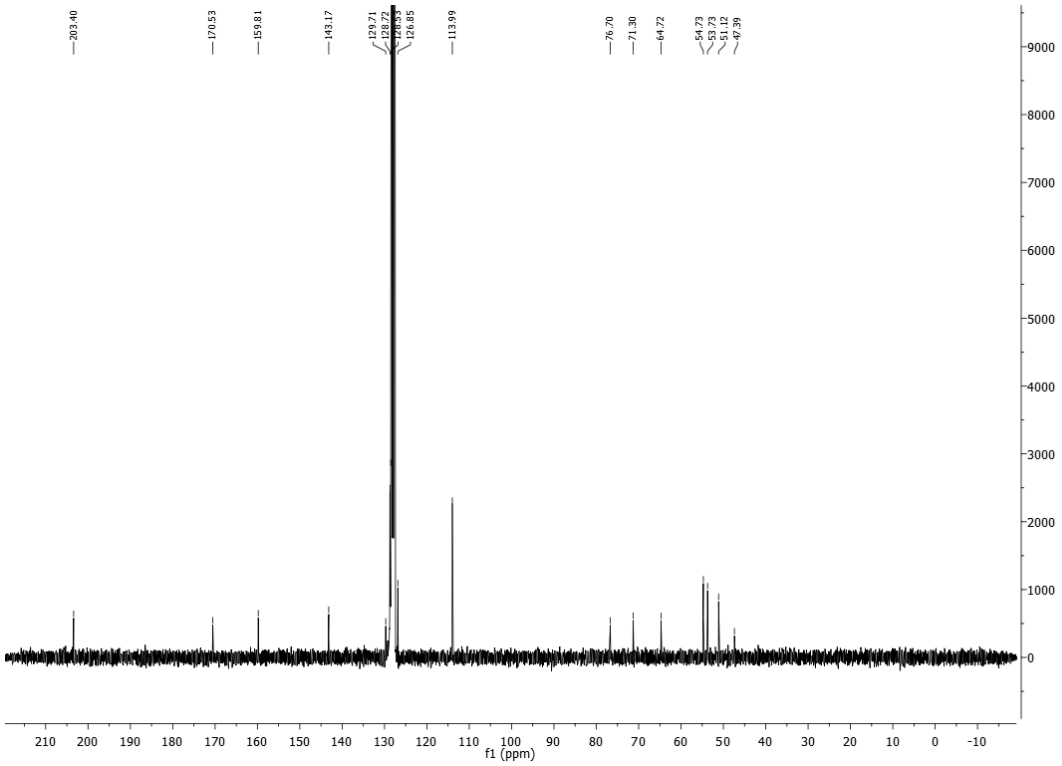

O
Ph
CO2Me
H3CO
N
H

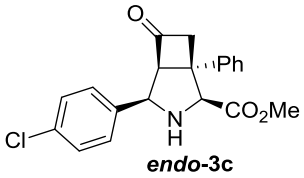
***endo*-3b**


7.45
7.42
7.40
7.38
7.36
7.34
7.32
7.31
7.26 Chloroform-d
6.91
6.88
4.70
4.68
4.20
3.90
3.89
3.88
3.87
3.86
3.81
3.73
3.56
3.56
3.49
3.49
3.46
3.45
3.40
3.39
7.09
2.01
1.00
1.02
1.08
2.97
2.90
1.04
0.95
f1 (ppm)

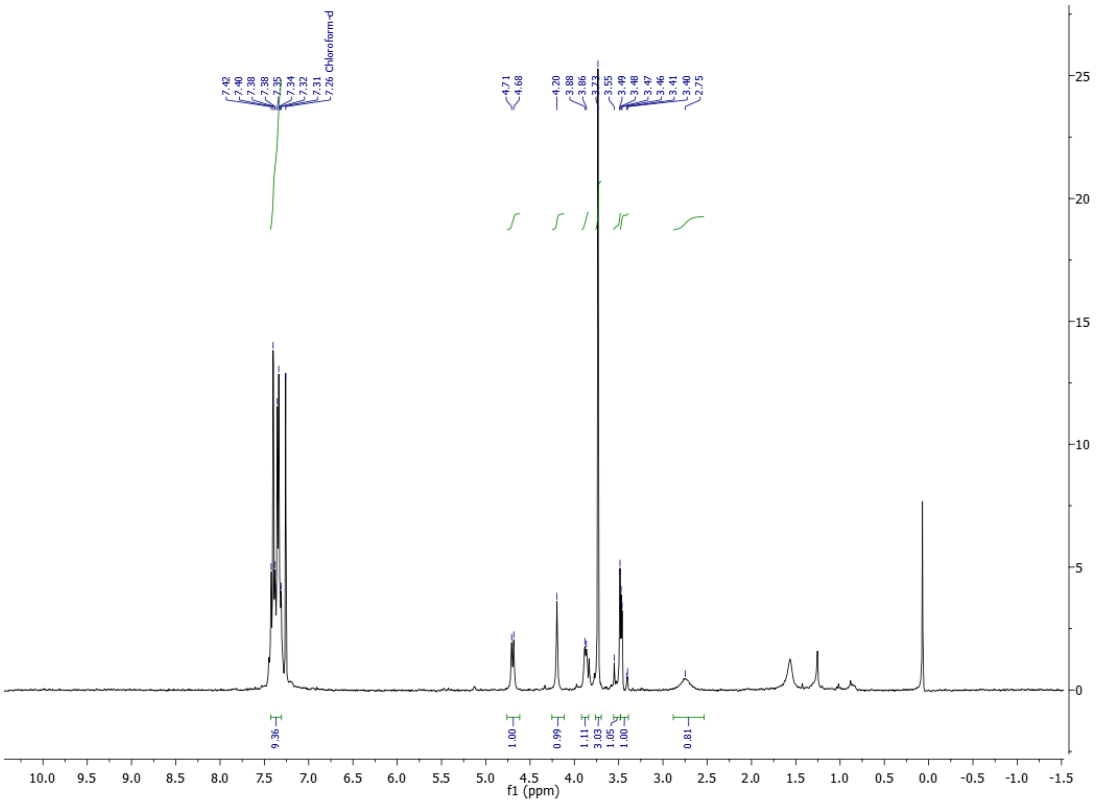

205.71
170.93
159.44
142.39
129.80
128.70
128.37
127.47
127.19
113.91
77.16 Chloroform-d
71.37
64.73
55.36
53.56
52.11
47.65
f1 (ppm)

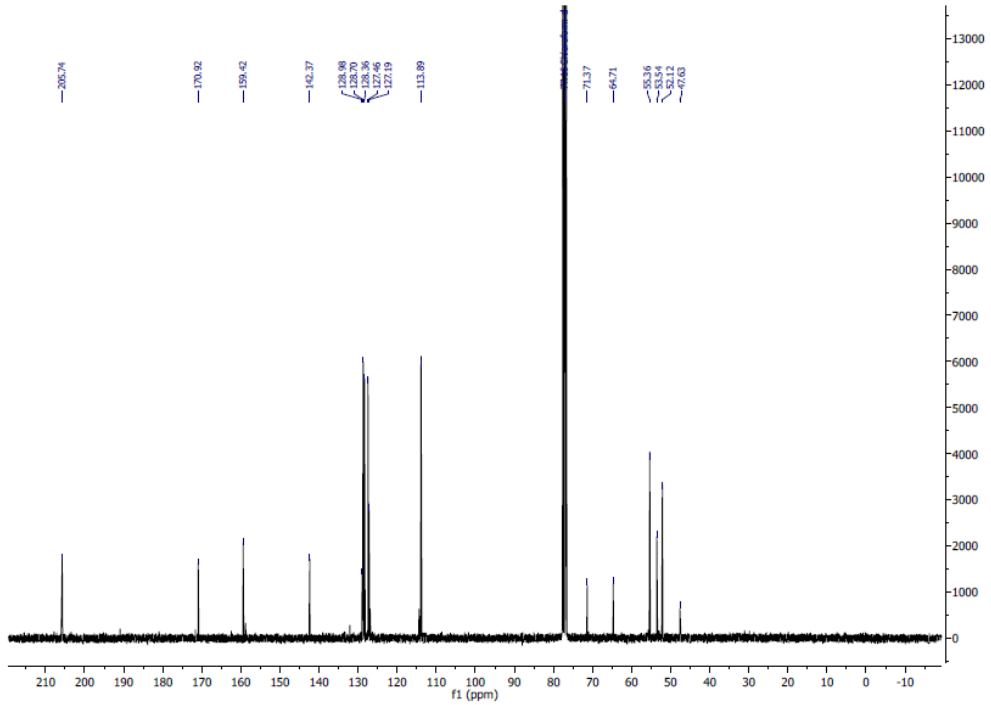
The existence of seven aliphatic carbons in compound *endo*-**3b** was determined by recording the ^{13}C-NMR in benzene-d_6.

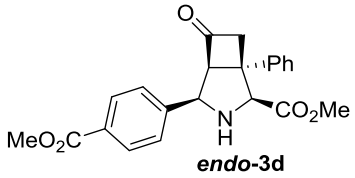



O
Ph
CO2Me
N
H
Cl

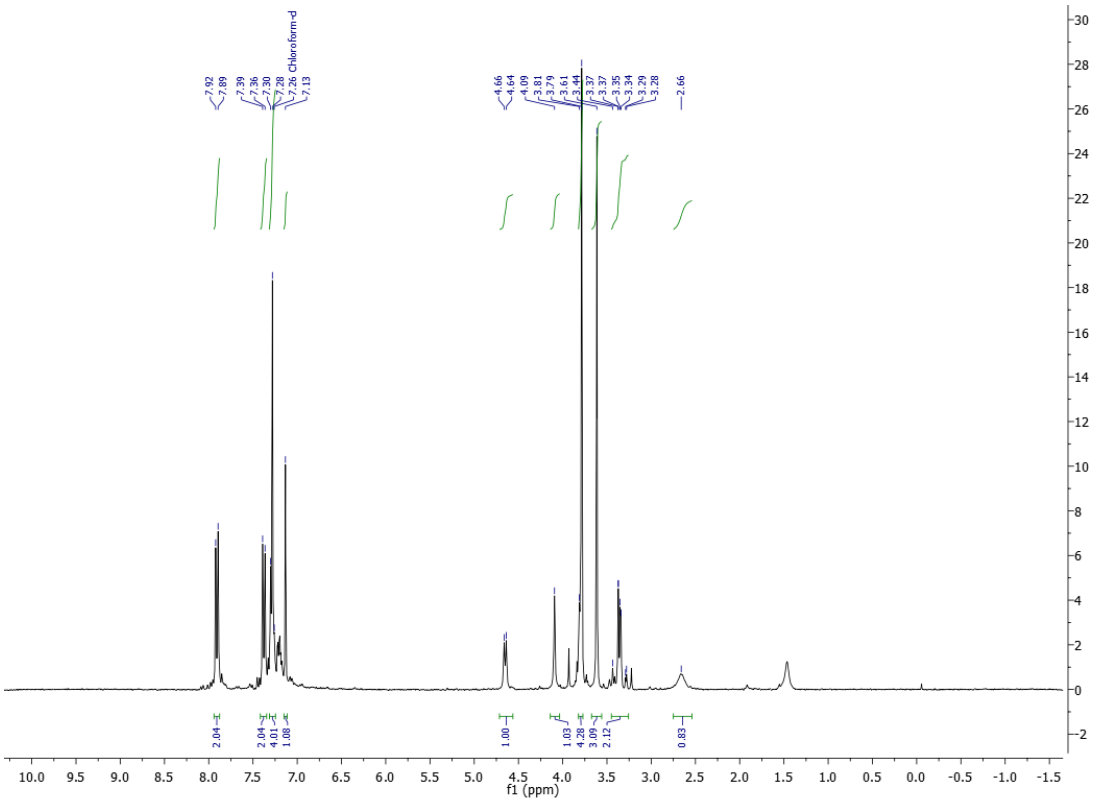
***endo*-3c**

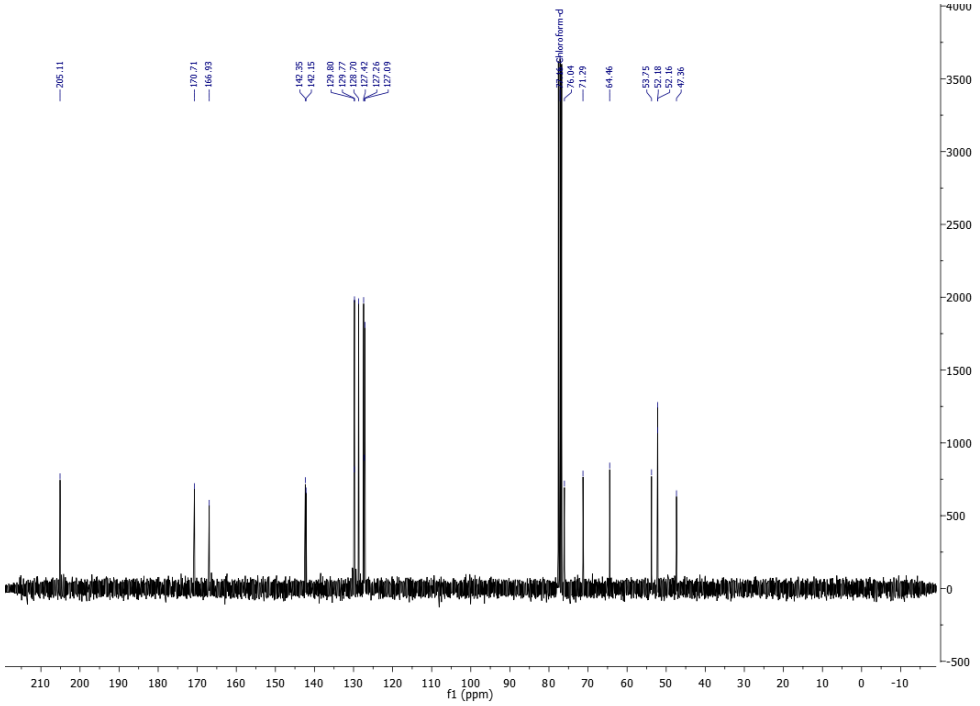

7.42
7.40
7.38
7.38
7.35
7.34
7.32
7.31
7.26 Chloroform-d
4.71
4.68
4.20
3.88
3.86
3.73
3.55
3.49
3.48
3.47
3.46
3.41
3.40
2.75
9.36
1.00
0.99
1.11
3.03
1.05
1.00
0.81
f1 (ppm)


205.74
170.92
159.42
142.37
128.98
128.70
128.36
127.46
127.19
113.89
71.37
64.71
55.36
53.54
52.12
47.63
f1 (ppm)

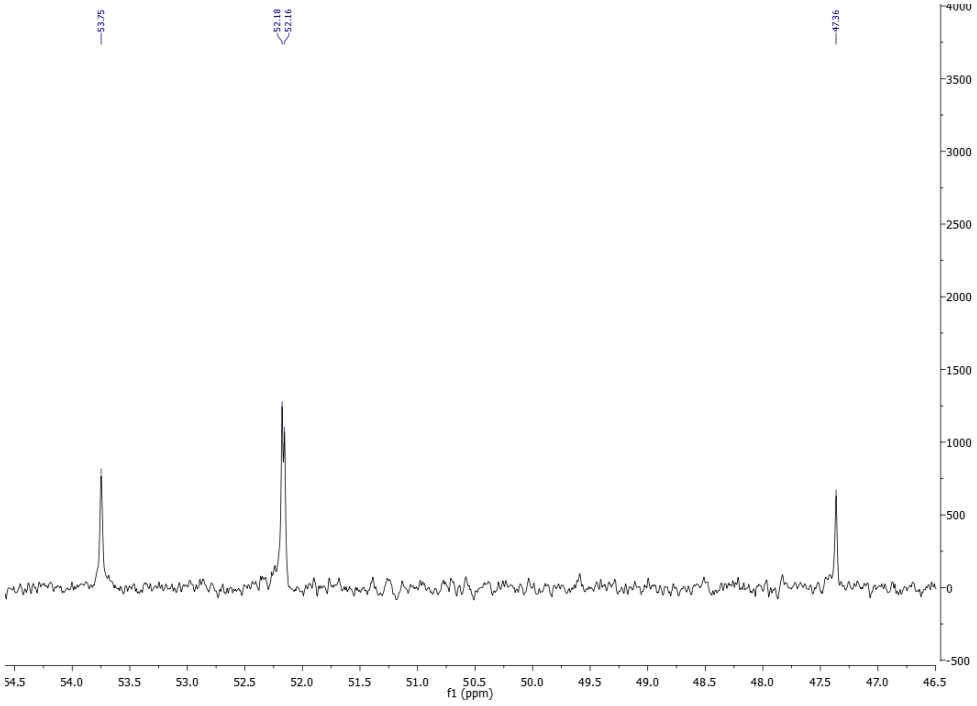

O
Ph
CO2Me
N
H
MeO2C

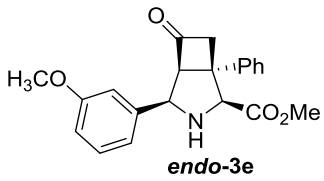
***endo*-3d**


7.92
7.89
7.39
7.36
7.30
7.28
Chloroform-d
7.26
7.13
4.66
4.64
4.09
3.81
3.79
3.61
3.44
3.37
3.35
3.34
3.29
3.28
2.66
2.04
2.04
4.01
1.08
1.00
1.03
4.28
3.09
2.12
0.83
f1 (ppm)

