Supporting Information

Chemoselective Intramolecular Functionalization of Methyl Groups in non-Constrained Molecules Promoted by *N*-iodosulfonamides.

Nieves R. Paz,[†] Dionisio Rodríguez-Sosa,[†] Haydee Valdés,[§] Ricardo Marticorena,[†] Daniel Melián,[‡] M. Belén Copano,[†] Concepción C. González*,[†] and Antonio J. Herrera*,[†]

[†]Instituto de Productos Naturales y Agrobiología C.S.I.C. Av. Astrofísico Francisco Sánchez 3, 38206 La Laguna, Tenerife, Spain

[‡]Departamento de Química Orgánica, Universidad de La Laguna, Av. Astrofísico Francisco Sánchez s/n, 38206 La Laguna, Tenerife, Spain

[§]Departamento de Física Teórica, Atómica y Óptica, Universidad de Valladolid, Paseo de Belén 7, 47011 Valladolid, Spain

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General Information and Instrumentation. Melting points were determined with a hot-stage apparatus and are uncorrected. Optical rotations were measured at the sodium line at ambient temperature in $CHCl_3$ solutions. IR spectra were measured as thin films on a NaCl plate. NMR spectra were determined at 400 MHz for ^1H and 100.6 MHz for ^{13}C in $CDCl_3$ unless otherwise stated, in the presence of TMS as internal standard. Mass spectra were determined at ESI+ unless otherwise stated. TLC was performed by using Merck silica gel coated aluminium 60 F_{254} plates; detection with UV or dipping into a solution of $KMnO_4$ (1.5 g in 400 mL H_2O, 5 g $NaHCO_3$) or a solution of nihidrin in EtOH (0.2%) and further heating until development of color. Merck silica gel 60 PF (0.063 – 0.2 mm) was used for column chromatography. Flash chromatography refers to a column chromatography accelerated by air pressure. Ascentis®Si columns (25 cm x 10 mm, 5μm or 15 cm x 4.6 mm, 3μm) were used for HPLC purifications. Commercially available reagents and solvents were analytical grade or were purified by standard procedures prior to use. All reactions involving air- or moisture-sensitive materials were carried out under argon atmosphere. The relative emission of light sources were measured with spectrophotometer [avantes AVS-USB2000 with grating #3(350-850)].UV-visible spectra were measured with spectrophotometer (Varian CARY-1E). The specifications for the light source were the following: [A] for tungsten lamps Philips PAR 38EC, Flood 30º, 80 W; [A+f] for tungsten lamps Philips PAR 38EC, Flood 30º, 80 W, filtered by 1 cm pathlength of aqueous solution of K_2CrO_4 (0.27 g/L) and Na_2CO_3 (1 g/L) into pyrex glasses (λ>445 nm); [B] for green LED lamps Lexman GU10, 0.9W; [C] for white LED lamps Lexman GU10, 4W, 285 Lumens.

General procedures:

Functionalization of methyl group conducted by slow addition of $PhI(OAc)_2$; General procedure for SHAT (GP1): To a solution of *N*-sulfonamidate (1 mmol) in DCE (10 mL), in a sealing tube equipped with a stirring bar, were added iodine (5 mmol, *saturated solution*) and $PhI(OAc)_2$ (0.25 mmol) and sealed off. The reaction mixture was stirred and irradiated with two tungsten filament lamps at 15-20 cm allowing to reach 65-75 ºC, and portions of $PhI(OAc)_2$ (0.25 mmol) were added each 15 min until the reaction was completed, monitored by TLC. The reaction mixture was further stirred for 1 hour and then poured into an aqueous solution of $Na_2S_2O_3$ (20%) and extracted with DCM. The organic phase was dried with Na_2SO_4 and concentrated. The residue was analyzed by ^1H NMR and then purified by flash chromatography (hexanes/EtOAc). Changes in amounts of reagents and use of other additives are specified in text or tables. All reactions were performed with 100-200 mg of *N*-sulfonamidates.

Functionalization of methyl group conducted by slow addition of $PhI(OAc)_2$; General procedure for SHAT $(GP1)_{CSA}$: Same as GP1 but iodine (0.6 mmol) and camphorsulfonic acid CSA (1 mmol) were added instead of the large amount of iodine (*saturated solution*).

Functionalization of methyl group conducted by slow addition of $PhI(OAc)_2$; General procedure for SHAT $(GP1)_{Zn(OTf)2}$: Same as GP1 but iodine (0.5 mmol) and $Zn(OTf)_2$ (0.6 mmol) were added instead of the large amount of iodine (*saturated solution*).

Functionalization of methyl group conducted by slow addition of iodine; General procedure for MHAT (GP2): To a solution of *N*-sulfonamidate (1 mmol) in DCE (33 mL) in a round bottomed flask, equipped with a stirring bar and a septum stopper, were added $PhI(OAc)_2$ (4-6 mmol) and $NaHCO_3$ (100%) (in most cases). The reaction mixture was stirred and irradiated with two tungsten filament lamps at 35 cm at rt (refrigerating with a fan) while a solution of iodine (0.6-1.5 mmol) in DCE (0.15 M) was added dropwise within 3-6 h with a syringe pump until consumption of the starting material, monitored by TLC. The reaction mixture was further stirred for 1-18 hours depending on the ability to afford the lactone product. Longer time of further stirring is needed if higher amount of the carboxylic acid intermediate is detected to promote its cyclization. The reaction mixture was then poured into an aqueous solution of $Na_2S_2O_3$ (20%) and extracted with DCM. The organic phase was dried with Na_2SO_4 and concentrated. The residue was analyzed by ^1H NMR and then purified by flash chromatography (hexanes/EtOAc). Changes in amounts of reagents and use of other additives are stated in text or tables.

Functionalization of methyl group conducted by simultaneously all-mixed protocol; General procedure for SHAT or MHAT (GP3): To a solution of *N*-sulfonamidate (1 mmol) in DCE (0.1-0.03M) in a sealing tube equipped with a stirring bar were added iodine (0.6-1.5 mmol), $PhI(OAc)_2$ (1.25-5 mmol) and, in some cases, additives such $NaHCO_3$ (100%), Na_2CO_3 (100-200%) or CSA (0.5-1 mmol) and sealed off. The reaction mixture was stirred and irradiated with two tungsten filament lamps at 35 cm at rt (refrigerating with a fan) until the reaction was completed, monitored by TLC. The reaction mixture was then poured into an aqueous solution of $Na_2S_2O_3$ (20%) and extracted with DCM. The organic phase was dried with Na_2SO_4 and concentrated. The residue was analyzed by ^1H NMR and then purified by flash chromatography (hexanes/EtOAc). Changes in amounts of reagents and use of other additives are stated in text or tables.

Functionalization of methyl group conducted by simultaneously all-mixed protocol; General procedure for MHAT (GP3)$_{Na2CO3}$: To a solution of *N*-sulfonamidate (1 mmol) in DCE or $CDCl_3$ (0.03M) in a sealing tube equipped with a stirring bar were added $PhI(OAc)_2$ (6-10 mmol), Na_2CO_3 (100-200%) and stirred for 20-30 min prior to the addition of iodine (1-2 mmol). The reaction mixture was stirred and irradiated at rt (refrigerating with a fan) until the reaction was completed, monitored by TLC. The reaction mixture was then poured into an aqueous solution of $Na_2S_2O_3$ (20%) and extracted with DCM. The organic phase was dried with Na_2SO_4 and concentrated. The residue was analyzed by ^1H NMR and then purified by flash chromatography (hexanes/EtOAc). Changes in amounts of reagents and source of light are stated in text or tables.

Functionalization of methyl group conducted by previous formation of AcOI in $CDCl_3$ and monitored by NMR; General procedure for SHAT or MHAT (GP4): A solution of iodine, $PhI(OAc)_2$ and, in some cases, additives such $NaHCO_3$ or Na_2CO_3 (100-200%) in $CDCl_3$ (0.03 – 0.2 M) was stirred for 30-45 min in the dark in a sealed tube, until the $PhI(OAc)_2$ was consumed (monitored by ^1H NMR). *N*-sulfonamidate was then added to this reaction mixture, which was vigorously stirred for 1-2 minutes and transferred to a NMR-tube. The evolution of the reaction was monitored by ^1H NMR either in the dark (usually, without taking the

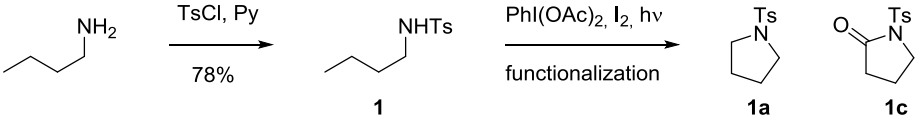
sample out of the NMR machine) or under irradiation (the NMR tube was rotated while it was irradiated outside of the NMR machine).

Note: When the reaction was performed under irradiation, we assumed that the processes promoted by radiation stopped during the measurement of the ^{1}H NMR (≈3 min of darkness), while the processes that could occur in absence of light continued ongoing, introducing an error that did not disturbed drastically the evolution of reactions.

General procedure for *N*-sulfonamidate products (GP5): $ClSO_2Ar$ (1.1 mmol) was added to a solution of the amine (1 mmol) in pyridine (1 mL) at 0 ºC and stirred at rt for 1-3 h. The reaction mixture was poured into a diluted aqueous solution of HCl (10%) and extracted twice with EtOAc. The organic extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc) of the residue afforded the corresponding products.

Synthesis and Functionalizacion of Tosylamine 1:

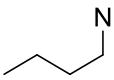
Table *S1*.



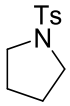
[scheme 2]

entry	substrate 1	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[c] ºC	time h	yield %[e]	1a %[f]	1c %[f]	products ratio[g]
1		GP3 (Fan)	3	1	-	0.25	25	5	?	complex mixture		-
2		GP1	3, 3	5	-	-	70	4	?	complex mixture		-
3		GP1	3, 3	1	CSA, 0.5	0.1	70	4	-	complex mixture		-
4		GP2	7	1.5, 6	$NaHCO_3$, 1	0.05	25	6.5	57	2.8	55	> 1:15
5		GP2	7	0.6, 4	$NaHCO_3$[h]	0.03	25	5	78	-	78	0:1

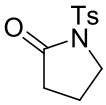
[a] millimoles per millimol of **1**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w. CSA = Camphorsulfonic acid.



***N*-Butyl-4-methylbenzenesulfonamide (1):**[1] According to GP5, *N*-tosylamine **1** was prepared from butan-1-amine in 78% as a crystalline solid: Mp 41.5-43.0 ºC (ethanol/*n*-hexane); ^{1}H NMR δ0.85 (t, *J* = 7.4 Hz, 3H), 1.24-1.33 (m, 2H), 1.40-1.47 (m, 2H), 2.43 (s, 3H), 2.93 (br dd, *J* = 7.0, 12.6 Hz, 2H), 4.47 (br s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR δ13.9 (CH_3), 20.1 (CH_2), 21.9 (CH_3), 31.9 (CH_2), 43.3 (CH_2), 127.5 (2 x CH), 130.0 (2 x CH), 137.8 (C), 143.6 (C).



1-Tosylpyrrolidine (1a):[2] Crystalline solid: ^{1}H NMR δ1.73-1.77 (m, 4H), 2.43 (s, 3H), 3.22-3.25 (m, 4H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H).



1-Tosylpyrrolidin-2-one (1c):[3] Crystalline solid: ^{1}H NMR δ2.03-2.11 (m, 2H), 2.41-2.45 (m, 2H), 2.44 (s, 3H), 3.90 (t, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.93 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ18.2 (CH_2), 21.6 (CH_3), 32.2 (CH_2), 47.2 (CH_2), 128.1 (2 x CH), 129.6 (2 x CH), 135.2 (C), 145.1 (C), 173.3 (C).

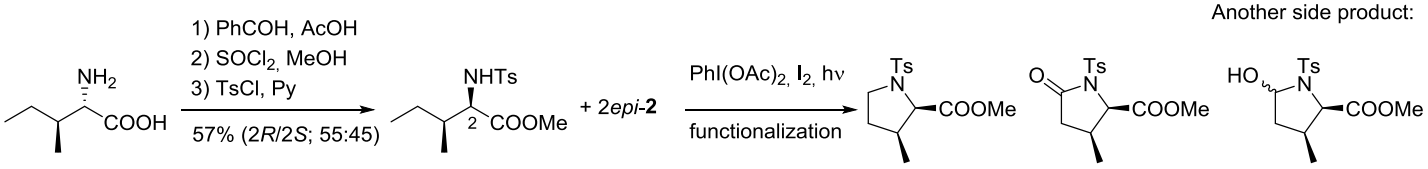
[1] Spectral data are in good agreement with those reported in the literature: (a) Rad, M. N. S.; Khlafi-Nezhad, A.; Asrari, Z.; Behrouz, S.; Amini, Z.; Behrouz, M. *Synthesis* **2009**, 3983; (b) Li, Y.; Zhao, Y.; Zhang, Z.;Xu, Y. *Tetrahedron Lett*. **2010**, *51*, 1434.

[2] Spectral data are in good agreement with those reported in the literature: Kato, Y.; Yen, D. H.; Fukudome, Y.; Hata, T.; Urabe, H. *Org. Lett*. **2010**, *12*, 4137.

[3] Spectral data are in good agreement with those reported in the literature: (a) Guo, J.; Harling, J. D.; Steel, P. G.; Woods, T. M. *Org. Biomol. Chem.* **2008**, *6*, 4053; (b) Boal, B. W.; Schammel, A. W.; Garg, N. K. *Org. Lett.* **2009**, *11*, 3458; (c) Schammel, A. W.; Boal, B. W.; Zu, L.; Mesganaw, T.; Garg N. *Tetrahedron* **2010**, *66*, 4687.

Synthesis and Functionalization of Tosylamine 2:

Table *S2*.

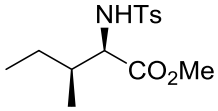


2 **2a** **2c** **2b(OH)**

table 1 [scheme 2, table 1]

entry	substrate **2**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] ºC	time h	yield %[e]	**2a** %[f]	**2c** %[f]	**2b(OH)**(*S*/*R*) %[f]	products ratio[g]
1		GP1	5, 5	5	-	0.1	70	4	95	95	-	-	1:0:0
2		GP2	6	0.6, 4	$NaHCO_3$[h]	0.03	25	5	11[i]	11	-	-	10.6:1:0
3		$GP3_{Na2CO3}$	6	1.4	Na_2CO_3[j]	0.03	25	2.25	88	-	81[k]	7[k]	0:1:0.14

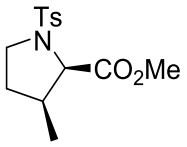
[a] millimoles per millimol of **2**; [b] Time of addition in hours: Portionwise (0.5 equiv / 30 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] [**2a**/**2c**/**2b(OH)**] calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w; [i] startingt material **2** was recovered (73%); [j] 200% w/w; [k] **2c** and **2b(OH)** were isolated together by column chromatography and independently isolated by further HPLC.



(2*R*,3*S*) Methyl 3-methyl-2-(4-methylphenylsulfonamido)pentanoate (2): A solution of L-isoleucine (5 g, 37.9 mmol) in glacial acetic acid (25 mL) was treated with benzaldehyde (400 mg), and the mixture heated at 100 ºC in a nitrogen atmosphere for 3 h. The mixture was cooled to 50 ºC and filtered through Celite. The solution was concentrated under vacuum to a volume of 5 mL. 2-Propanol (16 mL) was then added and the mixture stirred for 1 h. The mixture was filtered and washed with more 2-propanol (2x4 mL). The solid was dried under vacuum to afford an epimeric mixture of L-isoleucine and D-alloisoleucine (4.3 g, 86%, ≈1:1, estimated by ^{1}H NMR).[4] Part of this epimeric mixture (2.41 g, 20.6 mmol) was then dissolved in dry MeOH (80 mL) and treated at 0 ºC with $SOCl_2$ (2.99 mL, 41.2 mmol). The mixture was refluxed for 4 h and concentrated to give the crude methyl ester as viscous oil. The product was dissolved in pyridine (70 mL), TsCl (7.85 g, 41.2 mmol) was added and the mixture was heated at 40 ºC for 24 h. The mixture was concentrated, dissolved in EtOAc and washed with diluted aqueous solution of HCl (10%). The organic extract was washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 75:25) of the residue afforded pure D-alloisoleucine derivative **2** (165 mg, 0.55 mmol, 2.7%) as a white solid collecting the initial fractions of the column and the epimeric mixture (**2**/*2epi*-**2**, ≈1:1) (3.95 g, 13.2 mmol, 64%) with equal R_f by TLC analysis which was successively subjected to column chromatography to obtain further small portions of pure **2**: Crystalline solid; Mp 75.6-76.5 ºC (hexane / Et_2O); $[\alpha]_D$ -20.9 (*c* 1.0); ^{1}H NMR δ0.81 (d, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H), 1.23 (dquin, *J* = 7.4 x 4, 14.3 Hz, 1H), 1.46 (dquin, *J* = 7.4 x 4, 14.3 Hz, 1H), 1.77 (tqd, *J* = 4.1, 7.1 x 3, 7.4 x 2 Hz, 1H), 2.41 (s, 3H), 3.44 (s, 3H), 3.90 (dd, *J* = 4.1, 10.2 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR δ11.5 (CH_3), 14.3 (CH_3), 21.6 (CH_3), 26.0 (CH_2), 38.1

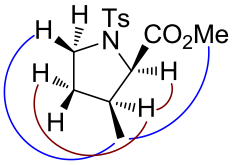
[4] Cambiè, M.; D'Arrigo, P.; Fasoli, E.; Servi, S.; Tessaro, D.; Canevotti, F.; Coron, L. D. *Tetrahedron: Asymmetry* **2003**, *14*, 3189.

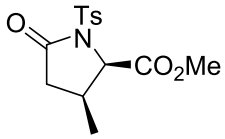
(CH), 52.2 (CH_3), 59.1 (CH), 127.4 (2 x CH), 129.6 (2 x CH), 136.7 (C), 143.6 (C), 172.1 (C); MS (ESI+) *m/z* (rel intensity) 322 (M^++ Na, 100); HRMS calcd for $C_{14}H_{21}NO_4NaS$, 322.1089, found 322.1088.



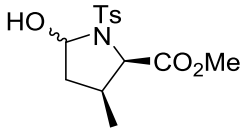
(2*R*,3*S*) Methyl 3-methyl-1-tosylpyrrolidine-2-carboxylate (2a): Colorless oil: $[\alpha]_D$ +53.2 (*c* 1.2); ^{1}H NMR δ 0.94 (d, *J* = 6.9 Hz, 3 H), 1.80 (dddd, *J* = 8.2, 10.1, 12.3, 12.3 Hz, 1 H), 1.92 (dddd, *J* = 2.2, 6.6, 6.6, 12.8 Hz, 1 H), 2.26 (ddquin, *J* = 6.9 x 4, 8.5, 11.7 Hz, 1 H), 2.43 (s, 3 H), 3.24 (ddd, *J* = 6.8, 9.1, 10.0 Hz, 1 H), 3.60 (ddd, *J* = 1.9, 8.2, 8.2 Hz, 1 H), 3.68 (s, 3 H), 4.24 (d, *J* = 8.5 Hz, 1 H), 7.31 (d, *J* = 8.5 Hz, 2 H), 7.73 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ 14.8 (CH_3), 21.9 (CH_3), 32.4 (CH_2), 37.9 (CH), 48.0 (CH_2), 52.1 (CH_3), 64.5 (CH), 127.8 (2 x CH), 130.0 (2 x CH), 135.9 (C), 143.8 (C), 171.5 (C); MS (ESI+) *m/z* (rel intensity) 320 (M^++ Na, 100); HRMS calcd for $C_{14}H_{19}NO_4NaS$, 320.0932, found 320.0937.

Main correlations observed by NOESY are shown in the figure:





(2*R*,3*S*) Methyl 3-methyl-5-oxo-1-tosylpyrrolidine-2-carboxylate (2c): Colorless oil: $[\alpha]_D$ +13.8 (*c* 0.5); ^{1}H NMR δ 1.05 (d, *J* = 6.9 Hz, 3 H), 2.30 (dd, *J* = 12.3, 17.0 Hz, 1 H), 2.44 (s, 3 H), 2.48 (dd, *J* = 8.0, 17.0 Hz, 1 H), 2.68-2.81 (m, 1 H), 3.76 (s, 3 H), 4.83 (d, *J* = 8.6 Hz, 1 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 7.92 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR (125 MHz) δ 15.3 (CH_3), 22.1 (CH_3), 31.1 (CH), 38.6 (CH_2), 52.6 (CH_3), 64.1 (CH), 129.3 (2 x CH), 129.7 (2 x CH), 135.4 (C), 145.7 (C), 170.1 (C), 172.5 (C); MS (ESI+) m/z (rel intensity) 334 (M^++ Na, 100); HRMS calcd for $C_{14}H_{17}NO_5NaS$, 334.0725, found 334.0723.



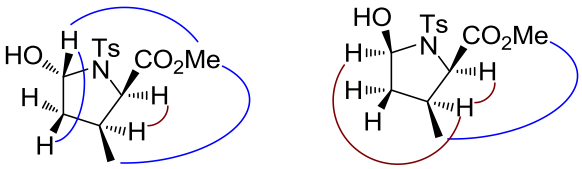
(2*R*,3*S*) Methyl 5-hydroxy-3-methyl-1-tosylpyrrolidine-2-carboxylate [2b(OH)]: Compound **2b(OH)** was isolated as an epimeric mixture [(5*S*/5*R*)-**2b(OH)**, 1.4:1.0] by HPLC (hexane/EtOAc, 8:2→6:4) as a colorless oil:

(5*S*)-**2b(OH)**: ^{1}H NMR (500 MHz) δ 0.95 (d, *J* = 6.9 Hz, 3 H), 1.90 (ddd, *J* = 5.0, 12.9 x 2 Hz, 1 H), 1.96 (dd, *J* = 6.3, 12.6 Hz, 1 H), 2.43 (s, 3 H), 2.93 (dddq, *J* = 6.9 x 4, 8.2, 13.6 Hz, 1 H), 3.55 (s, 3 H), 4.38 (d, *J* = 8.2 Hz, 1 H), 5.60 (d, *J* = 5.0 Hz, 1 H), 7.29 (d, *J* = 7.6 Hz, 2 H), 7.8 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ 14.2 (CH_3), 21.9 (CH_3), 35.0 (CH), 40.6 (CH_2), 52.1 (CH_3), 64.4 (CH), 84.5 (CH), 127.8 (2 x CH), 129.9 (2 x CH), 137.2 (C), 144.2 (C), 170.8 (C).

(5*R*)- **2b(OH**: ^{1}H NMR (500 MHz) δ 0.95 (d, *J* = 6.9 Hz, 3 H), 1.65 (ddd, *J* = 5.4, 11.7, 13.2 Hz, 1 H), 2.32-2.40 (m, 1 H), 2.42 (s, 3 H), 2.49 (ddd, *J* = 6.3, 6.9, 13.9 Hz, 1 H), 3.62 (s, 3 H), 4.31 (d, *J* = 8.2 Hz, 1 H), 5.62 (d, *J* = 6.3 Hz, 1 H), 7.31 (d, *J* = 7.6 Hz, 4 H), 7.8 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ 15.0 (CH_3), 21.9 (CH_3), 36.9 (CH), 42.1 (CH_2), 52.5 (CH_3), 64.4 (CH), 85.7 (CH), 127.8 (2 x CH), 129.9 (2 x CH), 137.2 (C),

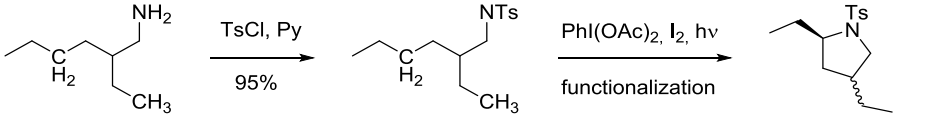
144.1 (C), 172.2 (C); MS (ESI+) *m/z* (rel intensity) 336 (M^++ Na, 100); HRMS calcd for $C_{14}H_{19}NO_6NaS$, 336.0882, found 336.0879.

Main correlations observed by NOESY are shown in the figure:



Synthesis and Functionalization of Tosylamine 3:

Table *S3*.

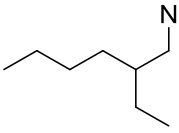


3 *rac*-**3a** (*syn*/*anti*, 1:1)

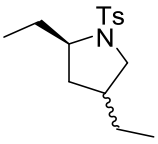
[scheme 2]

entry	substrate **3**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] °C	time h	yield %[e]	*rac*-**3a** (1:1) %[f]
1		GP1	3, 3	5	-	0.1	70	4	85	85
2		GP2	7	1.5, 3	$NaHCO_3$[g]	0.07	25	4	87	87

[a] millimoles per millimol of **3**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 °C (reaction mixture refrigerated by a fan) and 65-75 °C (without fan); [e] total isolated yield; [f] isolated yield; [g] 100% w/w.



***N*-(2-Ethylhexyl)-4-methylbenzenesulfonamide (3):** According to GP5, *N*-tosyl amine **3** was prepared from 2-ethylhexan-1-amine (1.16 g, 9.0 mmol) in 95% as a colorless oil: ^{1}H NMR δ0.78 (t, *J* = 7.4 Hz, 3H), 0.83 (t, *J* = 7.0 Hz, 3H), 1.10-1.31 (m, 8H), 1.35 (sept, *J* = 6.1 Hz, 1H), 2.24 (s, 3H), 2.83 (d, *J* = 5.7 Hz, 2H), 4.87 (br s, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR δ11.0 (CH_3), 14.4 (CH_3), 21.9 (CH_3), 23.3 (CH_2), 24.2 (CH_2), 29.0 (CH_2), 31.0 (CH_2), 39.6 (CH), 46.2 (CH_2), 127.5 (2 x CH), 130.0 (2 x CH), 137.5 (C), 143.6 (C); MS (ESI^+) *m/z* (rel intensity) 306 (M^++Na, 100); HRMS calcd for $C_{15}H_{25}NO_2NaS$, 306.1504, found 306.1505.

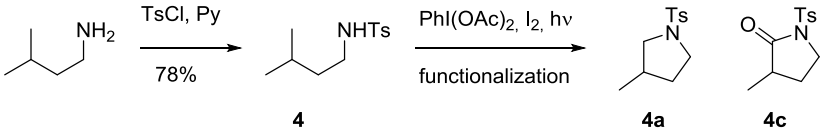


2,4-Diethyl-1-tosylpyrrolidine (3a): Crystalline solid; NMR showed a mixture of isomer *syn*/*anti* in 1:1 ratio. ^{1}H NMR (500Mz) δ0.80 (t, *J* = 7.3 Hz, 3H), 0.82 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H), 1.09-1.19 (m, 4H), 1.23-1.29 (m, 2H), 1.30-1.40 (m, 1H), 1.46-1.62 (m, 2H), 1.72 (ddd, *J* = 1.9, 6.2, 6.2 Hz, 1H), 1.80-1.88 (m, 1H), 1.97-2.15 (m, 3H), 2.43 (s, 6H), 2.63 (t, *J* = 9.5 Hz, 1H), 2.85 (br t, *J* = 11.0 Hz, 1H), 3.48-3.58 (m, 3H), 3.62 (br dd, *J* = 7.3, 11.3 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 4H), 7.72 (d, *J* = 8.0 Hz, 4H); ^{13}C NMR δ10.1 (CH_3), 10.9 (CH_3), 12.8 (CH_3), 12.9 (CH_3), 21.9 (2 x CH_3), 25.9 (CH_2), 26.3 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 36.3 (CH_2), 38.2 (CH_2), 39.2 (CH), 40.3 (CH), 54.5 (CH_2), 55.0 (CH_2), 62.2 (CH), 62.6 (CH), 127.8 (2 x CH), 127.9 (2 x CH), 129.9

(2 x CH), 130.0 (2 x CH), 135.2 (C), 136.2 (C), 143.5 (2 x C); MS (ESI^+) *m/z* (rel intensity) 304 (M^++Na, 100); HRMS calcd for $C_{15}H_{23}NO_2NaS$, 304.1347, found 304.1352.

Synthesis and Functionalization of Tosylamine 4:

Table *S4*.

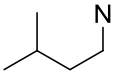


4 **4a** **4c**

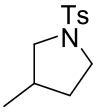
[table 1]

entry	substrate **4**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] °C	time h	yield %[e]	**4a** %[f]	**4c** %[f]	products ratio[g]
1		GP1	6, 6	7	-	0.1	70	6.5	68	61	7	7.5:1
2		GP1	3, 3	1	CSA, 1	0.1	70	5	-	complex mixture[h]		-
3		GP1	3, 3	1	*p*-TsOH, 1	0.1	70	5	-	complex mixture[i]		-
4		GP1	3, 3	1	TFA, 1	0.1	70	5	-	no reaction		-
5		GP2	7	0.6, 3	$NaHCO_3$[j]	0.03	25	4	77	-	77	0:1

[a] millimoles per millimol of **4**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] calculated by integration in the ^1H NMR of the crude of reaction; [h] aproximatly 60% of reaction was completed; [i] aproximatly 10% of reaction was completed; [j] 100% w/w. CSA = Camphorsulfonic acid; *p*-TsOH = *p*-toluenesulfonic acid; TFA = trifluoroacetic acid.

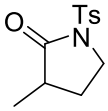


***N*-Isopentyl-4-methylbenzenesulfonamide (4):** According to GP5, *N*-tosylamine **4** was prepared from 3-methylbutan-1-amine (704 mg, 8.1 mmol) in 57% as a pale yellow oil: ^1H NMR δ0.81 (d, *J* = 6.6 Hz, 6H), 1.33 (q, *J* = 7.0 Hz, 2H), 1.57 (non, *J* = 6.7 x 8 Hz, 1H), 2.43 (s, 3H), 2.92 (t, *J* = 7.2 Hz, 2H), 4.97 (br s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR δ21.9 (CH_3), 22.6 (2 x CH_3), 25.8 (CH), 38.7 (CH_2), 41.9 (CH_2), 127.5 (2 x CH), 130.0 (2 x CH), 137.4 (C), 143.6 (C); MS (ESI^+) *m/z* (rel intensity) 264 (M^++Na, 100); HRMS calcd for $C_{12}H_{19}NO_2NaS$, 264.1034, found 264.1027.



3-Methyl-1-tosylpyrrolidine (4a):[5] Crystalline solid: Mp 69-71 ºC (Et_2O/hexane); [literature = 67-68 ºC (hexane/DCM)]; ^1H NMR (500 MHz) δ 0.92 (d, *J* = 6.6 Hz, 3H), 1.35 (dddd, *J* = 8.3, 8.3, 8.3, 12.3 Hz, 1H), 1.90 (dddd, *J* = 4.2, 7.3, 7.3, 12.3 Hz, 1H), 2.07-2.17 (m, 1H), 2.43 (s, 3H), 2.75 (dd, *J* = 7.9, 9.8 Hz, 1H), 3.22 (ddd, *J* = 7.3, 8.2, 9.8 Hz, 1H), 3.34 (ddd, *J* = 4.1, 8.2, 9.8 Hz, 1H), 3.42 (dd, *J* = 7.3, 9.8 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (125.7 MHz) δ 17.7 (CH_3), 21.5 (CH_3), 33.3 (CH_2), 33.3 (CH), 47.6 (CH_2), 54.8 (CH_2), 127.6 (2 x CH), 129.6 (2 x CH), 134.2 (C), 143.2 (C); MS (ESI^+) *m/z* (rel intensity) 262 (M^+ + Na, 100); HRMS calcd for $C_{12}H_{17}NO_2NaS$, 262.0878, found 262.0876.

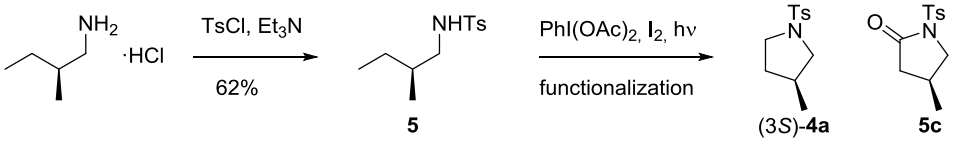
[5] Spectral data are in good agreement with those reported in the literature: (a) Tang, J.; Shinokubo, H.; Oshima, K. *Tetrahedron*, **1999**,*55*, 1893; (b) Rai, K. M. L.; Hassner, A. *Heterocycles*, **1990**, *30*, 817.



3-Methyl-1-tosylpyrrolidin-2-one (4c):[6] Crystalline solid. Mp 84-86 ºC (hexane/EtOAc); ^{1}H NMR δ1.13 (d, *J* = 7.1 Hz, 3H), 1.65-1.75 (m, 1H), 2.22-2.30 (m, 1H), 2.43 (s, 3H), 2.42-2.52 (m, 1H), 3.69 (ddd, *J* = 6.9, 9.7, 9.7 Hz, 1H), 3.94 (ddd, *J* = 2.4, 8.6, 9.9 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ 15.3 (CH_3), 22.0 (CH_3), 27.5 (CH_2), 38.6 (CH), 45.6 (CH_2), 128.4 (2 x CH), 130.0 (2 x CH), 135.6 (C), 145.5 (C), 176.2 (C); MS (ESI$^+$) *m/z* (rel intensity) 276 (M^++Na, 100); HRMS calcd for $C_{12}H_{15}NO_3NaS$, 276.0670, found 276.0674.

Synthesis and Functionalization of Tosylamine 5:

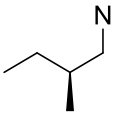
Table *S5*.



[table 1]

entry	substrate 5	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] ºC	time h	yield %[e]	(3*S*)-**4a** %[f]	**5c** %[f]	products ratio[g]
1		GP1	6, 6	7	-	0.1	70	6.5	65	65	-	1:0
2		GP1	2, 2	0.6	*p*-TSOH, 1	0.1	70	3	-	no reaction		-
3		GP2	7	0.6, 4	$NaHCO_3$[h]	0.1	25	4.5	61	9	52	1:3
4		GP2	7	0.6, 4	$NaHCO_3$[h]	0.03	25	4.5	78	-	78	0:1

[a] millimoles per millimol of **5**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w.