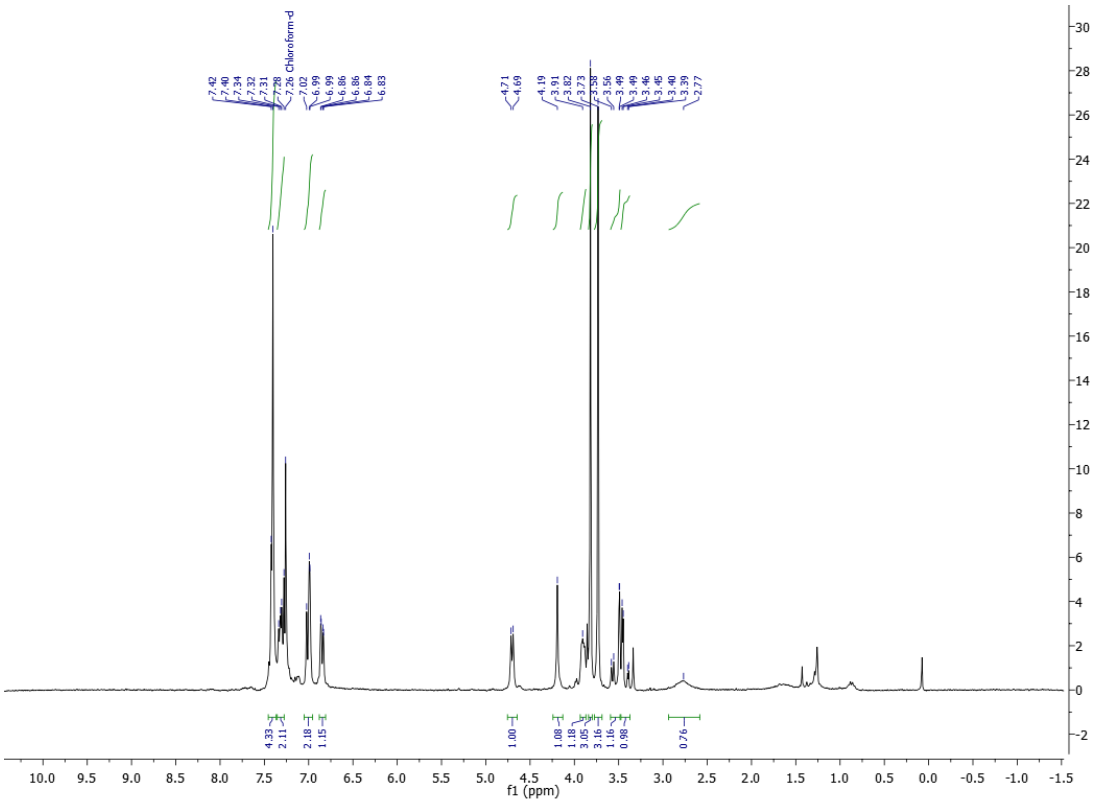

205.11
170.71
166.93
143.35
142.15
129.80
129.77
129.70
127.42
127.26
127.09
Chloroform-d
76.04
71.29
64.46
53.75
52.18
52.16
47.36
f1 (ppm)

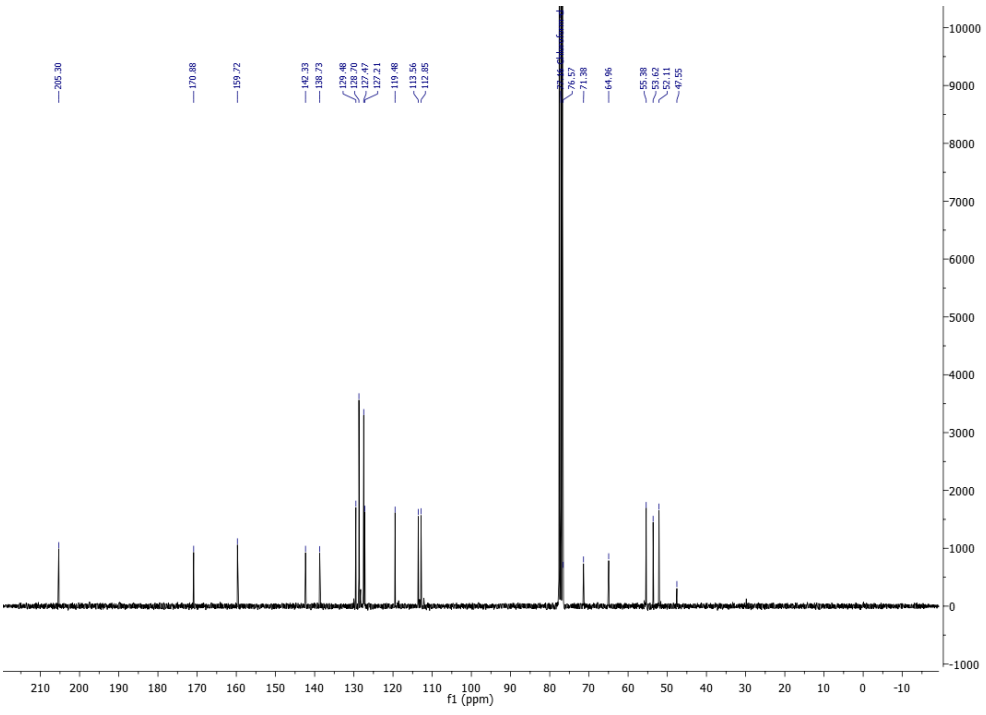
Scaling up in the region between 47.0-54.5 ppm:



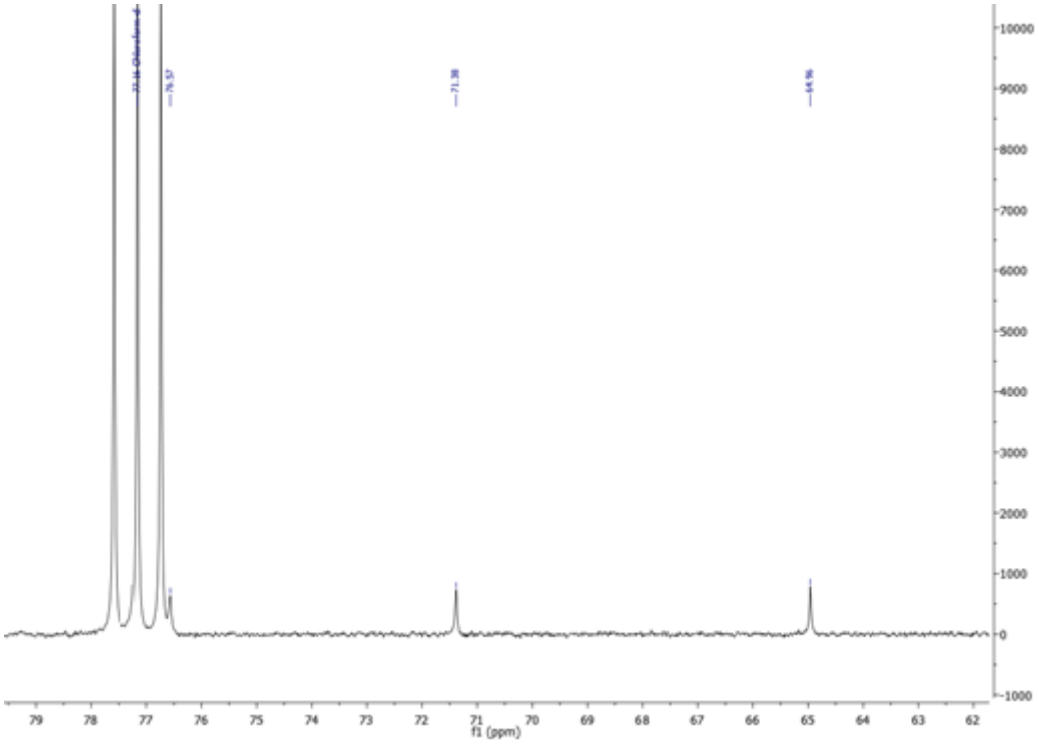

O
H3CO
Ph
CO2Me
N
H

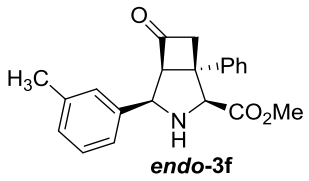
***endo*-3e**


Chloroform-d
f1 (ppm)

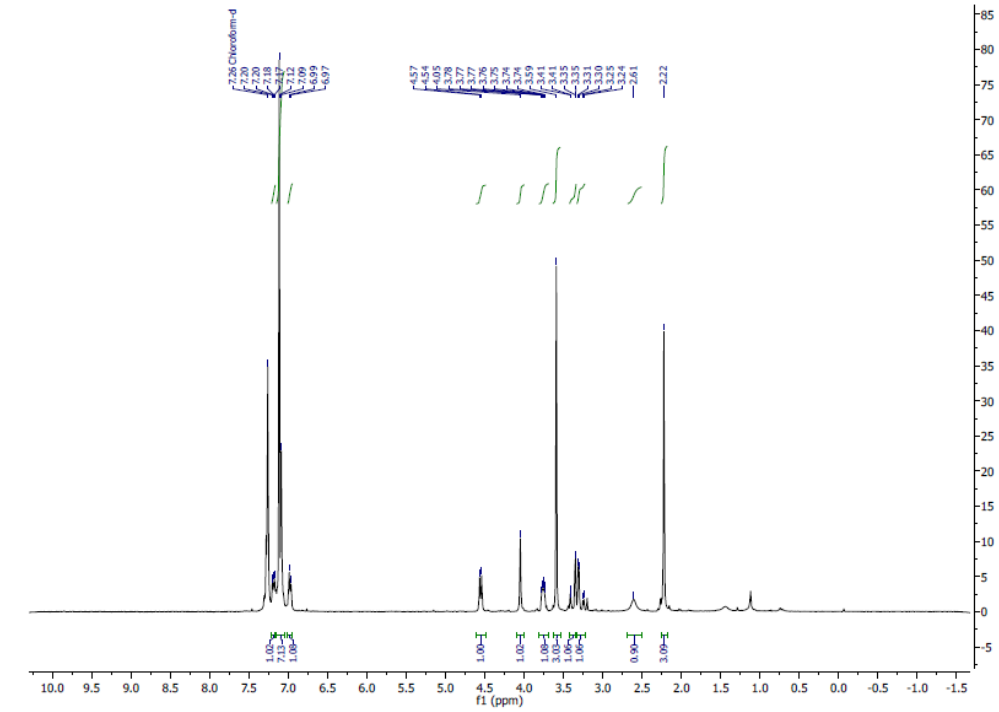

205.30
170.88
159.72
142.33
138.73
129.48
128.70
127.47
127.21
119.48
113.56
112.85
76.57
71.38
64.96
55.38
53.62
52.11
47.55
f1 (ppm)

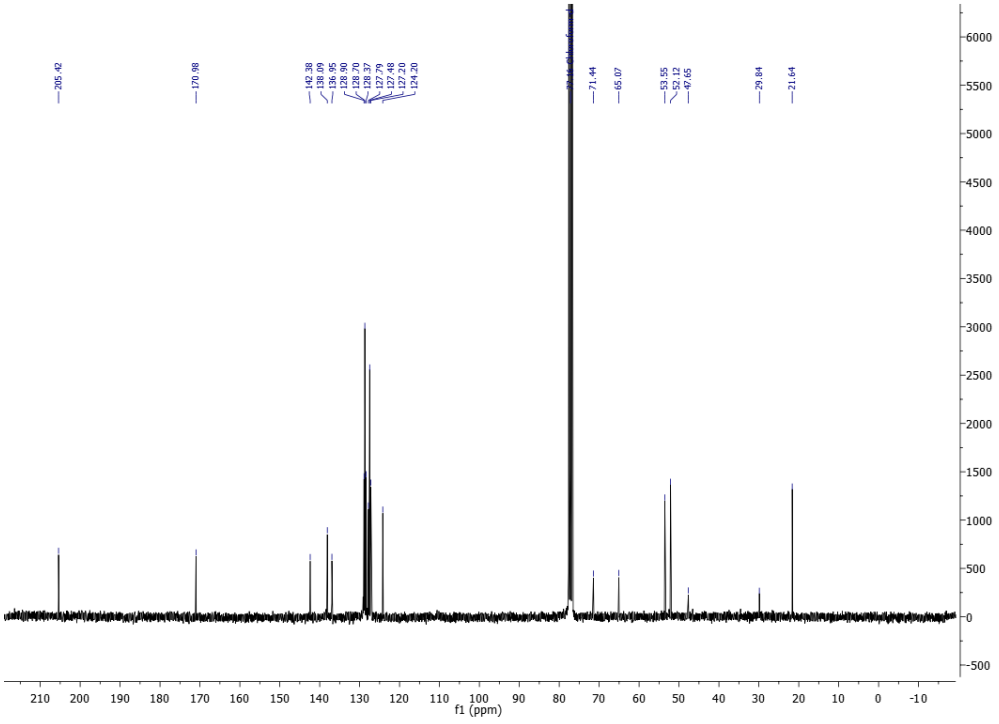
Scaling up in the region 62.0-79.0 ppm

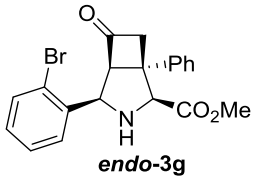




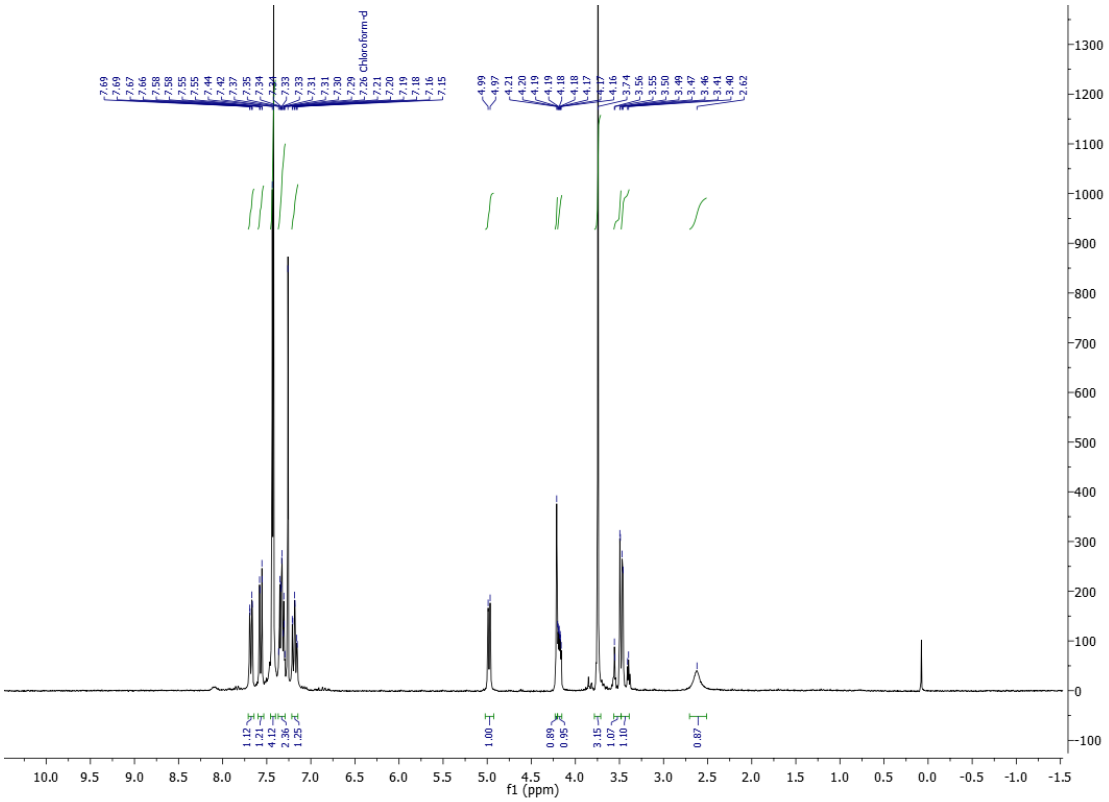
***endo*-3f**

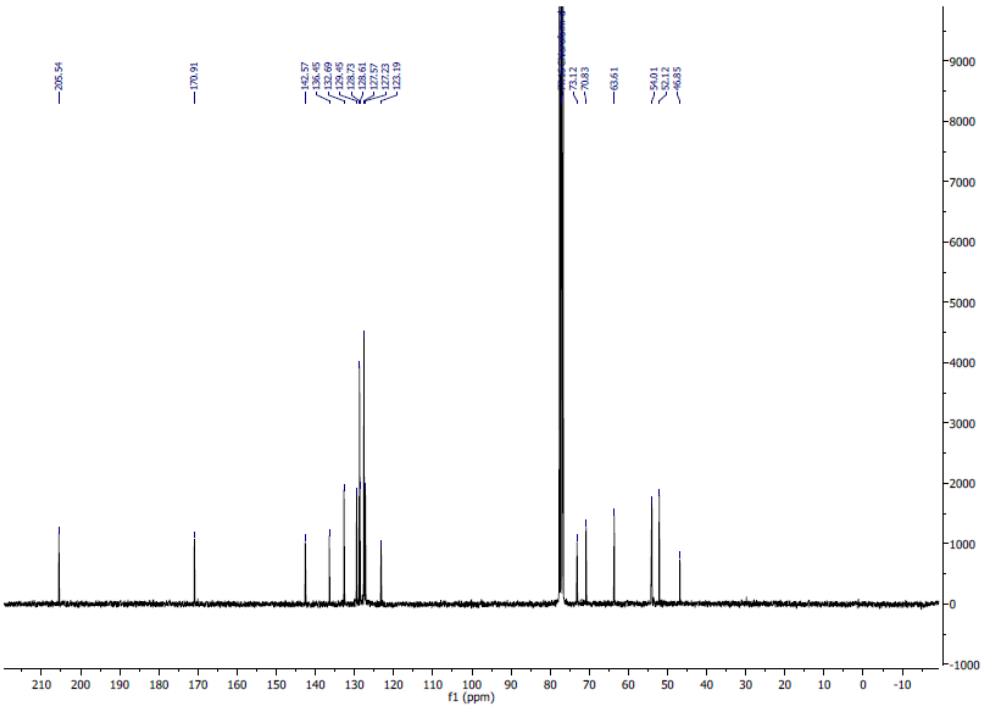


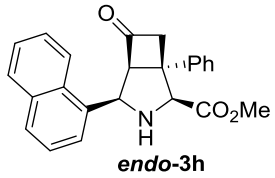



O
Br
Ph
CO2Me
N
H

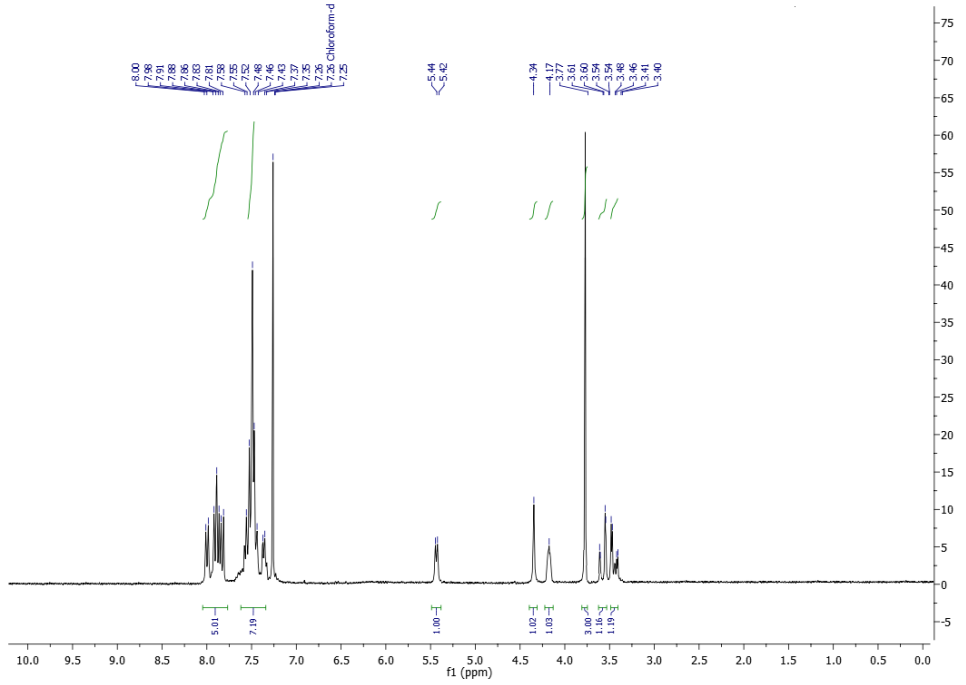
***endo*-3g**

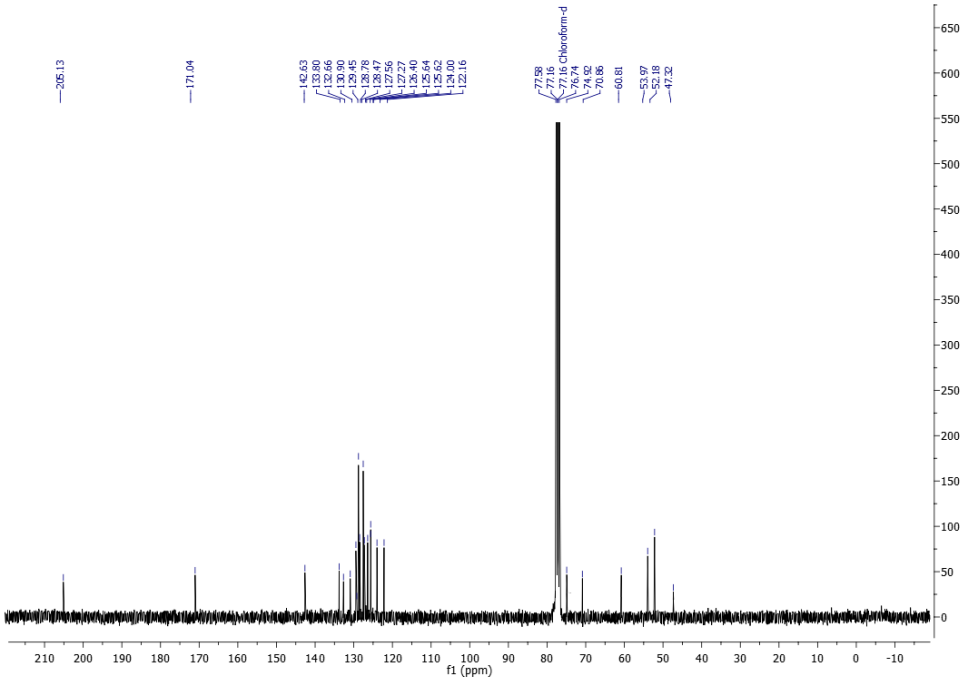

Chloroform-d
f1 (ppm)

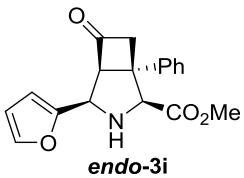

205.54
170.91
142.57
135.45
132.69
129.45
128.73
128.61
127.57
127.23
123.19
77.16
73.12
70.83
63.61
54.01
53.12
46.85
f1 (ppm)


O
Ph
CO2Me
N
H

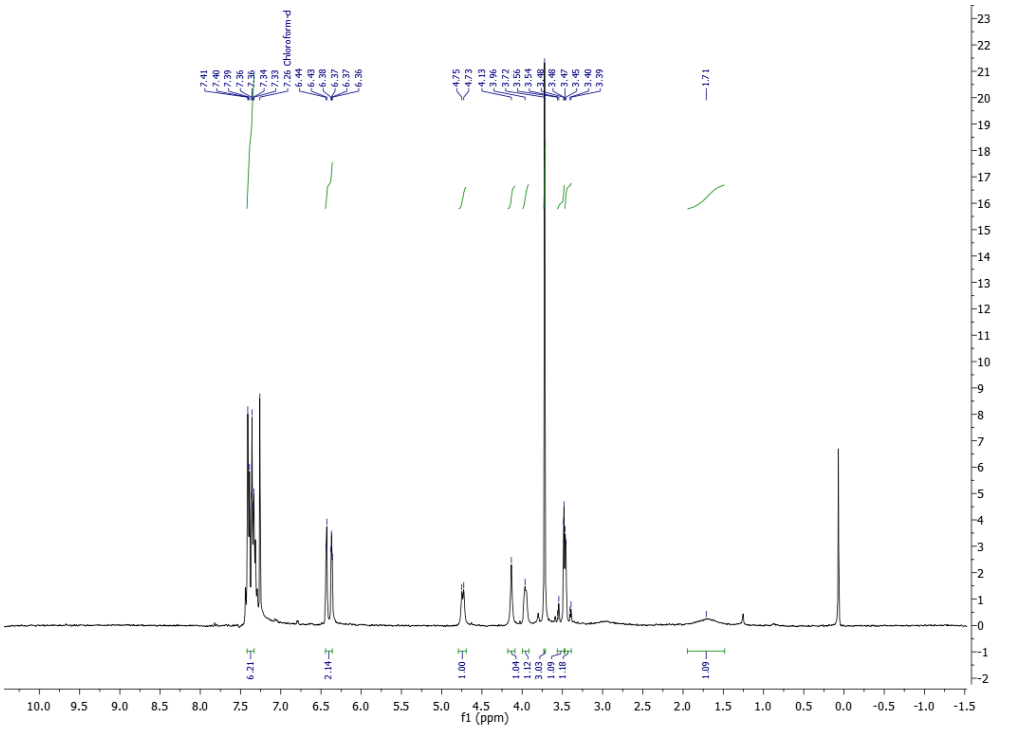
***endo*-3h**

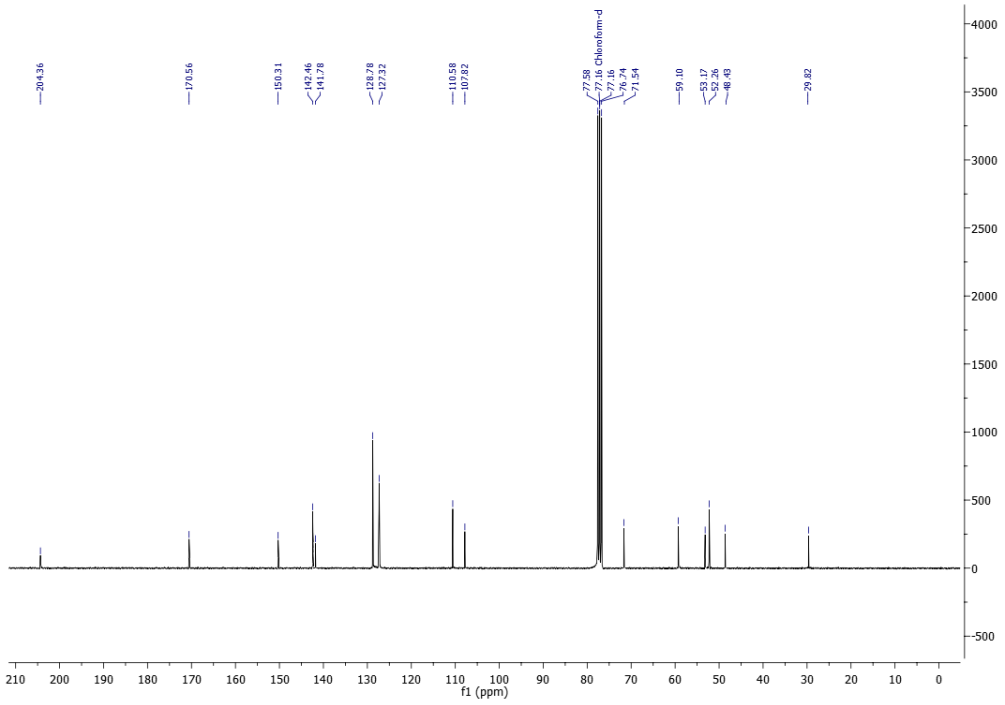

8.00
7.98
7.91
7.88
7.86
7.83
7.81
7.58
7.55
7.52
7.48
7.46
7.43
7.37
7.35
7.26
7.25
Chloroform-d
5.44
5.42
4.34
4.17
3.77
3.61
3.60
3.54
3.48
3.46
3.41
3.40
5.01
7.19
1.00
1.02
1.03
3.60
1.16
1.19
f1 (ppm)

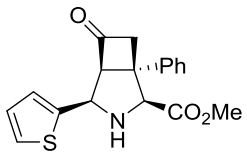

205.13
171.04
142.63
138.60
132.66
130.90
129.45
128.78
128.47
127.56
127.27
126.40
125.62
124.00
122.16
77.58
77.16
77.16
Chloroform-d
76.74
74.92
70.86
60.81
53.97
52.18
47.32
f1 (ppm)


O
Ph
CO2Me
N
H
O

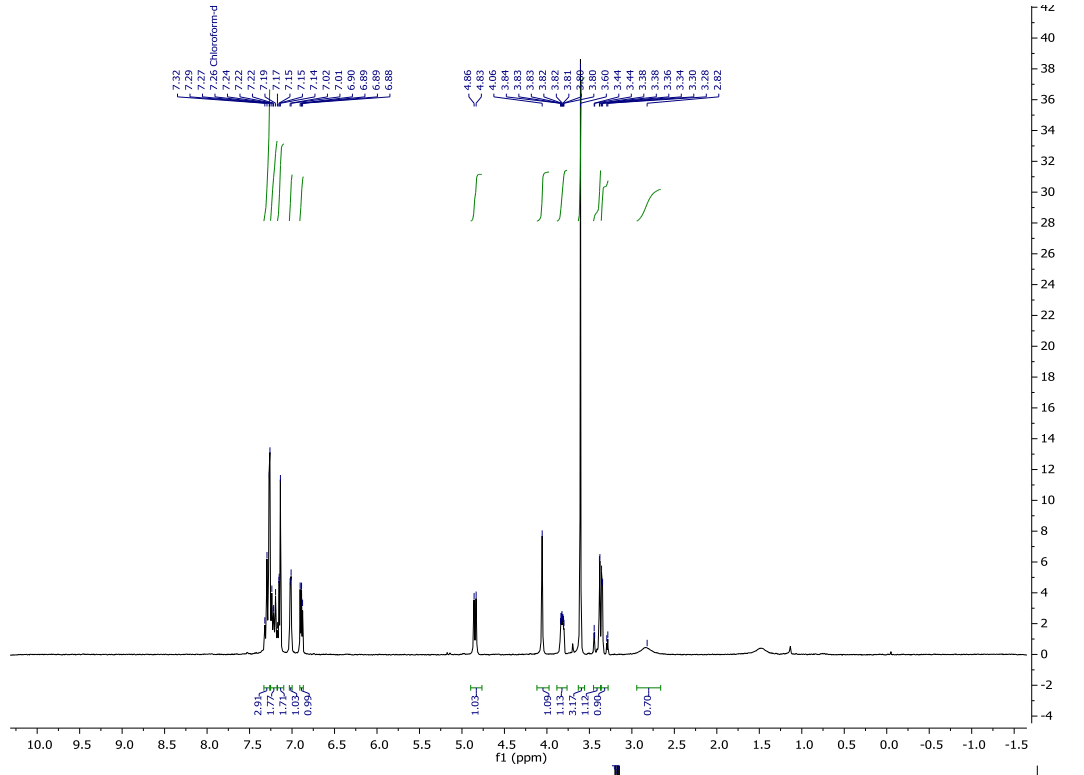
***endo*-3i**

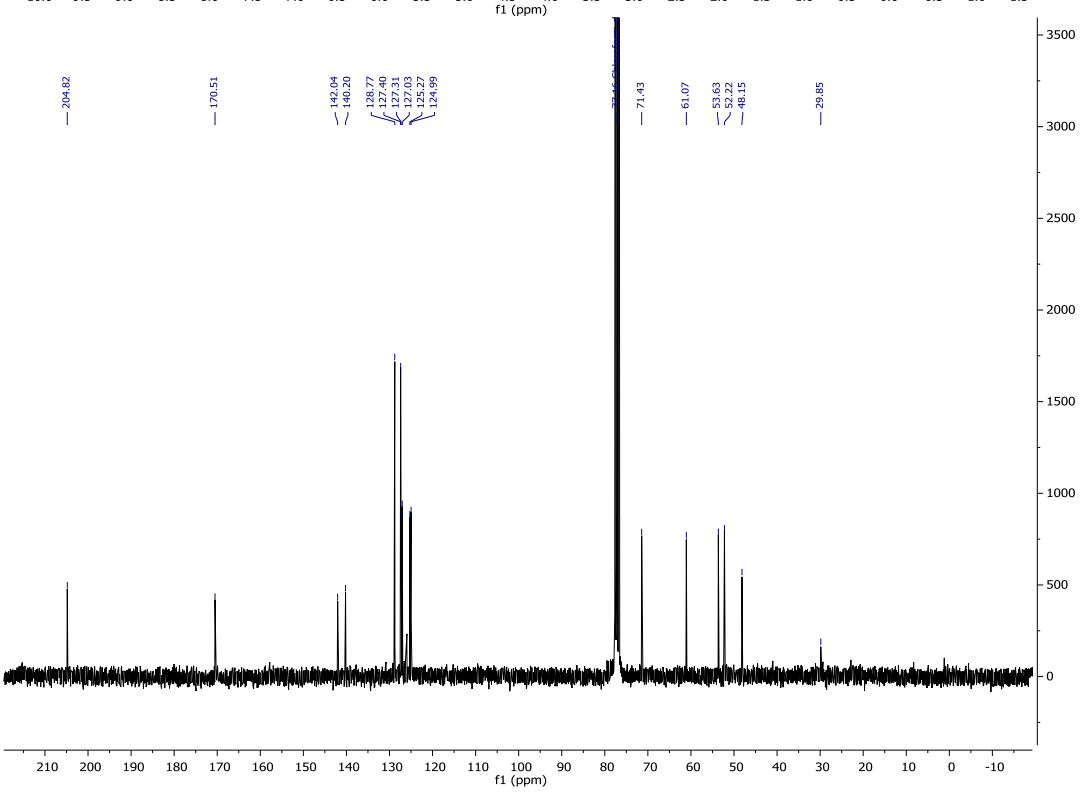

7.41
7.40
7.39
7.36
7.36
7.34
7.33
7.26 Chloroform-d
6.43
6.38
6.37
6.37
6.36
4.75
4.73
4.13
3.96
3.72
3.56
3.54
3.48
3.47
3.45
3.40
3.39
1.71
6.21
2.14
1.00
1.04
1.12
3.03
1.00
1.18
1.09
f1 (ppm)

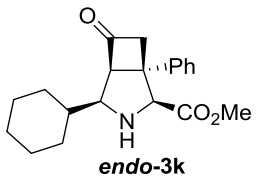

204.36
170.56
150.31
142.46
141.78
128.78
127.32
110.58
107.82
77.58
77.16 Chloroform-d
76.74
71.54
59.10
53.17
52.26
48.43
29.82
f1 (ppm)