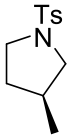
(*S*)-4-Methyl-*N*-(2-methylbutyl)benzenesulfonamide (5):[7] TsCl (3.59 g, 18.86 mmol) was added to a solution of (*S*)-2-methylbutan-1-amine[8] (1.16 g, 9.43 mmol) and Et_3N (7.9 mL, 56.58 mmol) in dry DCM (17 mL) at 0 ºC and stirred at rt for 2 h. The reaction mixture was poured into a diluted aqueous solution of HCl (10%) and extracted twice with EtOAc. The organic extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 95:5-90:10) of the residue afforded the corresponding sulfonamide **6** (1.41 g, 5.85 mmol, 62%) as a colorless oil: $[\alpha]_D$ +2.5 (*c* 0.7); ^{1}H NMR δ0.82 (t, *J* = 7.4 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H), 1.10 (dquin, *J* = 7.5 x 4, 13.5 Hz, 1H), 1.35 (ddq, *J* = 5.3, 7.5 x 3, 13.5 Hz, 1H), 1.48 (oct, *J* = 6.7 x 7 Hz, 1H), 2.43 (s, 3H), 2.72 (ddd, *J* = 6.8, 6.8, 12.4 Hz, 1H),

[6] Spectral data are in good agreement with those reported in the literature: (a) Padwa, A.; Kissel, W. S.; Eidell, C. K. *Can. J. Chem.* **2001**, *79*, 1681; (b) Boal, B. W.; Schammel, A. W.; Garg, N. K. *Org. Lett.* **2009**, *11*, 3458; (c) Schammel, A. W.; Boal, B. W.; Zu, L.; Mesganaw, T.; Garg N. *Tetrahedron* **2010**, *66*, 4687.

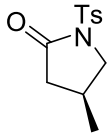
[7] Spectral data are in good agreement with those reported in the literature for the racemic compund: Zhu, M.; Fujita, K.-I.; Yamaguchi, R. *Org. Lett.* **2010**, *12*, 1336.

[8] This compound was obtained from L-isoleucine according the procedure reported in the literature: Hashimoto, M.; Eda, Y.; Osanai, Y.; Iwai, T.; Aoki, S. *Chem. Lett*. **1986**, 893.

2.84 (ddd, *J* = 6.3, 6.3, 12.3 Hz, 1H), 4.66 (t, *J* = 6.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ11.4 (CH_3), 17.3 (CH_3), 21.8 (CH_3), 27.0 (CH_2), 35.1 (CH), 49.1 (CH_2), 127.5 (2 x CH), 130.0 (2 x CH), 137.6 (C), 143.6 (C); MS (ESI$^+$) *m/z* (rel intensity) 264 (M^++ Na, 100); HRMS calcd for $C_{12}H_{19}NO_2NaS$, 264.1034, found 264.1032.



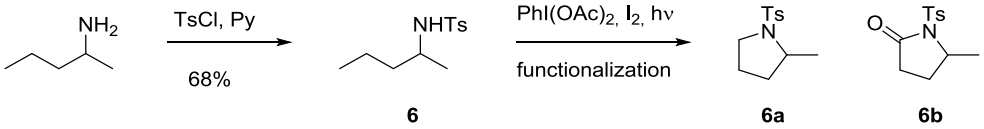
(*S*)-3-Methyl-1-tosylpyrrolidine [(3*S*)-4a]:[9] Crystalline solid: Mp 87–91 ºC (hexane/Et_2O); [α]$_D$ -8.51 (*c* 1.6); ^{1}H NMR δ0.91 (d, *J* = 6.9 Hz, 3H), 1.35 (dddd, *J* = 8.3, 8.3, 8.3, 12.3 Hz, 1H), 1.90 (dddd, *J* = 4.2, 7.3, 7.3, 12.3 Hz, 1H), 2.08-2.16 (m, 1H), 2.43 (s, 3H), 2.75 (dd, *J* = 7.8, 9.7 Hz, 1H), 3.22 (ddd, *J* = 7.1, 8.2, 9.8 Hz, 1H), 3.34 (ddd, *J* = 4.0, 8.3, 9.7 Hz, 1H), 3.42 (dd, *J* = 7.1, 9.5 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR δ18.0 (CH_3), 21.9 (CH_3), 33.6 (CH_2), 33.7 (CH), 48.0 (CH_2), 55.1 (CH_2), 127.9 (2 x CH), 130.0 (2 x CH), 134.6 (C), 143.6 (C); MS (ESI$^+$) *m/z* (rel intensity) 262 (M^++ Na, 100); HRMS calcd for $C_{12}H_{17}NO_2NaS$, 262.0878, found 262.0877.



(*S*)-4-Methyl-1-tosylpyrrolidin-2-one (5c):[10] Crystalline solid: Mp 87–88 ºC (hexane/Et_2O); [α]$_D$ +10.0 (*c* 0.9); ^{1}H NMR δ1.09 (d, *J* = 6.6 Hz, 3H), 2.07 (dd, *J* = 7.4, 16.7 Hz, 1H), 2.44 (s, 3H), 2.42-2.52 (m, 1H), 2.57 (dd, *J* = 7.9, 16.7 Hz, 1H), 3.42 (dd, *J* = 6.4, 9.8 Hz, 1H), 4.03 (dd, *J* = 7.3, 9.7 Hz, 1H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ18.1 (CH_3), 22.0 (CH_3), 27.2 (CH), 40.8 (CH_2), 54.4 (CH_2), 128.4 (2 x CH), 130.1 (2 x CH), 135.7 (C), 145.5 (C), 173.3 (C); MS (ESI$^+$) *m/z* (rel intensity) 276 (M^++ Na, 100); HRMS calcd for $C_{12}H_{15}NO_3NaS$, 276.0670, found 276.0676.

Synthesis and Functionalization of Tosylamine 6:

Table *S6*.

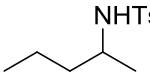


	entry	substrate **6**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives equiv	[C] M	temp[d] ºC	time h	yield %[e]	**6a** %[f]	**6b** %[f]	products ratio[g]
[table 1]	1		GP1	4.5, 4.5	7	-	0.1	70	5	65	65	-	1:0
	2		GP2	5	0.6, 3	$NaHCO_3$[h]	0.03	25	4	56	-	56	0:1

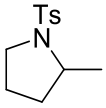
[a] millimoles per millimol of **6**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w.

[9] Spectral data are in good agreement with those reported in the literature: reference 5a.

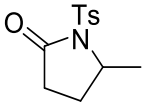
[10] This ^{1}H NMR spectral data was in good agreement with that reported in the literature: Ozaki, S.; Matsushita, H.; Ohmori, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2339.



***rac*-4-Methyl-*N*-(pentan-2-yl)benzenesulfonamide (6)**:[11] According to GP5, *N*-tosylamine **6** was prepared from pentan-2-amine (1.85 g, 21.27 mmol) in 68% as a crystalline solid: ^{1}H NMR δ 0.79 (t, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 1.15-1.40 (m, 4H), 2.42 (s, 3H), 3.25-3.35 (m, 1H), 4.48 (br s, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR δ 14.1 (CH_3), 19.1 (CH_2), 21.9 (CH_2), 22.0 (CH_3), 40.0 (CH_2), 50.1 (CH), 127.4 (2 x CH), 130.0 (2 x CH), 138.8 (C), 143.4 (C); MS (ESI$^+$) *m/z* (rel intensity) 264 (M^++ Na, 100); HRMS calcd for $C_{12}H_{19}NO_2NaS$, 264.1034, found 264.1032.



***rac*-2-Methyl-1-tosylpyrrolidine (6a):**[12] Crystalline solid: Mp 95–95.5 ºC (Et_2O); ^{1}H NMR δ 1.31 (d, *J* = 6.4 Hz, 3H), 1.45-1.57 (m, 2H), 1.64-1.74 (m, 1H), 1.77-1.88 (m, 1H), 2.43 (s, 3H), 3.15 (ddd, *J* = 7.3, 7.3, 10.3 Hz, 1H), 3.44 (ddd, *J* = 4.9, 7.1, 10.0 Hz, 1H), 3.71 (ddq, *J* = 4.0, 6.6, 6.6, 6.6, 7.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ 21.9 (CH_3), 23.2 (CH_3), 24.3 (CH_2), 33.9 (CH_2), 49.4 (CH_2), 56.5 (CH), 127.9 (2 x CH), 130.0 (2 x CH), 135.5 (C), 143.5 (C); MS (ESI$^+$) *m/z* (rel intensity) 262 (M^++ Na, 100); HRMS calcd for $C_{12}H_{17}NO_2NaS$, 262.0878, found 262.0877.



***rac*-5-Methyl-1-tosylpyrrolidin-2-one (6b):**[13] Crystalline solid: Mp 135–136 ºC (*n*-hexane/ Et_2O); ^{1}H NMR δ 1.46 (d, *J* = 6.4 Hz, 3H), 1.69-1.75 (m, 1H), 2.21-2.31 (m, 1H), 2.35 (ddd, *J* = 2.5, 9.3, 17.3 Hz, 1H), 2.43 (s, 3H), 2.56 (ddd, *J* = 8.9, 10.5, 17.2 Hz, 1H), 4.52 (ddq, *J* = 2.1, 6.4, 6.4, 6.4, 8.2 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 21.9 (CH_3), 22.0 (CH_3), 27.0 (CH_2), 30.9 (CH_2), 56.8 (CH), 128.7 (2 x CH), 129.9 (2 x CH), 136.6 (C), 145.3 (C), 173.7 (C); MS (ESI$^+$) *m/z* (rel intensity) 276 (M^++ Na, 100); HRMS calcd for $C_{12}H_{15}NO_3NaS$, 276.0670, found 276.0676.

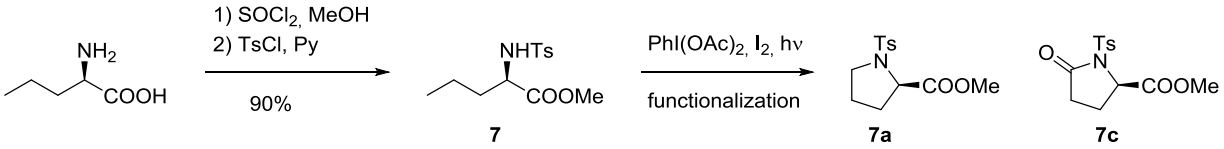
[11] Spectral data are in good agreement with those reported in the literature: Bossart, M.; Faessler, R.; Schoenberger, J.; Studer, A. *Eur. J. Org. Chem.* **2002**, 2742.

[12] Spectral data are in good agreement with those reported in the literature: (a) Andrés, J. M.; Herráiz-Sierra, I.; Pedrosa, R.; Pérez-Encabo, A. *Eur. J. Org. Chem.* **2000**, 1719; (b) Kato, Y.; Yen, D. H.; Fukudome, Y.; Hata, T.; Urabe, H. *Org. Lett.* **2010**, *12*, 4137.

[13] Spectral data are in good agreement with those reported in the literature: Wang, J.; Hou, Y. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1919.

Synthesis and Functionalization of Tosylamine 7:

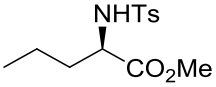
Table *S7*.



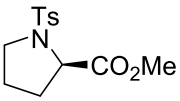
[table 1]

entry	substrate 7	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] °C	time h	yield %[e]	**7a** %[f]	**7c** %[f]	products ratio[g]
1		GP1	4.5, 4.5	5	-	0.1	70	5	86[h]	86	-	1:0
2		GP1	3, 3	1	CSA, 10%	0.04	70	10	60	60	-	1:0
3		GP2	7	1.2, 4	$NaHCO_3$[i]	0.03	25	20	82	9	73	1:9
4		GP3	6	1.4	$NaHCO_3$[i]	0.03	25	20	83	-	83	0:1

[a] millimoles per millimol of **7**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] calculated by integration in the ^{1}H NMR of the crude of reaction; [h] starting material **7** was recovered in 12%; [i] 100% w/w.



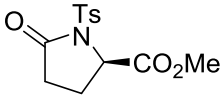
(*S*)-Methyl 2-(4-methylphenylsulfonamido)pentanoate (7): A solution of D-norvaline (1.17 g, 9.95 mmol) in MeOH (60 mL) was treated at 0 ºC with $SOCl_2$ (1.44 mL, 19.9 mmol). The mixture was refluxed for 4 h and concentrated to give the crude methyl ester as viscous oil. The product was dissolved in pyridine (47 mL), TsCl (5.69 g, 29.85 mmol) was added and the mixture was heated at 40 ºC for 24 h. The mixture was concentrated, dissolved in EtOAc and washed with diluted aqueous solution of HCl (10%). The organic extract was washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 75:25) of the residue afforded the corresponding compound **7** (2.56 g, 8.98 mmol, 90%) as a crystalline solid: Mp 57.5-58.5 ºC (hexane/AcOEt); $[\alpha]_D$ -18.1 (*c* 1.3); ^{1}H NMR δ0.87 (t, *J* = 7.3 Hz, 3H), 1.36 (sxt, *J* = 7.5 x 5 Hz, 2H), 1.55-1.73 (m, 2H), 2.41 (s, 3H), 3.48 (s, 3H), 3.91 (ddd, *J* = 5.3, 7.7, 9.3 Hz, 1H), 5.19 (d, *J* = 9.5 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ13.7 (CH_3), 18.6 (CH_2), 21.9 (CH_3), 35.8 (CH_2), 52.7 (CH_3), 55.9 (CH), 127.7 (2 x CH), 130.0 (2 x CH), 137.3 (C), 144.0 (C), 172.7 (C); MS (ESI$^+$) *m/z* (rel intensity) 308 (M^++ Na, 100); HRMS calcd for $C_{13}H_{19}NO_4NaS$, 308.0932, found 308.0934.



(*R*)-Methyl 1-tosylpyrrolidine-2-carboxylate (7a):[14] Crystalline solid: Mp 75.5-75.7 ºC (hexane/Et_2O); $[\alpha]_D$ +82.7 (*c* 1.5); ^{1}H NMR δ1.70-1.78 (m, 1H), 1.91-2.04 (m, 3H), 2.43 (s, 3H), 3.30 (ddd, *J* = 7.1, 7.1, 9.5 Hz, 1H), 3.49 (ddd, *J* = 4.7, 7.2, 9.8 Hz, 1H), 3.71 (s, 3H), 4.28 (dd, *J* = 4.6, 8.0 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ21.5 (CH_3), 24.6 (CH_2), 30.9 (CH_2), 48.5 (CH_2), 52.3 (CH_3), 60.4 (CH), 127.5 (2 x CH), 129.7 (2 x CH), 135.2 (C), 143.7 (C), 172.6

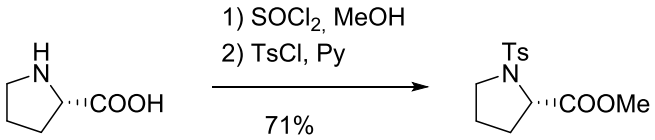
[14] Spectral data are consistent with previously published literature values of its enantiomer: Lalonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F.D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

(C); MS (ESI$^+$) *m/z* (rel intensity) 306 (M^++ Na, 100); HRMS calcd for $C_{13}H_{17}NO_4NaS$, 306.0776, found 306.0776.

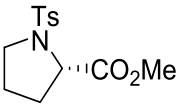


(*R*)-Methyl 5-oxo-1-tosylpyrrolidine-2-carboxylate (7c): Crystalline solid: Mp 119.5-121.5 ºC (Et_2O); $[\alpha]_D$ +44.1 (*c* 1.5); ^{1}H NMR (500 MHz) δ 2.09-2.14 (m, 1H), 2.39-2.48 (m, 2H), 2.44 (s, 3H), 2.51-2.57 (m, 1H), 3.78 (s, 3H), 4.89 (dd, *J* = 2.7, 8.7 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.96 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz) δ 21.7 (CH_3), 23.3 (CH_2), 30.5 (CH_2), 52.9 (CH_3), 59.4 (CH), 129.1 (2 x CH), 129.4 (2 x CH), 135.0 (C), 145.4 (C), 171.3 (C), 172.7 (C); MS (ESI+) *m/z* (rel intensity) 320 (M^++ Na, 100); HRMS calcd for $C_{13}H_{15}NO_5NaS$, 320.0569, found 320.0572.

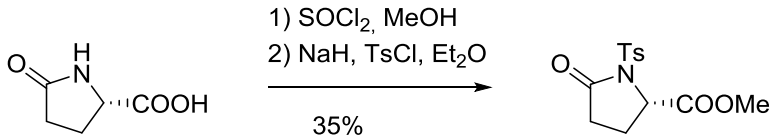
Synthesis of the enantiomers of 7a and 7c [(*S*)-7a and (*S*)-7c]:



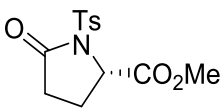
(*S*)-**7a**



(*S*)-Methyl 1-tosylpyrrolidine-2-carboxylate [(*S*)-7a]: A solution of L-proline (234 mg, 2.03 mmol) in MeOH (12 mL) was treated at 0 ºC with $SOCl_2$ (0.3 mL, 4.14 mmol). The mixture was refluxed for 4 h and concentrated to give the crude methyl ester as viscous oil. The product was dissolved in pyridine (8 mL), TsCl (450 mg, 2.36 mmol) was added and the mixture was heated at 40 ºC for 24 h. The mixture was concentrated, dissolved in EtOAc and washed with diluted aqueous solution of HCl (10%). The organic extract was washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 75:25) of the residue afforded the corresponding L-proline derivative (*S*)-**7a** (408 mg, 1.44 mmol, 71%) as a crystalline solid: Mp 75.0-75.5 ºC (hexane/Et_2O); $[\alpha]_D$ -82.7 (*c* 1.5) [Literature: -73.3 (c 1.0);[14] -93.3 (c 1.5)[15]]



(*S*)-**7c**



(*S*)-Methyl 5-oxo-1-tosylpyrrolidine-2-carboxylate [(*S*)-7c]: 1st step: A solution of (*S*)-2-pyrrolidinone-5-carboxylic acid (195 mg, 1.51 mmol) in MeOH (30 mL) was treated at 0 ºC with $SOCl_2$ (110 μL, 1.51 mmol). The mixture was stirred at rt for 40 min, then neutralized with amberjet 4400-OH resin, filtered and concentrated. The crude product was purified by silica gel column

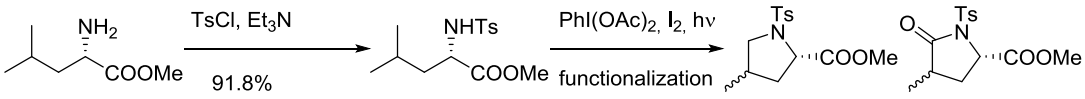
[15] Fujita, Y.; Gottlieb, A.; Peterkofsky, B.; Udenfriend, S.; Witkop, B. *J. Am. Chem. Soc.* **1964**, *86*, 4709.

chromatography (DCM/MeOH, 95:5) to afford the corresponding methyl ester (125 mg, 0.876 mmol, 58%) as viscous oil.

2nd step: To a suspension of NaH (60% in oil, 29 mg, 0.724 mmol) in dry ether (1 mL) were added at 0 ºC the previously obtained methyl ester (94 mg, 0.658 mmol) in dry ether (5 mL) and TsCl (125 mg, 0.658 mmol) in dry CH_2Cl_2 (2 mL). The reaction mixture was worked up according to the usual manner. The crude product was purified by silica gel column chromatography (hexane/AcOEt, 75:25) to give (*S*)-**7a** (117 mg, 0.39 mmol, 60%) as a crystalline solid: Mp 121.5–123.2 ºC (hexane/CH_2Cl_2); $[\alpha]_D$ -46.6 (*c* 1.6).

Synthesis and Functionalization of Tosylamine 8:

Table *S8*.

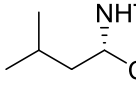


8 **8a**(*syn*/*anti*) **8c**(*syn*/*anti*)

[table 1]

entry	substrate **8**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] ºC	time h	yield %[e]	**8a**(*syn*/*anti*) %[f]	**8c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	3, 3	5	-	0.1	70	4.5	89	81(1:1.4)	8(1:0)	3.3:5:1:0
2		GP2	7	1, 6	$NaHCO_3$[h]	0.03	25	7	72	-	72(1.1:1)	0:0:1.1:1
3		$GP1_{CSA}$	2.5, 2.5	0.6	CSA, 1	0.1	70	3	92	92(1.1:1)	-	1.1:1:0:0
4		$GP1_{Zn(OTf)2}$	3, 3	0.5	$Zn(TfO)_2$, 0.6	0.1	70	4	88	88(1:1)	-	1:1:0:0
5		GP1	3, 3	3	$Zn(TfO)_2$, 0.6	0.1	70	4	85	85(1:1)	-	1:1:0:0
6		GP1	3, 3	3	$Zn(TfO)_2$, 0.6	0.1	-20	4	0	no reaction		-
7		GP3	3	0.5	$Zn(TfO)_2$, 1	0.2	30	4	85	85(1.2:1)	-	1.2:1:0:0
8		GP1	3, 3	-	$Zn(TfO)_2$, 0.6	0.1	70	4	0	no reaction		-
9		GP1	3, 3	0.5	-	0.1	70	4	nd	60% reaction completed		0.8:3:2.3:1

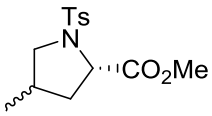
[a] millimoles per millimol of **9**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**9a**-*syn*/**9a**-*anti*/**9c**-*syn*/**9c**-*anti*/**9A**) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w. nd = not determined.



(*S*) Methyl 4-methyl-2-(4-methylphenylsulfonamido)pentanoate (8):[16] TsCl (4.24 g, 22.25 mmol) was added to a solution of L-leucine methyl ester hydrochloride (2.02 g, 11.13 mmol) and Et_3N (6 mL, 41.72 mmol) in dry DCM (50 mL) at 0 ºC and stirred at rt for 3 h. The reaction mixture was poured into a diluted aqueous solution of HCl (10%) and extracted twice with EtOAc. The organic extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous $NaSO_4$ and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 90:10) of the residue afforded the corresponding sulfonamide **8** (3.05 g, 10.21 mmol, 91.8%) as crystalline solid: Mp 49.4-50.2 ºC (hexane/Et_2O); $[\alpha]_D$ +7.3 (*c* 1.5); ^{1}H NMR δ0.88 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 1.48 (ddd, *J* = 0.8, 6.5, 7.8 Hz, 2H), 1.78 (non, *J* = 6.7 x 8 Hz, 1H), 2.42 (s, 3H), 3.44 (s, 3H), 3.93 (ddd, *J* = 6.2, 8.1, 10.1 Hz, 1H), 5.10 (br s, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ21.8

[16] Spectral data are in good agreement with those reported in the literature: Ordóñez, M.; Cruz-Cordero, R.; Fernández-Zertuche, M.; Muñoz-Hernández, M. A.; García-Barradas, O. *Tetrahedron: Asymmetry* **2004**, *15*, 3035.

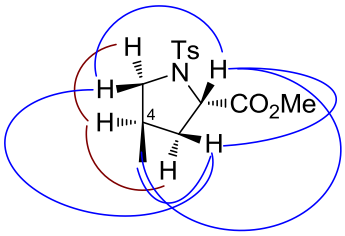
(CH_3), 21.9 (CH_3), 23.1 (CH_3), 24.7 (CH), 42.8 (CH_2), 52.6 (CH_3), 54.8 (CH), 127.7 (2 x CH), 129.9 (2 x CH), 137.2 (C), 144.0 (C), 173.1 (C); MS (ESI+) *m/z* (rel intensity) 322 (M^++ Na, 100); HRMS calcd for $C_{14}H_{21}NO_4NaS$, 322.1089, found 322.1101.



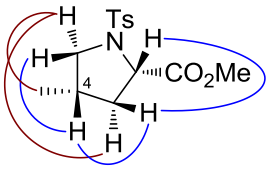
(2*S*) Methyl 4-methyl-1-tosylpyrrolidine-2-carboxylate (8a). Colorless oil: NMR showed a mixture of isomers (4*R*/4*S*)-**8a** in 7.2:1 ratio. (4*R*)-**8a**: ^{1}H NMR δ0.90 (d, *J* = 6.6 Hz, 3H), 1.64 (ddd, *J* = 9.6, 9.6, 12.6 Hz, 1H), 2.07 (ddd, *J* = 3.0, 6.3, 12.8 Hz, 1H), 2.43 (s, 3H), 2.42-2.48 (m, 1H), 2.81 (dd, *J* = 8.8, 8.8 Hz, 1H), 3.58 (dd, *J* = 7.1, 9.0 Hz, 1H), 3.71 (s, 3H), 4.34 (dd, *J* = 3.0, 9.0 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ17.2 (CH_3), 21.9 (CH_3), 32.9 (CH), 38.9 (CH_2), 52.7 (CH_3), 55.3 (CH_2), 60.7 (CH), 127.9 (2 x CH), 130.0 (2 x CH), 135.7 (C), 143.9 (C), 173.0 (C). (4*S*)-**8a**: ^{1}H NMR δ0.99 (d, *J* = 6.3 Hz, 3H), 1.59 (ddd, *J* = 8.8, 10.4, 12.6 Hz, 1H), 1.95 (ddq, *J* = 6.7 x 3, 9.9, 9.9 Hz, 1H), 2.34 (ddd, *J* = 7.3, 7.3, 12.6 Hz, 1H), 2.43 (s, 3H), 2.97 (dd, *J* = 9.8, 10.4 Hz, 1H), 3.54-3.62 (m, 1H), 3.75 (s, 3H), 4.25 (dd, *J* = 7.9, 8.8 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ17.0 (CH_3), 21.9 (CH_3), 33.9 (CH), 39.2 (CH_2), 52.7 (CH_3), 55.6 (CH_2), 61.4 (CH), 127.9 (2 x CH), 130.0 (2 x CH), 135.9 (C), 143.9 (C), 173.1 (C).

MS (ESI+) *m/z* (rel intensity) 320 (M^++ Na, 100); HRMS calcd for $C_{14}H_{19}NO_4NaS$, 320.0932, found 320.0935.

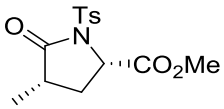
Main correlations observed by NOESY are shown in the figure:



(4*R*)



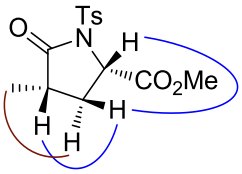
(4*S*)

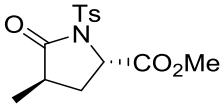


(2*S*,4*S*) Methyl 4-methyl-5-oxo-1-tosylpyrrolidine-2-carboxylate (*syn*-8c): Colorless oil: $[\alpha]_D$ -32.4 (*c* 0.5); ^{1}H NMR (500 MHz) δ1.17 (d, *J* = 6.9 Hz, 3H), 1.70 (ddd, *J* = 7.3, 7.3, 12.5 Hz, 1H), 2.44 (s, 3H), 2.54-2.64 (m, 1H), 2.65 (ddd, *J* = 8.8, 8.8, 12.6 Hz, 1H), 3.83 (s, 3H), 4.75 (dd, *J* = 6.9, 8.2 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz) δ15.8 (CH_3), 21.8 (CH_3), 31.1 (CH_2), 37.1 (CH), 52.9 (CH_3), 58.0 (CH), 129.2 (2 x CH), 129.4 (2 x CH), 135.1 (C), 145.4 (C), 171.7 (C), 175.4 (C).

^{1}H NMR (500 MHz, C_6D_6) δ0.69 (d, *J* = 7.3 Hz, 3H), 1.07 (ddd, *J* = 7.1, 8.3, 12.7 Hz, 1H), 1.61 (ddd, *J* = 8.7, 8.7, 12.7 Hz, 1H), 1.68-1.78 (m, 1H), 1.77 (s, 3H), 3.37 (s, 3H), 4.51 (dd, *J* = 7.1, 8.4 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 2H), 8.31 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125.7 MHz, C_6D_6) δ15.2 (CH_3), 20.8 (CH_3), 30.5 (CH_2), 36.5 (CH), 51.8 (CH_3), 57.7 (CH), 128.9 (2 x CH), 129.5 (2 x CH), 136.0 (C), 144.5 (C), 171.7 (C), 174.6 (C); MS (ESI+) *m/z* (rel intensity) 334 (M^++ Na, 100); HRMS calcd for $C_{14}H_{17}NO_5NaS$, 334.0725, found 334.0725.

Main correlations observed by NOESY (in C_6D_6) are shown in the figure:

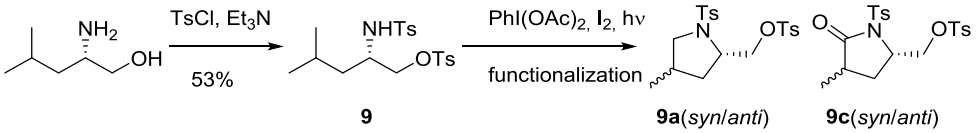




(2*S*,4*R*) Methyl 4-methyl-5-oxo-1-tosylpyrrolidine-2-carboxylate (*anti*-8c): [data obtained from the mixture (*anti/syn*)-**8c**; 1.0:1.7]: ^{1}H NMR δ1.15 (d, J = 7.2 Hz, 3H), 2.07 (ddd, J = 9.3, 11.9, 13.8 Hz, 1H), 2.35 (ddd, J = 1.2, 8.2, 13.8 Hz, 1H), 2.44 (s, 3H), 2.54-2.69 (m, 1H), 3.79 (s, 3H), 4.86 (dd, J = 1.2, 9.3 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.97 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ14.5 (CH_3), 21.7 (CH_3), 32.2 (CH_2), 36.1 (CH), 52.8 (CH_3), 57.3 (CH), 129.1 (2 x CH), 129.2 (2 x CH), 134.7 (C), 145.3 (C), 171.6 (C), 175.3 (C).

Synthesis and Functionalization of Tosylamine 9:

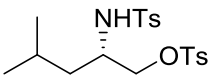
Table S9.



[table 1]

entry	substrate **9**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] °C	time h	yield %[e]	**9a**(*syn*/*anti*) %[f]	**9c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	1.5, 1.5	5	-	0.1	40	10	77	72(1:1.7)	5(1:0)	9:6:1:0:0
2		GP2	7	1.2, 6	$NaHCO_3$[h]	0.02	25	10	88	-	88(2.8:1)	0:0:3.7:1:0
3		GP3	5	1.2	$NaHCO_3$[h]	0.02	25	12	79	-	79(2.7:1)	0:0:2.6:1:0

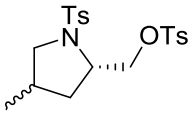
[a] millimoles per millimol of **9**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 °C (reaction mixture refrigerated by a fan) and 65-75 °C (without fan); [e] total isolated yield; [f] isolated yield; [g] (**9a**-*syn*/**9a**-*anti*/**9c**-*syn*/**9c**-*anti*) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w.



(*S*)-4-Methyl-2-(4-methylphenylsulfonamido)pentyl 4-methylbenzenesulfonate (9):[17] According to GP5, *N*-tosylamine **9** was prepared from L-leucinol (1 mmol) employing TsCl (2.2 mmol) in 53% as a crystalline solid: Mp 100.5-102.0 °C (hexane/Et_2O); $[\alpha]_D$ –47.6 (*c* 1.0); ^{1}H NMR δ0.58 (d, J = 6.5 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H), 1.26 (dd, J = 7.0, 7.0 Hz, 2H), 1.36-1.46 (m, 1H), 2.41 (s, 3H), 2.44 (s, 3H), 3.36-3.46 (m, 1H), 3.83 (dd, J = 4.8, 9.9 Hz, 1H), 3.94 (dd, J = 3.5, 10.0 Hz, 1H), 5.01 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), ^{13}C NMR δ21.9 (2 x CH_3), 22.0 (CH_3), 23.1 (CH_3), 24.4 (CH), 41.2 (CH_2), 51.0 (CH), 72.0 (CH_2), 127.4 (2 x CH), 128.4 (2 x CH), 130.1 (2 x CH), 130.3 (2 x CH), 132.9 (C), 138.0 (C), 143.9

[17] Spectral data are in good agreement with those reported in the literature: Craven, A. P.; Dyke, H. J.; Thomas, E. J. *Tetrahedron* **1989**, *45*, 2417.

(C), 145.5 (C); MS (ESI+) *m/z* (rel intensity) 448 (M^++ Na, 100); HRMS calcd for $C_{20}H_{27}NO_5NaS_2$, 448.1228, found 448.1224.

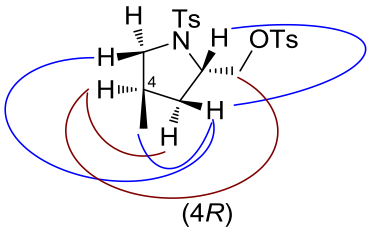


(2*S*)-4-Methyl-1-tosylpyrrolidin-2-yl)methyl 4-methylbenzenesulfonate (**9a**): Colorless oil. NMR showed a mixture of isomers (*anti*/*syn*)-**9a** in 1.7:1 ratio. ***Anti*-9a**: ^{1}H NMR δ0.84 (d, *J* = 6.6 Hz, 3H), 1.20 (ddd, *J* = 8.8, 11.0, 12.9 Hz, 1H), 1.98 (dd, *J* = 6.3, 13.2 Hz, 1H), 2.26-2.35 (m, 1H), 2.44 (s, 3H), 2.47 (s, 3H), 2.49 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.49 (dd, *J* = 6.6, 9.1 Hz, 1H), 3.75-3.78 (m, 1H), 3.97 (dd, *J* = 8.2, 10.1 Hz, 1H), 4.23 (dd, *J* = 3.5, 9.8 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H) 7.82 (d, *J* = 8.2 Hz, 2H), ^{13}C NMR δ16.7 (CH_3), 21.6 (CH_3), 21.7 (CH_3), 31.4 (CH), 36.4 (CH_2), 55.9 (CH_2), 57.9 (CH), 71.5 (CH_2), 127.7 (2 x CH), 128.1 (2 x CH), 129.8 (2 x CH), 130.0 (2 x CH), 132.7 (C), 133.3 (C), 143.9 (C), 145.1 (C).