O
Ph
CO2Me
N
H
S

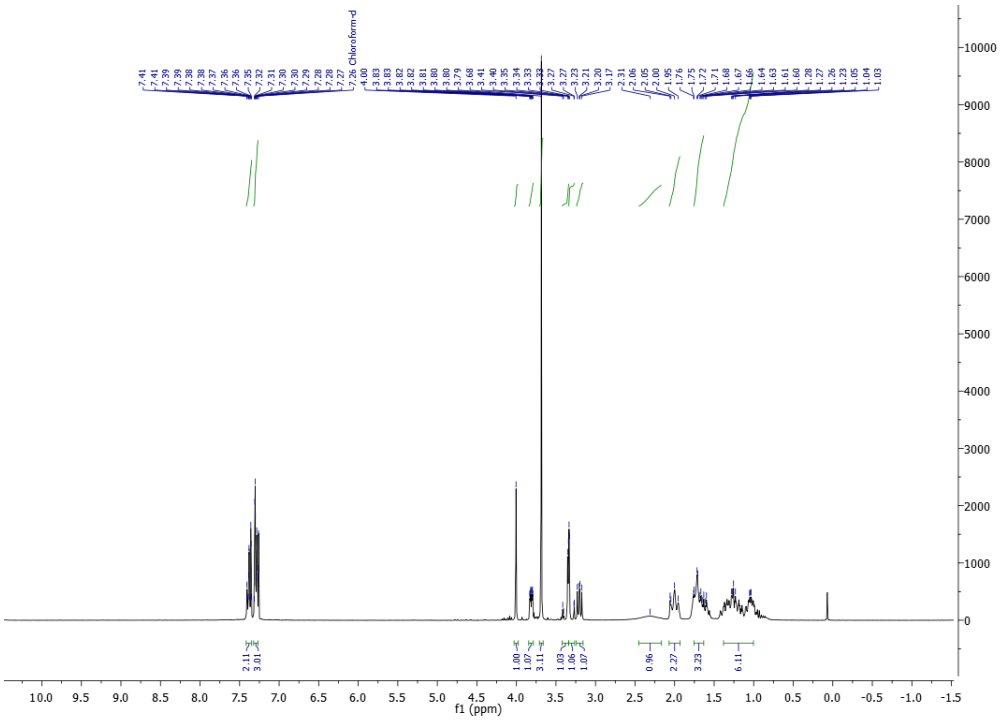
***endo*-3j**

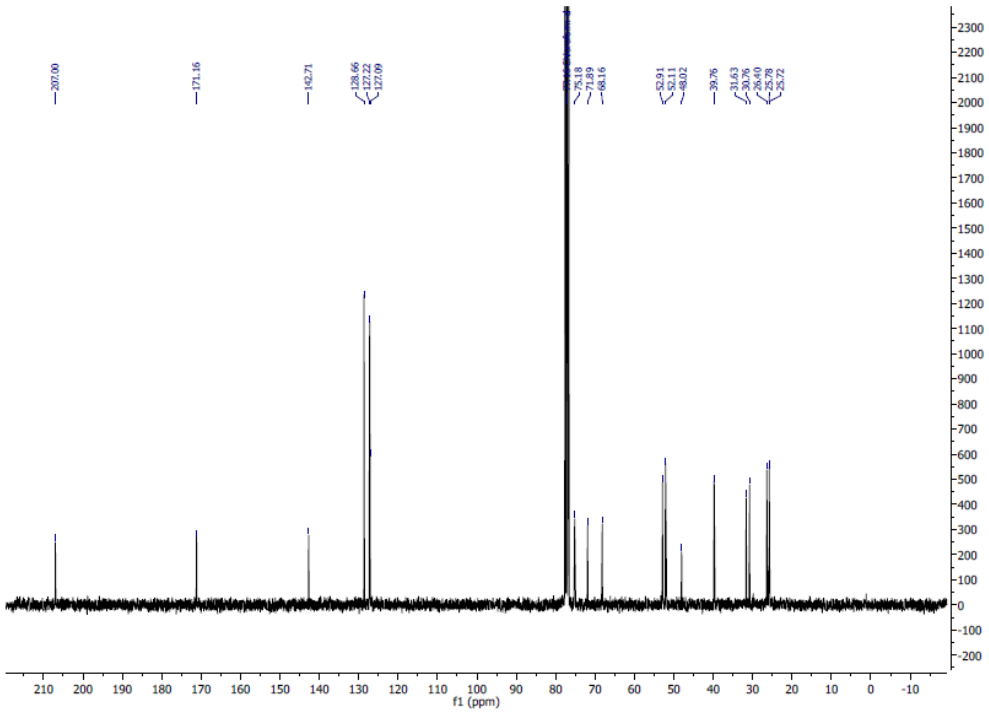

7.32
7.29
7.27
7.26 Chloroform-d
7.24
7.22
7.22
7.19
7.17
7.15
7.15
7.14
7.02
7.01
6.90
6.89
6.89
6.88
4.86
4.83
4.06
3.84
3.83
3.83
3.82
3.81
3.80
3.80
3.60
3.44
3.44
3.38
3.38
3.36
3.34
3.30
3.28
2.82
2.91
1.77
1.71
1.03
0.99
1.03
1.09
1.13
1.12
1.12
0.90
0.70
f1 (ppm)

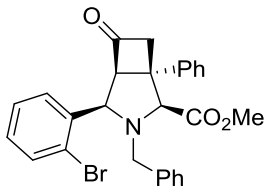

204.82
170.51
142.04
140.20
128.77
127.40
127.31
127.03
125.27
124.99
77.46
71.43
61.07
53.63
52.22
48.15
29.85
f1 (ppm)

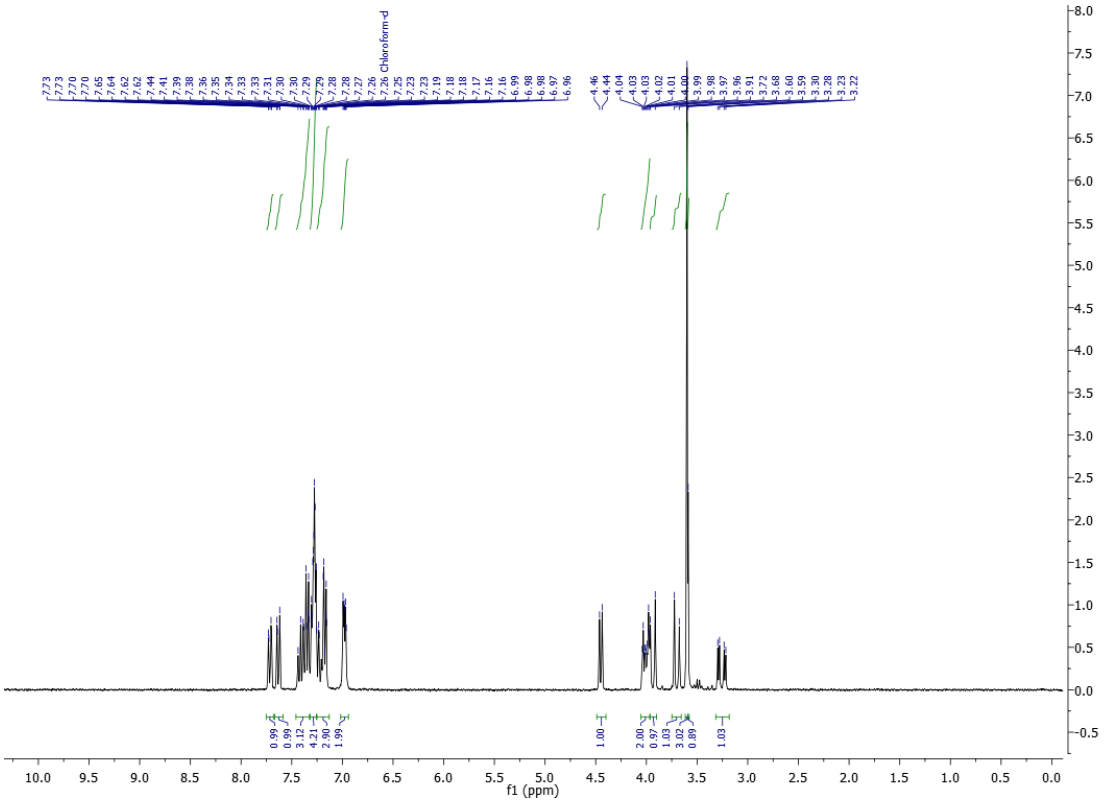


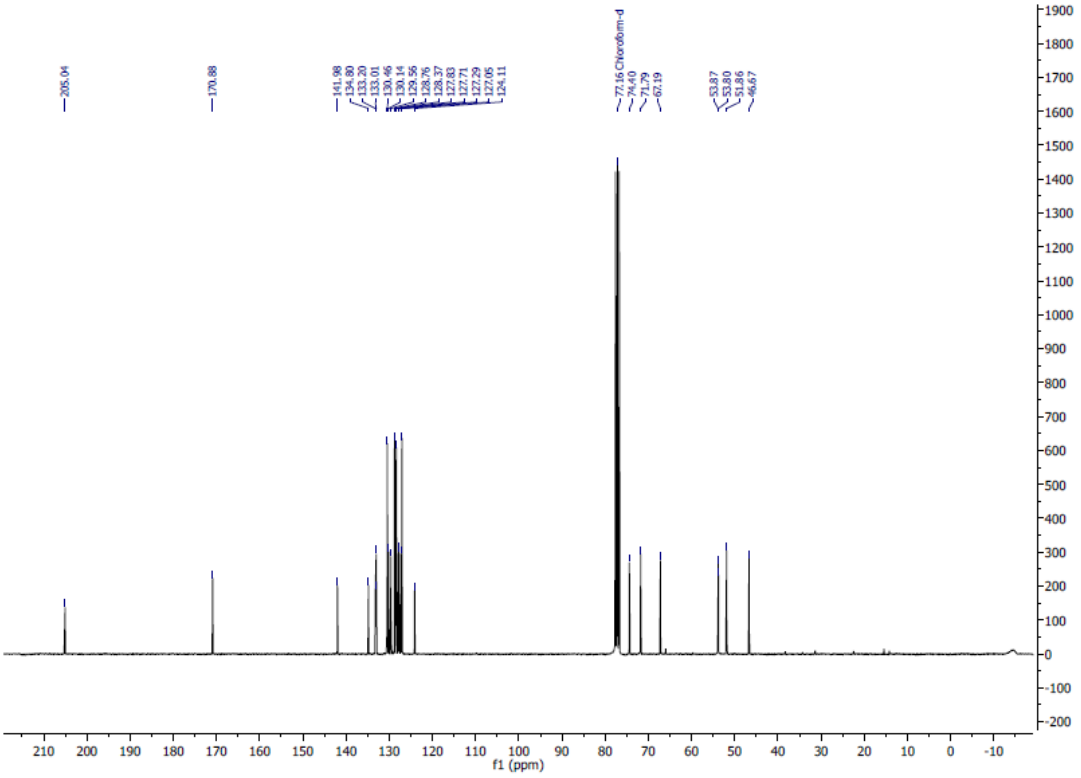
***endo*-3k**

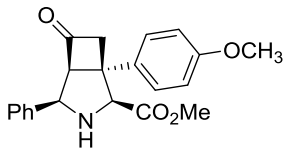




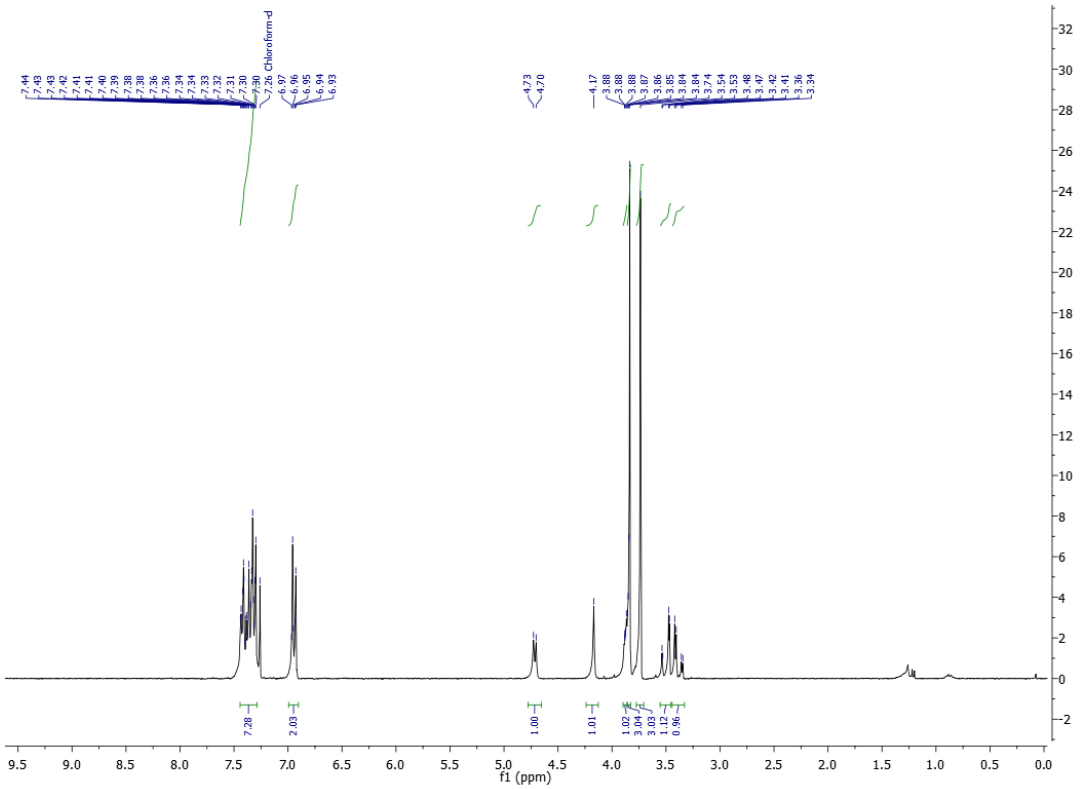

O
Ph
CO2Me
N
Br
Ph

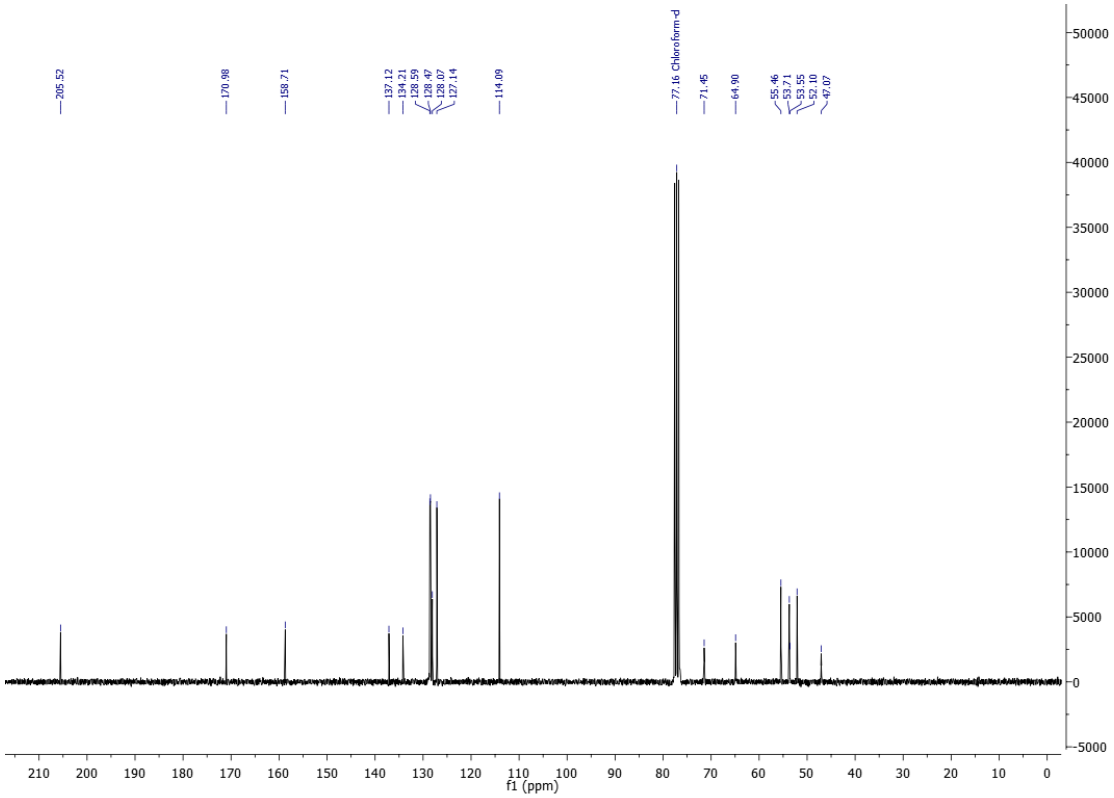

Chloroform-d
f1 (ppm)

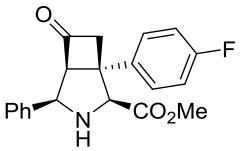

Chloroform-d
f1 (ppm)


O
OCH3
Ph
N
H
CO2Me

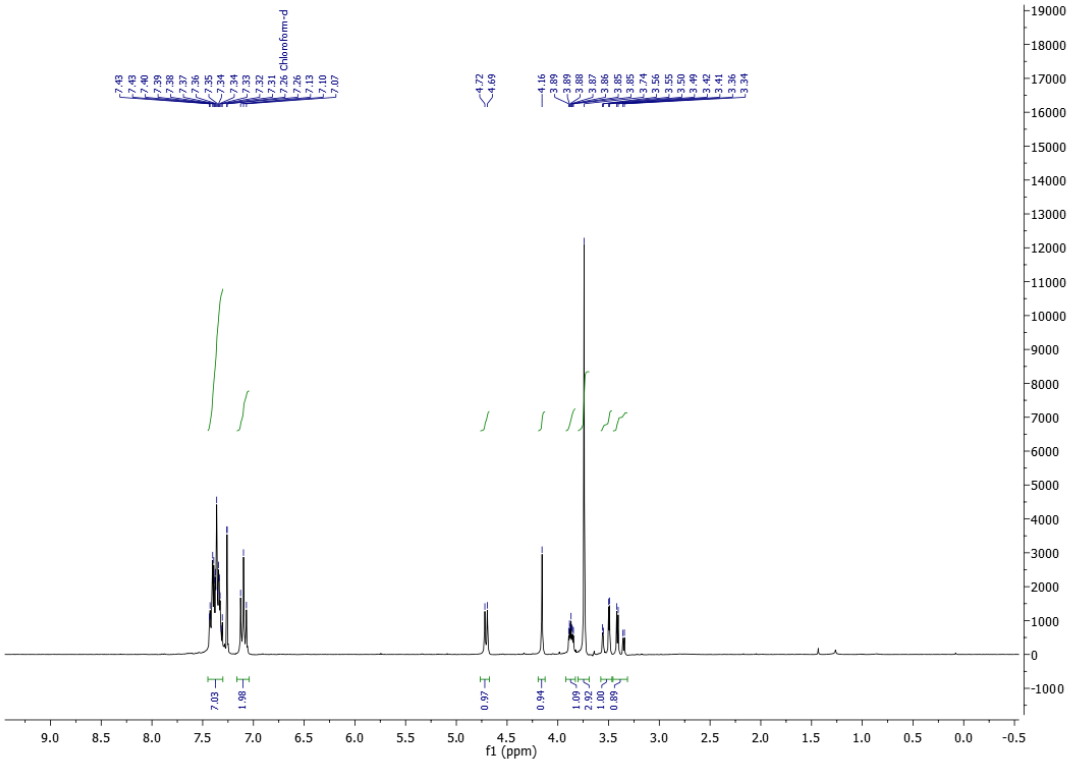
***endo*-3l**

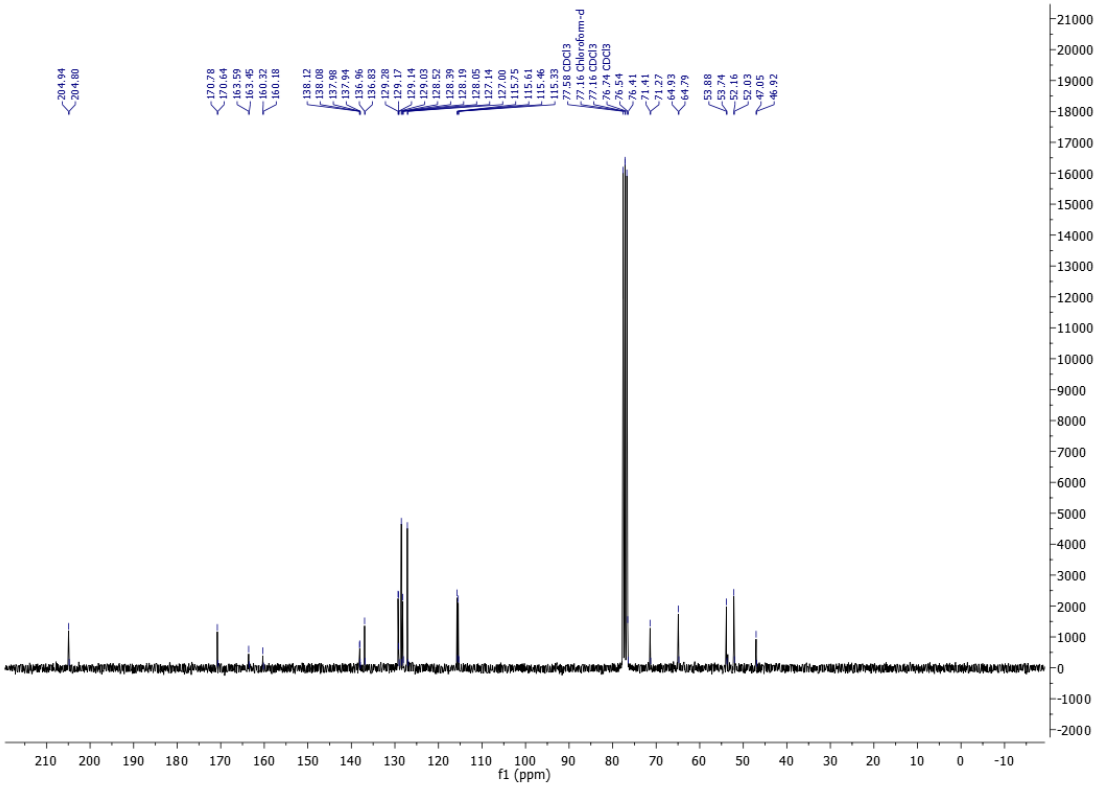

7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.36
7.36
7.34
7.34
7.33
7.32
7.31
7.30
7.30
7.26 Chloroform-d
6.97
6.96
6.95
6.94
6.93
4.73
4.70
4.17
3.88
3.88
3.88
3.87
3.86
3.85
3.84
3.84
3.74
3.54
3.53
3.48
3.47
3.42
3.41
3.36
3.34
7.28
2.03
1.00
1.01
1.02
3.04
3.03
1.12
0.96
f1 (ppm)


205.52
170.98
158.71
137.12
134.21
128.59
128.47
128.07
127.14
114.09
77.16 Chloroform-d
71.45
64.90
55.46
53.71
53.55
53.10
47.07
f1 (ppm)

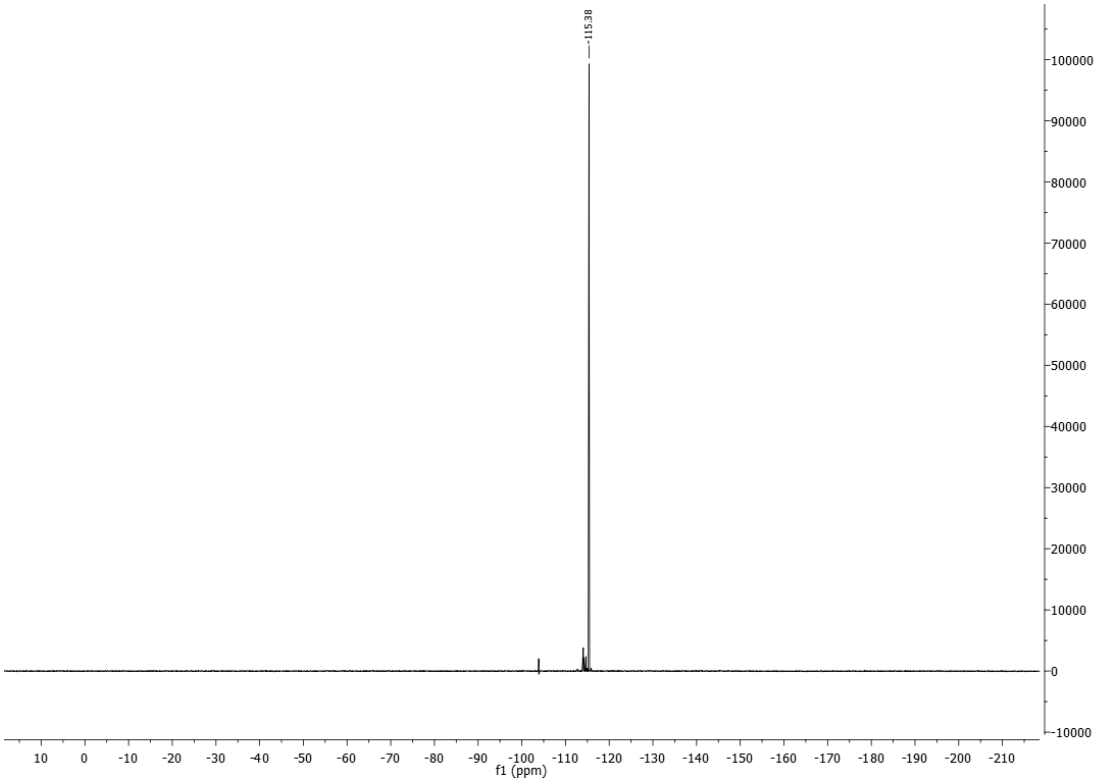


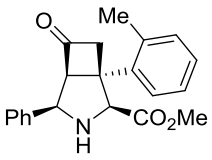
***endo*-3m**



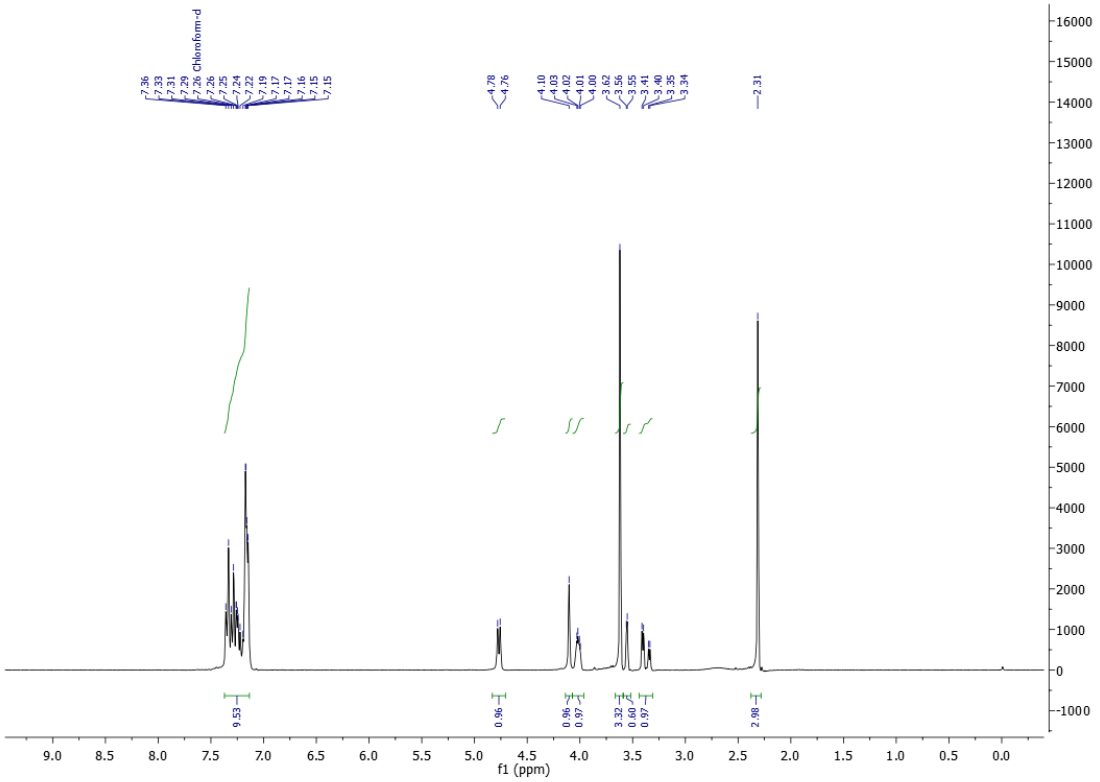


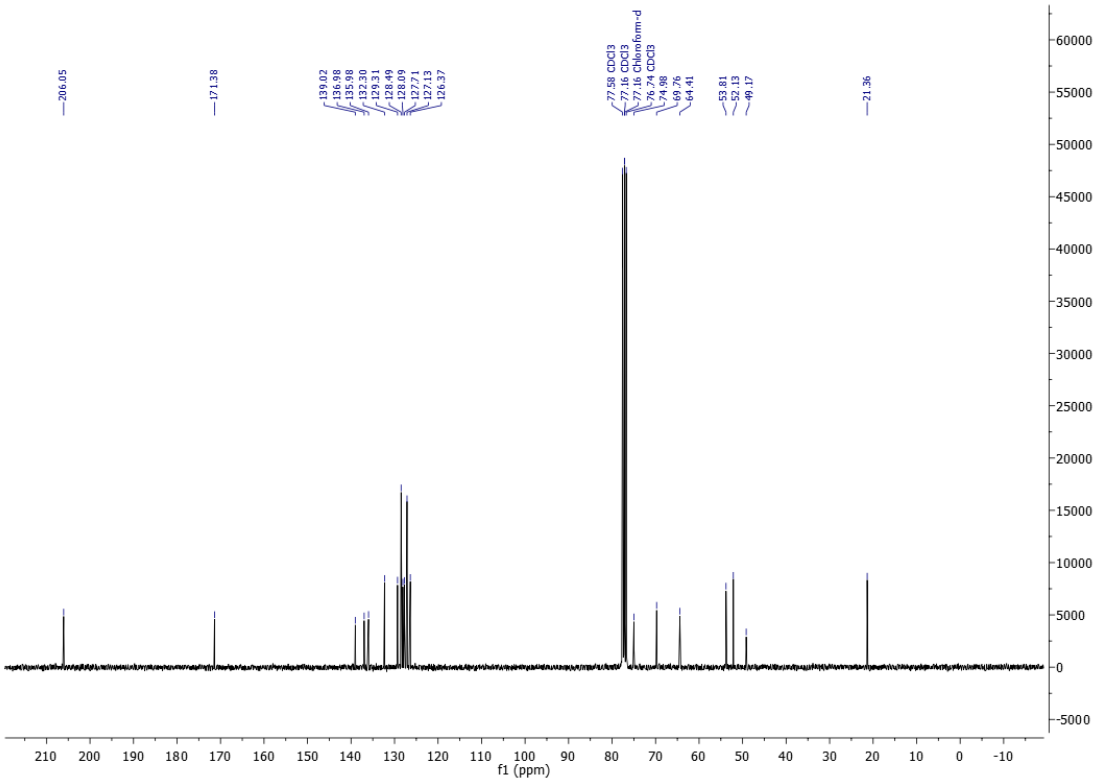
^{19}F-NMR spectrum:

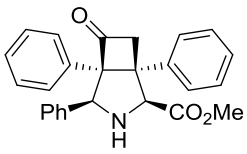



O
Me
Ph
N
H
CO2Me

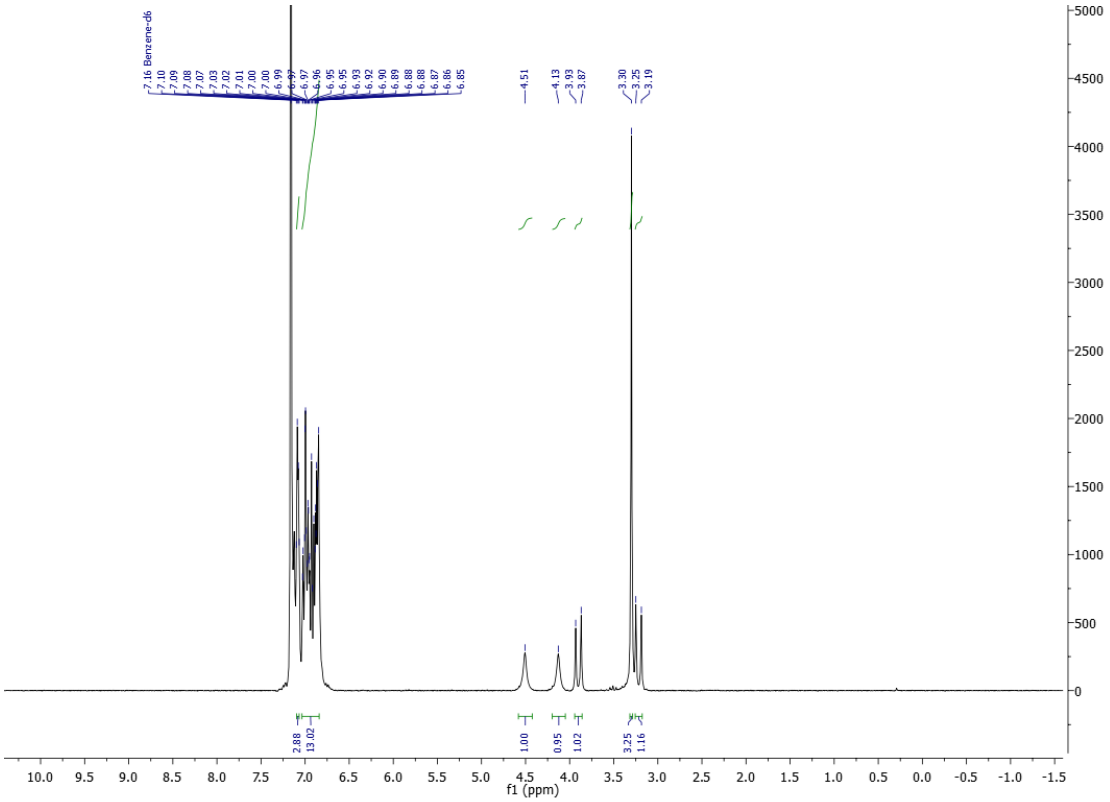
***endo*-3n**

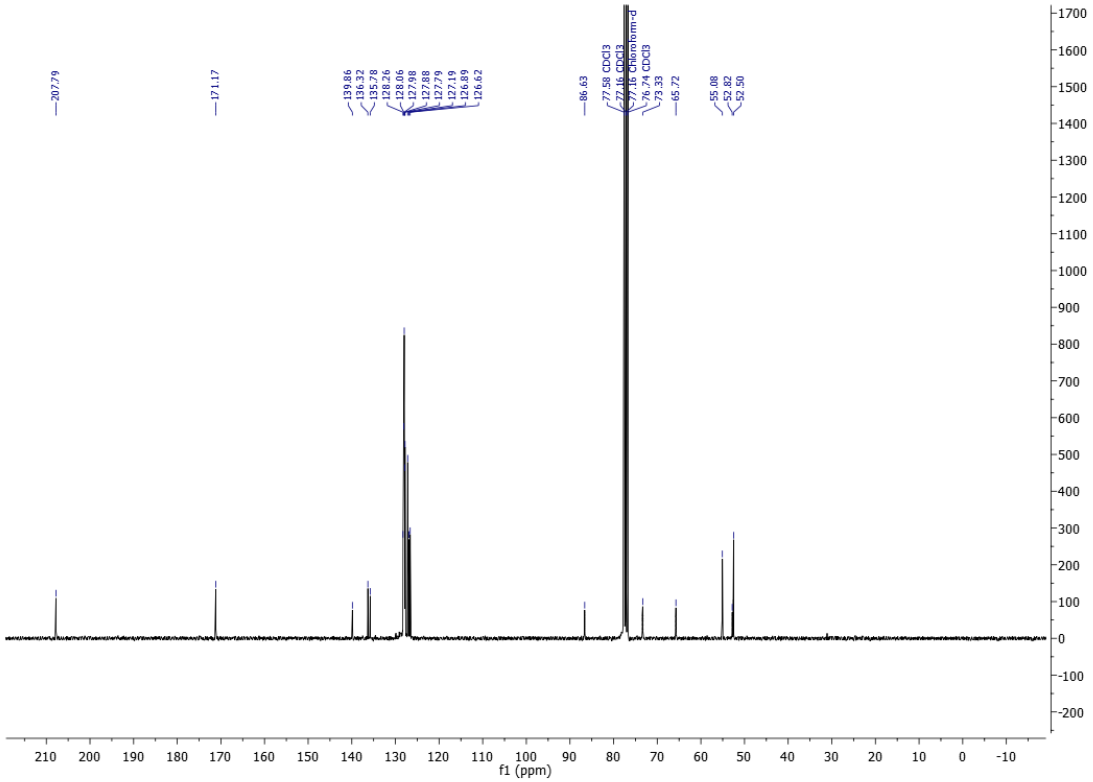

7.36
7.33
7.31
7.29
7.26 Chloroform-d
7.26
7.25
7.24
7.22
7.19
7.17
7.17
7.16
7.15
7.15
4.78
4.76
4.10
4.03
4.02
4.01
4.00
3.62
3.56
3.55
3.41
3.40
3.35
3.34
2.31
9.53
0.96
0.96
0.97
3.32
0.60
0.97
2.98
f1 (ppm)

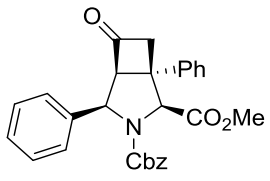

206.05
171.38
139.02
136.98
135.98
132.30
129.31
128.49
128.09
127.71
127.13
126.37
77.58 CDCl3
77.16 CDCl3
77.16 Chloroform-d
76.74 CDCl3
69.88
69.76
64.41
53.81
52.13
49.17
21.36
f1 (ppm)