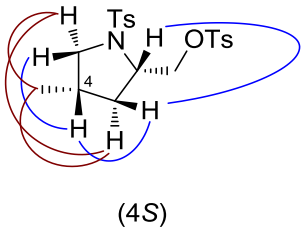
***Syn*-9a**: ^{1}H NMR δ0.90 (d, *J* = 6.6 Hz, 3H), 1.42 (ddd, *J* = 8.5, 11.0, 12.6 Hz, 1H), 1.48-1.58 (m, 1H), 2.10 (ddd, *J* = 6.5, 6.5, 12.5 Hz, 1H), 2.43 (s, 3H), 2.47 (s, 3H), 2.83 (dd, *J* = 10.4, 11.4 Hz, 1H), 3.47-3.49 (m, 1H), 3.70-3.76 (m, 1H), 4.04 (dd, *J* = 7.6, 9.8 Hz, 1H), 4.41 (dd, *J* = 3.8, 9.8 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H) 7.82 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ16.4 (CH_3), 21.6 (CH_3), 21.7 (CH_3), 32.7 (CH), 37.8 (CH_2), 56.3 (CH_2), 58.6 (CH), 72.6 (CH_2), 127.6 (2 x CH), 128.1 (2 x CH), 129.9 (2 x CH), 130.0 (2 x CH), 132.8 (C), 134.4 (C), 143.8 (C), 145.0 (C).

MS (ESI+) *m/z* (rel intensity) 446 (M^++ Na, 100); HRMS calcd for $C_{20}H_{25}NNaO_5S_2$, 446.1072, found 446.1062.

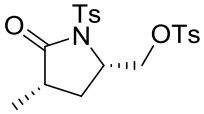
Main correlations observed by NOESY are shown in the figure:



(4*R*)



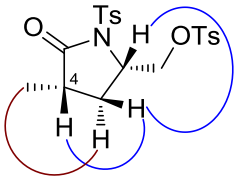
(4*S*)



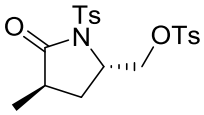
[(2*S*,4*S*)-4-Methyl-5-oxo-1-tosylpyrrolidin-2-yl]methyl 4-methylbenzenesulfonate (***syn*-9c**): Crystalline solid: Mp 172.5-174.0 ºC (hexane/CH_2Cl_2); $[\alpha]_D$ -18.9 (*c* 3.0); ^{1}H NMR (500 MHz) δ1.16 (d, *J* = 6.6 Hz, 3H), 1.61-1.68 (m, 2H), 2.44 (s, 3H), 2.40-2.50 (m, 1H), 2.47 (s, 3H), 4.36-4.42 (m, 3H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H) 7.86 (d, *J* = 8.2 Hz, 2H); ^{1}H NMR (500 MHz, C_6D_6) δ0.76 (d, *J* = 7.3 Hz, 3H), 1.10 (ddd, *J* = 6.3, 8.2, 13.2 Hz, 1H), 1.52 (ddd, *J* = 8.2, 10.2, 13.2 Hz, 1H), 1.64-1.74 (m, 1H), 1.80 (s, 3H), 1.83 (s, 3H), 3.92-4.00 (m, 1H), 4.23 (dd, *J* = 2.7, 10.3 Hz, 1H), 4.40 (dd, *J* = 5.4, 10.4 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 7.9 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H) 8.07 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz) δ 16.0 (CH_3), 21.7 (2 x CH_3), 29.2 (CH_2), 36.4 (CH), 55.9 (CH), 70.0 (CH_2), 128.0 (2 x CH), 128.4 (2 x CH), 129.6 (2 x

CH), 130.1 (2 x CH), 132.3 (C), 135.1 (C), 145.4 (2 x C), 176.5 (C); MS (ESI+) *m/z* (rel intensity) 460 (M^++ Na, 100); HRMS calcd for $C_{20}H_{23}NNaO_6S_2$, 460.0865, found 460.0873.

Main correlations observed by NOESY (in C_6D_6) are shown in the figure:

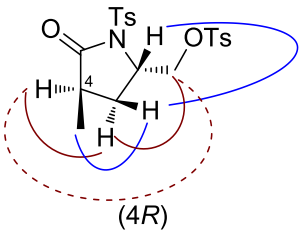


(4*S*)



[(2*S*,4*R*)-4-Methyl-5-oxo-1-tosylpyrrolidin-2-yl]methyl 4-methylbenzenesulfonate (***anti*-9c**): Crystalline solid: Mp 163.0-164.5 ºC (hexane/CH_2Cl_2); $[\alpha]_D$ -9.6 (*c* 1.6); ^{1}H NMR δ 1.08 (d, *J* = 6.9 Hz, 3H), 1.85 (ddd, *J* = 9.0, 12.4, 12.4 Hz, 1H), 2.28 (dd, *J* = 8.8, 12.3 Hz, 1H), 2.44 (s, 3H), 2.47 (s, 3H), 2.71-2.75 (m, 1H), 4.26 (dd, *J* = 2.5, 10.4 Hz, 1H), 4.38 (dd, *J* = 4.4, 10.4 Hz, 1H), 4.41-4.48 (m, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H) 7.86 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 15.2 (CH_3), 21.7 (CH_3), 22.0 (CH_3), 31.2 (CH_2), 36.1 (CH), 55.4 (CH), 70.2 (CH_2), 127.9 (2 x CH), 128.4 (2 x CH), 129.6 (2 x CH), 130.1 (2 x CH), 132.2 (C), 135.2 (C), 145.4 (C), 145.4 (C), 175.8 (C); MS (ESI+) *m/z* (rel intensity) 460 (M^++ Na, 100); HRMS calcd for $C_{20}H_{23}NNaO_6S_2$, 460.0865, found 460.0869.

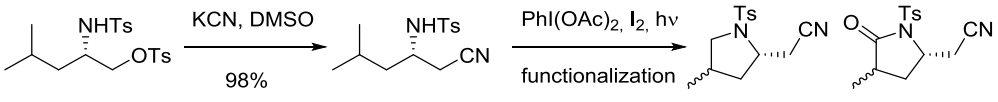
Main correlations observed by NOESY are shown in the figure:



(4*R*)

Synthesis and Functionalization of Tosylamine 10:

Table *S10*.

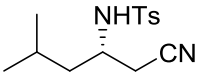


9 **10** **10a**(*syn*/*anti*) **10c**(*syn*/*anti*)

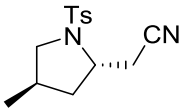
entry	substrate **10**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] ºC	time h	yield %[e]	**10a**(*syn*/*anti*) %[f]	**10c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	3, 3	5	-	0.1	70	4	72	32(1:2.8)	40(4:1)	1:3.4:4.8:1.6
2		GP1$_{CSA}$	2.5, 2.5	0.6	CSA, 1	0.1	70	3.5	86	86(1.25:1)	-	1.25:1:0:0
3		GP2	7	0.6, 4	$NaHCO_3$[h]	0.03	25	6	72	-	72(2.5:1)	0:0:2.5:1

[table 1]

[a] millimoles per millimol of **10**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**10a**-*syn*/**10a**-*anti*/**10c**-*syn*/**10c**-*anti*) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 100% w/w.

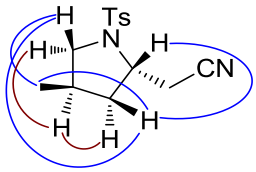


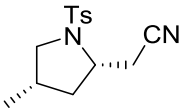
(*S*)-*N*-(1-Cyano-4-methylpentan-2-yl)-4-methylbenzenesulfonamide (10): KCN (217 mg, 3.34 mmol) was added to a solution of **10** (710 mg, 1.67 mmol) in DMSO (4 mL) and stirred at rt for 5 h. The reaction mixture was poured into brine and extracted with EtOAc. The organic phase was dried with Na_2SO_4, filtrated and concentrated. The residue was purified by column chromatography (hexanes/EtOAc, 60:40) to afford the product **10** (435 mg, 1.64 mmol, 98%) as a crystalline solid: Mp 83.0-83.5 ºC (hexane/Et_2O); $[\alpha]_D$ -75.5 (*c* 1.6); ^{1}H NMR δ0.61 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H), 1.30-1.40 (m, 1H), 1.42-1.52 (m, 2H), 2.44 (s, 3H), 2.51 (dd, *J* = 3.5, 16.7 Hz, 1H), 2.63 (dd, *J* = 6.1, 16.7 Hz, 1H), 3.45-3.54 (m, 1H), 5.03 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR δ21.6 (CH_3), 21.9 (CH_3), 23.1 (CH_3), 24.6 (CH), 25.7 (CH_2), 43.4 (CH_2), 48.7 (CH), 117.5 (C), 127.5 (2 x CH), 130.3 (2 x CH), 137.7 (C), 144.3 (C); MS (ESI+) *m/z* (rel intensity) 303 (M^++ Na, 100); HRMS calcd for $C_{14}H_{20}N_2O_2NaS$, 303.1143, found 303.1145.



2-[(2*S*,4*R*)-4-Methyl-1-tosylpyrrolidin-2-yl]acetonitrile (*anti*-10a): Colorless oil: $[\alpha]_D$ -72.7 (*c* 1.0); ^{1}H NMR δ0.87 (d, *J* = 6.4 Hz, 3H), 1.47 (ddd, *J* = 8.6, 10.3, 13.1 Hz, 1H), 1.99 (ddd, *J* = 2.5, 6.2, 13.1 Hz, 1H), 2.45 (s, 3H), 2.45-2.52 (m, 1H), 2.61 (dd, *J* = 9.1, 9.1 Hz, 1H), 2.77 (dd, *J* = 8.1, 16.8 Hz, 1H), 2.88 (dd, *J* = 3.7, 16.7 Hz, 1H), 3.60 (dd, *J* = 6.4, 9.0 Hz, 1H), 3.85 (dddd, *J* = 3.1, 3.1, 8.4, 8.4, 1H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ17.1 (CH_3), 21.9 (CH_3), 25.8 (CH_2), 31.7 (CH), 39.3 (CH_2), 56.3 (CH), 56.5 (CH_2), 117.9 (C), 128.1 (2 x CH), 130.3 (2 x CH), 133.9 (C), 144.5 (C); MS (ESI+) *m/z* (rel intensity) 301 (M^++ Na, 100); HRMS calcd for $C_{14}H_{18}N_2O_2NaS$, 301.0987, found 301.0989.

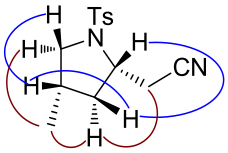
Main correlations observed by NOESY are shown in the figure:

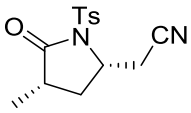




2-[(2*S*,4*S*)-4-Methyl-1-tosylpyrrolidin-2-yl]acetonitrile (*syn*-10a): Colorless oil: $[\alpha]_D$ -88.5 (*c*, 1.0); ^{1}H NMR δ0.96 (d, *J* = 6.4 Hz, 3H), 1.49 (ddd, *J* = 9.3, 11.6, 12.5 Hz, 1H), 1.59-1.69 (m, 1H), 2.25 (ddd, *J* = 6.1, 6.1, 12.2 Hz, 1H), 2.45 (s, 3H), 2.89 (dd, *J* = 6.6, 16.7 Hz, 1H), 2.95 (dd, *J* = 4.1, 16.8 Hz, 1H), 2.97 (d, *J* = 10.6 Hz, 1H), 3.56 (ddd, *J* = 1.3, 7.2, 11.4 Hz, 1H), 3.79 (dddd, *J* = 4.1, 6.8, 6.8, 9.2, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ16.6 (CH_3), 21.9 (CH_3), 25.7 (CH_2), 33.2 (CH), 40.6 (CH_2), 56.6 (CH_2), 57.1 (CH), 117.6 (C), 127.9 (2 x CH), 130.3 (2 x CH), 135.0 (C), 144.4 (C); MS (ESI+) *m/z* (rel intensity) 301 (M^++ Na, 100); HRMS calcd for $C_{14}H_{18}N_2O_2NaS$, 301.0987, found 301.0989.

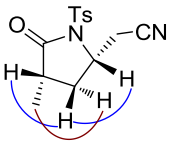
Main correlations observed by NOESY are shown in the figure:

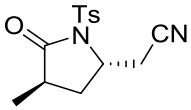




2-((2*S*,4*S*)-4-Methyl-5-oxo-1-tosylpyrrolidin-2-yl)acetonitrile (*syn*-10c): Crystalline solid: Mp 137.5-139.0 ºC (hexane/Et_2O); $[\alpha]_D$ -72.6 (*c* 1.0); ^{1}H NMR δ 1.23 (d, *J* = 7.0 Hz, 3H), 1.64 (ddd, *J* = 8.0, 9.8, 13.0 Hz, 1H), 2.45 (s, 3H), 2.48-2.56 (m, 1H), 2.65 (ddd, *J* = 7.5, 9.7, 13.0 Hz, 1H), 3.12 (dd, *J* = 3.7, 16.6 Hz, 1H), 3.18 (dd, *J* = 6.3, 16.6 Hz, 1H), 4.39 (dddd, *J* = 3.9, 6.4, 7.7, 7.7 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR δ 15.8 (CH_3), 22.1 (CH_3), 25.6 (CH_2), 33.0 (CH_2), 37.0 (CH), 54.0 (CH), 116.3 (C), 128.9 (2 x CH), 130.1 (2 x CH), 135.6 (C), 146.1 (C), 176.5 (C); MS (ESI+) *m/z* (rel intensity) 315 (M^++ Na, 100); HRMS calcd for $C_{14}H_{16}N_2O_3NaS$, 315.0779, found 315.0771.

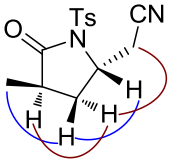
Main correlations observed by NOESY are shown in the figure:





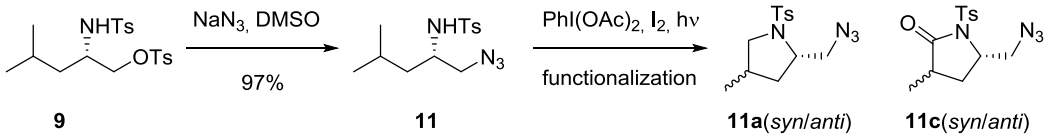
2-[(2*S*,4*R*)-4-Methyl-5-oxo-1-tosylpyrrolidin-2-yl]acetonitrile (*anti*-10c): Crystalline solid: Mp 123.5-124.0 ºC (hexane/Et_2O); $[\alpha]_D$ -46.8 (*c* 0.4); ^{1}H NMR δ 1.14 (d, *J* = 6.9 Hz, 3H), 2.01 (ddd, *J* = 8.7, 11.6, 13.5 Hz, 1H), 2.33 (ddd, *J* = 1.3, 8.7, 13.4 Hz, 1H), 2.45 (s, 3H), 2.82-2.92 (m, 1H), 2.98 (d, *J* = 5.5 Hz, 2H), 4.52 (dddd, *J* = 1.3, 5.0, 6.1, 8.8 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 15.3 (CH_3), 22.1 (CH_3), 24.2 (CH_2), 33.3 (CH_2), 35.9 (CH), 53.6 (CH), 116.8 (C), 128.7 (2 x CH), 130.2 (2 x CH), 135.4 (C), 146.2 (C), 175.4 (C); MS (ESI+) *m/z* (rel intensity) 315 (M^++ Na, 100); HRMS calcd for $C_{14}H_{16}N_2O_3NaS$, 315.0779, found 315.0771.

Main correlations observed by NOESY are shown in the figure:



Synthesis and Functionalization of Tosylamine 11:

Table S11.

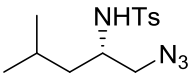


9 **11** **11a**(*syn*/*anti*) **11c**(*syn*/*anti*)

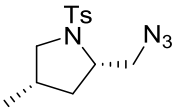
[table 1]

entry	substrate **11**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives equiv	[C] M	temp[d] °C	time h	yield %[e]	**11a**(*syn*/*anti*) %[f]	**11c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	3, 3	5	-	0.1	70	7	67	52(1.5:1)	15(1:1)	3.3:2:1:1.2
2		GP1	4, 8[h]	0.6	CSA, 1	0.03	70	10	65	38(1:2.8)	27(4:1)	1.5:3:3.3:1
3		$GP1_{CSA}$	5, 5	0.6	CSA, 1	0.1	70	8	59	36(1:3)	23(4.3:1)	1.7:5:3:1
4		GP2	7	1.5, 3	$NaHCO_3$[i]	0.03	25	4	68	68(2:1)	-	0:0:2.2:1

[a] millimoles per millimol of **11**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hopurs); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**11a**-*syn*/**11a**-*anti*/**11c**-*syn*/**11c**-*anti*) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] Portionwise (0.25 equiv / 30 min); [i] 100% w/w.

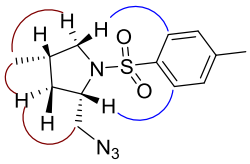


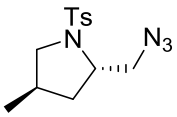
(*S*)-*N*-(1-Azido-4-methylpentan-2-yl)-4-methylbenzenesulfonamide (11): NaN_3 (0.59 g, 9.16 mmol) was added to a solution of **9** (973 mg, 2.29 mmol) in DMSO (13 mL) and stirred at rt for 24 h. The reaction mixture was poured into brine and extracted with EtOAc. The organic phase was dried with Na_2SO_4, filtrated and concentrated. The residue was purified by column chromatography (hexanes/EtOAc, 60:40) to afford the product **11** (658 mg, 2.22 mmol, 97%) as a crystalline solid: Mp 59.0-60.3 ºC (hexane/Et_2O); $[\alpha]_D$ -45.4 (*c* 1.1); ^{1}H NMR δ0.60 (d, *J* = 6.4 Hz, 3H), 0.73 (d, *J* = 6.6 Hz, 3H), 1.13-1.28 (m, 2H), 1.37-1.47 (m, 1H), 2.35 (s, 3H), 3.18 (dd, *J* = 3.9, 12.2 Hz, 1H), 3.22 (dd, *J* = 4.8, 12.5 Hz, 1H), 3.26-3.35 (m, 1H), 5.01 (br s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ20.5 (CH_3), 20.7 (CH_3), 21.8 (CH_3), 23.3 (CH), 40.9 (CH_2), 50.5 (CH), 54.3 (CH_2), 126.1 (2 x CH), 128.7 (2 x CH), 136.9 (C), 142.6 (C); MS (ESI+) *m/z* (rel intensity) 319 (M^++ Na, 100); HRMS calcd for $C_{13}H_{20}N_4O_2NaS$, 319.1205, found 319.1210.



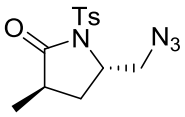
(2*S*,4*S*)-2-(Azidomethyl)-4-methyl-1-tosylpyrrolidine (*syn*-11a): ***syn*-11a** was isolated from a mixture (*syn*/*anti*)-**11a** (1.5:1 ratio) by HPLC (hexanes / EtOAc, 90:10) as a colorless oil: $[\alpha]_D$ -32.0 (*c* 0.2); ^{1}H NMR (500 MHz) δ0.94 (d, *J* = 6.6 Hz, 3H), 1.43 (ddd, *J* = 8.8, 11.4, 12.6 Hz, 1H), 1.51-1.63 (m, 1H), 2.05 (ddd, *J* = 1.2, 7.2, 12.6 Hz, 1H), 2.44 (s, 3H), 2.88 (dd, *J* = 10.7, 11.3 Hz, 1H), 3.57 (dd, *J* = 3.2, 12.3 Hz, 1H), 3.58 (dd, *J* = 1.3, 11.3 Hz, 1H), 3.64 (dd, *J* = 6.3, 12.3 Hz, 1H), 3.70-3.75 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz) δ16.4 (CH_3), 21.6 (CH_3), 32.9 (CH), 38.2 (CH_2), 55.5 (CH_2), 56.3 (CH_2), 60.0 (CH), 127.5 (2 x CH), 129.9 (2 x CH), 134.9 (C), 143.7 (C); MS (ESI+) *m/z* (rel intensity) 317 (M^++ Na, 100); HRMS calcd for $C_{13}H_{18}N_4O_2NaS$, 317.1048, found 317.1041.

Main correlations observed by NOESY are shown in the figure:



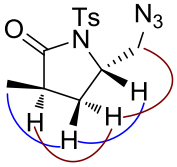


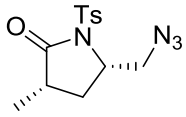
(*2S*,*4R*)-2-(Azidomethyl)-4-methyl-1-tosylpyrrolidine (*anti*-11a): [data obtained from the mixture (*anti/syn*)-**11a**; 1.0:1.1]: Colorless oil; ^{1}H NMR (500 MHz) δ 0.86 (d, J = 6.6 Hz, 3H), 1.22-1.32 (m, 1H), 1.91 (ddd, J = 2.2, 6.3, 12.9 Hz, 1H), 2.32-2.41 (m, 1H), 2.45 (s, 3H), 2.58 (dd, J = 9.3, 9.3 Hz, 1H), 3.48 (dd, J = 7.9, 12.3 Hz, 1H), 3.55-3.60 (m, 2H), 3.68-3.73 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz) δ 16.9 (CH_3), 21.6 (CH_3), 31.6 (CH), 37.3 (CH_2), 55.4 (CH_2), 56.1 (CH_2), 58.9 (CH), 127.7 (2 x CH), 129.8 (2 x CH), 133.7 (C), 143.8 (C).



(3*R*,5*S*)-5-(Azidomethyl)-3-methyl-1-tosylpyrrolidin-2-one (*anti*-11c): Colorless oil: $[\alpha]_D$ -68.0 (*c* 0.5); ^{1}H NMR (500 MHz) δ 1.12 (d, J = 7.3 Hz, 3H), 1.86 (ddd, J = 8.8, 11.6, 13.0 Hz, 1H), 2.20 (ddd, J = 1.0, 9.0, 12.8 Hz, 1H), 2.44 (s, 3H), 2.79 (ddq, J = 7.1 x 3, 8.7, 11.6 Hz, 1H), 3.68 (dd, J = 2.8, 12.6 Hz, 2H), 3.84 (dd, J = 5.4, 12.9 Hz, 1H), 4.40 (dddd, J = 1.0, 2.8, 5.4, 8.8 Hz, 1H), 7.34 (d, J = 7.9 Hz, 2H), 7.95 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 15.4 (CH_3), 21.7 (CH_3), 31.9 (CH_2), 36.2 (CH), 54.3 (CH), 56.1 (CH_2), 128.4 (2 x CH), 129.7 (2 x CH), 135.5 (C), 145.4 (C), 175.9 (C); MS (ESI+) m/z (rel intensity) 331 (M^++ Na, 100); HRMS calcd for $C_{13}H_{16}N_4O_3NaS$, 331.0841, found 331.0836.

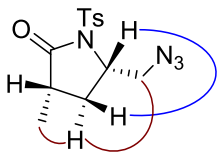
Main correlations observed by NOESY are shown in the figure:





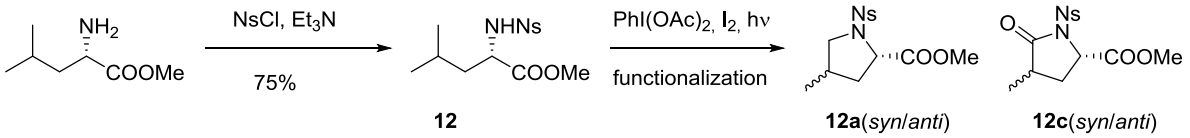
(3*S*,5*S*)-5-(Azidomethyl)-3-methyl-1-tosylpyrrolidin-2-one (*syn*-11c): Crystalline solid: Mp 98-99 ºC (hexane/Et_2O); $[\alpha]_D$ -8.4 (*c* 1.0); ^{1}H NMR (500 MHz) δ 1.21 (d, J = 6.9 Hz, 3H), 1.60 (ddd, J = 6.0, 7.3, 13.9 Hz, 1H), 2.43 (ddd, J = 8.2, 10.4, 13.0 Hz, 1H), 2.44 (s, 3H), 2.48 (ddq, J = 6.9 x 4, 10.1 Hz, 1H), 3.75 (dd, J = 2.5, 12.6 Hz, 1H), 3.94 (dd, J = 5.7, 12.6 Hz, 1H), 4.33 (dddd, J = 2.8, 5.7, 6.9, 8.2 Hz, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 16.3 (CH_3), 22.1 (CH_3), 30.4 (CH_2), 36.9 (CH), 54.8 (CH_2), 57.1 (CH), 128.7 (2 x CH), 130.0 (2 x CH), 135.9 (C), 145.7 (C), 176.9 (C); MS (ESI+) *m/z* (rel intensity) 331 (M^++ Na, 100); HRMS calcd for $C_{13}H_{16}N_4O_3NaS$, 331.0841, found 331.0840.

Main correlations observed by NOESY are shown in the figure:



Synthesis and Functionalization of 4-nitrophenylsulfonamine 12:

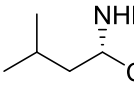
Table *S12*.



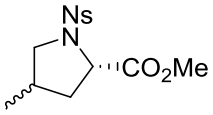
entry	substrate **12**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives equiv	[C] M	temp[d] ºC	time h	yield %[e]	**12a**(*syn*/*anti*) %[f]	**12c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	5, 5	5	-	0.1	70	6	93.5	69.5(1:1.8)	24(2.5:1)	4:6.9:2.3:1
2		$GP1_{CSA}$	2.5, 2.5	0.6	CSA (1)	0.1	25	4	82	82(1:1.2)	-	1:1.3:0:0
3		GP2	7	0.6, 3	$NaHCO_3$[h]	0.03	25	5	60	-	60(1:1.1)	0:0:1:1.1

[table 1]

[a] millimoles per millimol of **12**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**12a**-*syn*/**12a**-*anti*/**12c**-*syn*/**12c**-*anti*) calculated by integration in the ^1H NMR of the crude of reaction; [h] 100% w/w.



(*S*)-Methyl 4-methyl-2-(4-nitrophenylsulfonamido)pentanoate (12):[18] Triethylamine (2 mL) was added to a suspension of L-leucine methyl ester hydrochloride (1.04 g, 5.74 mmol) in dry CH_2Cl_2 (7 mL) at room temperature and stirred for 30 min. The resulting mixture was cold at 0 ºC and *p*-nitrobenzenesulfonyl chloride (1.91 g, 8.60 mmol) was added in one portion, allowed to reach rt and stirred for further 3-4 h. The reaction was poured into ice–water and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. Column chromatography (hexanes–EtOAc, 85:15) of the residue afforded compound **13** (1.42 g, 4.31 mmol, 75%) as a pale yellow solid: Mp 97.5-99.0 ºC (*n*-hexane/Et_2O); $[\alpha]_D$ +27.4 (*c* 1.5); ^1H NMR δ0.90 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 1.54 (t, *J* = 6.9 Hz, 2H), 1.70-1.82 (m, 1H), 3.51 (s, 3H), 4.03 (ddd, *J* = 6.8, 7.9, 9.8 Hz, 1H), 5.45 (br s, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 8.35 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR δ21.7 (CH_3), 23.0 (CH_3), 24.8 (CH), 42.6 (CH_2), 52.9 (CH_3), 55.0 (CH), 124.6 (2 x CH), 128.9 (2 x CH), 146.2 (C), 150.5 (C), 172.7 (C); MS (ESI+) *m/z* (rel intensity) 353 (M^++ Na, 100); HRMS calcd for $C_{13}H_{18}N_2O_6NaS$, 353.0783, found 353.0783.

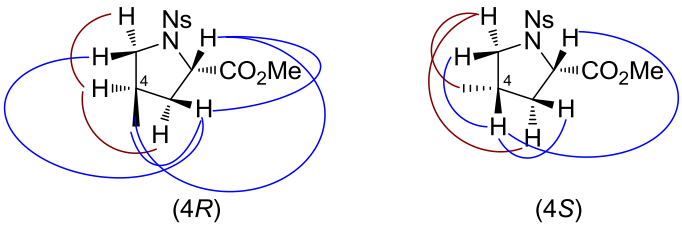


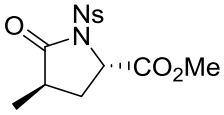
(2*S*)-Methyl 4-methyl-1-((4-nitrophenyl)sulfonyl)pyrrolidine-2-carboxylate (12a): Colorless oil. NMR showed a mixture of isomer (*anti*/*syn*)-**12a** in 1.8:1.0 ratio. ***anti*-12a**: ^1H NMR (500 MHz) δ0.99 (d, *J* = 6.9 Hz, 3H), 1.80 (ddd, *J* = 9.6, 9.6, 12.9 Hz, 1H), 2.14 (ddd, *J* = 2.8, 6.2, 13.0 Hz, 1H), 2.41-2.49 (m, 1H), 2.96 (dd, *J* = 8.8, 8.8 Hz, 1H), 3.57 (dd, *J* = 7.1, 9.0 Hz, 1H), 3.71 (s, 3H), 4.49 (dd, *J* = 2.8, 9.1 Hz, 1H), 8.08 (d, *J* = 8.8 Hz, 2H), 8.38 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR δ17.2 (CH_3), 33.0 (CH), 38.9 (CH_2), 52.8 (CH_3), 55.1 (CH_2), 61.0 (CH), 124.5 (2 x CH), 129.1 (2 x CH), 145.0 (C), 150.5 (C), 172.5 (C).

[18] Spectral data are in good agreement with those reported in the literature: (a) Reichwein, J. F.; Liskamp, R. M. J. *Eur. J. Org. Chem.* **2000**, 2335; (b) Gioia, M. L. D.; Leggio, A.; Pera, A. L.; Liguori, A.; Napoli, A.; Siciliano, C.; Sindona, G. *J. Org. Chem.* **2003**, *68*, 7416.

***syn*-12a**: ^{1}H NMR (500 MHz) δ1.03 (d, J = 6.6 Hz, 3H), 1.62 (ddd, J = 8.7, 10.2, 12.6 Hz, 1H), 2.14-2.24 (m, 1H), 2.40-2.47 (m 1H), 2.94 (dd, J = 9.8, 9.8 Hz, 1H), 3.68-3.75 (m, 1H), 3.74 (s, 3H), 4.43 (dd, J = 8.3, 8.3 Hz, 1H), 8.10 (d, J = 8.8 Hz, 2H), 8.38 (d, J = 8.8 Hz, 2H); ^{13}C NMR δ17.2 (CH_3), 34.2 (CH), 39.2 (CH_2), 52.8 (CH_3), 55.5 (CH_2), 61.5 (CH), 124.5 (2 x CH), 129.1 (2 x CH), 145.3 (C), 150.5 (C), 172.7 (C). MS (ESI+) *m/z* (rel intensity) 351 (M^++ Na, 100); HRMS calcd for $C_{13}H_{16}N_2O_6NaS$, 351.0627, found 351.0621.

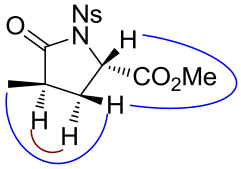
Main correlations observed by NOESY are shown in the figure:

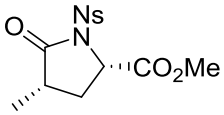




(2*S*,4*R*) Methyl 4-methyl-1-((4-nitrophenyl)sulfonyl)-5-oxopyrrolidine-2-carboxylate (*anti*-12c): Colorless oil: $[\alpha]_D$ -32.7 (*c* 1.0); ^{1}H NMR δ1.18 (d, J = 7.0 Hz, 3H), 2.13 (ddd, J = 9.5, 12.6, 12.6 Hz, 1H), 2.41 (dd, J = 8.4, 13.1 Hz, 1H), 2.55-2.66 (m, 1H), 3.82 (s, 3H), 4.91 (d, J = 9.4 Hz, 1H), 8.31 (d, J = 8.8 Hz, 2H), 8.38 (d, J = 8.8 Hz, 2H); ^{13}C NMR δ14.8 (CH_3), 32.6 (CH_2), 36.5 (CH), 53.4 (CH_3), 57.9 (CH), 124.0 (2 x CH), 131.2 (2 x CH), 143.5 (C), 151.4 (C), 171.3 (C), 175.3 (C); MS (ESI+) *m/z* (rel intensity) 365 (M^++ Na, 100); HRMS calcd for $C_{13}H_{14}N_2O_7NaS$, 365.0419, found 365.0420.

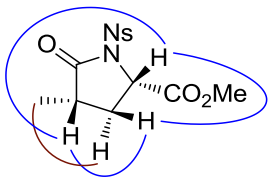
Main correlations observed by NOESY are shown in the figure:





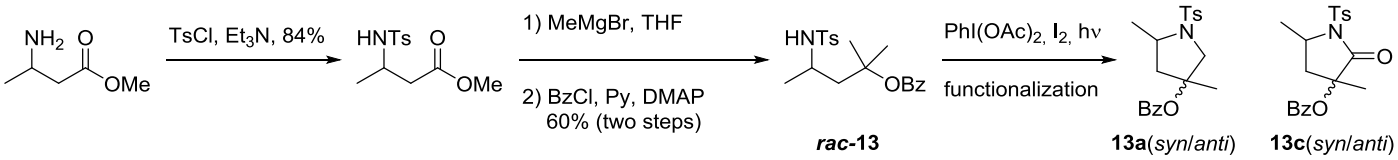
(2*S*,4*S*)-Methyl 4-methyl-1-((4-nitrophenyl)sulfonyl)-5-oxopyrrolidine-2-carboxylate (*syn*-12c): Crystalline solid: Mp 146.0-146.5 ºC (hexane/Et_2O); $[\alpha]_D$ -17.2 (*c* 0.8); ^{1}H NMR δ1.17 (d, J = 6.9 Hz, 3H), 1.73 (ddd, J = 6.8, 6.8, 11.8 Hz, 1H), 2.65-2.76 (m, 2H), 3.85 (s, 3H), 4.84 (dd, J = 7.5, 7.5 Hz, 1H), 8.35 (d, J = 8.8 Hz, 2H), 8.39 (d, J = 8.8 Hz, 2H); ^{13}C NMR δ16.0 (CH_3), 31.5 (CH_2), 37.4 (CH), 53.4 (CH_3), 58.3 (CH), 124.1 (2 x CH), 131.1 (2 x CH), 143.8 (C), 151.4 (C), 171.9 (C), 175.8 (C); MS (ESI+) *m/z* (rel intensity) 365 (M^++ Na, 100); HRMS calcd for $C_{13}H_{14}N_2O_7NaS$, 365.0419, found 365.0422.

Main correlations observed by NOESY are shown in the figure:



Synthesis and Functionalization of Tosylamine 13:

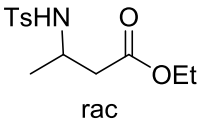
Table *S13*.



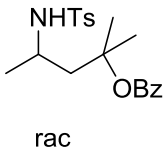
[table 1]

entry	substrate *rac*-**13**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	[C] M	temp[d] °C	time h	yield %[e]	**13a**(*syn*/*anti*) %[f]	**13c**(*syn*/*anti*) %[f]	products ratio[g]
1		GP1	3, 3	7	-	0.1	70	6	-	complex mixture of products		-
2		$GP1_{CSA}$	3, 6[h]	1.1	CSA, 1.1	0.07	70	8	76	52(1.7:1)	24(1:0)	(3.3:1:2.2:0)
3		GP2	4	0.7, 3 h	-	0.03	25	12	83	-	83(7.5:1)	(0:0:10:1)

[a] millimoles per millimol of **13**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**13a**-*syn*/**13a**-*anti*/**13c**-*syn*/**13c**-*anti*) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] portionwise (0.5 equiv / 60 min).



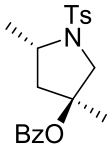
Ethyl 3-(4-methylphenylsulfonamido)butanoate:[19] TsCl (570 mg, 3 mmol) was added portionwise to a suspension of 3-amino-butyric acid ethyl ester (175 mg, 1.5 mmol) and distilled Et_3N (0.56 mL, 4 mmol) in dry DCM (15 mL). The resulting mixture was stirred at room temperature for 4 h. 1 N Aqueous HCl was then added and the acidified solution (pH = 2) was extracted with DCM. The organic phase was carefully washed with a saturated aqueous $NaHCO_3$, brine and finally dried with Na_2SO_4 and the solvent was evaporated. The crude material was purified by column chromatography (hexane/EtOAc 70:30) to give the desired product as colorless oil (341 mg, 84% yield). ^{1}H NMR δ1.15 (d, J = 6.9 Hz, 3H), 1.22 (dd, J = 7.2, 7.2 Hz, 3H), 2.41 (d, J = 6.9 Hz, 2H), 2.42 (s, 3H), 3.65-3.73 (m, 1H), 4.06 (dd, J = 4.5, 7.1 Hz, 1H), 4.09 (dd, J = 4.5, 7.1 Hz, 1H), 5.17 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H); ^{13}C NMR δ14.4 (CH_3), 21.4 (CH_3), 21.8 (CH_3), 41.5 (CH_2), 47.1 (CH), 61.0 (CH_2), 127.4 (2 x CH), 130.0 (2 x CH), 138.5 (C), 143.6 (C), 171.5 (C).



2-Methyl-4-(4-methylphenylsulfonamido)pentan-2-yl benzoate (*rac*-13): A solution of the previously prepared *N*-tosyl derivative (100 mg, 0.29 mmol) in THF (1 mL) was added to a slurry of MeMgCl in THF (ca. 2 M, 0.72 mL, 5 equiv) at 0 °C. The resulting mixture was stirred for 4 h at 0 °C and poured into ice-cooled aqueous NH_4Cl. The phases were separated and the aqueous phase was extracted with EtOAc twice. The combined organic phase was dried over Na_2SO_4 and filtered. To the concentrated crude residue was added DCM (1 mL), BzCl (203 mg, 0.17 mL, 1.45 mmol) and DMAP (88 mg, 0.86 mmol) and stirred for 16 h at room temperature. The reaction was quenched by the addition of aqueous HCl solution (10 %) and diluted with EtOAc. The layers were separated and the aqueous phase was extracted with more EtOAc. The combined organic layer was washed with aqueous HCl

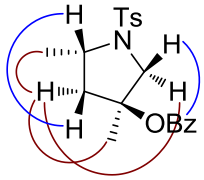
[19] Spectral data are in good agreement with those reported in the literature: Jefford, C. W.; McNulty, J.; Lu, Z-H.; Wang, J. B. *Helv. Chim. Acta* **1996**, *79*, 1203.

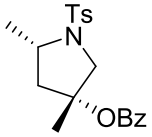
(10%), saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, and the solvent was evaporated under vacuum. The residue was purified by column chromatography (hexane/EtOAc 70:30) to give the desired benzoyl derivative as colorless oil (60 mg, 60% after 2 steps). ^{1}H NMR δ1.09 (d, *J* = 6.4, Hz, 3H), 1.50 (s, 3H), 1.55 (s, 3H), 2.01 (dd, *J* = 5.3, 14.8 Hz, 1H), 2.10 (dd, *J* = 7.4, 14.8 Hz, 1H), 2.36 (s, 3H), 3.57-3.67 (m, 1H), 5.32 (d, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.42 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.95 (d, *J* = 7.7 Hz, 2H), 8.11 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR δ21.8 (CH_3), 23.5 (CH_3), 26.7 (CH_3), 26.9 (CH_3), 47.4 (CH), 48.3 (CH_2), 82.8 (C), 127.4 (2 x CH), 128.7 (2 x CH), 129.8 (2 x CH), 130.0 (2 x CH), 131.9 (C), 133.1 (CH), 138.6 (C), 143.6 (C), 166.2 (C); MS (ESI+) *m/z* (rel intensity) 398 (M^++ Na, 100); HRMS calcd for $C_{20}H_{25}NO_4NaS$, 398.1402, found 398.1404.



***rac*-3,5-*syn*-Dimethyl-1-tosylpyrrolidin-3-yl benzoate (*syn*-13a):** Colorless oil; ^{1}H NMR δ1.47 (d, *J* = 6.0 Hz, 3 H), 1.56 (s, 3 H), 1.66 (dd, *J* = 10.4, 13.6 Hz, 1 H), 1.89 (s, 3 H), 2.48 (ddd, *J* = 2.2, 6.3, 13.6 Hz, 1 H), 3.49 (d, *J* = 13.2 Hz, 1 H), 3.70 (ddq, *J* = 6.2 x 4, 10.3 Hz, 1 H), 4.21 (dd, *J* = 2.1, 13.1 Hz, 1 H), 6.86 (d, *J* = 7.9 Hz, 2 H), 7.22-7.29 (m, 2 H), 7.44 (tt, *J* = 1.3, 7.3 Hz, 1 H), 7.49 - 7.57 (m, 4 H); ^{13}C NMR δ21.1 (CH_3), 21.3 (CH_3), 22.1 (CH_3), 48.0 (CH_2), 55.6 (CH), 58.1 (CH_2), 84.7 (C), 127.4 (2 x CH), 128.0 (2 x CH), 129.3 (2 x CH), 129.4 (2 x CH), 130.4 (C), 132.8 (CH), 134.2 (C), 143.1 (C), 165.2 (C); MS (EI+) *m/z* (rel intensity) 251 (M^+- PhCOOH, 97), 236 [M^+- (PhCOOH + Me), 17]; HRMS calcd for $C_{13}H_{17}NO_2S$, 251.0980, found 251.0986; IR 1714, 1599, 1453, 1337, 1295, 1241, 1158, 1097 cm^{-1}.

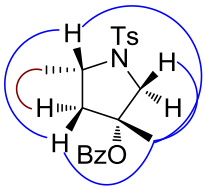
Main correlations observed by NOESY are shown in the figure:

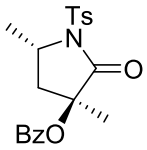




***rac*-3,5-*anti*-Dimethyl-1-tosylpyrrolidin-3-yl benzoate (*anti*-13a):** Colorless oil: ^{1}H NMR (500 MHz) δ1.36 (s, 3 H), 1.43 (d, *J* = 6.6 Hz, 3 H), 2.15 (dd, *J* = 8.8, 13.6 Hz, 1 H), 2.26 (dd, *J* = 5.5, 13.7 Hz, 1 H), 2.44 (s, 3 H), 3.50 (d, *J* = 11.3 Hz, 1 H), 3.79 (dquin, *J* = 6.2 x 4, 8.1 Hz, 1 H), 3.90 (d, *J* = 11.3 Hz, 1 H), 7.33 (d, *J* = 7.9 Hz, 2 H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.56 (tt, *J* = 1.3, 7.4 Hz, 1 H), 7.76 (d, *J* = 8.5 Hz, 2 H), 7.96 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz) δ21.6 (CH_3), 22.2 (CH_3), 22.8 (CH_3), 45.4 (CH_2), 55.0 (CH), 59.0 (CH_2), 84.0 (C), 127.6 (2 x CH), 128.4 (2 x CH), 129.6 (2 x CH), 129.7 (2 x CH), 130.6 (C), 133.1 (CH), 134.8 (C), 143.6 (C), 165.6 (C); MS (EI+) *m/z* (rel intensity) 251 (M^+- PhCOOH, 100), 236 [M^+- (PhCOOH + Me), 27]; HRMS calcd for $C_{13}H_{17}NO_2S$, 251.0980, found 251.0979.

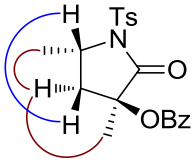
Main correlations observed by NOESY are shown in the figure:

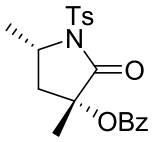




***rac*-3,5-*syn*-Dimethyl-2-oxo-1-tosylpyrrolidin-3-yl benzoate (*syn*-13c):** Colorless oil; NMR showed a mixture of isomers (*syn*/*anti*)-**13c** in 7.5:1.0 ratio; ^{1}H NMR δ1.63 (d, *J* = 6.6 Hz, 3H), 1.67 (s, 3H), 1.92 (dd, *J* = 2.8, 13.9 Hz, 1H), 2.45 (s, 3H), 2.88 (dd, *J* = 9.8, 13.9 Hz, 1H), 4.50-4.57 (m, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.53 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.82 (dd, *J* = 1.2, 8.5 Hz, 2H), 7.98 (d, J 0 8.5 Hz, 2H); ^{13}C NMR δ21.7 (CH_3), 23.9 (CH_3), 25.2 (CH_3), 39.6 (CH_2), 52.5 (CH), 79.5 (C), 128.3 (2 x CH), 128.9 (2 x CH), 129.3 (2 x CH), 129.7 (2 x CH), 133.4 (CH), 133.5 (C), 135.0 (C), 145.0 (C), 164.9 (C), 171.7 (C); MS (ESI+) *m/z* (rel intensity) 410 (M^++ Na, 100); HRMS calcd for $C_{20}H_{21}NO_5NaS$, 410.1038, found 410.1050.

Main correlations observed by NOESY are shown in the figure:

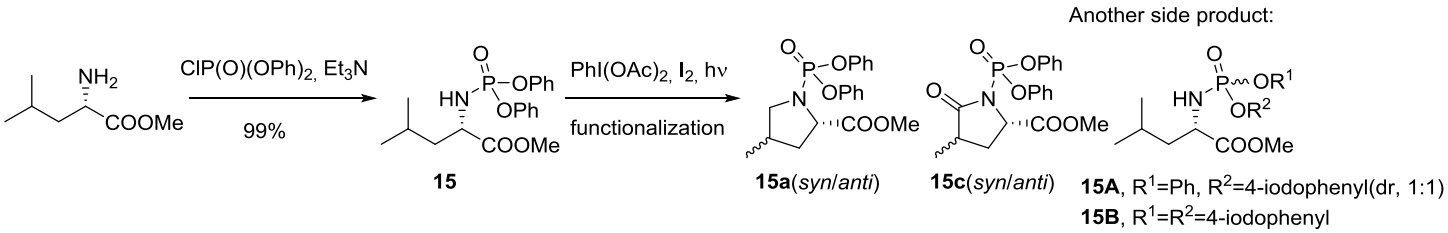




***rac*-3,5-*anti*-Dimethyl-2-oxo-1-tosylpyrrolidin-3-yl benzoate (*anti*-13c):** colorless oil; NMR showed a mixture of isomers (*syn*/*anti*)-**13c** in 7.5:1.0 ratio; ^{1}H NMR δ1.54 (s, 3H), 1.61 (d, *J* = 6.0 Hz, 3H), 2.31 (dd, *J* = 6.9, 13.2 Hz, 1H), 2.44 (s, 3H), 2.46 (dd, *J* = 7.9, 13.2 Hz, 1H), 4.33-4.37 (m, 1H), 7.33-7.99 (m, 9H).

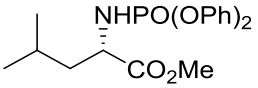
Synthesis and Functionalization of (diphenoxyphosphoryl)amine 15:

Table *S14*.

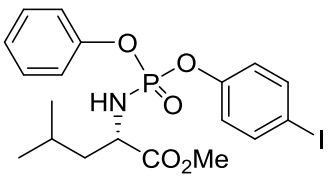


entry	substrate **15**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives mmol[a]	temp[d] °C	time h	yield %[e]	[C] M	**15a**(*syn*/*anti*) %[f]	**15c**(*syn*/*anti*) %[f]	**15A**(1:1) %[f]	**15B** %[f]	products ratio[g]
1		GP1	4, 4	5	-	70	5	-[h]	0.1	-	-	41	21.5	0:0:0:0
2		GP1$_{CSA}$	4, 4	0.6	CSA, 1	70	6	21.5[i]	0.03	21.5(1:2)	-	-	-	1:2:0:0
3		GP2	7	1.2, 9	$NaHCO_3$[j]	25	24	29[k]	0.03	5(0:1)	24(1:1.4)	-	-	0:1:3:3.8
4		GP2[l]	7(x3)	1.2, 9 (x3)	$NaHCO_3$[j]	25	96	47	0.03	11(1:8)	36(1:1.3)	-	-	0:1:1.5:2

[a] millimoles per millimol of **15**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] total isolated yield; [f] isolated yield; [g] (**15a**-*syn*/**15a**-*anti*/**15c**-*syn*/**15c**-*anti*) calculated by integration in the ^{1}H NMR of the crude of reaction; [h] 10% of **15** was recovered; [i] 45% of **15** was recovered; [j] 100% w/w; [k] 50% of **15** was recovered; [l] addition of PhI(OAc)$_2$ and I_2 was equally repited every 3 continous days. reaction performed with 300 mg.

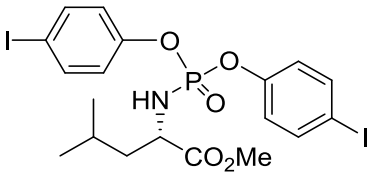


(*S*)-Methyl 2-[(diphenoxyphosphoryl)amino]-4-methylpentanoate (15) L-Leucine methylester hydrochloride (1.01 g, 5.58 mmol) was dissolved in dry CH_2Cl_2 (62 mL) and treated with TEA (3.1 mL, 22.32 mmol) and diphenylchlorophosphate (2.3 mL, 11.16 mmol). The mixture was stirred at rt for 1.5 h under nitrogen, poured into a dilute hydrochloric acid (5%) solution, and extracted with $CHCl_3$. The organic layer was washed with an aqueous saturated solution of $NaHCO_3$ and concentrated in vacuo. Column chromatography of the residue (hexanes–EtOAc, 85:15) afforded the title compound **15** (1.43 g, 3.79 mmol, 68%) as colorless oil: $[\alpha]_D$ -2.0 (*c* 1.2); ^{1}H NMR δ0.86 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 1.46 (ddd, *J* = 6.3, 8.5, 13.7 Hz, 1H), 1.55 (ddd, *J* = 2.6, 5.7, 13.7 Hz, 1H), 1.64 (non, *J* = 6.6 x 8 Hz, 1H), 3.62 (s, 3H), 3.66 (dd, *J* = 11.0, 11.0 Hz, 1H), 4.03-4.10 (m, 1H), 7.13-7.34 (m, 10H); ^{13}C NMR δ22.3 (CH_3), 23.0 (CH_3), 24.7 (CH), 44.3 (CH_2), 52.6 (CH_3), 53.8 (CH), 120.6 (4 X CH), 125.4 (2 x CH), 130.1 (4 X CH), 151.1 (2 x C), 174.1 (C); MS (ESI+) *m/z* (rel intensity) 400 (M^++ Na, 100); HRMS calcd for $C_{19}H_{24}NO_5NaP$, 400.1290, found 400.1282.

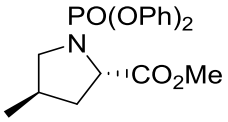


(2*S*)-Methyl 2-[((4-iodophenoxy)(phenoxy)phosphoryl)amino]-4-methylpentanoate (15A). NMR showed only one diastereoisomer: Pale brown syrup: $[\alpha]_D$ +1.3 (*c* 1.0); ^{1}H NMR δ0.86 (d, *J* = 6.6 Hz, 1H), 0.87 (d, *J* = 6.6 Hz, 1H), 0.87 (d, *J* = 6.6 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H), 1.47 (ddd, *J* = 7.2, 7.2, 14.8 Hz, 1H), 1.51-1.58 (m, 1H), 1.60-1.69 (m, 1H), 3.59 (dd, *J* = 11.0, 11.0 Hz, 1H), 3.64 (s, 3H), 4.02-4.09 (m, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 7.15-7.24 (m, 3H), 7.30-7.34 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR δ22.2 (CH_3), 23.0 (CH_3), 24.7 (CH), 44.2 (CH_2), 52.6 (CH_3), 53.8 (CH), 89.0 (C), 120.5 (2 x CH), 122.9 (2 x CH), 125.5 (CH), 130.1 (2 x CH), 139.0

(2 x CH), 151.0 (C), 151.1 (C), 174.1 (C); MS (ESI+) *m/z* (rel intensity) 526 (M^++ Na, 100); HRMS calcd for $C_{19}H_{23}NO_5NaPI$, 526.0253, found 526.0256.

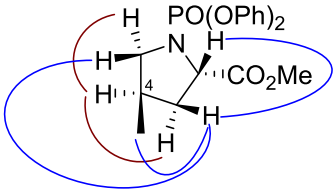


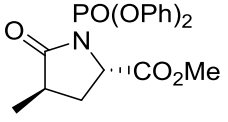
(*S*)-Methyl 2-((bis(4-iodophenoxy)phosphoryl)amino)-4-methyl pentanoate (15B): Pale brown syrup: $[\alpha]_D$ -0.3 (*c* 1.0); ^{1}H NMR δ0.87 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 1.46 (ddd, *J* = 6.0, 8.4, 13.9 Hz, 1H), 1.51-1.58 (m, 1H), 1.60-1.69 (m, 1H), 3.60 (dd, *J* = 11.0, 11.0 Hz, 1H), 3.65 (s, 3H), 4.00-4.05 (m, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR δ22.2 (CH_3), 23.0 (CH_3), 24.7 (CH), 44.2 (CH_2), 52.7 (CH_3), 53.7 (CH), 89.2 (2 x C), 122.7 (4 x CH), 139.1 (4 x CH), 150.9 (2 x C), 174.0 (C); MS (ESI+) *m/z* (rel intensity) 652 (M^++ Na, 100); HRMS calcd for $C_{19}H_{22}NO_5NaPI_2$, 651.9223, found 651.9223.



(2*S*,4*R*)-Methyl 1-(diphenoxyphosphoryl)-4-methylpyrrolidine-2-carboxylate (*anti*-15a): Colorless oil: $[\alpha]_D$ -0.3 (*c* 1.0); ^{1}H NMR (500 MHz) δ0.97 (d, *J* = 6.6 Hz, 3H), 1.71 (ddd, *J* = 8.8, 9.8, 12.6 Hz, 1H), 2.08-2.13 (m, 1H), 2.40-2.46 (m, 1H), 2.97 (ddd, *J* = 2.8, 8.6, 8.6 Hz, 1H), 3.59 (s, 3H), 3.63 (dd, *J* = 8.6, 8.6 Hz, 1H), 4.42 (ddd, *J* = 3.2, 3.2, 8.7 Hz, 1H), 7.13-7.34 (m, 10H); ^{13}C NMR δ17.3 (CH_3), 32.9 (CH, $^3J_{CP}$ = 9.5 Hz), 39.0 (CH_2, $^3J_{CP}$ = 9.5 Hz), 52.1 (CH_3), 54.3 (CH_2, $^2J_{CP}$ = 3.2 Hz), 60.9 (CH, $^2J_{CP}$ = 6.4 Hz), 120.0 (2 x CH, $^4J_{CP}$ = 5.3 Hz), 120.4 (2 x CH, $^4J_{CP}$ = 4.2 Hz), 124.8 (2 x CH, $^5J_{CP}$ = 7.4 Hz), 129.6 (4 x CH, $^3J_{CP}$ = 10.6 Hz), 150.9 (2 x C, $^2J_{CP}$ = 5.3 Hz), 173.6 (C); MS (ESI+) *m/z* (rel intensity) 398 (M^++ Na, 100); HRMS calcd for $C_{19}H_{22}NO_5NaP$, 398.1133, found 398.1122.

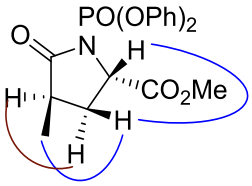
Main correlations observed by NOESY are shown in the figure:

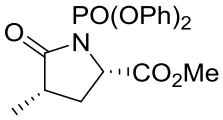




(2*S*,4*R*)-Methyl 1-(diphenoxyphosphoryl)-4-methyl-5-oxopyrrolidine-2-carboxylate (*anti*-15c): Colorless oil: $[\alpha]_D$ -31.1 (*c* 2.0); ^{1}H NMR (500 MHz) δ1.13 (d, *J* = 7.2 Hz, 3H), 1.81 (ddd, *J* = 9.1, 11.8, 13.1 Hz, 1H), 2.33 (dddd, *J* = 1.7, 1.7, 8.2, 13.0 Hz, 1H), 2.62-2.69 (m, 1H), 3.54 (s, 3H), 4.49 (ddd, *J* = 1.6, 4.6, 9.1Hz, 1H), 7.18-7.35 (m, 10H); ^{13}C NMR δ15.3 (CH_3), 33.8 (CH_2, $^3J_{CP}$ = 7.8 Hz), 36.5 (CH, $^3J_{CP}$ = 8.5 Hz), 52.9 (CH_3), 58.7 (CH, $^2J_{CP}$ = 5.0 Hz), 121.2 (4 x CH, $^4J_{CP}$ = 22.6 Hz), 126.0 (2 x CH, $^5J_{CP}$ = 24.0 Hz), 130.0 (4 x CH, $^3J_{CP}$ = 21.9 Hz), 150.4 (2 x C), 171.8 (C), 179.3 (C); MS (ESI+) *m/z* (rel intensity) 412 (M^++ Na, 100); HRMS calcd for $C_{19}H_{20}NO_6NaP$, 412.0926 found 412.0930.

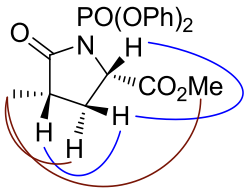
Main correlations observed by NOESY are shown in the figure:





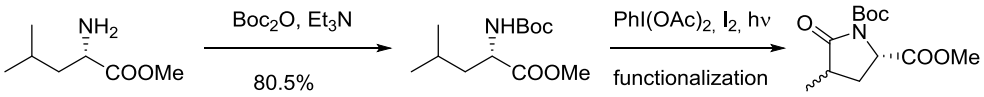
(2*S*,4*S*)-Methyl 1-(diphenoxyphosphoryl)-4-methyl-5-oxopyrrolidine-2-carboxylate (*syn*-15c): colorless oil; $[\alpha]_D$ -25.1 (*c* 1.2); ^{1}H NMR (500 MHz) δ1.25 (d, *J* = 6.6 Hz, 3H), 1.78 (dd, *J* = 6.2, 12.9 Hz, 1H), 2.48-2.60 (m, 2H), 3.55 (s, 3H), 4.43 (dd, *J* = 6.9, 8.8 Hz, 1H), 7.18-7.36 (m, 10H); ^{13}C NMR δ16.3 (CH_3), 32.7 (CH_2, $^3J_{CP}$ = 8.5 Hz), 37.6 (CH, $^3J_{CP}$ = 9.2 Hz), 52.9 (CH_3), 59.3 (CH, $^2J_{CP}$ = 5.0 Hz), 121.2 (4 x CH, $^4J_{CP}$ = 42.4 Hz), 126.0 (2 x CH, $^5J_{CP}$ = 17.0 Hz), 130.0 (4 x CH, $^3J_{CP}$ = 30.4 Hz), 150.4 (2 x C), 172.1 (C), 179.5 (C); MS (ESI+) *m/z* (rel intensity) 412 (M^++ Na, 100); HRMS calcd for $C_{19}H_{20}NO_6NaP$, 412.0926 found 412.0928.

Main correlations observed by NOESY are shown in the figure:



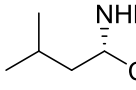
Synthesis and Functionalization of (*tert*-butoxycarbonyl)amine 16:

Table *S15*.



entry	substrate **16**	procedure	PhI(OAc)$_2$ mmol,[a] t[b]	I$_2$ mmol,[a] t[c]	aditives equiv	[C] M	temp[d] °C	time h	yield %[e]	**16a**(*syn*/*anti*) %[f]	**16c**(*syn*/*anti*) %[f]
1		GP1	3, 3	5	-	0.1	70	24	-	-	-
2		GP2	7	1.2, 6	$NaHCO_3$[g]	0.03	25	24	13[h]	-	13(<1:9)

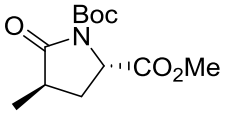
[a] millimoles per millimol of **16**; [a] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [b] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [c] 25 °C (reaction mixture refrigerated by a fan) and 65-75 °C (without fan); [d] total isolated yield; [e] isolated yield; [f] calculated by integration in the ^{1}H NMR of the crude of reaction; [g] 100% w/w; [h] large amount of products without the Boc group were observed in the ^{1}H NMR spectra after column chromatography.



(*S*)-Methyl 2-[(*tert*-butoxycarbonyl)amino]-4-methylpentanoate (16):[20] $(Boc)_2O$ (6.7 mmol, 1.5 g) was added to a solution of L-leucine methyl ester (5.9 mmol, 1 g) and triethylamine (11.2 mmol, 1.6 mL) in anhydrous THF (14 mL) at room temperature. The reaction mixture

[20] Spectral data are in good agreement with those reported in the literature: Jahani, F.; Tajbakhsh, M.; Golchoubian, H.; Khaksar, S. *Tetrahedron Lett.* **2011**, *52*, 1260.

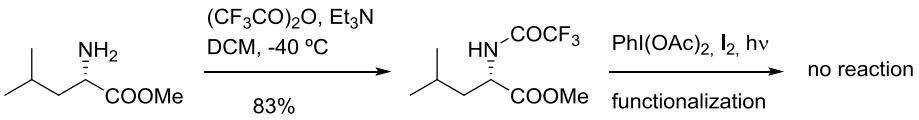
was stirred for 24 h at room temperature, quenched by the addition of aqueous HCl solution (10 %) and diluted with EtOAc. The layers were separated and the aqueous phase was extracted with EtOAc twice. The combined organic layer was washed with aqueous solution HCl (10%), saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, and evaporated under vacuum. The residue was purified by column chromatography (hexane/EtOAc 70:30) to give the desired *N-tert*-butoxycarbonyl-L-leucine methyl ester as a crystalline solid (1.1 g, 80%). $[\alpha]_D$ -4.2 (*c* 1.5); ^{1}H NMR δ0.94 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.44 (s, 9H), 1.44-1.77 (m, 3H), 3.73 (s, 3H), 4.28-4.36 (m, 1H), 4.91 (d like, *J* = 7.1 Hz, 1H); ^{13}C NMR δ22.3 (CH_3), 23.2 (CH_3), 25.2 (CH), 28.7 (3 x CH_3), 42.3 (CH_2), 52.5 (CH + CH_3), 80.3 (C), 155.8 (C), 174.2 (C); MS (ESI+) *m/z* (rel intensity) 268 (M^++ Na, 100); HRMS calcd for $C_{12}H_{23}NO_4Na$, 268.1525, found 268.1523.



(2*S*,4*R*)-1-*tert*-Butyl 2-methyl 4-methyl-5-oxopyrrolidine-1,2-dicarboxylate (*anti*-16c):[21] Colorless oil: $[\alpha]_D$ -9.6 (*c* 0.7); ^{1}H NMR δ 1.22 (d, *J* = 7.0 Hz, 3H), 1.50 (s, 9H), 1.93 (ddd, *J* = 9.6, 11.7, 13.2 Hz, 1H), 2.28 (ddd, *J* = 1.3, 8.6, 13.2 Hz, 1H), 2.62-2.74 (m, 1H), 3.78 (s, 3H), 4.57 (dd, *J* = 1.5, 9.5 Hz, 1H); ^{13}C NMR δ15.1 (CH_3), 27.9 (3 x CH_3), 30.5 (CH_2), 36.6 (CH), 52.5 (CH_3), 56.9 (CH), 83.5 (C), 149.6 (C), 171.8 (C), 175.5 (C). MS (ESI+) *m/z* (rel intensity) 280 (M^++ Na, 100); HRMS calcd for $C_{12}H_{19}NO_5Na$, 280.1161, found 280.1168.

Synthesis and Functionalization of Trifluoroacetylamine 17:

Table *S16*.



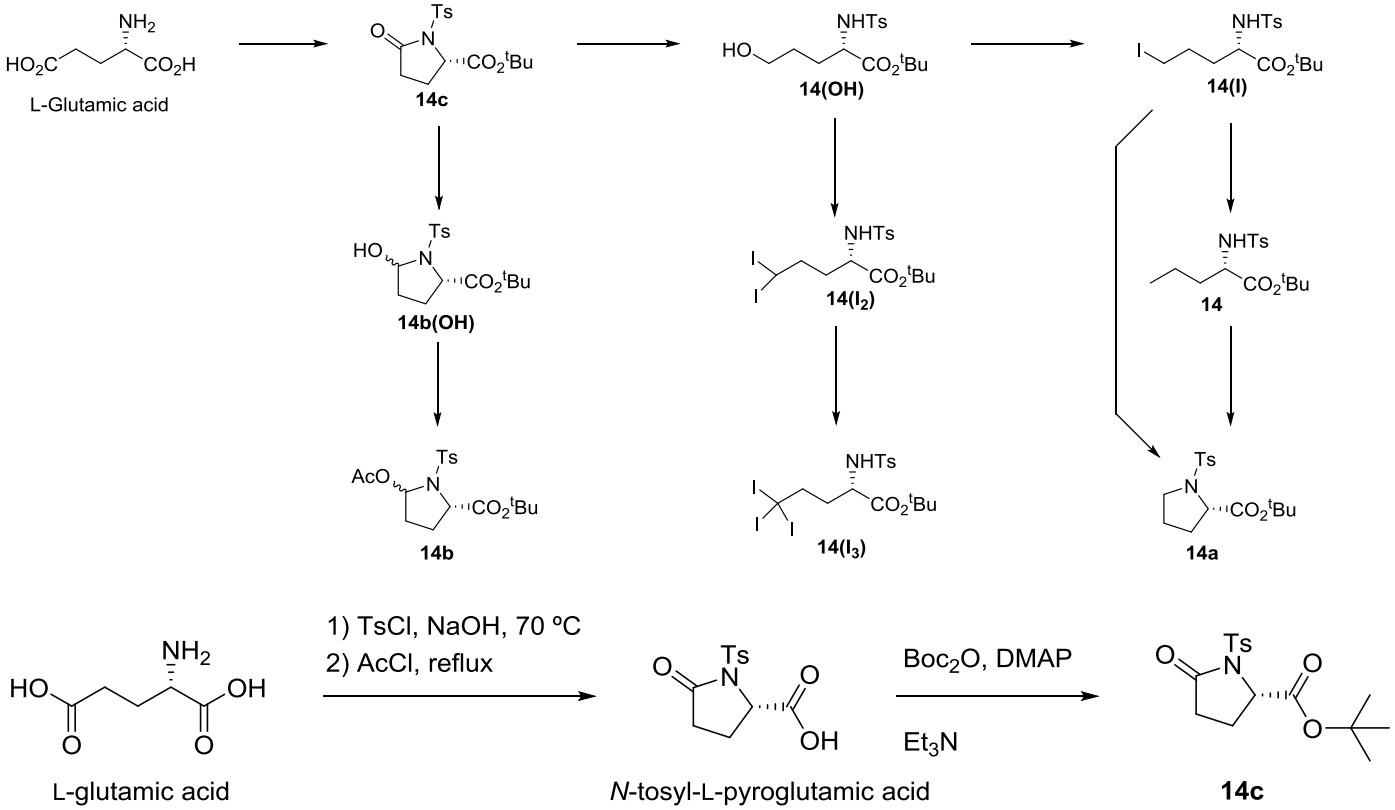
entry	substrate **17**	procedure	$PhI(OAc)_2$ mmol,[a] t[b]	I_2 mmol,[a] t[c]	aditives equiv	[C] M	temp[d] ºC	time h	yield %[e]
1		GP1	3, 3	5	-	0.1	70	24	-[f]
2		GP2	7	1.2, 6	$NaHCO_3$[g]	0.03	25	24	-[f]

[a] millimoles per millimol of **17**; [b] Time of addition in hours: Portionwise (0.25 equiv / 15 min); [c] time of continous addition of I_2 disolved in DCE (0.15M) by syringe pump (in hours); [d] 25 ºC (reaction mixture refrigerated by a fan) and 65-75 ºC (without fan); [e] isolated yield; [f] **17** was quantitatively recovered; [g] 100% w/w.

[21] Spectral data are in good agreement with those reported in the literature for its enantiomer: Katoh, M.; Mizutani, H.; Honda, T. *Heterocycles* **2006**, *69*, 193.