O
Ph
N
H
CO2Me

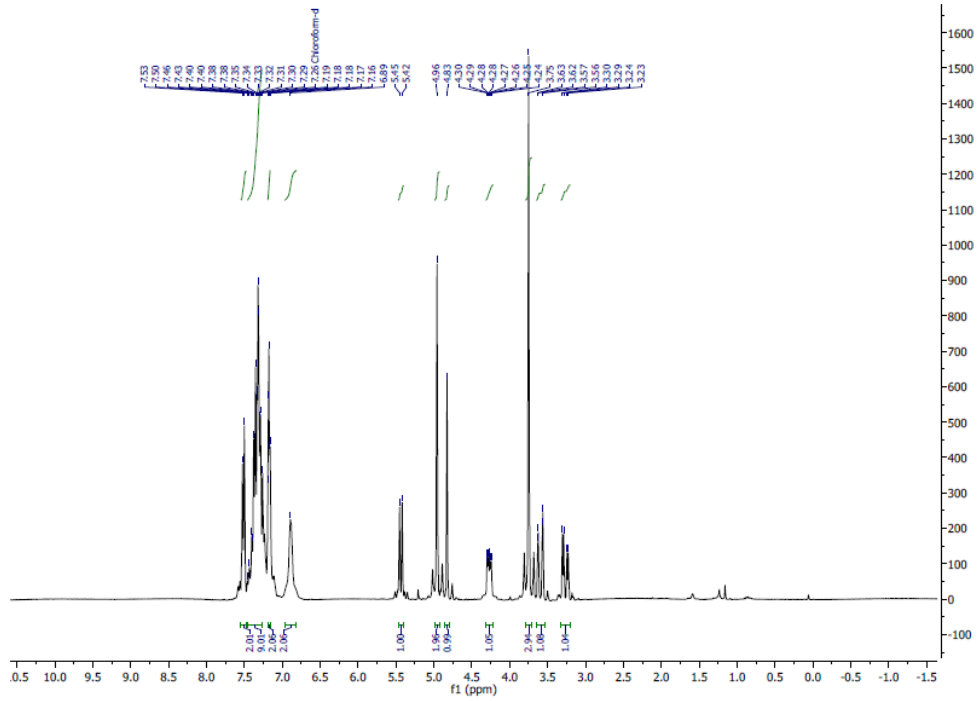
***endo*-3o**

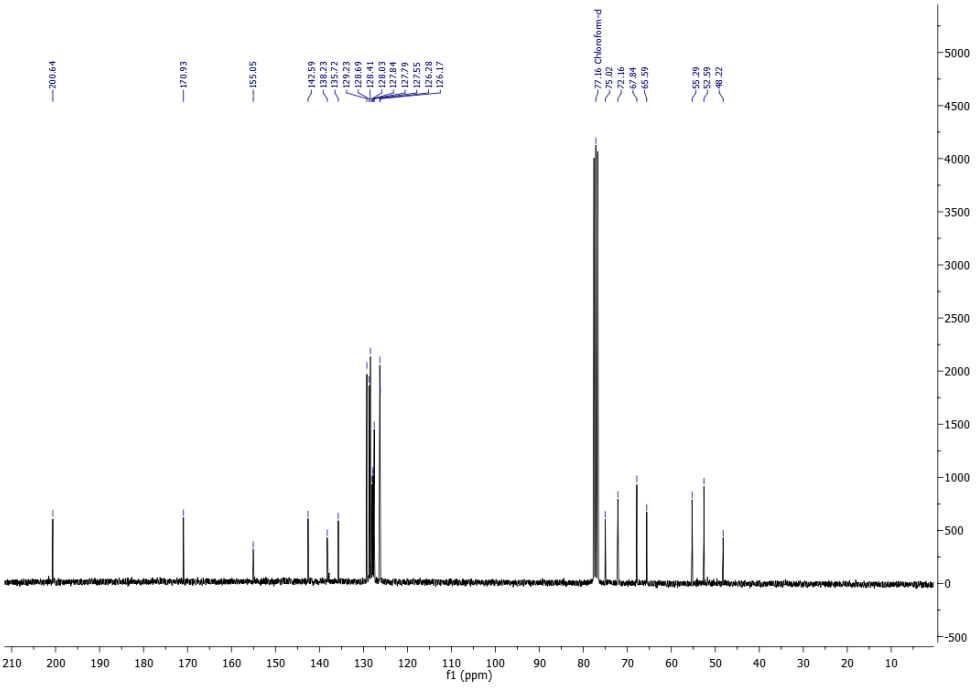

7.16 Benzene-d6
7.10
7.09
7.08
7.07
7.03
7.02
7.01
7.00
6.99
6.97
6.96
6.95
6.93
6.92
6.90
6.89
6.88
6.87
6.86
6.85
4.51
4.13
3.93
3.87
3.30
3.25
3.19
2.88
13.02
1.00
0.95
1.02
3.25
1.16
f1 (ppm)

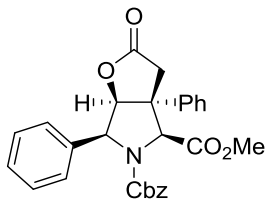

207.79
171.17
139.86
136.32
135.28
128.26
128.06
127.98
127.88
127.79
127.19
126.89
126.62
86.63
77.58 CDCl3
77.16 CDCl3
77.16 Chloroform-d
76.74 CDCl3
73.33
65.72
55.08
52.82
52.50
f1 (ppm)



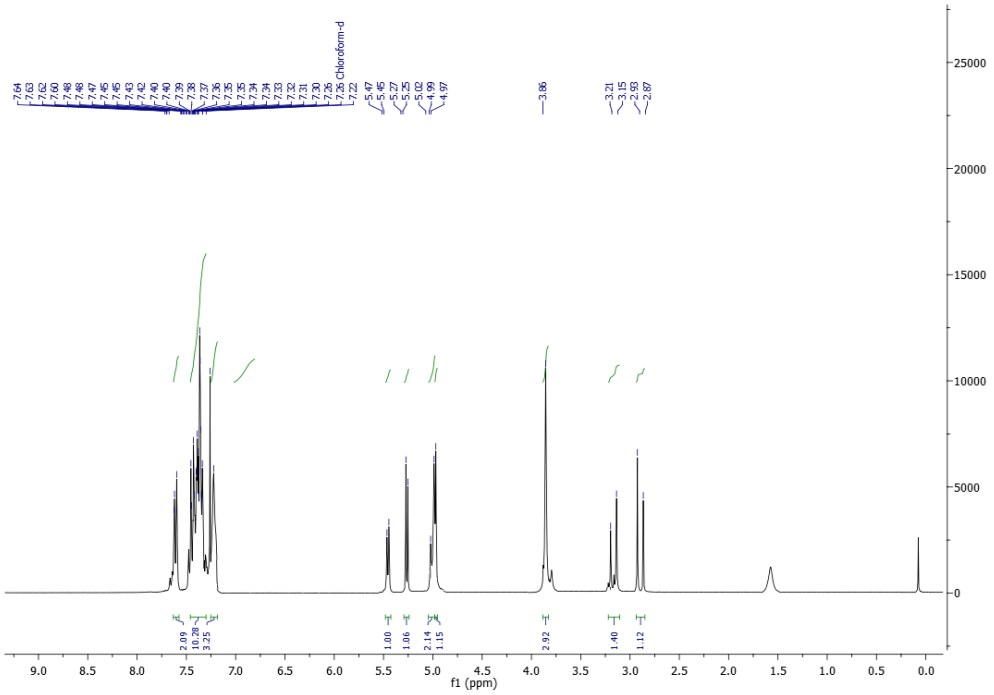
7

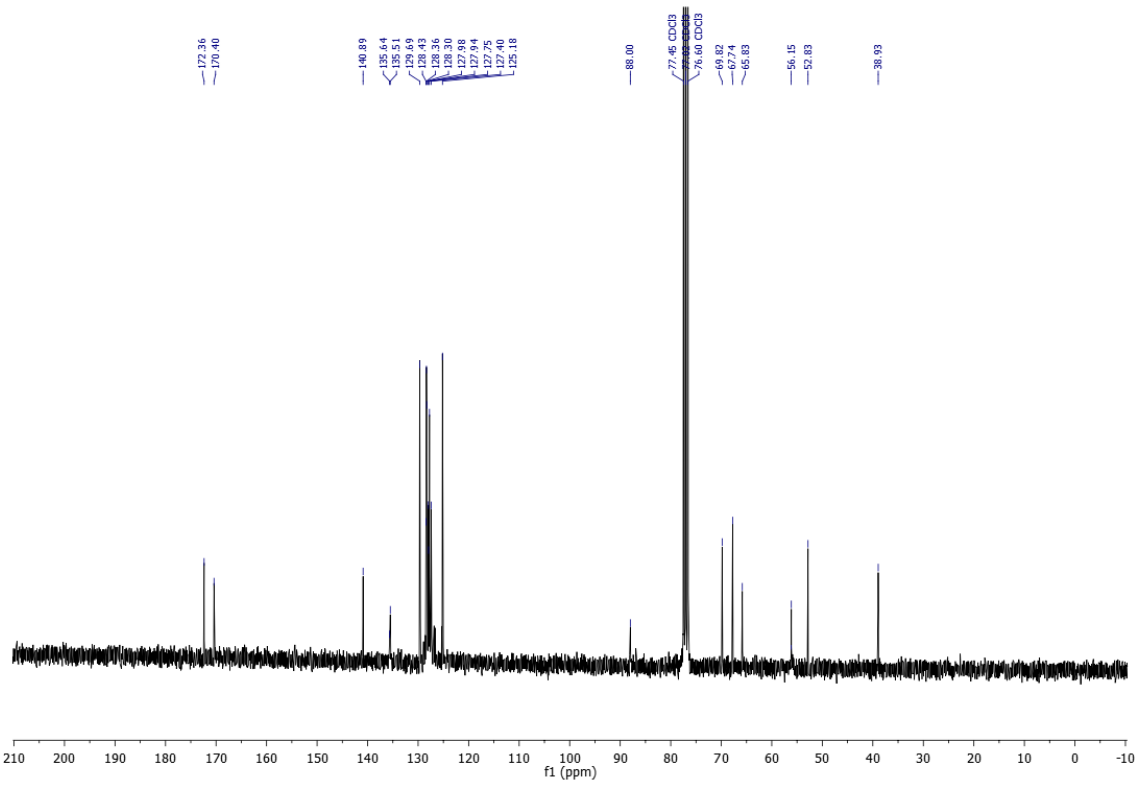


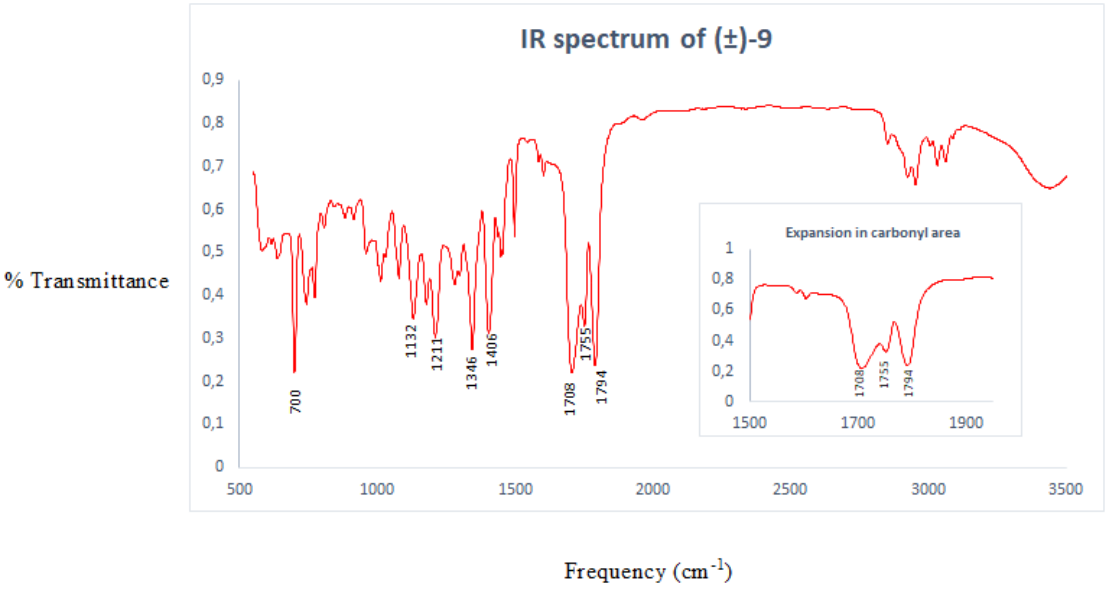


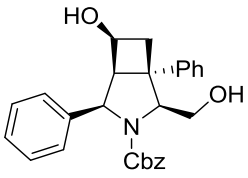

O
O
H
Ph
CO2Me
N
Cbz

8

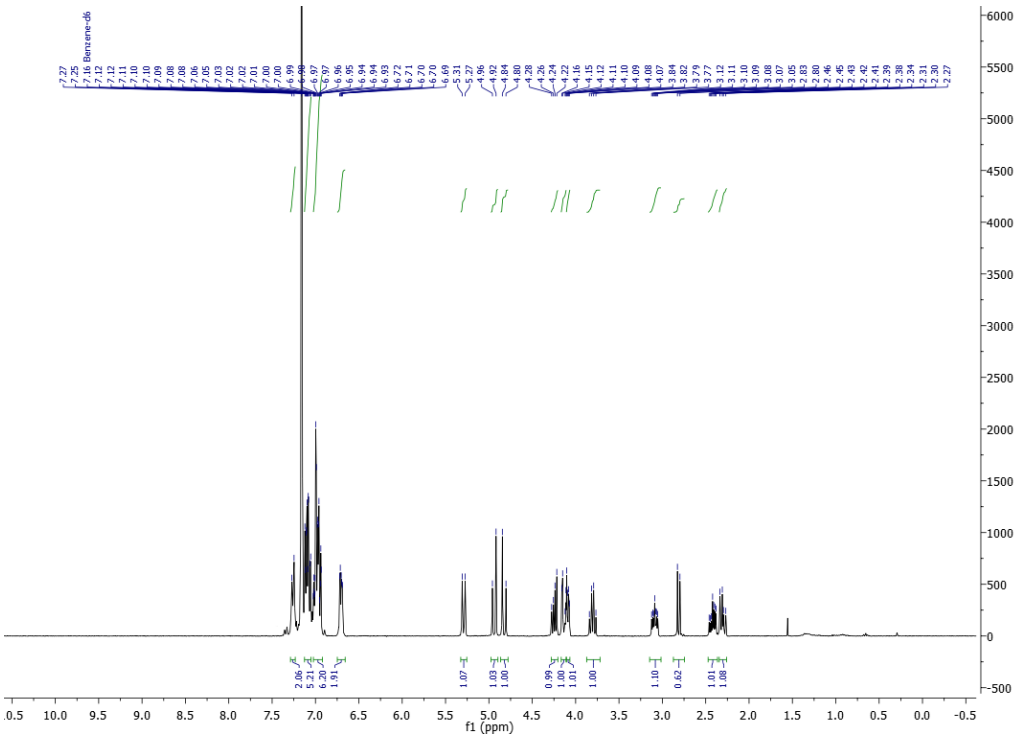

7.64
7.63
7.62
7.60
7.48
7.47
7.45
7.45
7.43
7.42
7.40
7.40
7.39
7.38
7.37
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.31
7.30
7.26
7.26 Chloroform-d
7.22
5.47
5.45
5.27
5.25
5.02
4.99
4.97
3.86
3.21
3.15
2.93
2.87
2.09
1.28
3.25
1.00
1.06
2.14
1.15
2.92
1.40
1.12
25000
20000
15000
10000
5000
0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

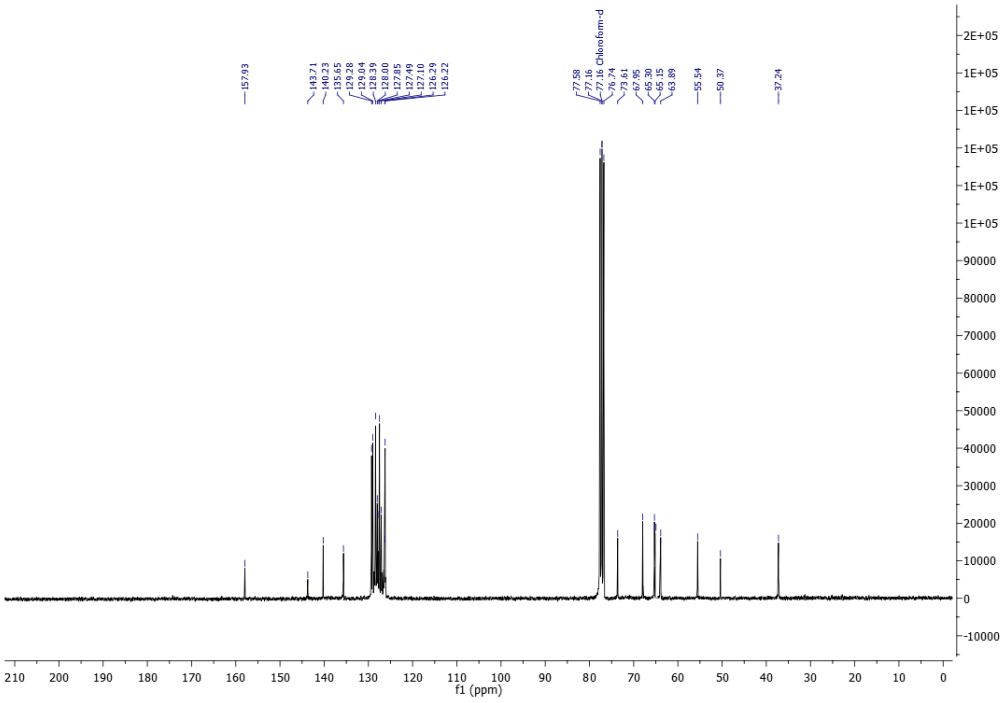

172.36
170.40
140.89
135.64
135.51
129.69
128.43
128.36
128.30
128.08
127.94
127.75
127.40
125.18
88.00
77.45 CDCl3
77.20 CDCl3
76.60 CDCl3
69.82
67.74
65.83
56.15
52.83
38.93
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


IR spectrum of (±)-9
% Transmittance
Frequency (cm-1)
700
1132
1211
1346
1406
1708
1755
1794
Expansion in carbonyl area
1708
1755
1794