MECHANISTIC STUDIES
Description of products:

Scheme *S1*. Synthetic approaches



***tert*-Butyl (2*S*)-1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinecarboxylate (14c):**

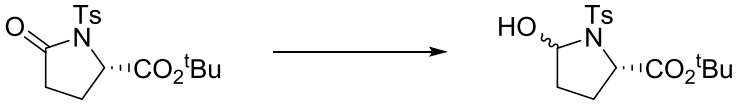
Step 1: L-Glutamic acid (14.7 g, 0.1 mol) was placed in a 250-mL conical flask and NaOH solution (2N) was added slowly until all glutamic acid was dissolved and the mixture became distinctly alkaline. The reaction mixture was then stirred on the magnetic stirrer at 70ºC using a hot water bath. TsCl (0.15 mol) was added in small portions with constant stirring and also, from time to time, small addition of NaOH (2 N) to keep the reaction mixture alkaline. The stirring was continued until a clear homogeneous solution resulted or the TLC showed that the reaction was completed. After cooled and filtered to separate non dissolved solid matter, the filtrate was acidified with concentrated HCl, saturated with sodium chloride and extracted with EtOAc. The organic phase was washed with brine solution and dried overnight over anhydrous sodium sulphate. The solvent was distilled off to get the *N*-tosyl-L-glutamic acid derivative (26.6 g, 0.093 mol, 93%).

Step 2:[22] *N*-Tosyl-L-glutamic acid (0.01 mol) was placed in 100-mL round-bottomed flask, fitted with reflux condenser and calcium chloride guard tube. Acetyl chloride (0.025 mol) was added and refluxed for 2 h in a boiling water bath. After the reaction was completed (tested by TLC), the reaction mixture was cooled and then poured onto crushed ice with continuous stirring. The precipitated product was filtered, recrystallized from water, and directly used for the next step.

[22] Steps 1-2: Srikanth, K.; Kumar, Ch. A.; Ghosh, B.; Jha, T. *Bioorg. Med. Chem*. **2002**, *10*, 2119.

Step 3: To the *N*-tosyl-L-pyroglutamic acid (7.2 g, 25.4 mmol) in CH_3CN (70 ml) was added DMAP (297 mg, 2.5 mmol), Et_3N (5 ml) and $(Boc)_2O$ (8.1 g, 36.2 mmol) in CH_3CN (15 mL) and was stirred for 24 h at room temperature, before quenching by the addition of HCl (10 %) solution. After the reaction mixture was diluted with EtOAc, the layers were separated and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with HCl (10%) solution, saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, and the solvent was evaporated to give the crude product. The residue was purified by column chromatography (hexane/EtOAc, 70:30) to give **14c** (4.3 g, 12.7 mmol, 50%) as a crystalline solid: ^{1}H NMR δ1.50 (s, 9H), 2.05 (dddd, *J* = 1.6, 4.1, 9.2, 11.1 Hz, 1H), 2.36–2.42 (m, 2H), 2.43 (s, 3H), 2.48–2.61 (m, 1H), 4.74 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.97 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ21.7 (CH_3), 23.3 (CH_2), 27.9 (3 x CH_3), 30.5 (CH_2), 60.2 (CH), 83.0 (C), 129.1 (2 x CH), 129.2 (2 x CH), 135.2 (C), 145.2 (C), 169.9 (C), 171.0 (C).[23]

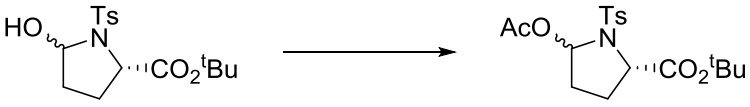
(2*S*)-*tert*-Butyl 5-hydroxy-1-tosylpyrrolidine-2-carboxylate [14b(OH)]:



14c **14b(OH)**

Diisobutylaluminium hydride 1.0 M in toluene (0.19 mL, 0.19 mmol) was added dropwise to a solution of lactam **14c** (43 mg, 0.13 mmol) in anhydrous THF (0.65 mL) at -78 ºC under Ar atmosphere. The reaction was allowed to reach room temperature, and was stirred for 1 h. Then, it was cooled at -78 ºC and MeOH (0.2 mL) was added, stirred for 10 min, poured into a saturated aqueous solution of K_2CO_3 and extracted with EtOAc. The organic phase was dried over sodium sulfate and concentrated under vacuum. The residue was purified by column chromatography (hexanes/EtOAc, 70:30) to yield **14b(OH)** (32 mg, 74 %) as a colorless oil. NMR showed a mixture of isomers in 1:1.7 ratio. ^{1}H NMR δ1.38 (s, 9 H), 1.42 (s, 9 H), 1.87-2.22 (m, 6 H), 2.42 (s, 6 H), 2.39-2.45 (m, 1 H), 2.46-2.59 (m, 1 H), 4.21 (dd, *J* = 8.3, 5.5 Hz, 1 H), 4.40 (dd, *J* = 9.2, 0.9 Hz, 1 H), 5.55 (d, *J* = 5.0 Hz, 1 H), 5.57 (dt, *J* = 5.4, 2.8 Hz, 1 H), 7.29 (d, *J* = 8.5 Hz, 4 H), 7.77 (d, *J* = 8.2 Hz, 2 H), 7.79 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ21.47 (CH_3), 21.49 (CH_3), 27.8 (CH_3 x 6), 28.4 (CH_2), 29.0 (CH_2), 32.5 (CH_2), 34.0 (CH_2), 60.7 (CH), 61.4 (CH), 81.7 (C), 82.4 (C), 84.3 (CH), 85.2 (CH), 127.4 (2 x CH), 127.6 (2 x CH), 129.5 (2 x CH), 129.6 (2 x CH), 136.8 (C), 137.3 (C), 143.7 (2 x C), 170.6 (C), 173.3 (C); MS (ESI$^+$) *m/z* (rel intensity) 364 (M^++ Na, 100); HRMS calcd for $C_{16}H_{23}NO_5NaS$, 364.1195, found 364.1190.

(2*S*)-*tert*-Butyl 5-acetoxy-1-tosylpyrrolidine-2-carboxylate (14b):

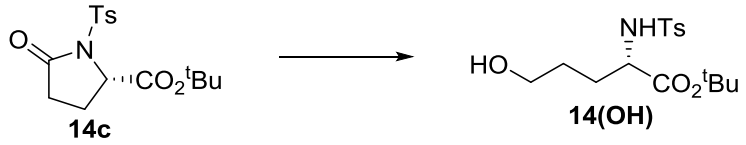


14b(OH) **14b**

[23] spectral data are in good agreement with those reported in the literature: Yar, M.; Unthank, M. G.; McGarrigle, E. M.; Aggarwal V. K. *Chem. Asian J.* **2011**, *6*, 372 – 375.

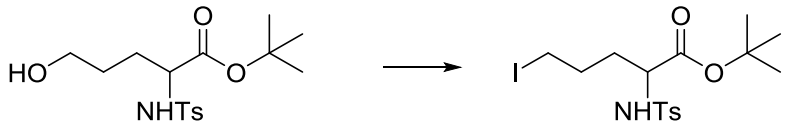
Acetic anhydride (0.05 mL) and pyridine (0.02 mL) were added to a solution of hemiaminal **14b(OH)** (32 mg, 0.094 mmol) in DCM (0.8 mL). The reaction was stirred for 17 h at room temperature and concentrated under vaccum to yield **14b** (35 mg, 97%) as colorless oil, unstable on silica gel and acidic conditions in general. NMR showed a mixture of isomers in 1:1.3 ratio. ^{1}H NMR δ1.40 (s, 9 H), 1.40 (s, 9 H), 1.79 (s, 3 H), 1.82-2.32 (m, 8 H), 1.84 (s, 3 H), 2.35 (s, 3 H), 2.35 (s, 3 H), 4.20-4.26 (m, 2 H), 6.38 (t, *J* = 3.4 Hz, 1 H), 6.44 (d, *J* = 3.9 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 4 H), 7.69 (d, *J* = 8.3 Hz, 2 H), 7.74 (d, *J* = 8.3 Hz, 2 H); ^{1}H NMR (500 MHz, C_6D_6) δ1.26–1.36 (m, 2H), 1.39 (s, 9H), 1.40 (s, 9H), 1.44–1.64 (m, 4H), 1.55 (s, 3H), 1.59 (s, 3H), 1.81–1.95 (m, 1H), 1.85 (s, 6H), 2.00–2.08 (m, 1H), 4.28 (t, *J* = 8.0 Hz, 1H), 4.42 (d, *J* = 9.1 Hz, 1H), 6.72 (d, *J* = 5.4 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 4H), 6.81 (d, *J* = 4.7 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125.7 MHz, C_6D_6) δ20.9 (CH_3), 21.1 (CH_3), 21.4 (2 x CH_3), 28.2 (3 x CH_3), 28.2 (3 x CH_3), 28.5 (CH_2), 28.7 (CH_2), 32.7 (CH_2), 33.4 (CH_2), 62.2 (CH), 63.2 (CH), 81.6 (C), 81.8 (C), 85.1 (CH), 85.3 (CH), 128.7 (2 x CH), 129.8 (2 x CH), 129.9 (4 x CH), 138.1 (C), 138.7 (C), 143.7 (2 x C), 169.4 (C), 169.7 (C), 171.0 (C), 171.2 (C); MS (ESI$^+$) *m/z* (rel intensity) 406 (M^++ Na, 100); HRMS calcd for $C_{18}H_{25}NO_6NaS$, 406.1300, found 406.1304.

***tert*-Butyl (2*S*)-5-hydroxy-2-{[(4-methylphenyl)sulfonyl]amino}pentanoate [14(OH)]**:



To a solution of **14c** (660 mg, 1.9 mmol) in anhydrous THF (47 mL) was added $NaBH_4$ (216 mg, 5.7 mmol), and the mixture was heated at 50-60ºC. Then a solution of *tert*-butyl alcohol:THF (1:1, 10mL) was added dropwise. After the reaction was completed, the reaction mixture was cooled at room temperature and quenched by the slow addition of saturated citric acid solution (pH~4), diluted with EtOAc and washed with brine. After the layers were separated, the aqueous phase was extracted with EtOAc twice. The combined organic layer was dried over anhydrous Na_2SO_4, evaporated and purified by column chromatography (hexane/EtOAc 6:4) to give the desired product **14(OH)** (481 mg, 72%) as a crystalline solid: Mp. 68.9-70.1ºC (hexane/EtOAc); $[\alpha]_D$ +20.0º (*c* 0.35); ^{1}H NMR δ1.24 (s, 9H), 1.64–1.71 (m, 3H), 1.80–1.86 (m, 1H), 2.40 (s, 3H), 3.60–2.69 (m, 2H), 3.81 (dd, *J* = 4.4, 7.2 Hz, 1H), 5.50 (bs, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ21.3 (CH_3), 27.9 (3 x CH_3), 28.0 (CH_2), 30.1 (CH_2), 56.0 (CH), 62.0 (CH_2), 82.4 (C), 127.3 (2 x CH), 129.6 (2 x CH), 136.9 (C), 143.2 (C), 170.8 (C); MS (ESI$^+$) *m/z* (rel intensity) 366 (M^++ Na, 100); HRMS (ESI+) calcd for $C_{16}H_{25}NO_5SNa$, 366.1353 found 366.1353.

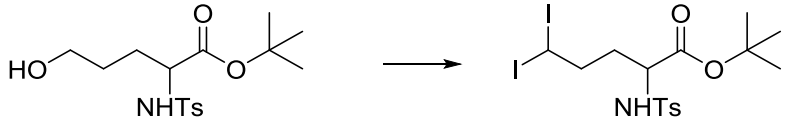
***tert*-Butyl (2*S*)-5-iodo-2-{[(4-methylphenyl)sulfonyl]amino}pentanoate [14(I)]:**



14(OH) **14(I)**

I_2 (350 mg, 1.4 mmol) was added to a solution of PPh_3 (913 mg, 3.5 mmol) and imidazole (254 mg, 3.7 mmol) in anhydrous dichloromethane (5 ml) at 0ºC and allowed to warm at room temperature. Then a solution of alcohol **14(OH)** (600 mg, 1.75 mmol) in anhydrous dichloromethane (3 mL) was added at 0ºC and the reaction was stirred during 2h at this temperature. The reaction mixture was poured into a saturated aqueous solution of $Na_2S_2O_3$ and extracted with dichloromethane. The organic phase was dried over sodium sulfate and concentrated under vacuum. The residue was purified by column chromatography (hexanes/EtOAc, 70:30) to yield **14(I)** (760 mg, 1.7 mmol, 96 %) as a crystalline solid. Mp. 122.5-123.7ºC (hexane-EtOAc); $[\alpha]_D$ +51º (*c* 0.21), ^{1}H NMR δ1.26 (s, 9H), 1.64–1.73 (m, 1H), 180–1.97 (m, 3H), 2.40 (s, 3H), 3.12–3.23 (m, 2H), 3.76 (ddd, *J* = 4.2, 8.5, 8.5 Hz, 1H), 5.23 (d, *J* = 8.5 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR δ5.38 (CH_2), 21.4 (CH_3), 27.6 (3 x CH_3), 28.7 (CH_2), 34.2 (CH_2), 55.2 (CH), 82.8 (C), 127.3 (2 x CH), 129.6 (2 x CH), 136.7 (C), 143.6 (C), 170.3 (C). MS (ESI^+) *m/z* (rel intensity) 476 (M^++ Na, 100); HRMS (ESI+) calc for $C_{16}H_{24}NO_4SINa$, 476.0369 found 476.0363.

***tert*-Butyl (2*S*)-5,5-diiodo-2-{[(4-methylphenyl)sulfonyl]amino}pentanoate [14(I_2)]:**



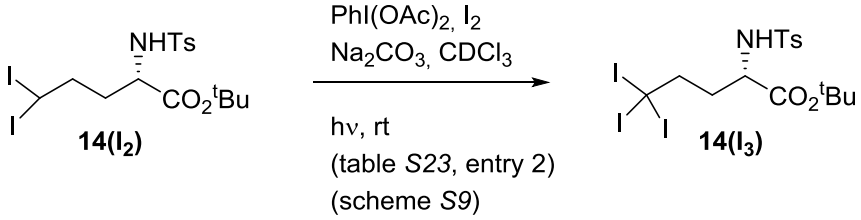
14(OH) **14(I_2)**

Dess-Martin periodinane (488 mg, 1.15 mmol) was added to a solution of alcohol **14(OH)** (329 mg, 0.96 mmol) in DCM (10 mL) and stirred at room temperature during 45 min. Then, the reaction was poured into a saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic phase was dried over sodium sulfate and concentrated under vacuum. The crude residue was used in the next step without further purification. Hydrazine monohydrate (0.9 mL) was added to a solution of the crude in dry DCM (1mL) and stirred at room temperature during 1 h. Then, water and DCM were added and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under vacuum. To this crude pale yellow oil were added, at room temperature and under argon, TEA (0.25 mL), CH_2Cl_2 (1mL) and iodine in 3 portions (300 mg) and the reaction was stirred for 10 min. After hydrolysis with an aqueous solution of Na_2SO_3, the aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over $MgSO_4$, filtered and concentrated under vacuum.[24] Purification by chromatography gave the diiodo derivative **14(I_2)** as a yellow solid (110 mg, 21% after 3 steps). Mp.

[24] Français, A.; Leyva-Pérez, A.; Etxebarria-Jardi, G.; Peña, J.; Ley, S. V. *Chem. Eur. J.* **2011**, *17*, 329.

117-119ºC (hexane/EtOAc); $[\alpha]_D$ +24.1º (*c* 0.22); ^{1}H NMR δ1.29 (s, 9H), 1.73 (dddd, *J* = 5.0, 8.2, 10.2, 12.9 Hz, 1H), 1.92 (dddd, *J* = 5.0, 5.3. 10.2, 13.9 Hz, 1H), 2.35–1.49 (m, 2H), 2.41 (s, 3H), 3.79 (ddd, *J* = 5.0, 8.2, 8.2 Hz, 1H), 5.13 (dd, *J* = 5.6, 6.7 Hz, 1H), 5.17 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR δ–29.0 (CH), 21.5 (CH_3), 27.7 (3 x CH_3), 35.4 (CH_2), 43.3 (CH_2), 54.5 (CH), 83.2 (C), 127.4 (2 x CH), 129.8 (2 x CH), 136.6 (C), 143.8 (C), 170.0 (C); MS (ESI$^+$) *m/z* (rel intensity) 602 (M^++ Na, 100); HMRS (ESI +) *m/z* calc for $C_{16}H_{23}NO_4SNa$, 601.9335 found 601.9341.

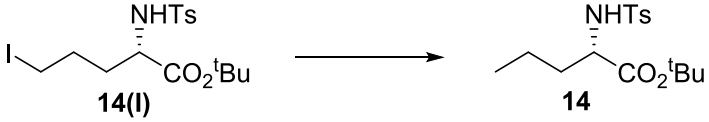
***tert*-Butyl (2*S*)-5,5,5-triiodo-2-{[(4-methylphenyl)sulfonyl]amino}pentanoate [14(I_3)]:**



Following conditions described in table *S23*, entry 2, compound **14(I_3)** was detected as major product in the crude reaction by ^{1}H NMR (87.2% conversion)(scheme *S9*). **14(I_3)** was relatively stable when reaction mixture was kept at -22 ºC in the dark.

Description of the compound **14(I_3)** from a crude reaction. ^{1}H NMR (500 MHz, -20 ºC) δ1.27 (s, 9H), 1.81–1.90 (m, 1H), 1.90–2.00 (m, 1H), 3.10 (ddd, *J* = 3.5, 14.8, 15.1 Hz, 1H), 3.14 (ddd, *J* = 4.7, 14.8, 15.1 Hz, 1H), 3.87 (ddd, *J* = 4.4, 7.9, 8.2 Hz, 1H), 5.53 (d, *J* = 8.2 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, -20 ºC) δ–108.8 (C), 21.5 (CH_3), 27.5 (3 x CH_3), 38.1 (CH_2), 52.8 (CH), 60.4 (CH_2), 83.3 (C), 127.2 (2 x CH), 129.8 (2 x CH), 135.6 (C), 143.9 (C), 169.8 (C); MS (ESI$^+$) *m/z* (rel intensity) 728 (M^++ Na, 100); HMRS (ESI+) *m/z* calc for $C_{16}H_{22}I_3SNaNO_4$, 727.8302, found 727.8303.

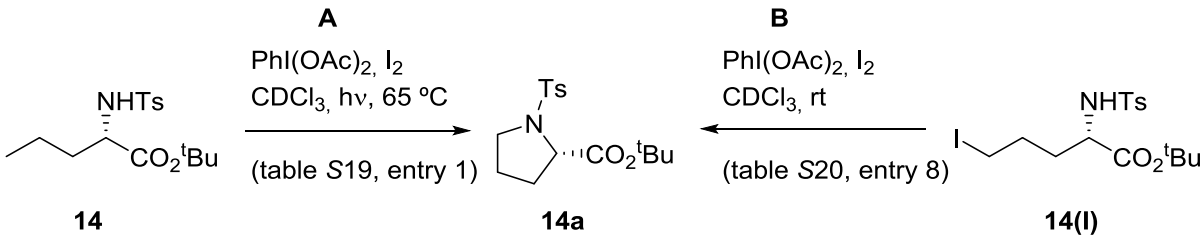
***tert*-Butyl (2*S*)-2-{[(4-methylphenyl)sulfonyl]amino}pentanoate (14)**:[25]



Bu_3SnH (0.9 mL, 3.3 mmol) and AIBN (54 mg, 0.33 mmol) were added to a solution of **14(I)** (760 mg, 1.65 mmol) in benzene (80 mL) and was refluxed during 1 h. Then, the reaction mixture was concentrated under vacuum and the residue was purified by column chromatography (hexanes and gradient elution to 30 % EtOAC) to give the derivate **14** (512 mg, 1.57 mmol, 94 %) as a crystalline solid. ^{1}H NMR δ 0.90 (dd, *J* = 7.4, 7.4 Hz, 3H), 1.24 (s, 9H), 1.35-1.45 (m, 2H), 1.52-1.68 (m, 2H), 2.40 (s, 3H), 3.76 (ddd, *J* = 5.0, 7.7, 9.2 Hz, 1H), 5.10 (d, *J* = 9.2 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ13.5 (CH_3), 18.2 (CH_2), 21.4 (CH_3), 27.7 (3 x CH_3), 35.7 (CH_2), 56.0 (CH), 82.2 (C), 127.4 (2 x CH), 129.6 (2 x CH), 137.1 (C), 143.4 (C), 171.0 (C).

[25] spectral data are in good agreement with those reported in the literature: Baldwin, J. E.; Spivey, A. C.; Schofield, C. J.; Sweeney, J. B. *Tetrahedrom* **1993**, *49*, 6309–6330.

(*S*)-*tert*-Butyl 1-tosylpyrrolidine-2-carboxylate (**14a**):[26]



14 **14a** **14(I)**

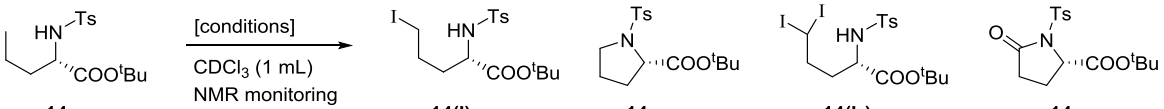
According to GP1 (table *S*19, entry 1), pyrrolidine **14a** was prepared from **14** (100 mg, 0.306 mmol) in 71% following approach **A** or from **14(I)** (100 mg, 0.22 mmol) according to GP3 (table *S*20, entry 8) in quantitative yield following approach **B,** as a crystalline solid compound. ^{1}H NMR δ1.45 (s, 9H), 1.72–1.79 (m, 1H), 1.91–2.04 (m, 3H), 2.42 (s, 3H), 3.32 (ddd, J = 7.0, 7.0, 9.2 Hz, 1H), 3.44–3.49 (m, 1H), 4.19 (dd, J = 3.5, 8.0 Hz, 1H), 7.30 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.1 Hz, 2H); ^{13}C NMR δ 21.5 (CH_3), 24.5 (CH_2), 27.9 (3 x CH_3), 30.9 (CH_2), 48.3 (CH_2), 61.2 (CH), 81.5 (C), 127.5 (2 x CH), 129.5 (2 x CH), 136.0 (C), 143.3 (C), 171.3 (C).

[26] spectral data are in good agreement with those reported in the literature: Foschi, F.; Landini, D.; Lupi, V.; Mihali, V.; Penso, M.; Pilati, T.; Tagliabue, A. *Chem. Eur. J.* **2010**, *16*, 10667 – 10670.

MECHANISTIC STUDIES (NMR monitored reactions):

NMR monitored experiments with 14.

Table *S17.* Monitored experiments with **14**:



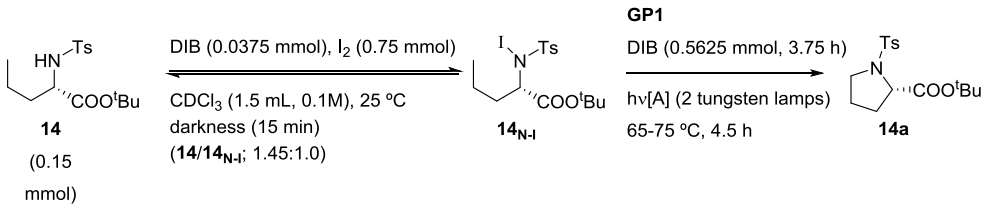
14 **14(I)** **14a** **14(I$_2$)** **14c**

[table 3]

entry	substrate **14** mmol	procedure[a]	$PhI(OAc)_2$ mmol[b]	I_2 mmol[b]	aditives w/w	[C] M	temp ºC	time h	conv. %[c]	**14a** %[d]	**14c** %[d]	notes[e]
1	0.15	GP1	4	5	-	0.1	65	4.5	73	73	-	hν [A]
2	0.15	$GP3_{Na2CO3}$	6	1.4	Na_2CO_3, 100%	0.03	27	6	95[f]	5	84.3	hν [A]
3	0.05	$GP3_{Na2CO3}$	6	1.4	Na_2CO_3, 100%	0.03	27	6	100[g]	4	88	hν [A+f]
4	0.05	GP3	2	2	-	0.05	27	0.41	0[h]	-	-	dark
5	0.05	GP3	2	2	Na_2CO_3, 100%	0.05	27	3.6	0[i]	-	-	dark

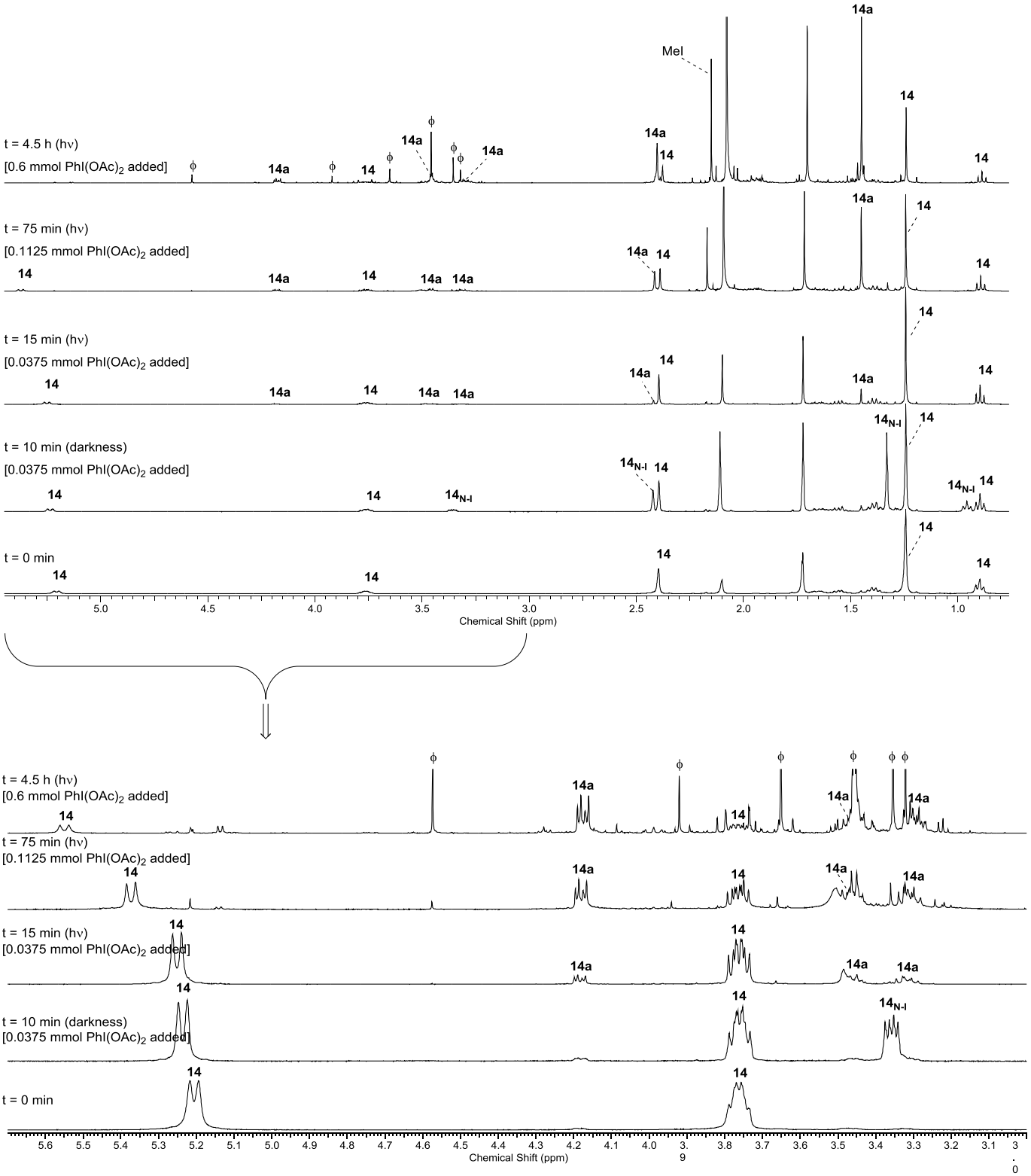
[a] GP1: $PhI(OAc)_2$ added portionwise (0.25 mmol per mmol of **14**, every 15 min), GP3: all reagents added in one portion; [b] millimols per millimol of **14**; [c] global convertion of starting material. Detection of $\mathbf{14_{N\text{-}I}}$, was not considered as converted product since this afforded starting material after quenching; [d] convertions; [e] [A] = tungsten lamps (80W), [A+f] = light filtered by 1 cm pathlength of aqueous solution of K_2CrO_4 (0.27 g/L) and Na_2CO_3 (1 g/L) into pyrex glasses (λ>445 nm); [f] besides **14**, **14a** and **14c**, **14(I)** (5.7%) was detected by ^{1}H NMR; [g] besides **14a** and **14c**, **14(I)** (8%) was detected by ^{1}H NMR; [h] $\mathbf{14_{N\text{-}I}}$ was detected by ^{1}H NMR (**14**/$\mathbf{14_{N\text{-}I}}$, 1:1.52) after 20 min; [i] $\mathbf{14_{N\text{-}I}}$ was detected by ^{1}H NMR (**14**/$\mathbf{14_{N\text{-}I}}$, 1:0.31) after 3.6 h.

Scheme *S2*: Table *S17* (entry 6):

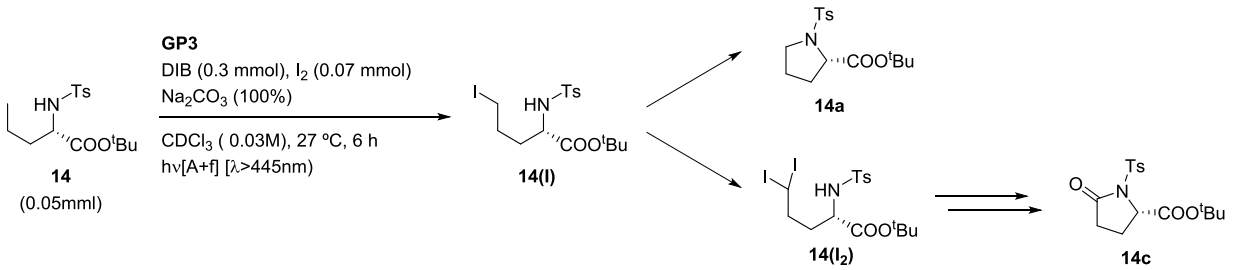


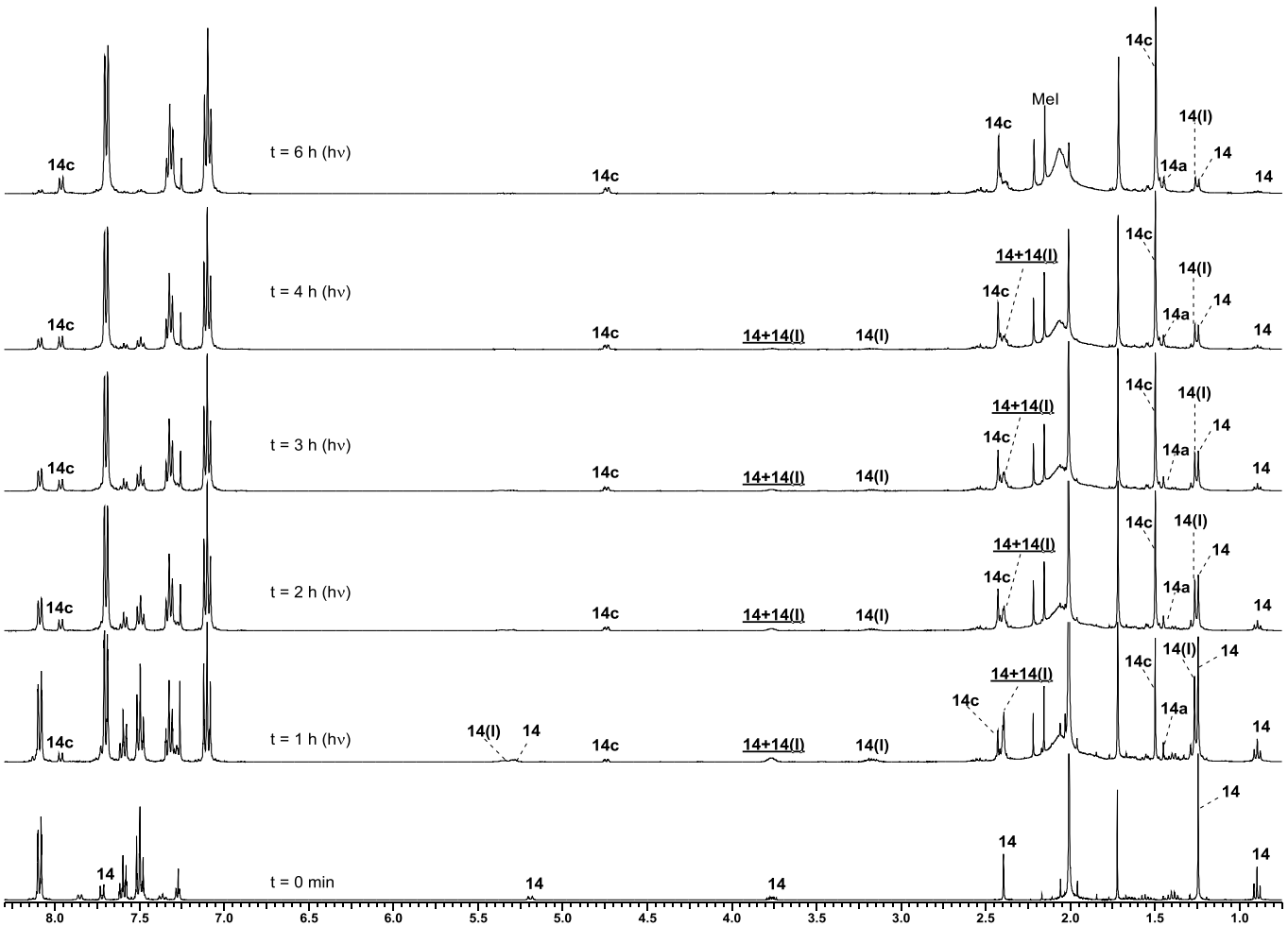
GP1: $PhI(OAc)_2$ added portionwise (0.25 equiv/15 min)

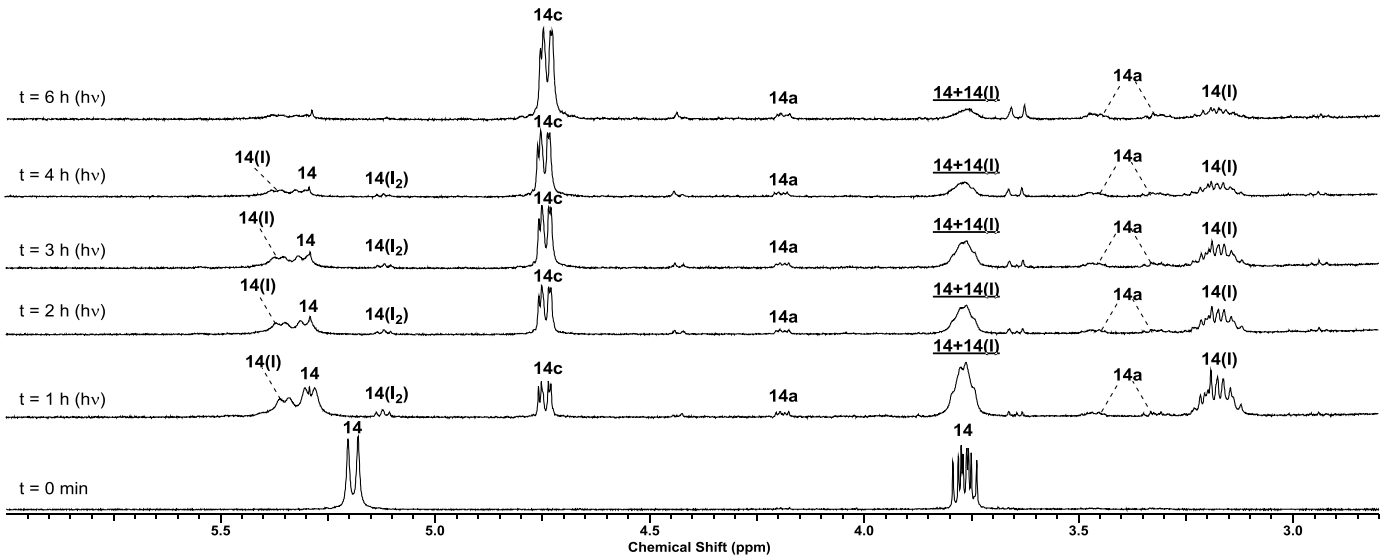
(ϕ) signals from side products that appear along the time when the reaction is performed with the system $PhI(OAc)_2/I_2$ in $CDCl_3$ as solvent and tungsten lamps as light source (see scheme *S5*). These signals are independent from our substrates.



Scheme *S3*: Table *S17* (entry 8):

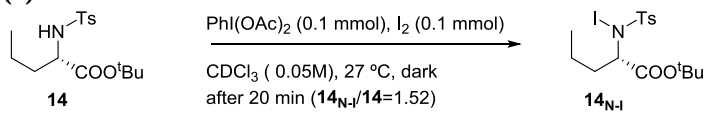


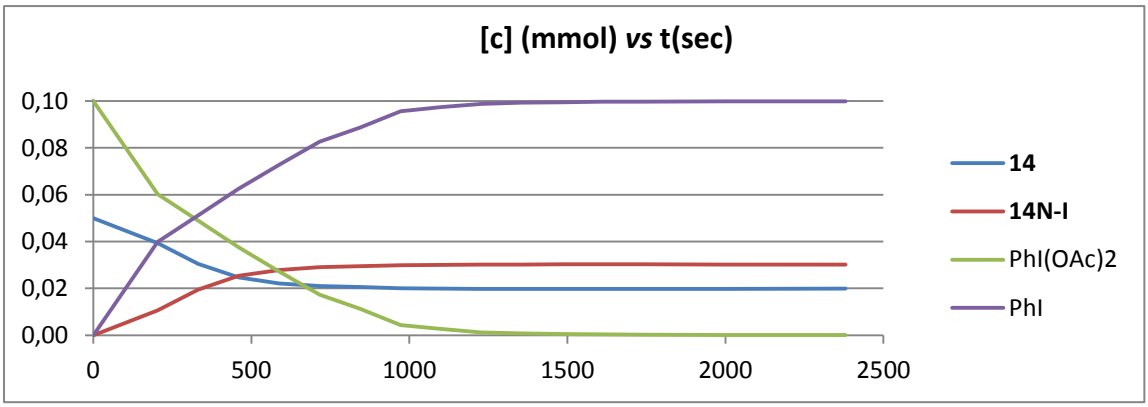




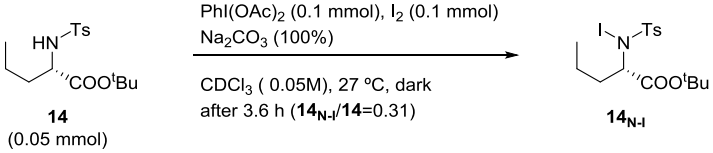
Scheme *S4*: (a) Formation of $\mathbf{14_{N\text{-}I}}$ in absence of Na_2CO_3. **(b)** Formation of $\mathbf{14_{N\text{-}I}}$ in presence of Na_2CO_3. **(c)** Consumption of $PhI(OAc)_2$ in the presence of I_2: (A) in absence of Na_2CO_3, (B) in presence of Na_2CO_3.

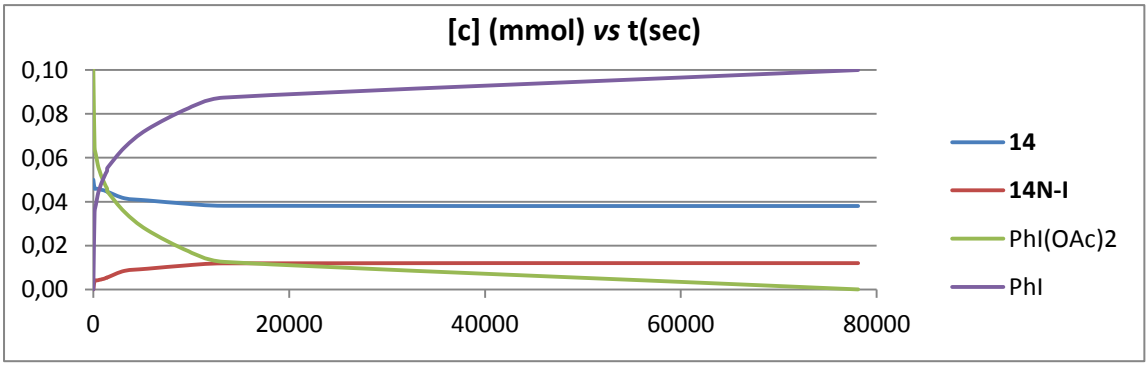
(a):



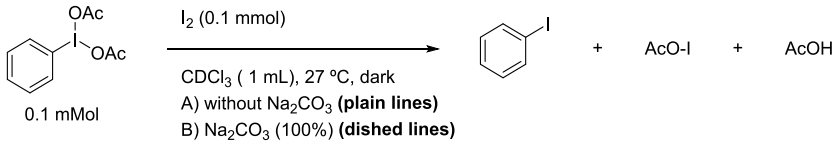


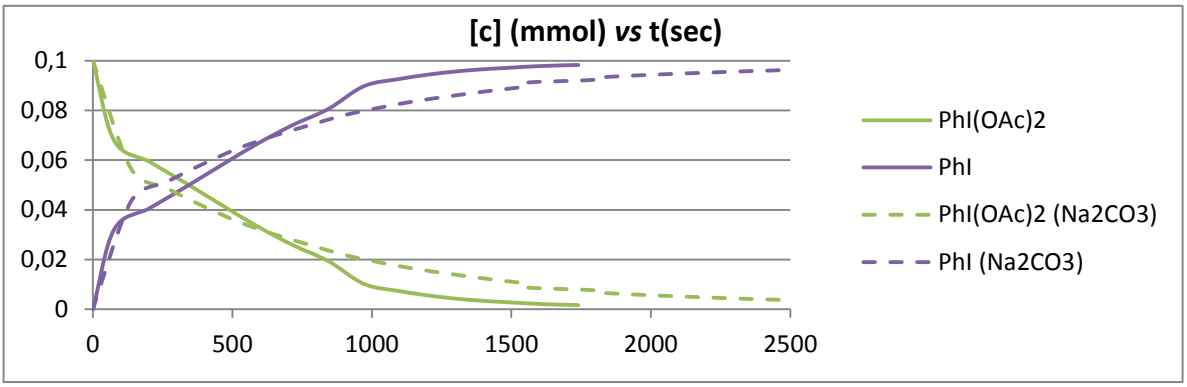
(b):





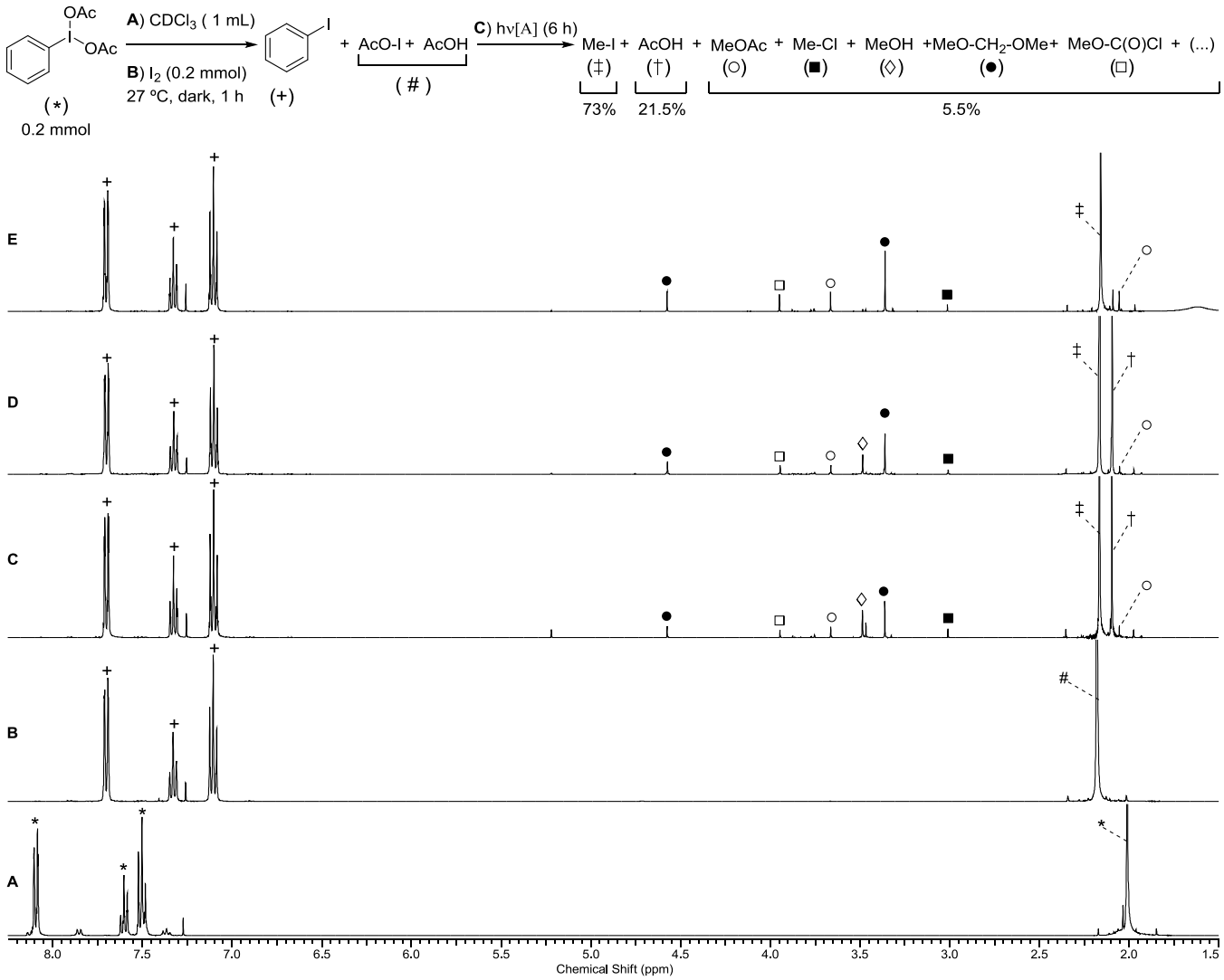
(c):





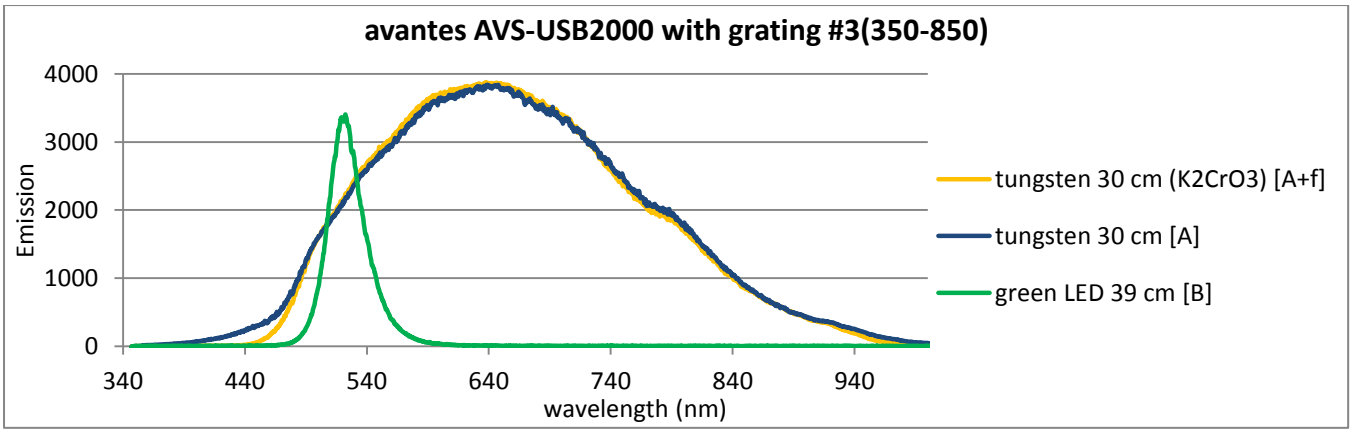
Determination of products from photolysis of $PhI(OAc)_2$ with I_2:

Scheme *S5*: Formation of side products derived from photolysis of AcOI and I_2 in $CDCl_3$ under irradiation with tungsten lamps (hν[A]).



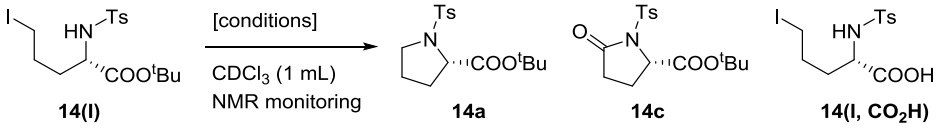
[a] **A**: $PhI(OAc)_2$ in $CDCl_3$; **B**: I_2 was added and stirred in the darknes for 1 h; **C**: Reaction mixture was irradiated with 2 tunsgten lamps at 20 cm for 6 h while flask was refrigerated with a fun; **D**: Reaction mixture was further irradiated for 6 h; **E**: Reaction mixture was quenched with 20% aqueous solution of $Na_2S_2O_3$. MeOH and AcOH were extracted into the water phase.

Scheme *S6*: Relative emission spectrum of different light sources in the region 340-950 nm



NMR monitored experiments with 14(I).

Table *S18*. Monitored experiments with **14(I)**

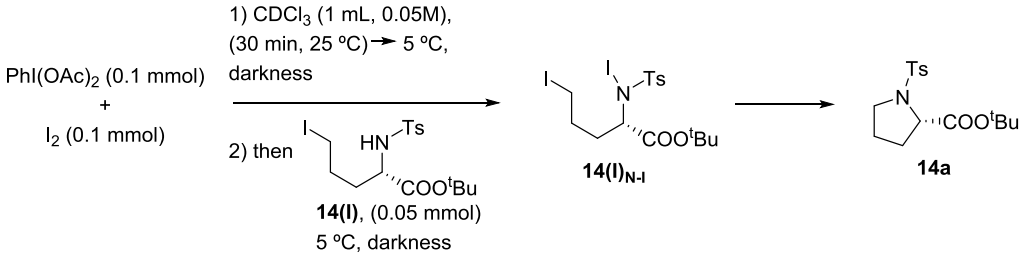


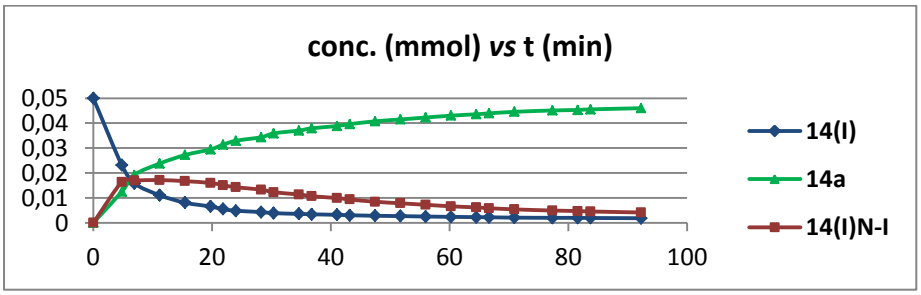
14(I) **14a** **14c** **14(I, CO_2H)**

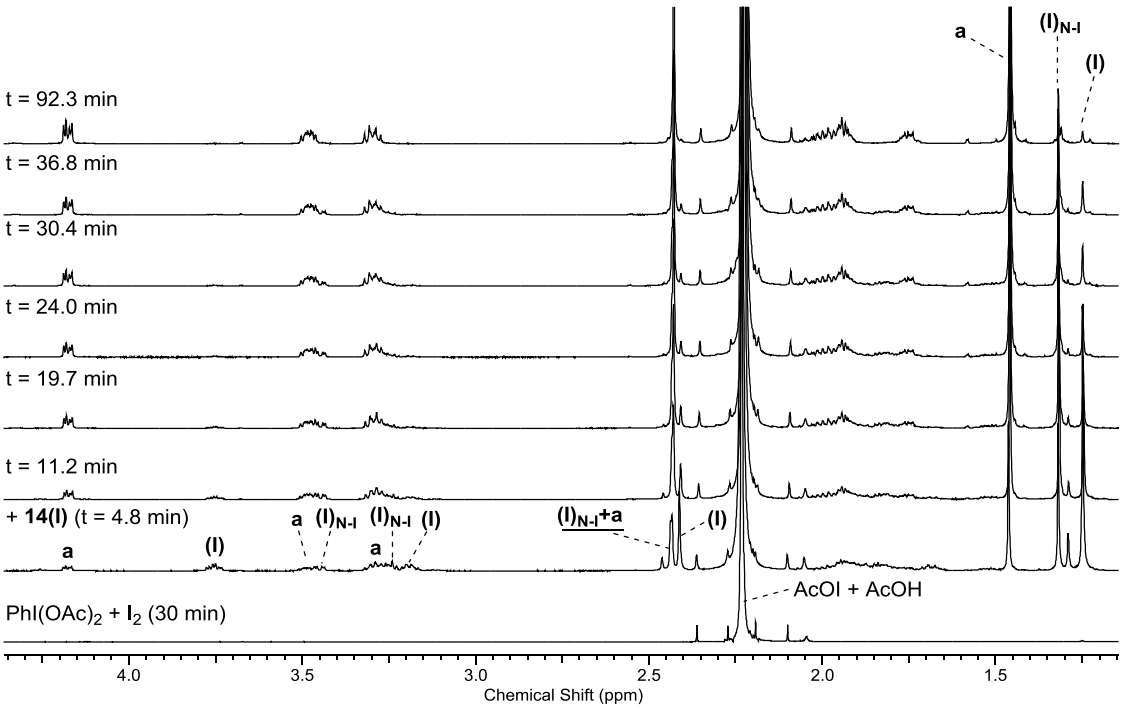
	entry	substrate **14(I)** mmol	procedure[a]	$PhI(OAc)_2$ mmol[b]	I_2 mmol[b]	aditives mmol[b] or w/w	[C] M	temp[c] ºC	time h	conv. %[d]	**14a** %[e]	**14c** %[e]	notes[f]
	1	0.1	-	-	-	-	0.1	60	10	0	no reaction		dark or hν [A]
	2	0.1	GP3	-	5	-	0.1	27	14	50[g]	no reaction		dark or hν [A]
	3	0.1	GP3	-	1	-	0.05	27	48	0	no reaction		dark or hν [B]
	4	0.1	GP3	-	-	AcOH, 2	0.1	60	16	0	no reaction		dark or hν [A]
	5	0.1	GP3	-	-	CSA, 1	0.1	27	12	15[g]	no reaction		dark
	6	0.1	GP3	-	-	$Zn(OTf)_2$, 1	0.1	27	12	0	no reaction		dark
	7	0.052	GP3	2	-	-	0.052	27	10	0	no reaction		dark or hν [A]
	8	0.05	GP3	2	1	-	0.05	27	<5 min	100	100	-	dark
	9	0.05	GP4	2	2	-	0.05	27	<3 min	100	100	-	dark
[equation 1]	10	0.05	GP4	2	2	-	0.05	5	1	100	100	-	dark
[equation 1]	11	0.05	GP3	2	2	-	0.05	5	3.5	100	100	-	dark
[equation 1]	12	0.05	GP3	2	0.2	-	0.05	5	10	100	100	-	dark
[equation 1]	13	0.05	GP3	2	2	Na_2CO_3, 200%	0.05	5	12	0	-	-	dark
[equation 1]	14	0.05	GP3	2	0.2	Na_2CO_3, 200%	0.05	27	24	86	86	-	dark, 11.1 h / 50%
[equation 1]	15	0.05	GP4	2	2	Na_2CO_3, 200%	0.05	27	257	71.6	71.6	-	dark, 87.5 h / 50%
[equation 2]	16	0.03	GP3	4	1	$NaHCO_3$, 100%	0.05[k]	25	16	95	49.7	45.3	hν [A]
[equation 2]	17	0.03	$GP3_{Na2CO3}$	6	1.3	Na_2CO_3, 200%	0.03	24	10	100[l]	12	82	hν [A]
[equation 2]	18	0.03	$GP3_{Na2CO3}$	6	1.3	Na_2CO_3, 200%	0.03	24	7.5	100[m]	8	87	hν [B]

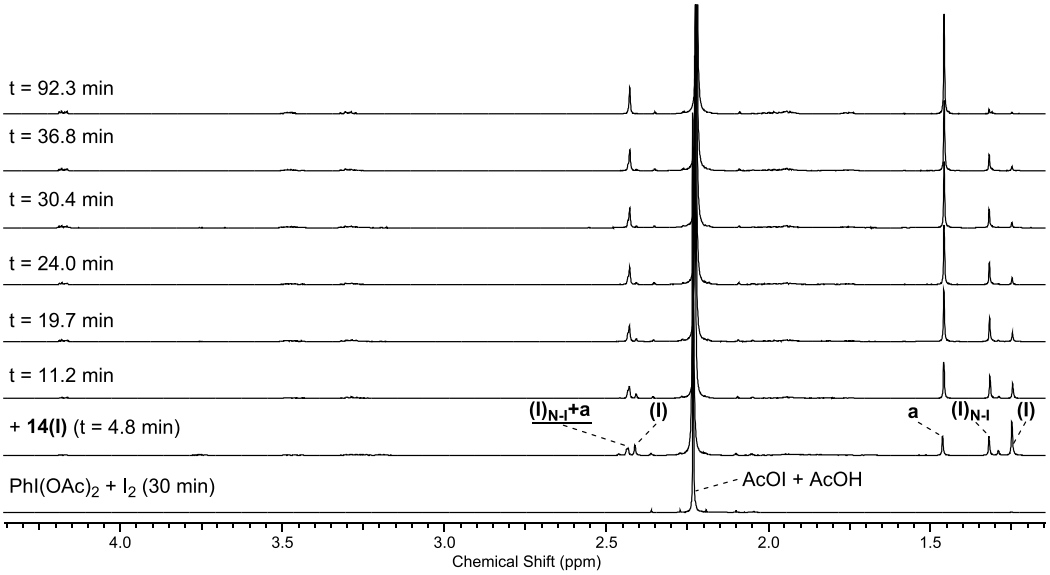
[a] GP3: all reagents added in one portion, GP4: $PhI(OAc)_2$ and I_2 were stirred in the solvent at room temperature untill the $PhI(OAc)_2$ desappeared (15-45 min), previous to the addition of **14(I)**; [b] millimols per millimol of **14(I)**; [c] temperature controled by the NMR apparatus; [d] global conversion of starting material; [e] conversions; [f] [A] = tungsten lamps (80W), [B] = green LED light; [g] deprotected compound **14(I, COOH)** was observed; [h] equivalents of reagents added every 12 h; [i] 200% w/w; [j] DIB + I_2 previouly mixed; [k] DCE as solvent; [l] 6% of another not identified product seems to be formed; [m] 5% of another not identified product seems to be formed.

Scheme *S7*: Table *S18* (entry 10):

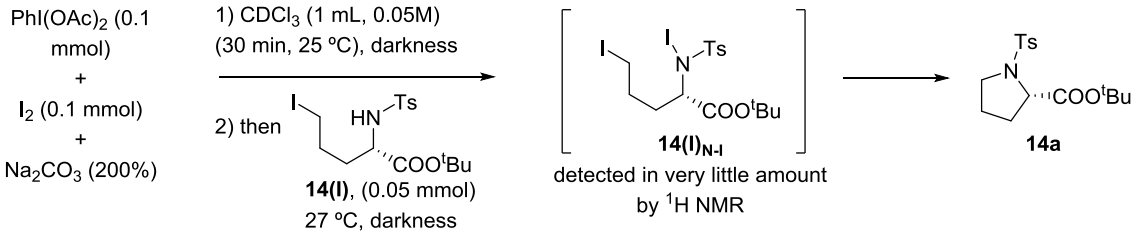




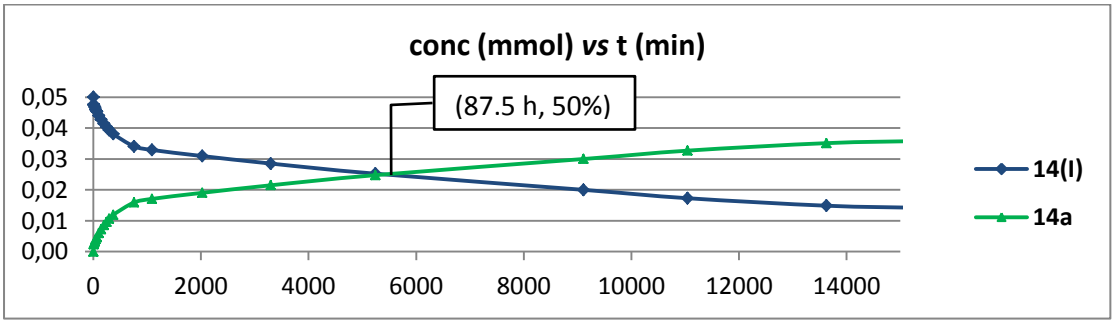




Scheme *S8*: Table *S18* (entry 15):

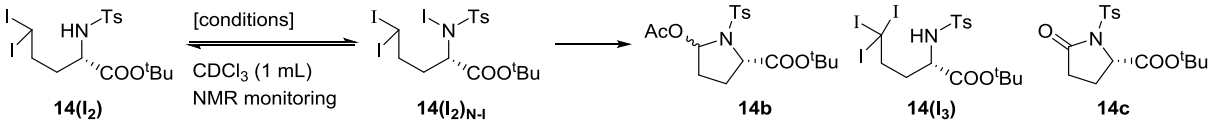


Note: **14(I)$_{N-I}$** was detected by ^{1}H NMR during the whole time in very little amount (<0.002 mmol) indicating that the equilibrium **14(I)**↔**14(I)$_{N-I}$** is displaced toward **14(I)** in these conditions.



NMR monitored experiments with $14(I_2)$

Table *S19*. Monitored experiments with **$14(I_2)$**

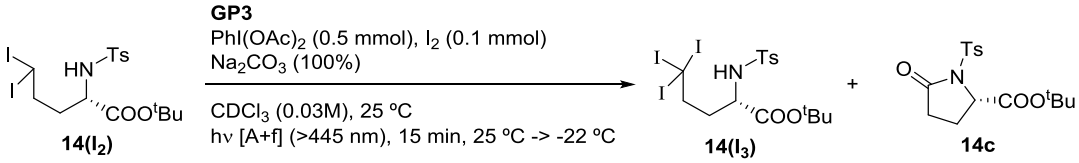


[table 3]

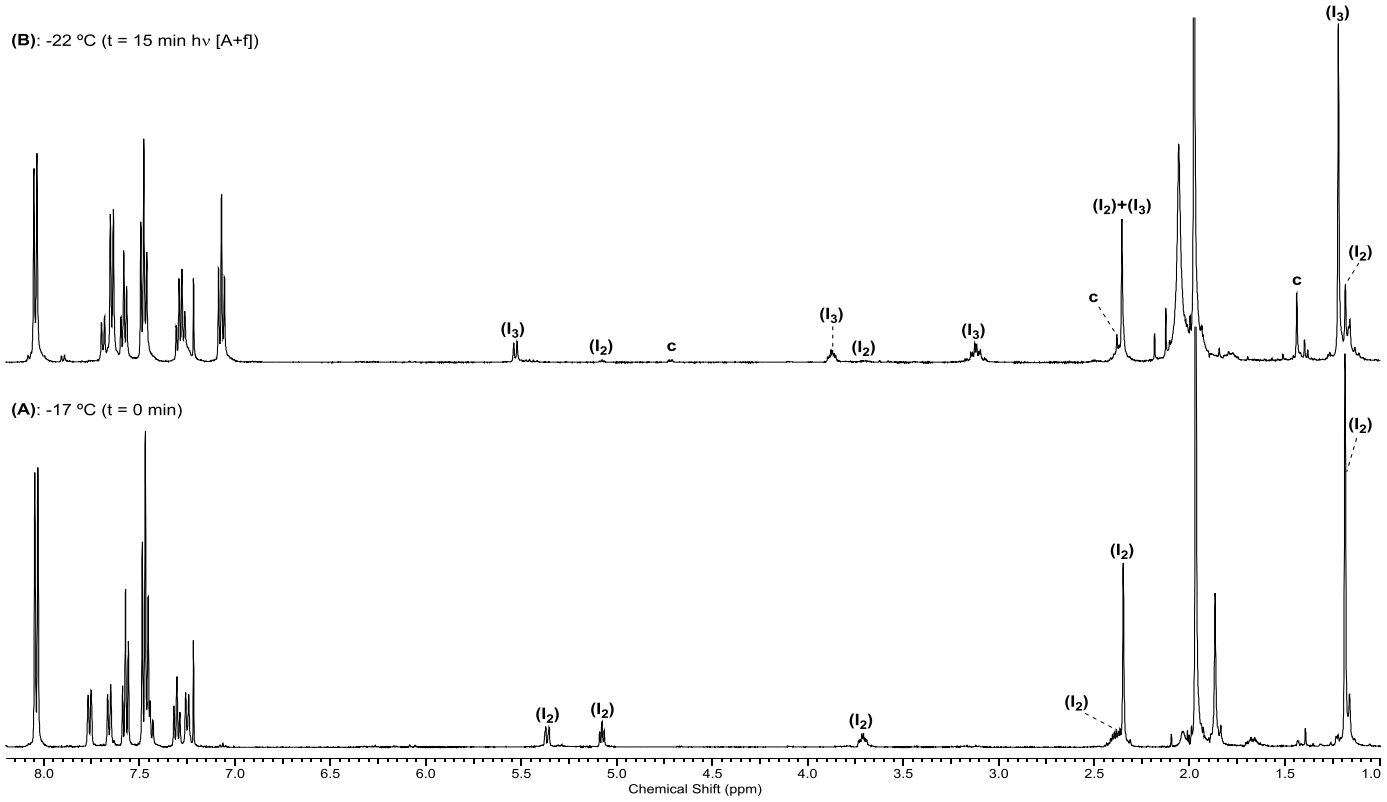
entry	substrate **14(I_2)** mmol	procedure[a]	$PhI(OAc)_2$ mmol[b]	I_2 mmol[b]	aditives mmol[b]	[C] M	temp ºC	time h	conv. %[c]	**14b** %[d]	**14c** %[d]	**14(I_3)** %[d]	notes[e]
1	0.05	GP3	3.5	1	Na_2CO_3, 100%	0.03	27	2	87[f]	-	78.3	-	hν [A]
2	0.05	GP3	10	2	Na_2CO_3, 100%	0.03	25	0.25	95.3	-	8.1	87.2[g]	hν [A+f]
3	0.05	GP3	3	1	-	0.03	5-35	4	71.6[h]	11.2	8.8	40.8	dark + hν [A+f][i]
4	0.05	GP3	3	1	Na_2CO_3, 100%	0.03	27	2.4	58[j]	-	34.0	13.4	dark + hν [A+f][i]
5	0.05	GP4	4	1	-	0.03	27	3	100	>95	-	-	dark
6	0.05	GP4	4	1	Na_2CO_3, 200%	0.03	27	3	12[k]	7	-	-	dark

[a] GP1: $PhI(OAc)_2$ added portionwise (0.25 equiv/15 min), GP3: all reagents added in one portion, GP4: $PhI(OAc)_2$ and I_2 were stirred in the $CDCl_3$ for 24 h, previous to the addition of **$14(I_2)$**; [b] millimols per millimol of **$14(I_2)$**; [c] global convertion of starting material; [d] convertions; [e] [A] = tungsten lamps (80W), [A+f] = tungsten lamps (80W) filtered by 1 cm pathlength of aqueous solution of [K_2CrO_4 (0.27 g/L) and Na_2CO_3 (1 g/L)] into pyrex glasses (λ>445 nm); [f] **14a** (8.7%) was also detected by ^{1}H NMR; [g] **$14(I_3)$** was relatively stable when reaction mixture was keept at -22 ºC; [h] **14a** (10.8%) was also detected by ^{1}H NMR; [i] procedure described in schemes *S10* and *S11*, with more detail; [j] **14a** (10.3%) was also detected by ^{1}H NMR; [k] besides **$14(I_2)$** (66%) and **14b**, **$14(I_2)_{N-I}$** (22%) and **14a** (5%) were detected by ^{1}H NMR. **$14(I_2)_{N-I}$** was considered as non-converted compound.