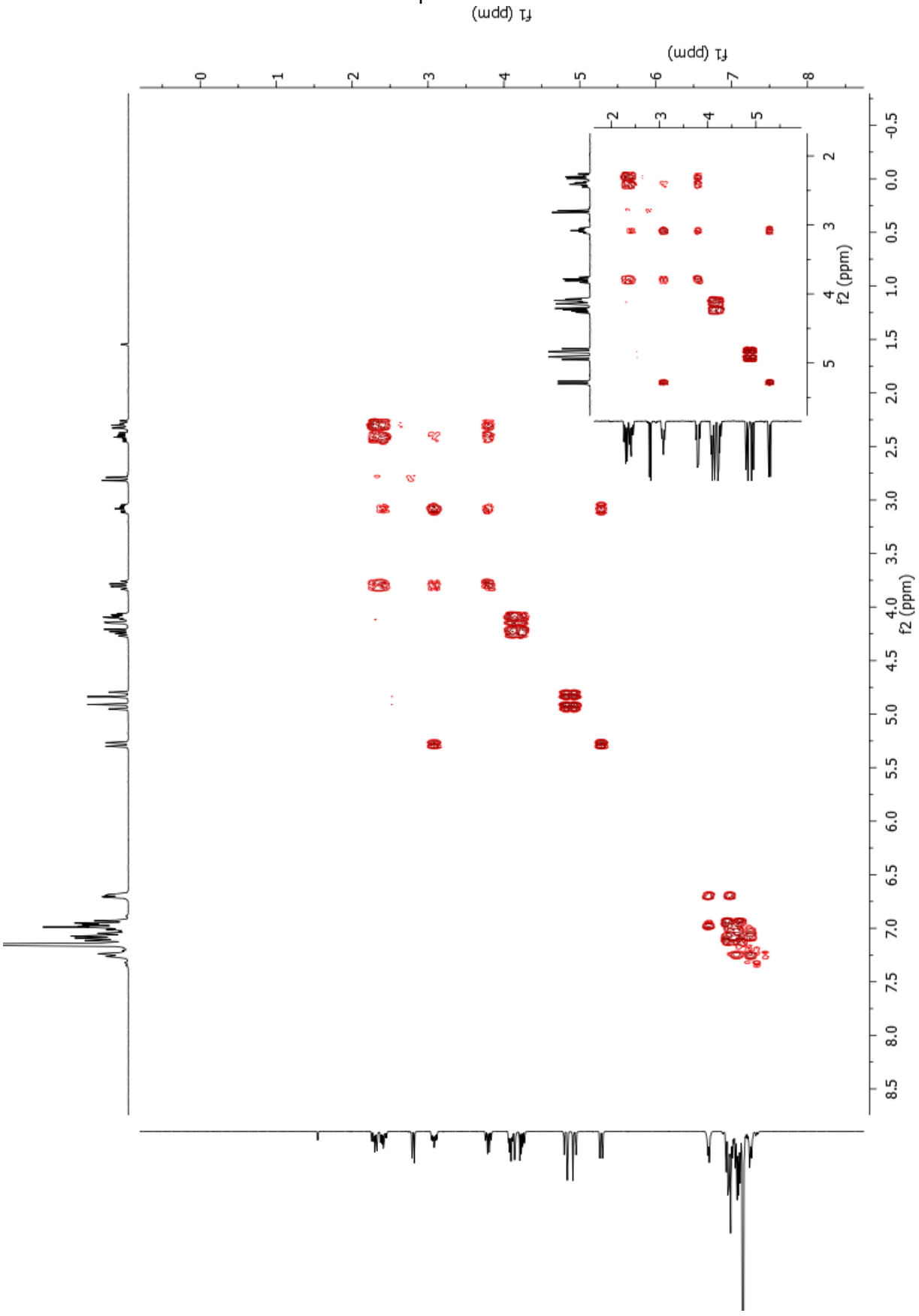


9

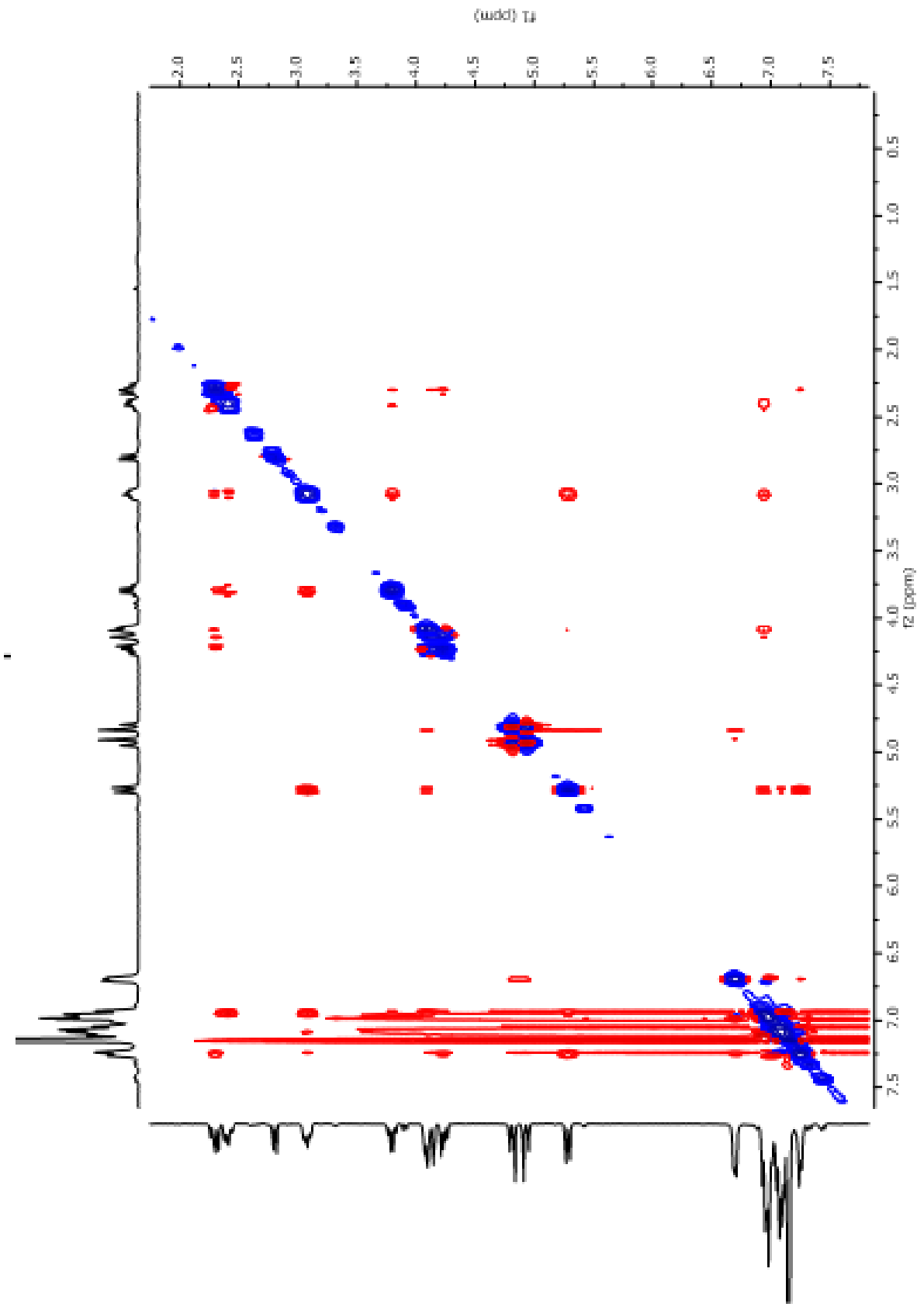


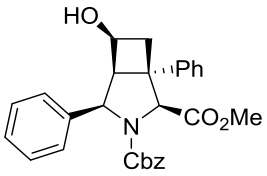


COSY spectrum:

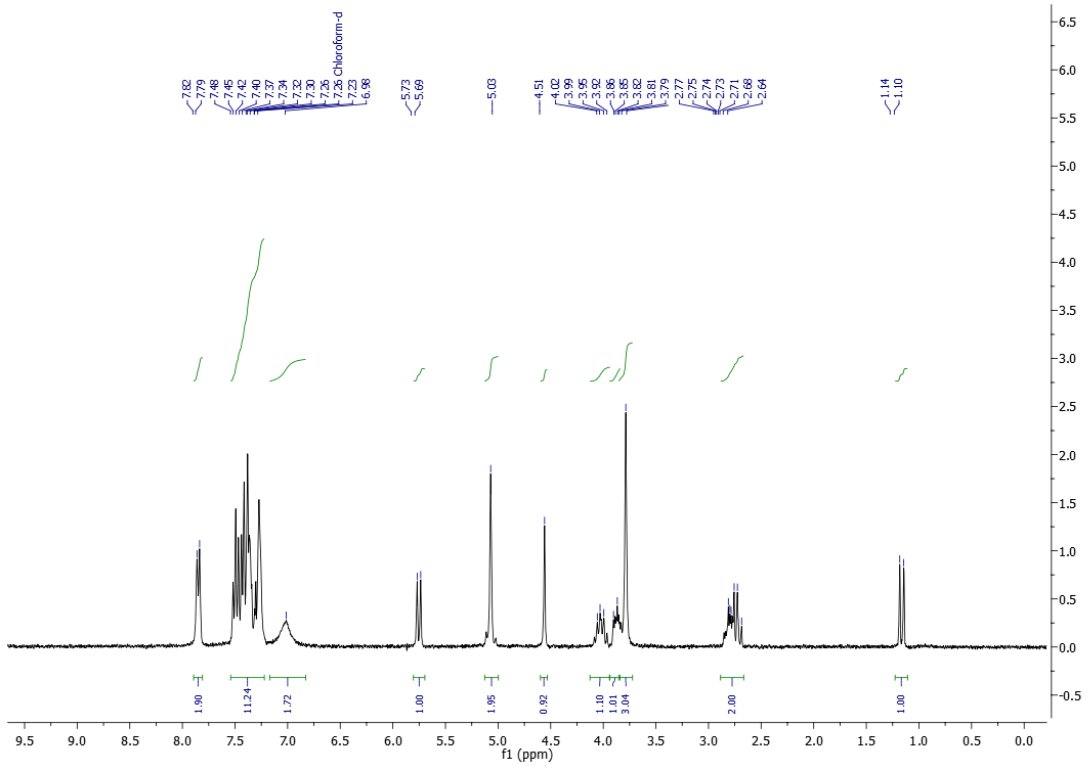


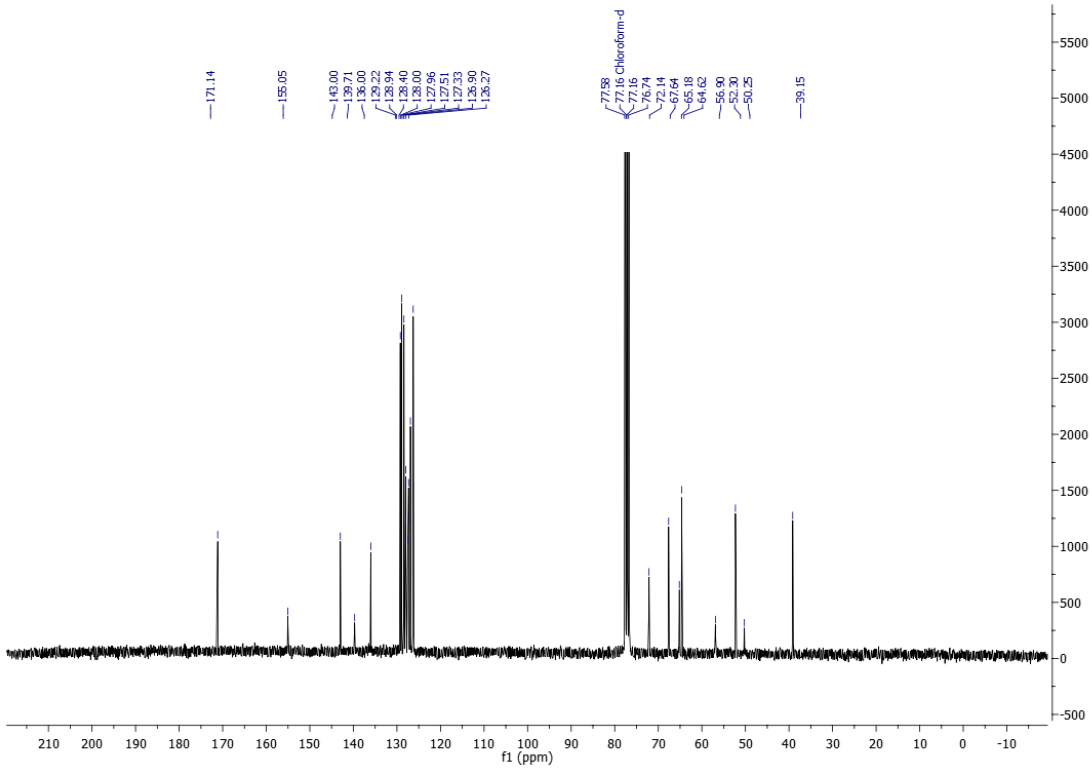
NOESY spectrum:

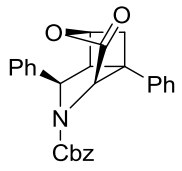



HO
Ph
CO2Me
N
Cbz

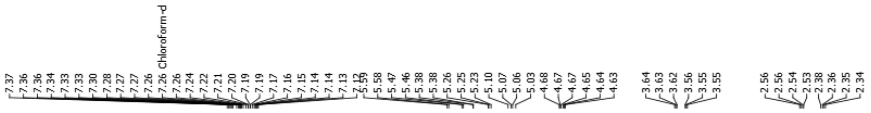
10

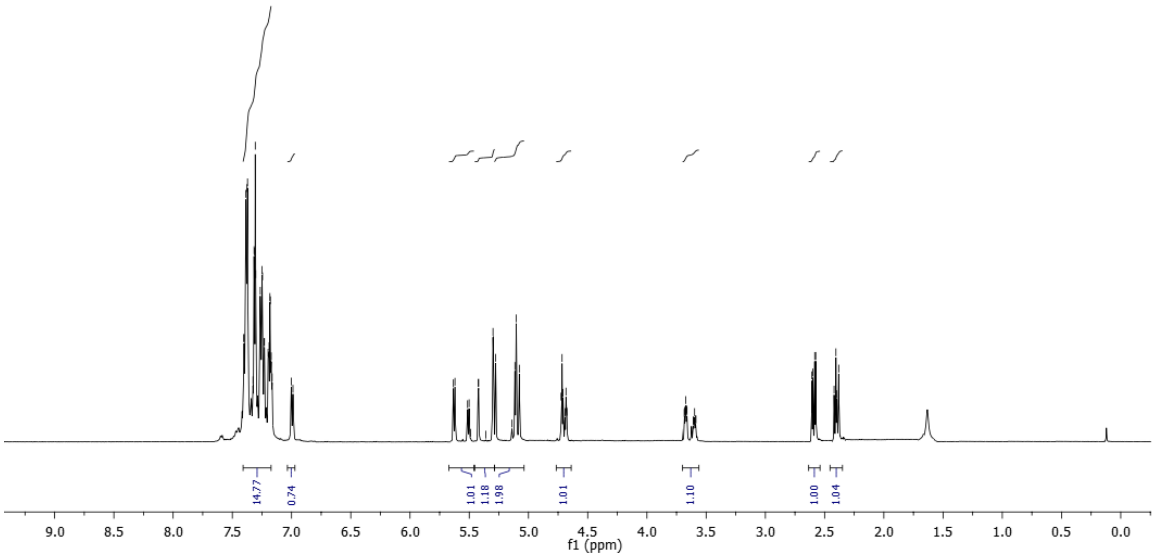

7.82
7.79
7.48
7.45
7.42
7.40
7.37
7.34
7.32
7.30
7.26
7.26 Chloroform-d
7.23
6.98
5.73
5.69
5.03
4.51
4.02
3.99
3.95
3.92
3.86
3.85
3.82
3.81
3.79
2.77
2.75
2.74
2.73
2.71
2.68
2.64
1.14
1.10
1.90
11.24
1.72
1.00
1.95
0.92
1.10
1.01
3.04
2.00
1.00
f1 (ppm)

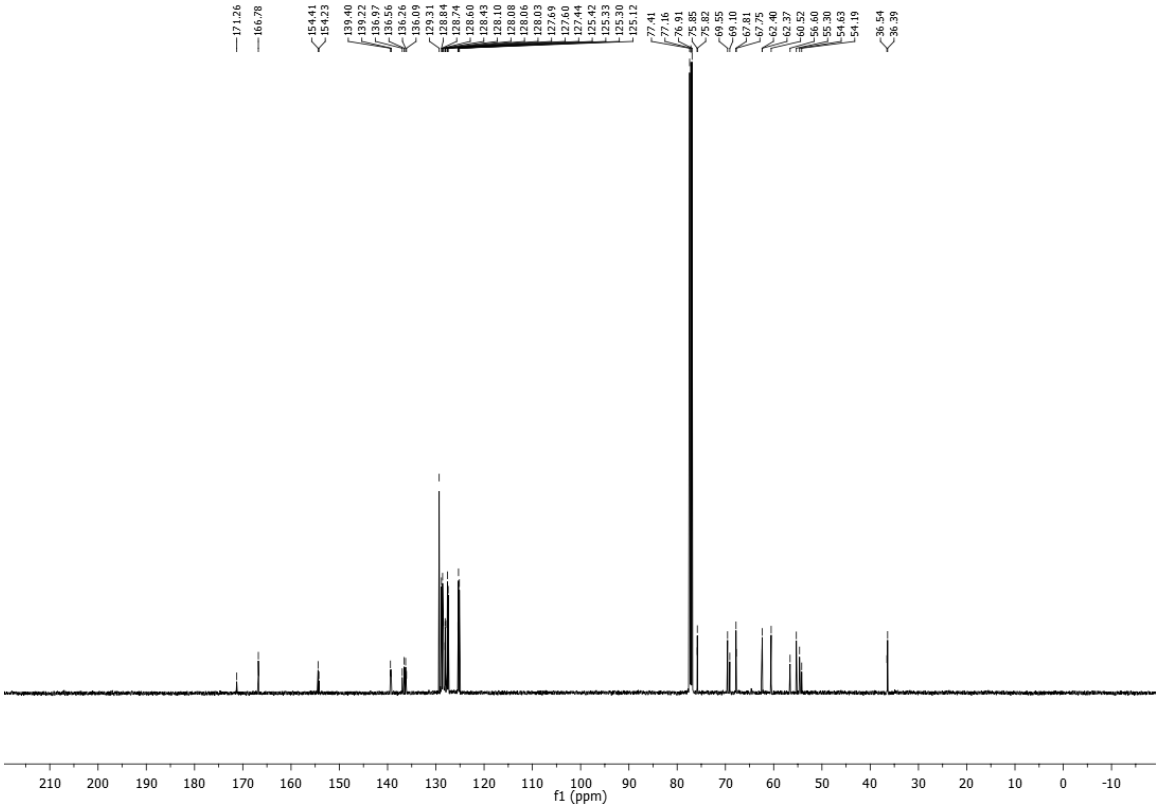

171.14
155.05
143.00
139.71
136.00
129.22
128.94
128.40
128.00
127.96
127.51
127.33
126.90
126.27
77.58
77.16 Chloroform-d
76.74
72.14
67.64
65.18
64.62
56.90
52.30
50.25
39.15
f1 (ppm)