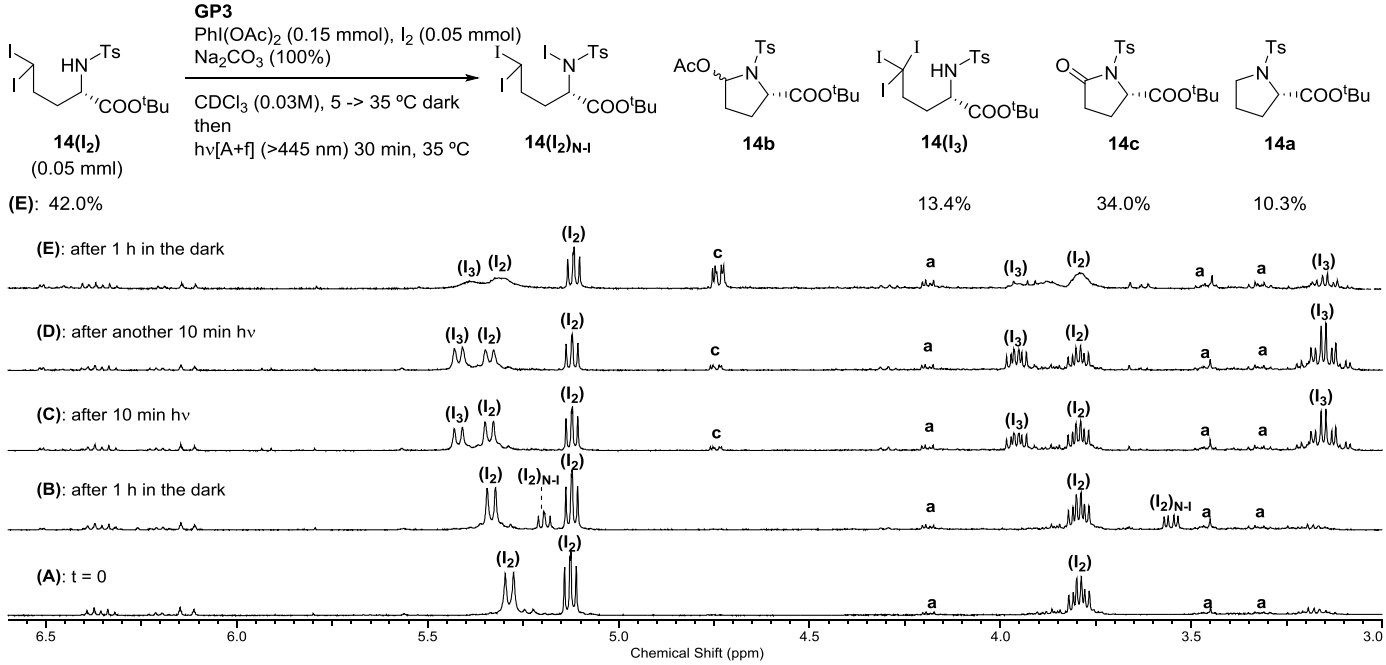
Scheme *S9*: Table *S19* (entry 2)



Procedure: $PhI(OAc)_2$ and Na_2CO_3 were added to a solution of **$14(I_2)$** in $CDCl_3$ at rt, and the mixture was submitted to a ^{1}H NMR at – 17 ºC **(A)**. Then, the mixture was allowed to reach 25 ºC, iodine was added and the reaction was irradiated with filtered light [A+f] for 15 min. Finally, the crude reaction was submitted to a ^{1}H NMR at -22 ºC **(B)**.

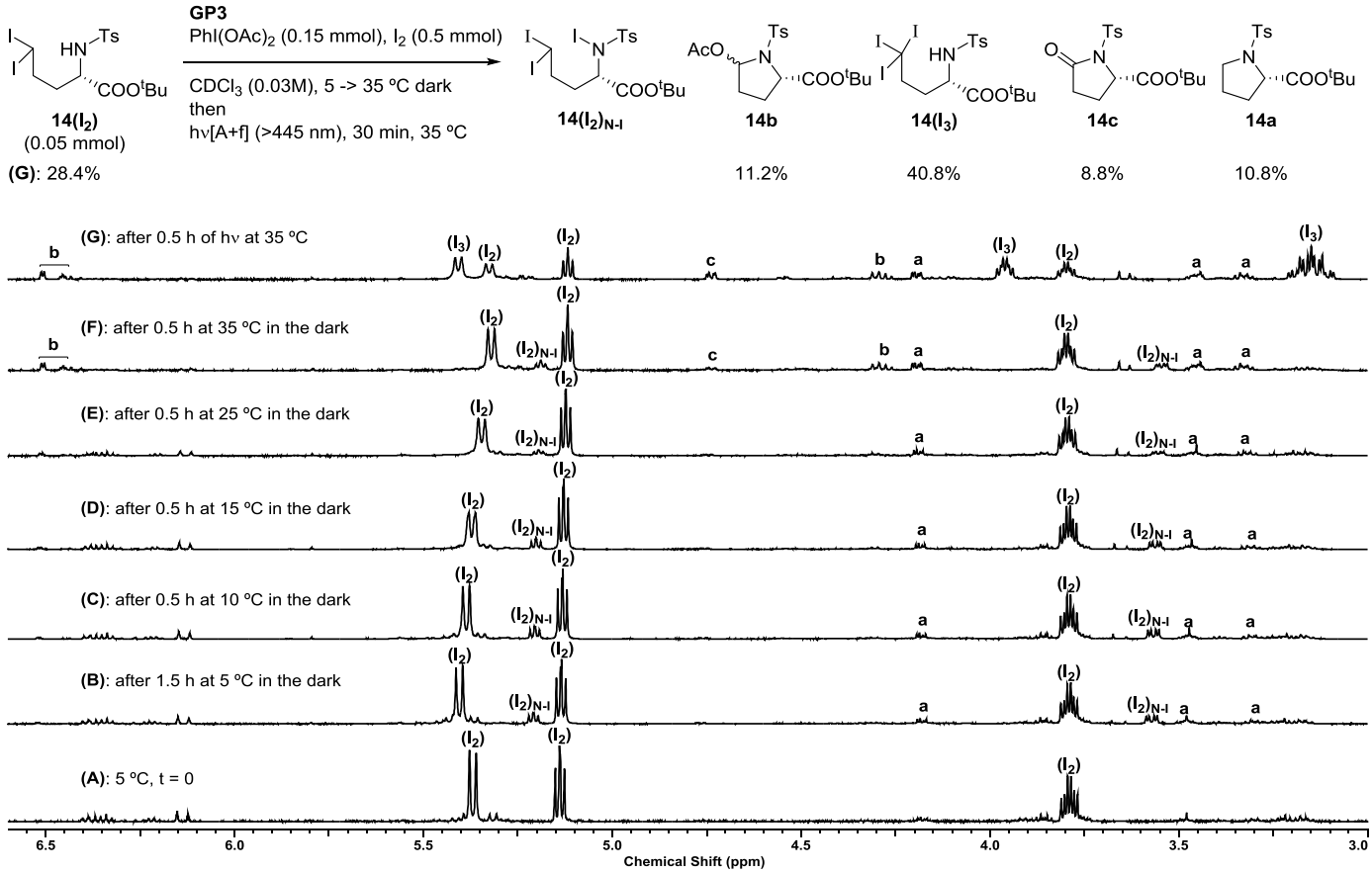


Scheme *S10*: Table *S19* (entry 4)



Note: When **14(I$_2$)** [**A**] was submitted to MHAT conditions in the dark and kept during one hour, formation of **14(I$_2$)$_{N\text{-}I}$** was observed, which did not lead to cyclic compound **14b** [**B**]. [**C** and **D**] show how irradiation is necessary to further functionalize the iodinated moiety, however, more interestingly is the evolution between [**D**→**E**] indicating that the conversion of **14(I$_3$)** toward **14c** did not need either light or aqueous quenching.

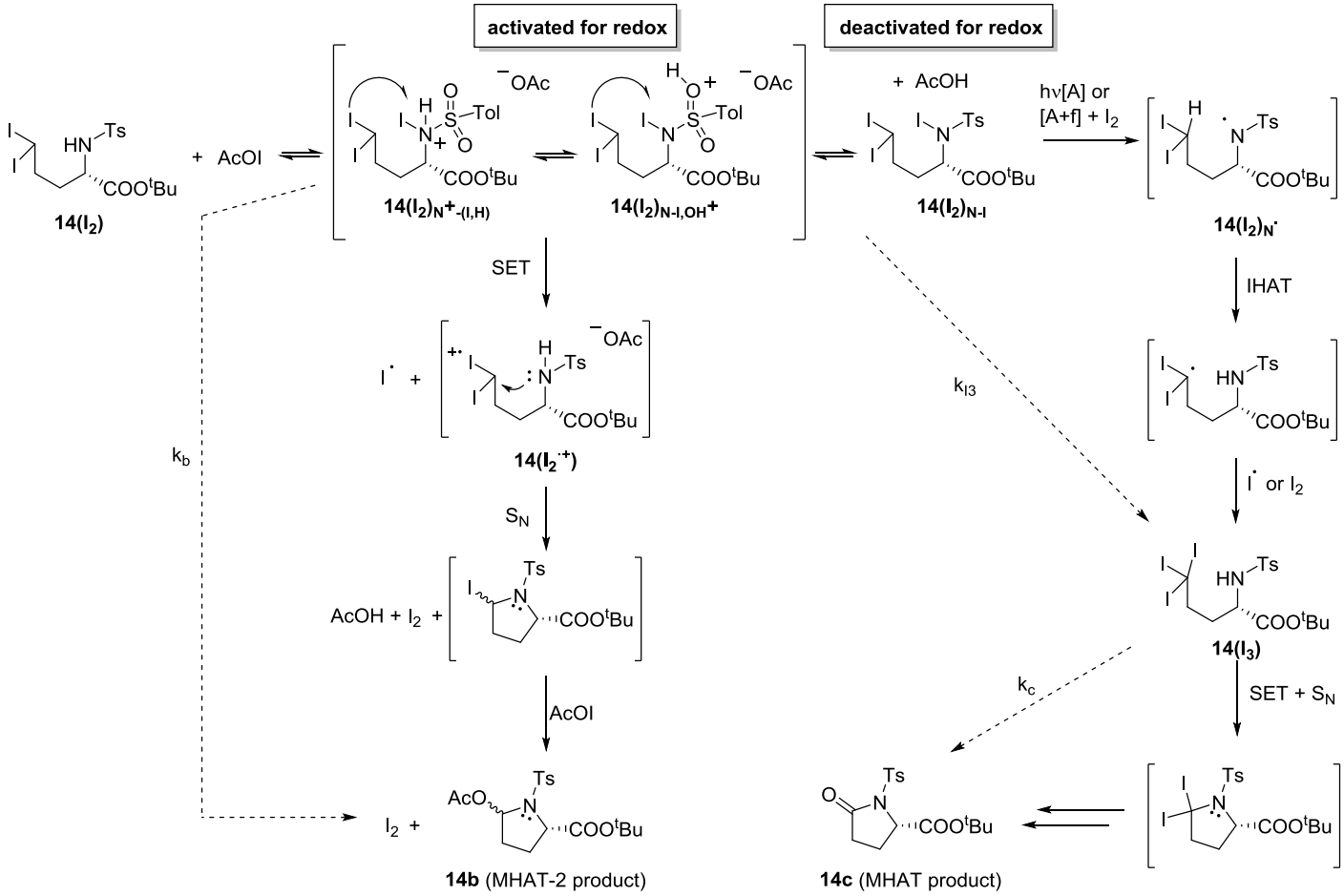
Scheme *S11*: Table *S19* (entry 3)



Note: When **14(I$_2$)** [**A**] was submitted to standard conditions in the dark at 5 ºC and kept during 1.5 hours, formation of **14(I$_2$)$_{N\text{-}I}$** was observed, which did not lead to cyclic compound **14b** [**B**]. Then, temperature was increased to 10, 15 and 25 ºC keeping the reaction in the dark for half an hour at each temperature, not observing considerable formation of cyclic compound **14b** [**C**, **D** and **E**]. Temperatures above 30 ºC were

necessary to observe considerable formation of **14b** [**F**]. Irradiation of reaction mixture [**F**] with filtered light led to a complete consumption of intermediate **14(I$_2$)$_{N-I}$** affording **14(I$_3$)** as major product. As a conclusion, it seems to be evident that, under irradiation, the IHAT reaction with **14(I$_2$)** toward **14(I$_3$)** is much faster than its cyclization toward **14b** (Scheme *S12*: k_{I3}>>k_b).

Scheme *S12*: Proposed mechanism for **14(I$_2$)** towards **14b** and **14c**.



Note 1: k_{I3} >> k_b under irradiation [A] or ([A+f] + I_2), with or without Na_2CO_3 (schemes *S9*, *S10* and *S11*)
Note 2: k_c > k_a and k_b in MHAT conditions with Na_2CO_3 in the darkness: Compare scheme *S8* and (table *S19*, entry 6) with the scheme *S10*.
Note 3: Conversion of **14(I$_3$)** into **14c** did not need light (scheme *S10*).
Note 4: Conversion of **14(I$_3$)** into **14c** did not need previous aqueous quenching (scheme *S10*).
Note 5: Conversion of **14(I$_3$)** into **14c** required the presence of AcOI, either in absence or presence of Na_2CO_3. Conversion of **14(I$_3$)** into **14c** was dramatically slowed down when reactions were carried out in deficiency of $PhI(OAc)_2$, and, moreover, side products derived from **14(I$_3$)** were formed.

DFT CALCULATIONS

Density Functional Theory (DFT) calculations have been performed using two different density functionals, namely, M06-L (1,2) and M06-2X (2,3). The first one is a meta GGA whereas the second one is a hybrid meta functional. Geometries have been optimized using M06-L in conjunction with the cc-pVDZ basis set (4,5,6). Diffuse functions have been added to iodine in order to correctly describe its more diffuse electron density since we have found that iodine is involved in halogen-π interactions with the benzene ring. As a matter of fact, our calculations show that conformers that feature halogen-π bonding have enhanced stability. Only diffuse functions of low angular momentum have been added (minimally augmented basis or maug-cc-pVDZ) following the procedure described by Truhlar et al. (7). Thermochemical data based on the rigid rotor-harmonic oscillator-ideal approximations have been obtained at this level of theory. In order to improve the quality of the electronic energies we have carried out M06-2X/maug-cc-pVTZ (4,5,6) calculations on the M06-L geometries. The chosen level of theory for this work is therefore M06-2X/maug-cc-pVTZ//M06-L/maug-cc-pVDZ. All DFT calculations have been carried out with the G09 program package (8). We have additionally model bulk solvent effects through the Polarizable Continuum Model (PCM) as implemented in G09. In particular, we have used the polarizable conductor calculation model (CPCM) (9) using the united atom topological model (radii=uaks). The chosen solvent was diethylether.

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Scheme *S13*: Regioselectivity observed with **3**.

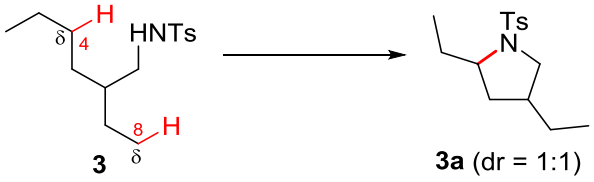
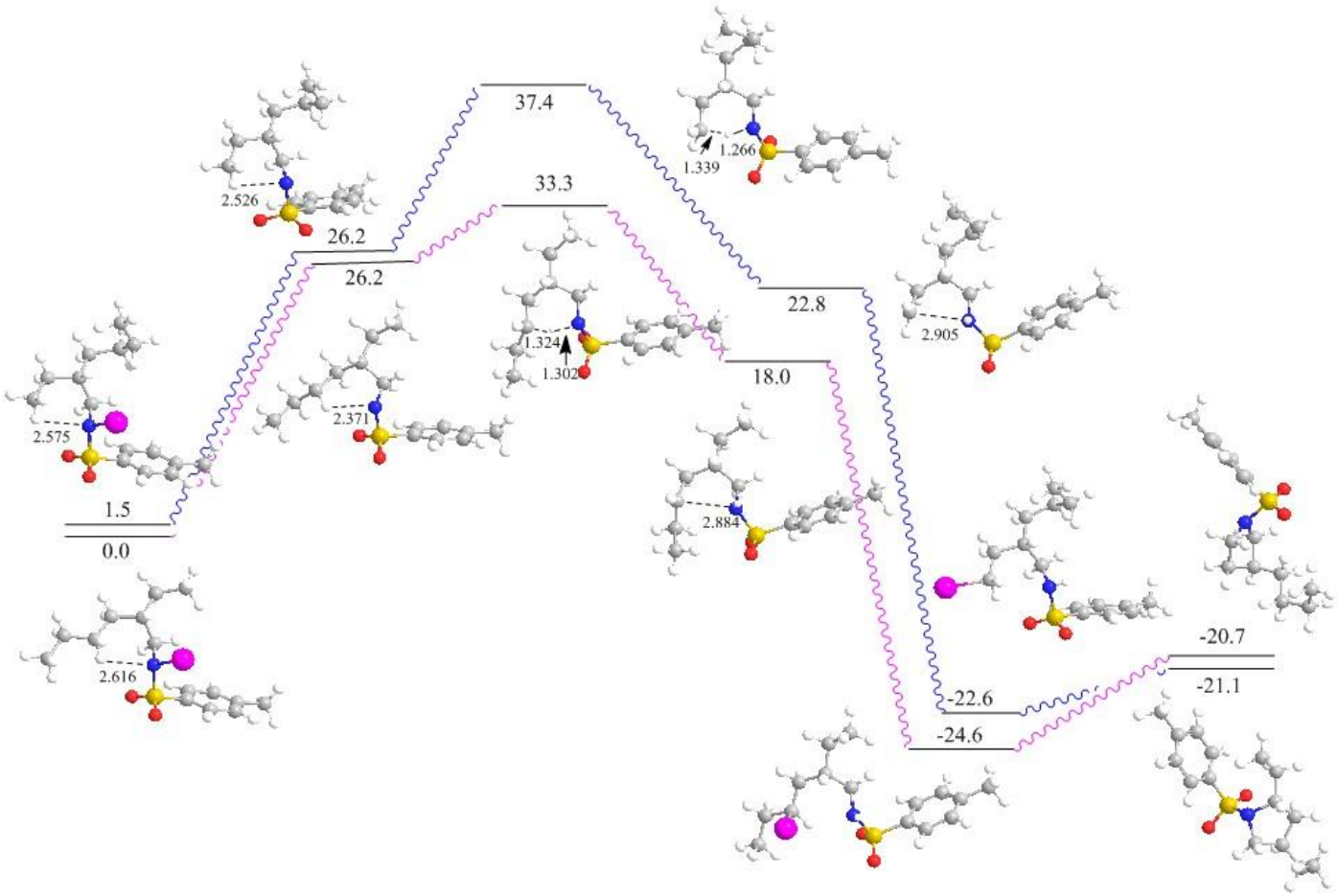


Table *S3*, entry 1	GP1	85%
Table *S3*, entry 2	GP2	87%

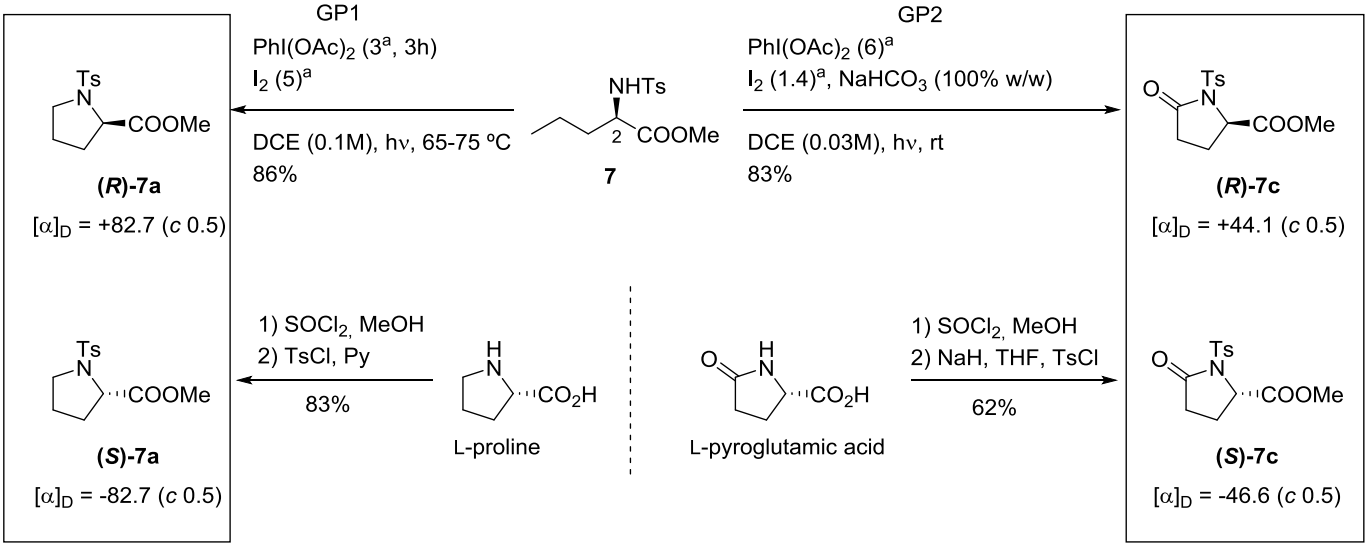
Note: The step of hydrogen atom transfer from C–H bond to Nitrogen centered radical is determinant for the regioselectivity observed within the functionalization of **3**. $BDE_{C4–H}$ = 93.9 kcal/mol; $BDE_{C8–H}$ = 97.5 kcal/mol



Schematic representation of the Gibbs Free Energy Surface (FES) (at 298.15 K; kcal/mol) showing the equilibrium structures involved in the functionalization of **3**. Solvent effects have been taken into account as described above. Notice the larger stability (4.8 kcal/mol) of the methylene radical over the methyl radical in agreement with the observed regioselectivity for this functionalization.

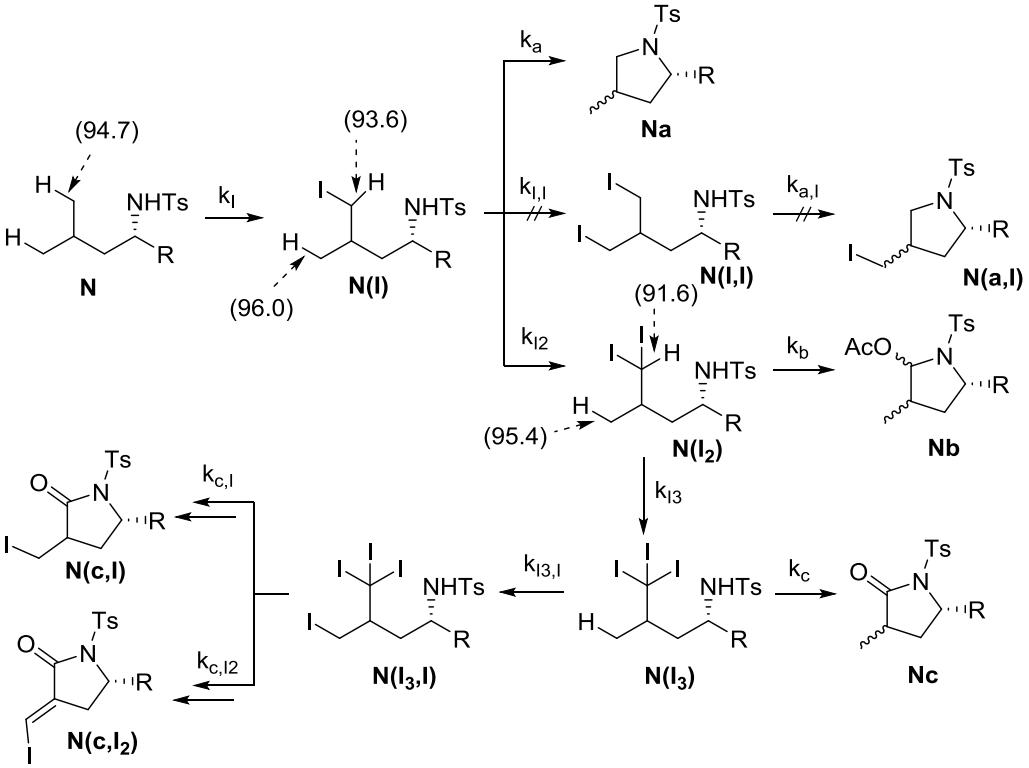
ADDITIONAL SCHEMES

Scheme *S14*: Checking whether GP1 and GP2 promote epimerization at C2.



[a] millimoles per millimol of **7**.

Scheme *S15*: Chemo-, regio- and stereoselectivity.

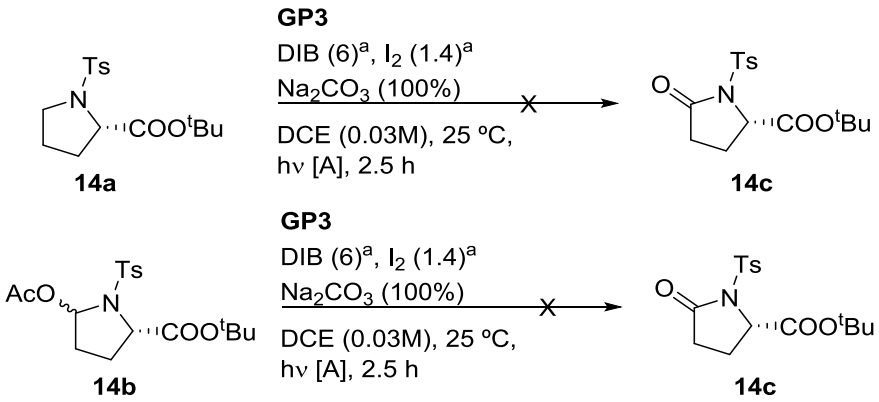


[a] Values in parentheses indicate ab initio C–H BDE (kcal mol^{-1}) for derivatives of **8** (**N** = **8**) at the M06-2X/cc-pVTZ level.

Experimental data support the following conclusions:

- $k_{I3} > k_{I2} > k_I$
- k_{I2} and $k_a > k_{I,I}$
- $k_{I3} > k_b$ (under irradiation)
- $k_c > k_{I3,I}$

Scheme *S16*: Determination whether **14a** and **14b** are intermediates toward **14c.**

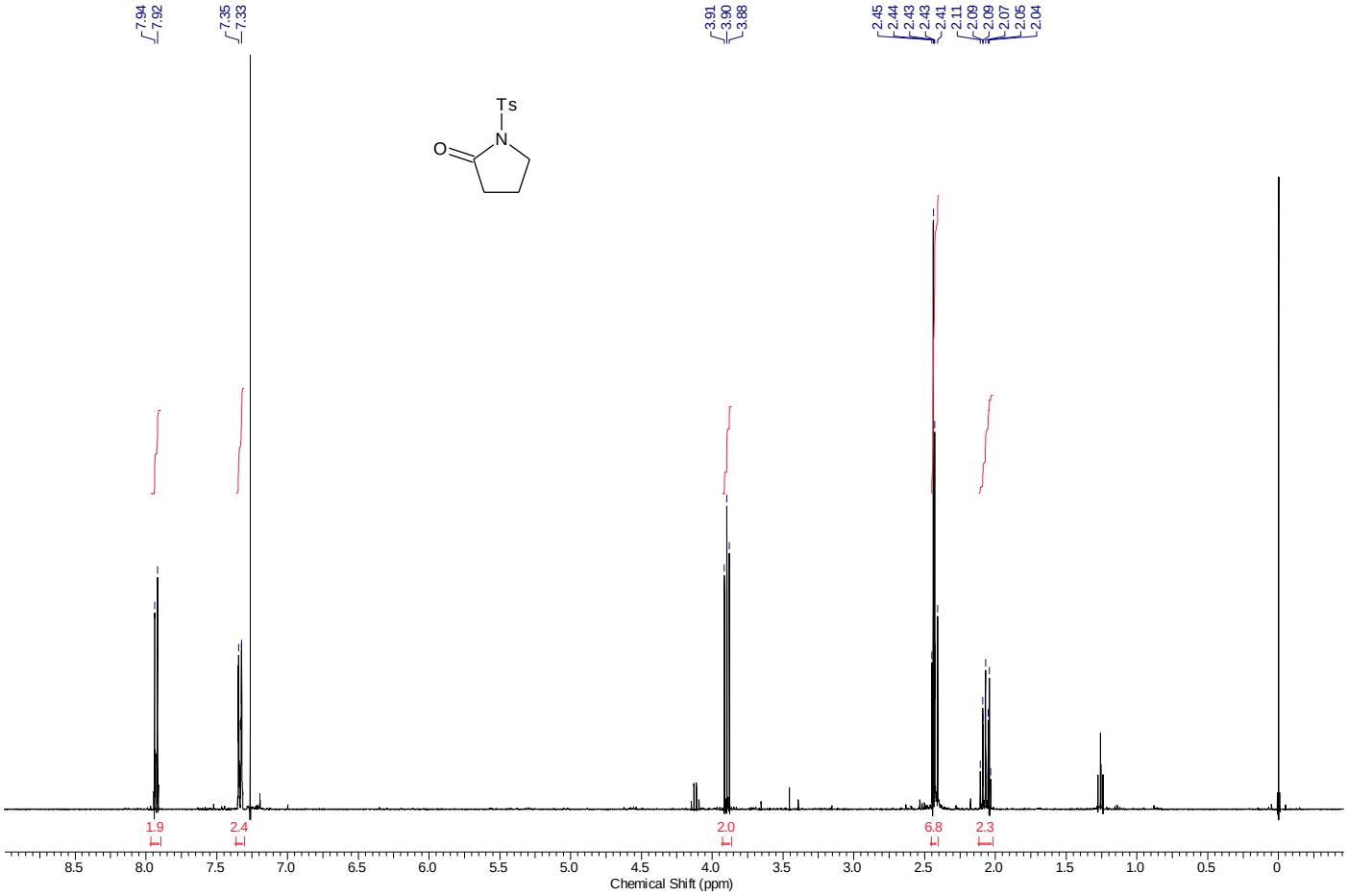


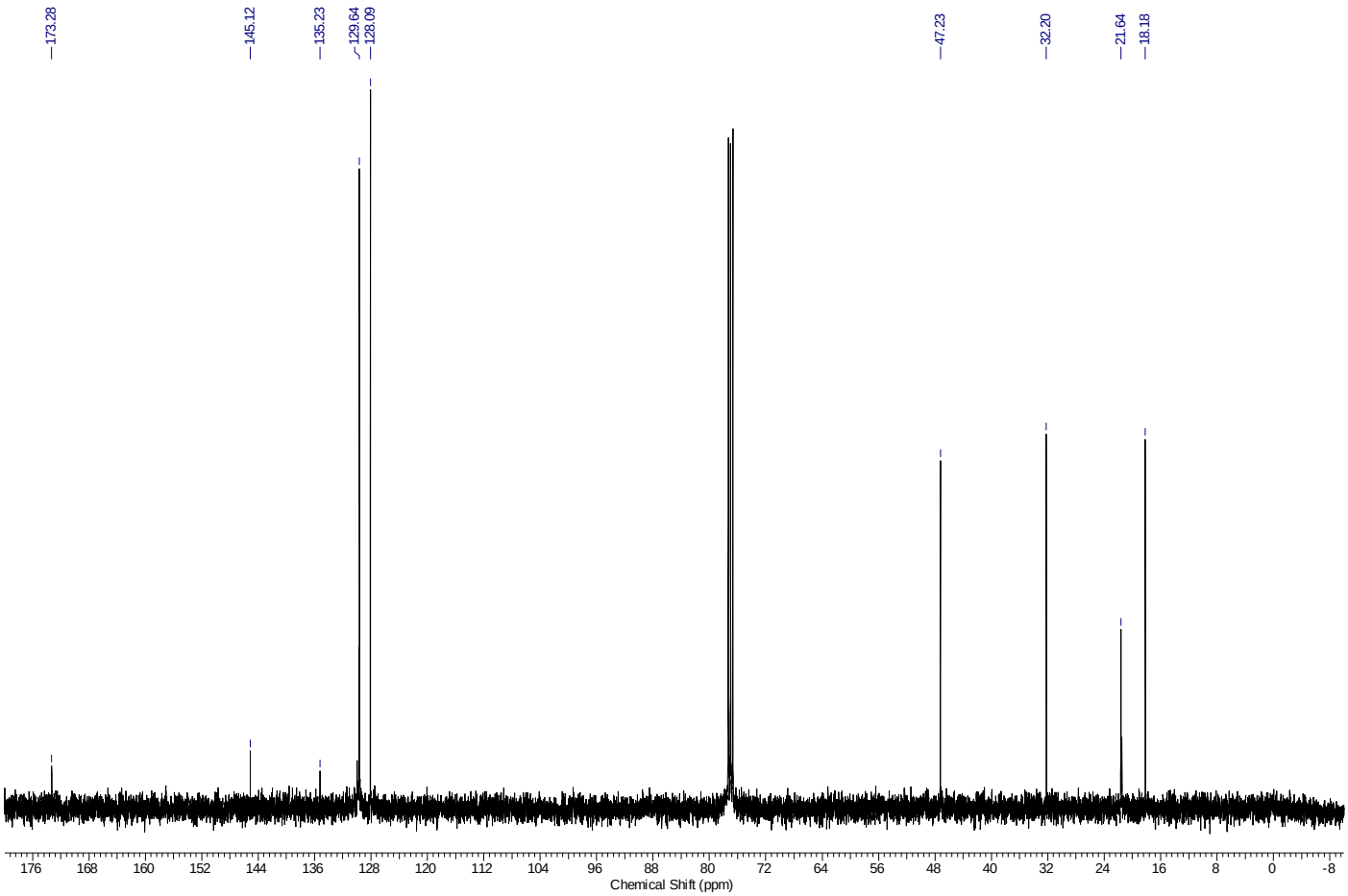
[a] millimoles per millimol of **14a** and **14b**, respectively.

Note: starting material (**14a** and **14b**) was completely recovered after 2.5 h of irradiation.