O
O
Ph
Ph
N
Cbz

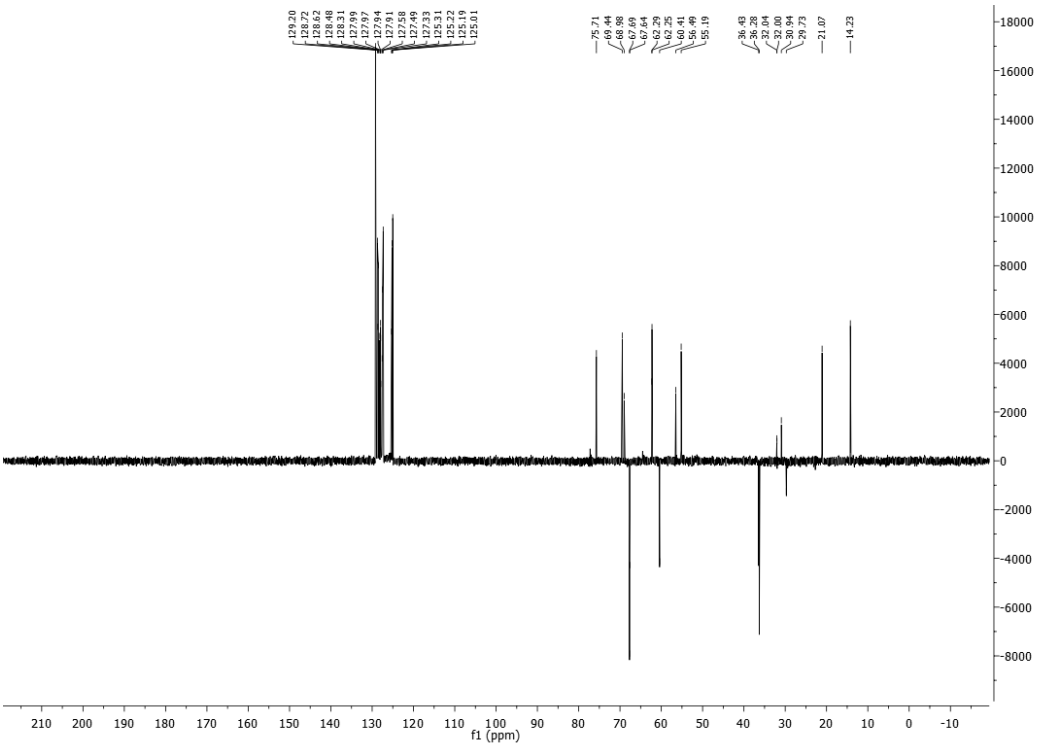
11


Chloroform-d

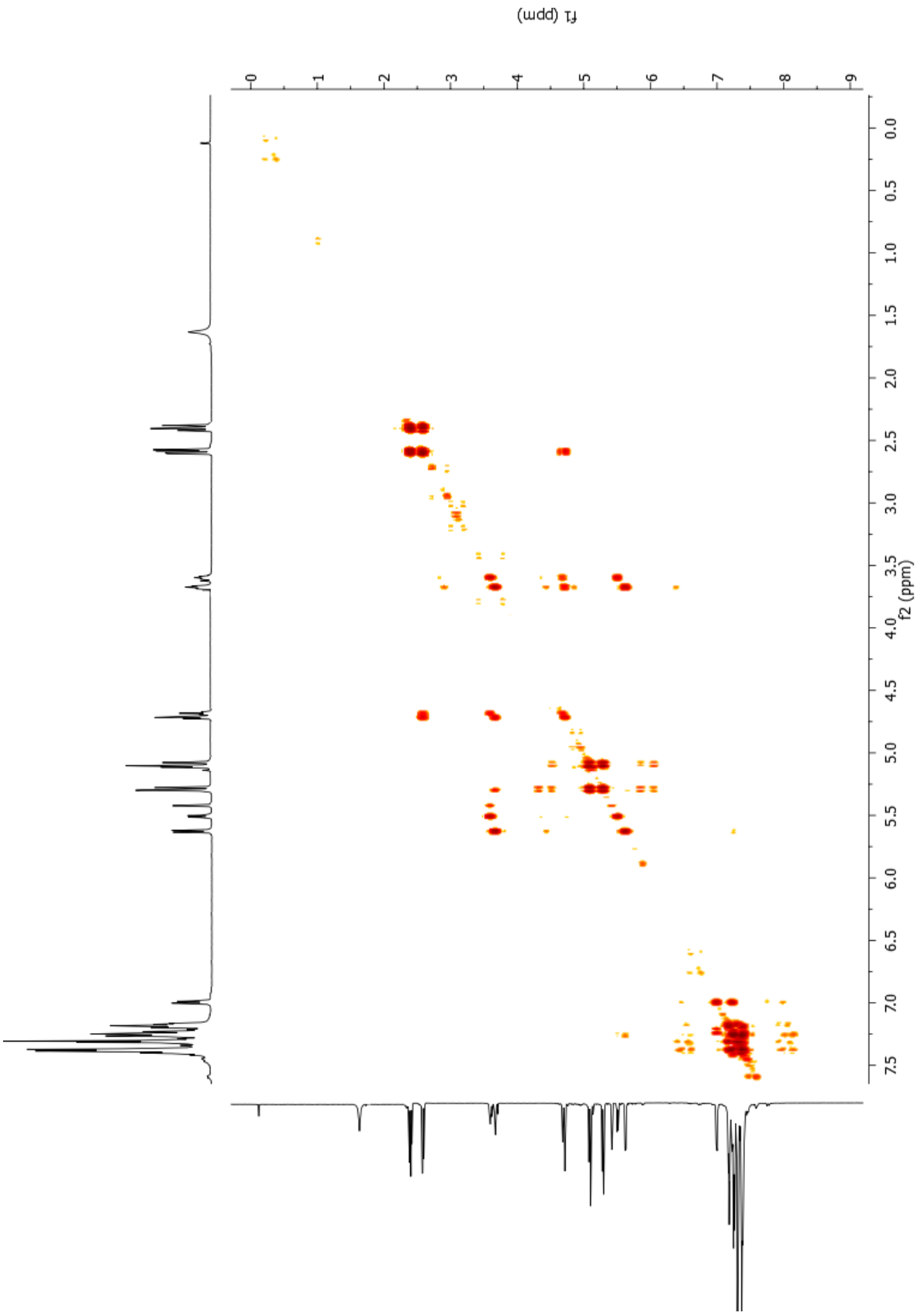

14.77
0.74
1.01
1.18
1.98
1.01
1.10
1.00
1.04
f1 (ppm)


f1 (ppm)

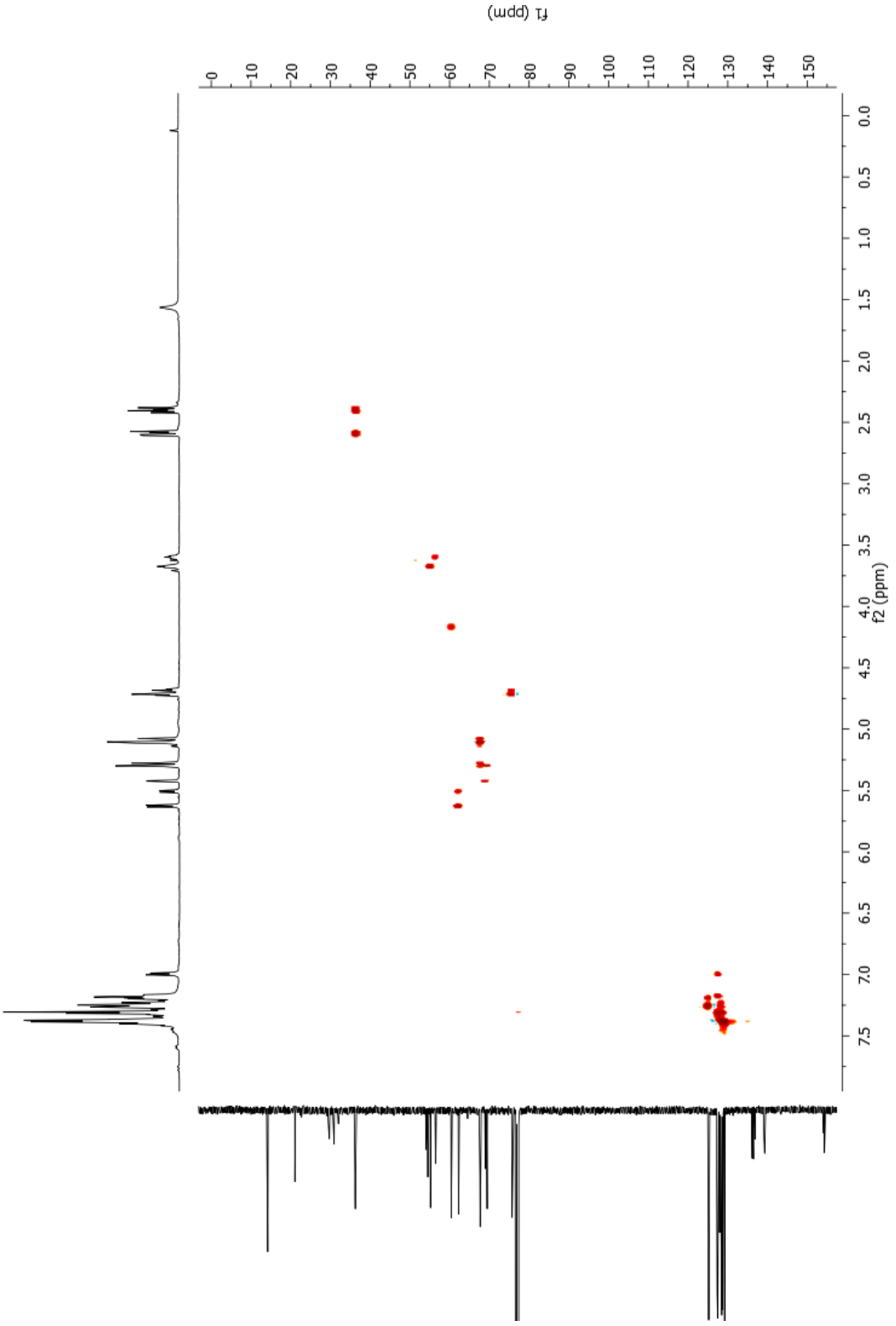
DEPT 135 spectrum:



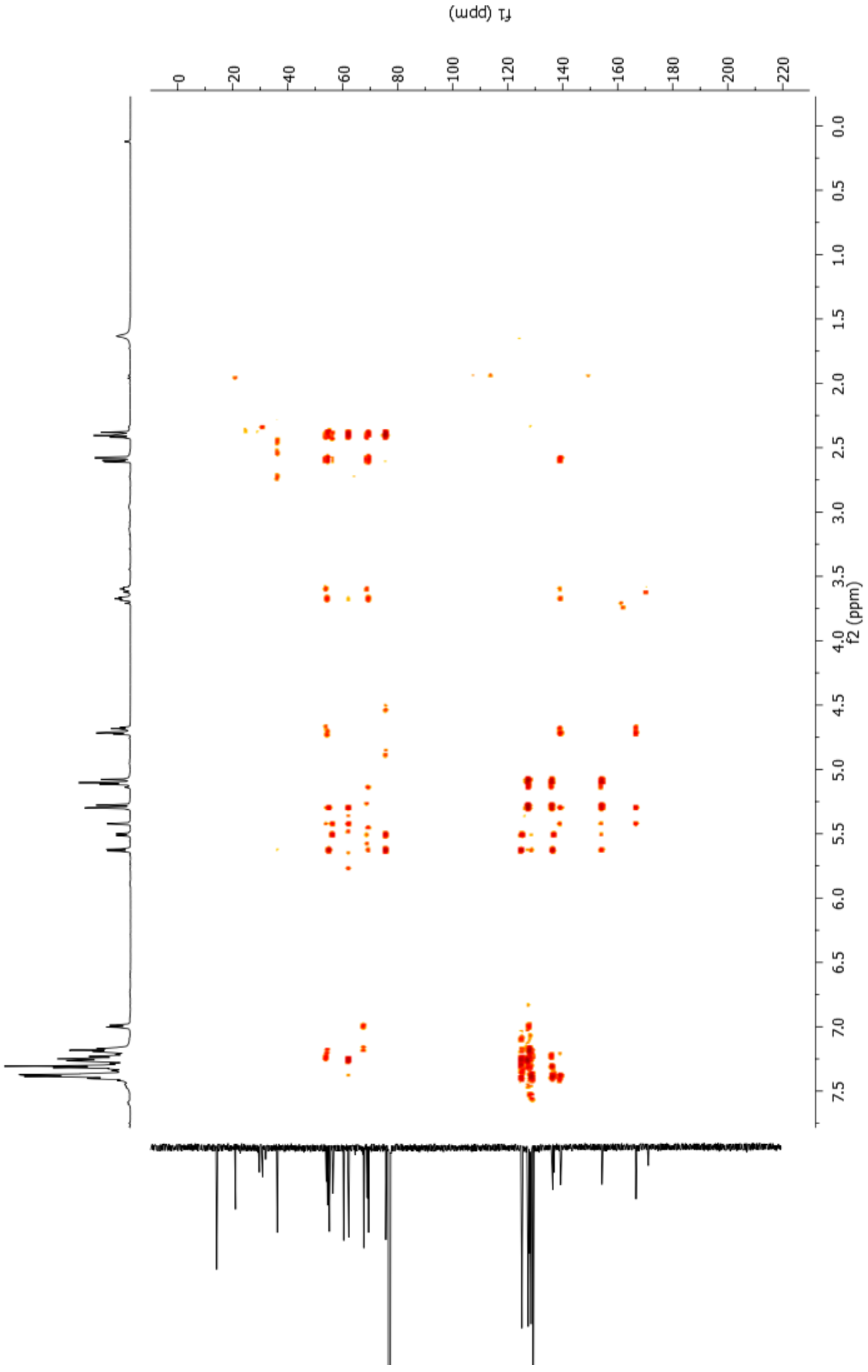
COSY spectrum:



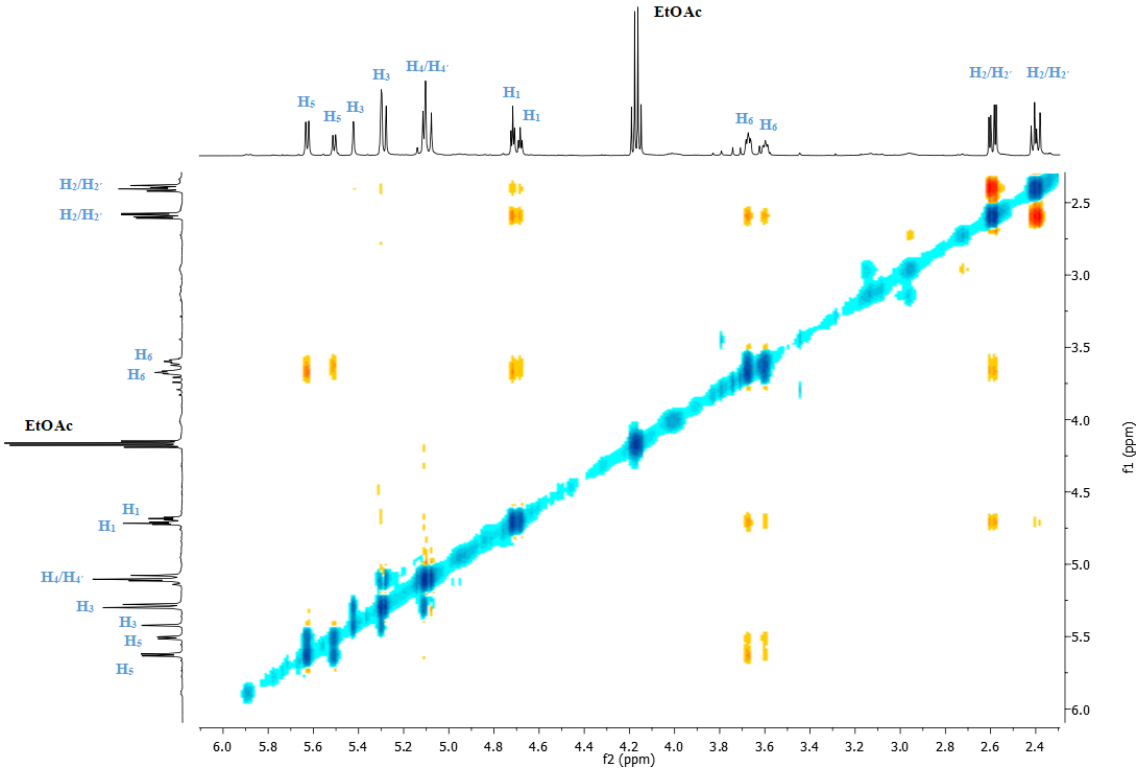
HMQC spectrum:



HMBC spectrum:



The existence of an equilibrium between rotamers was evidenced qualitatively from the performance of a 2D NOESY experiment of compound **12** in $CDCl_3$ (see below). In addition to the signals corresponding to the nuclear Overhauser effect (nOe, indicated in yellow) strong peaks of cross between protons in equivalent equilibrium of a pair of rotamers were detected (peaks EXSY, indicated in blue). These two types of signals easily differentiate between them in the spectrum since they appear in different phases (positive peaks NOE, in yellow, negative peaks EXSY, in blue).[4]



4. For other examples of the use of this technique for the discrimination between rotamers, see: Rayyan, S.; Fossen, T.; Solheim Nateland, H.; Andersen, M. *Phytochem. Anal.*, **2005**, *16*, 334 and references cited therein.