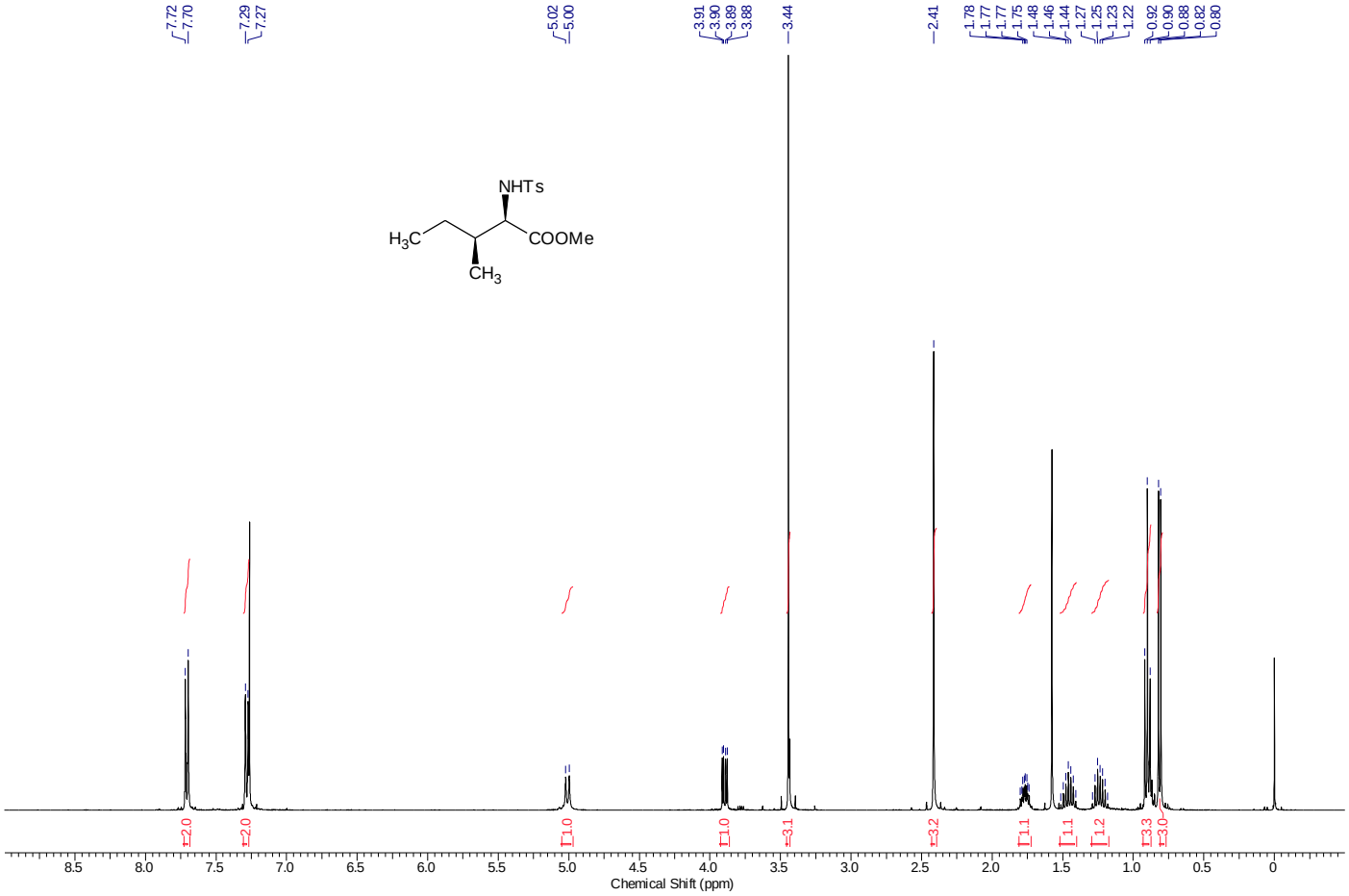
Copies of ^{1}H NMR and ^{13}C NMR spectra of new compounds:

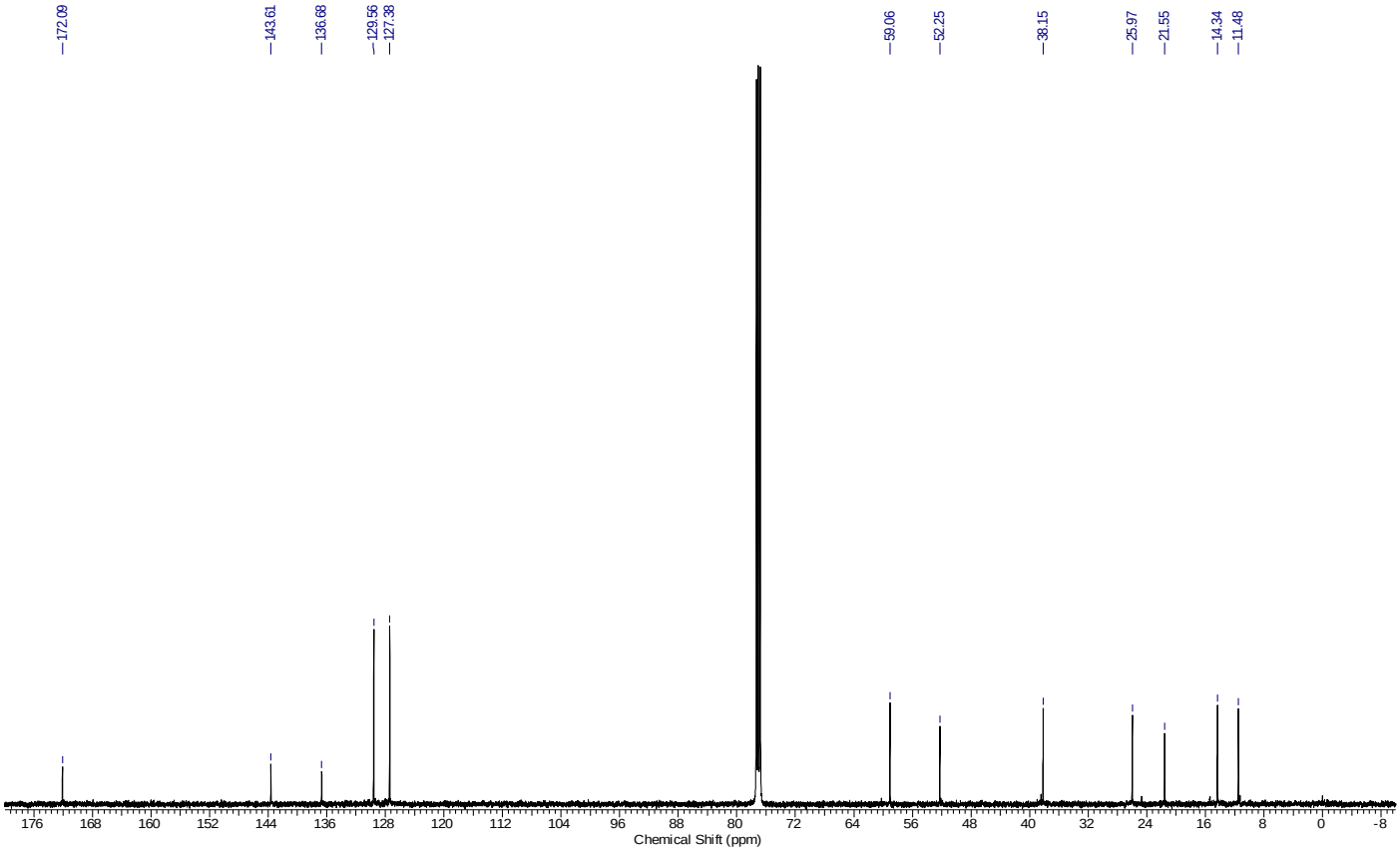
^{1}H NMR and ^{13}C NMR of 1c:



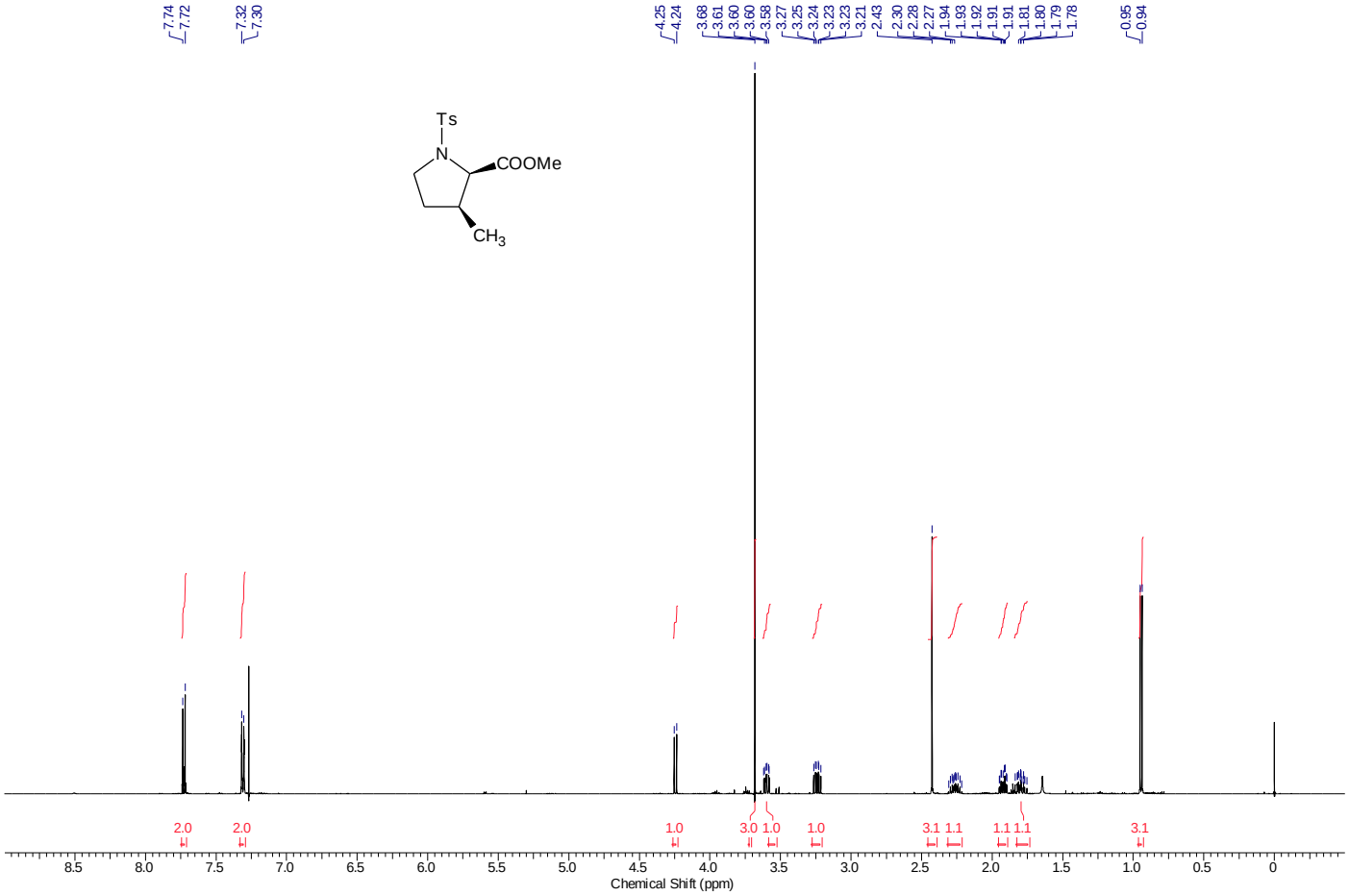


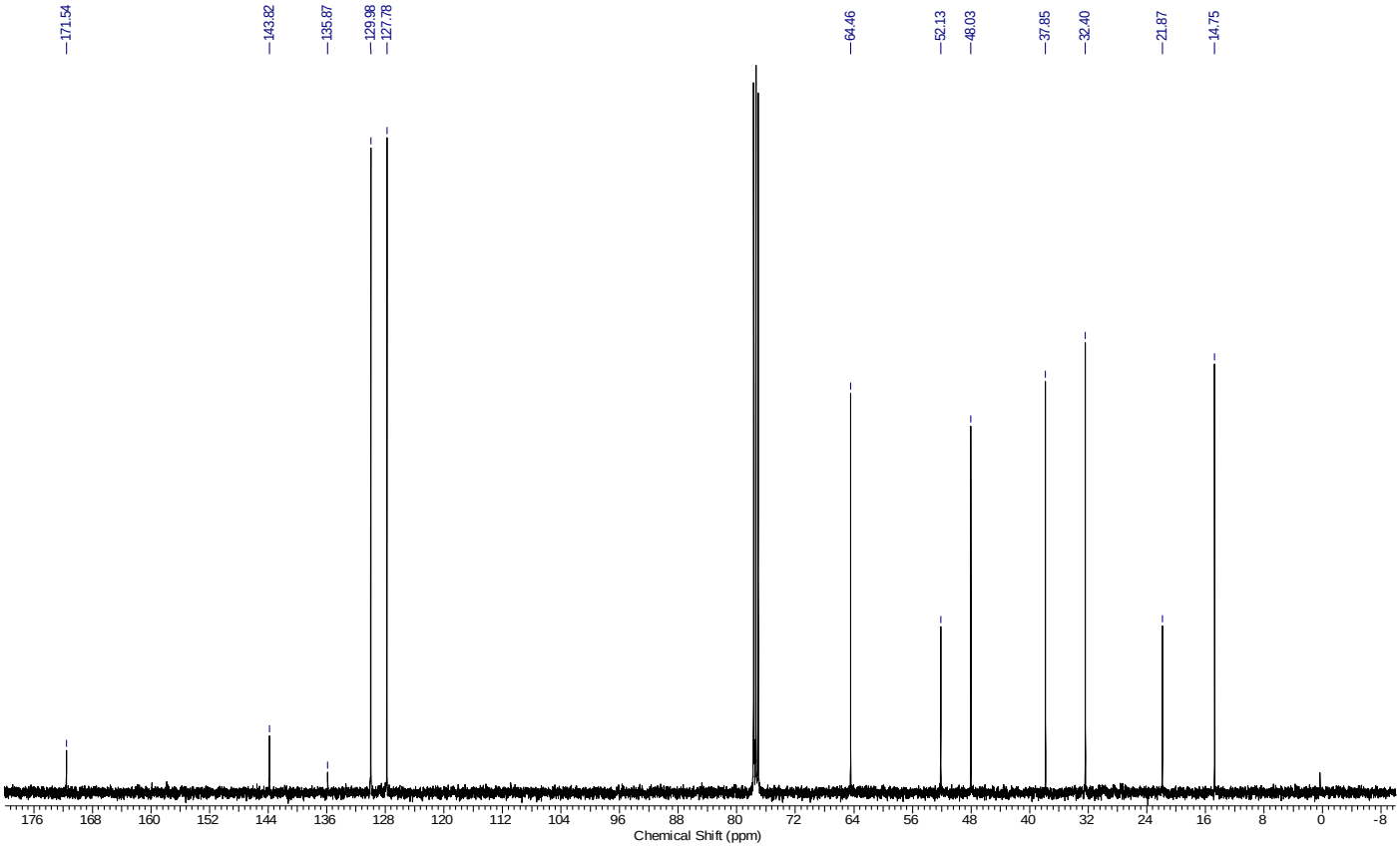
^{1}H NMR and ^{13}C NMR of 2:



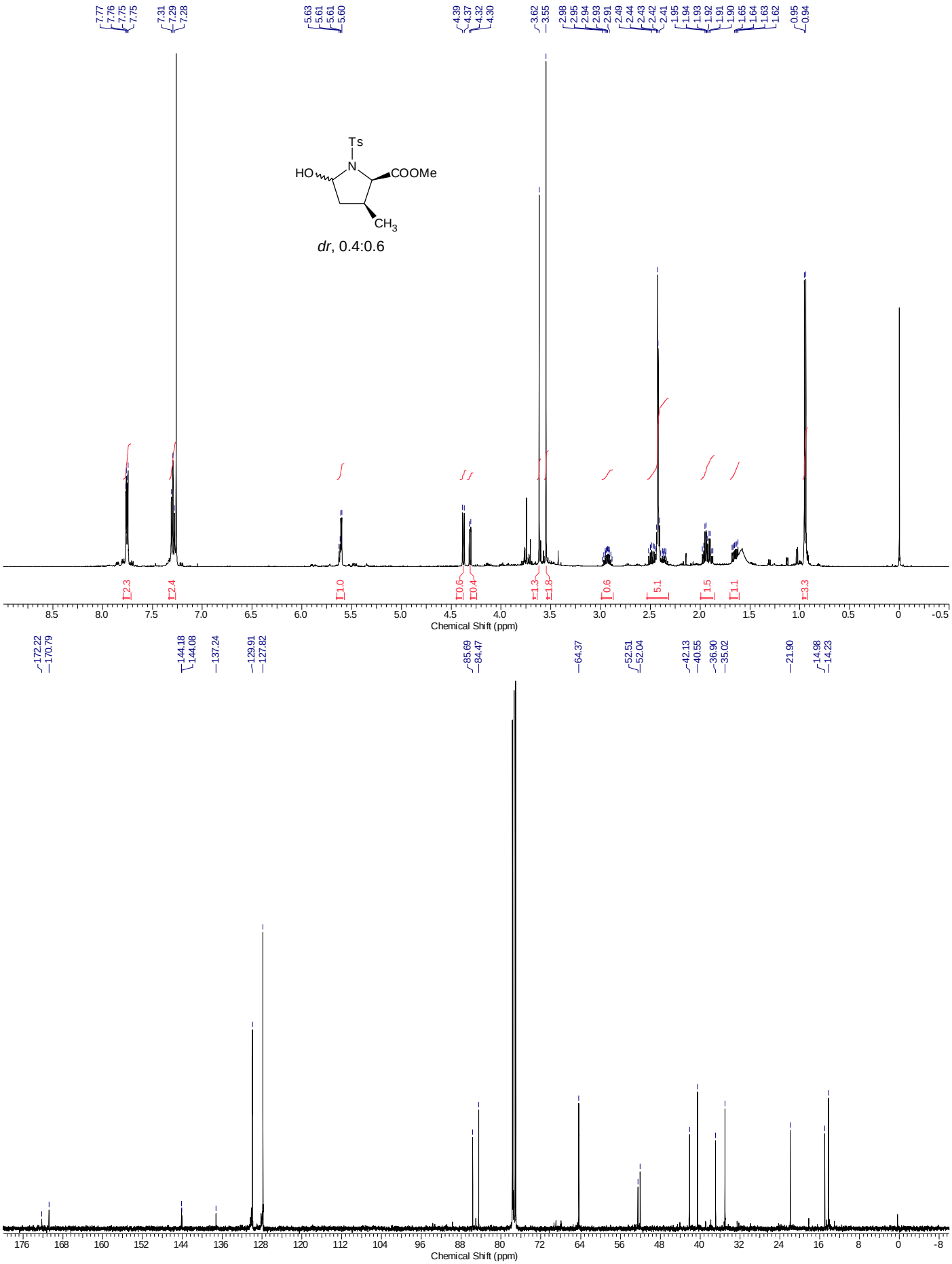


^{1}H NMR and ^{13}C NMR of 2a:

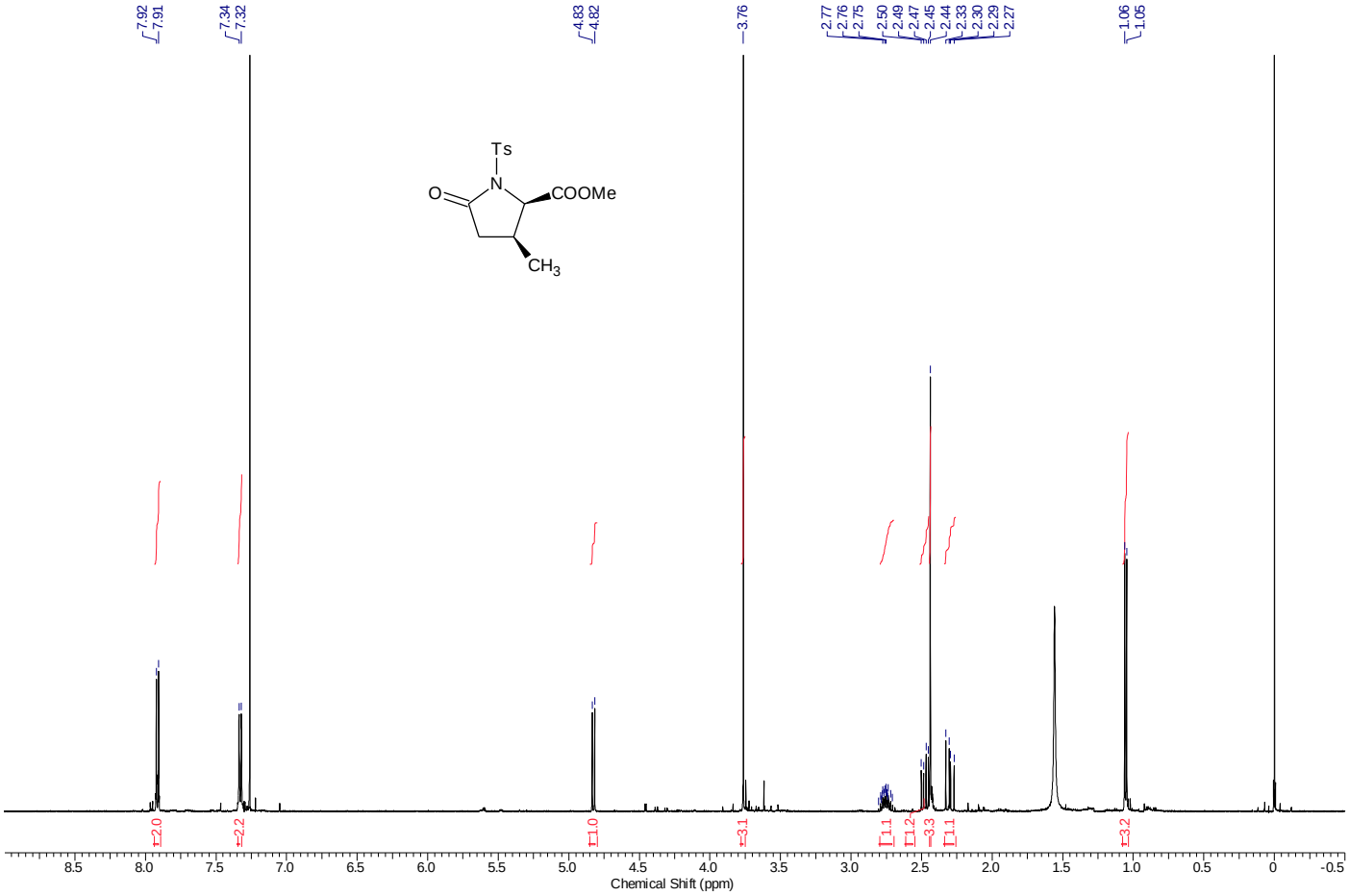


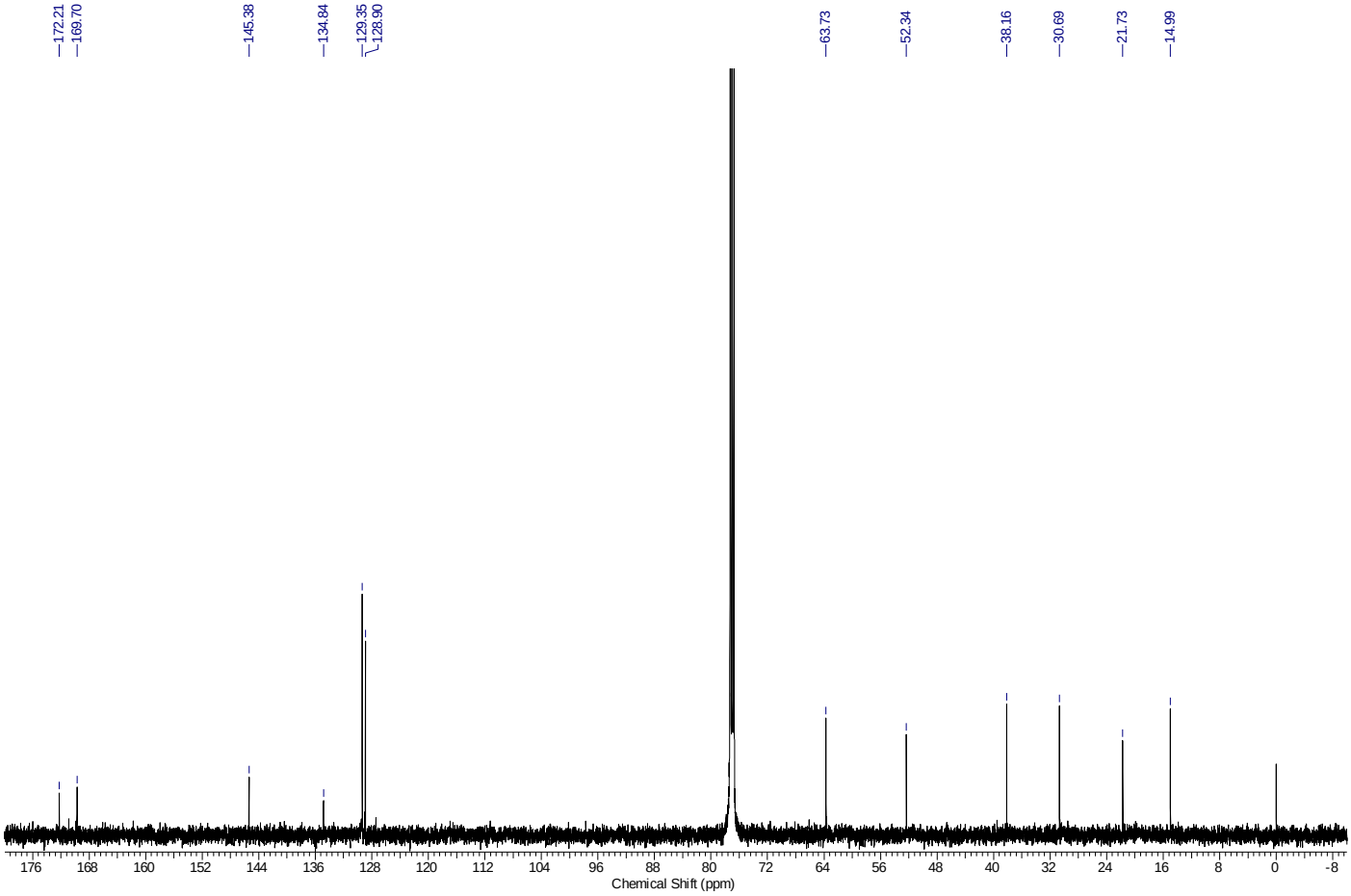


^{1}H NMR and ^{13}C NMR of 2b:

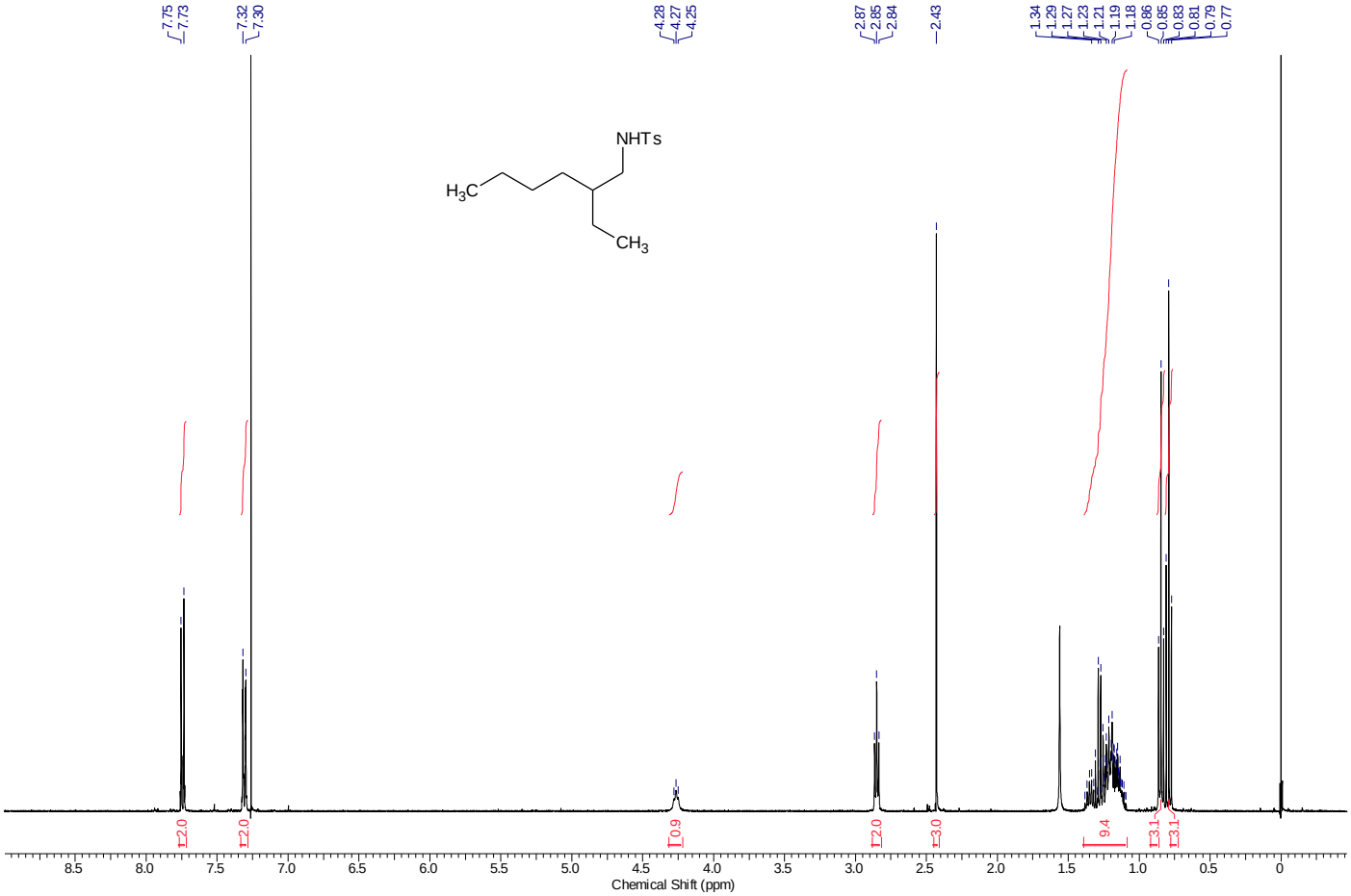


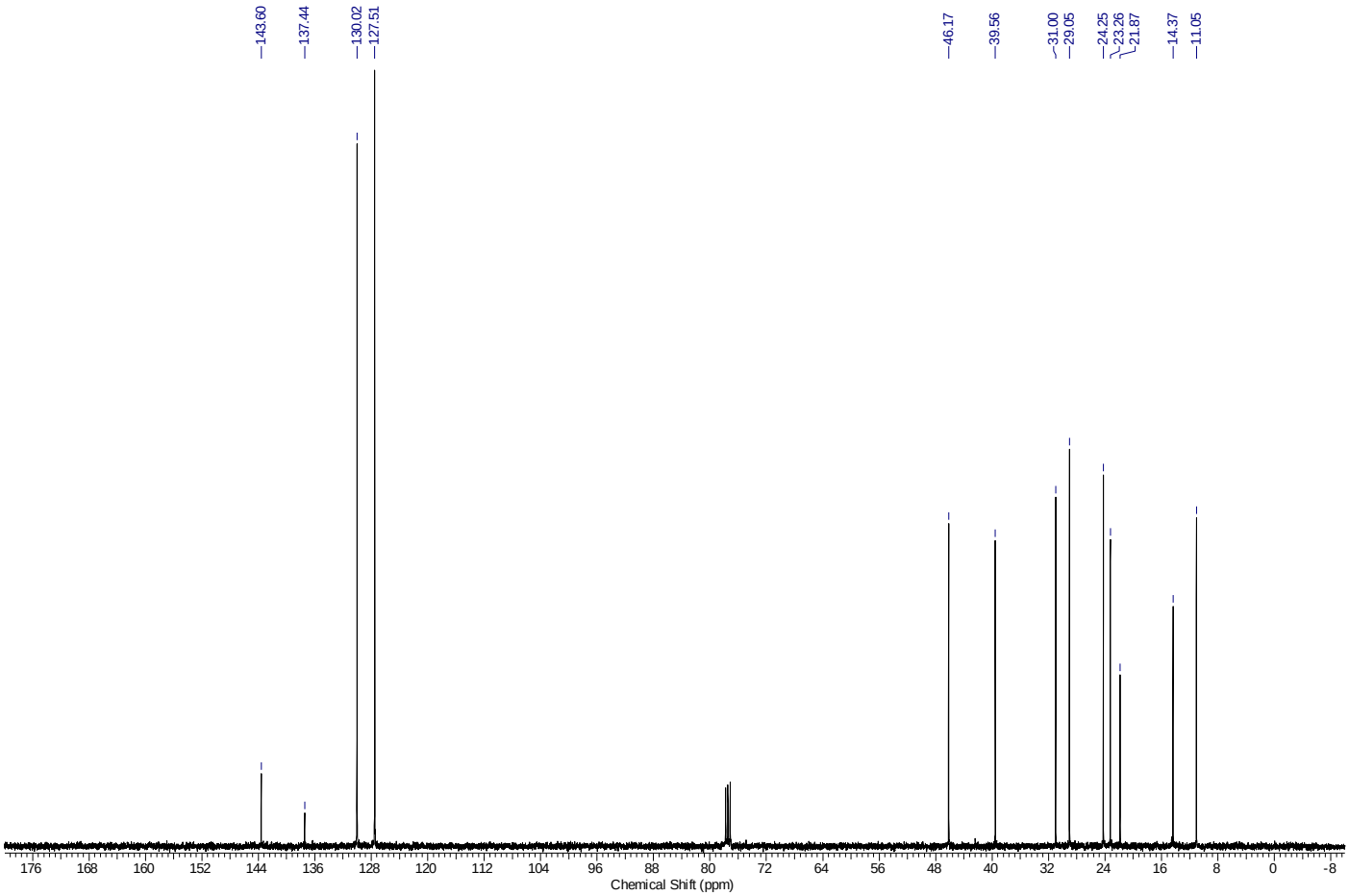
^{1}H NMR and ^{13}C NMR of 2c:



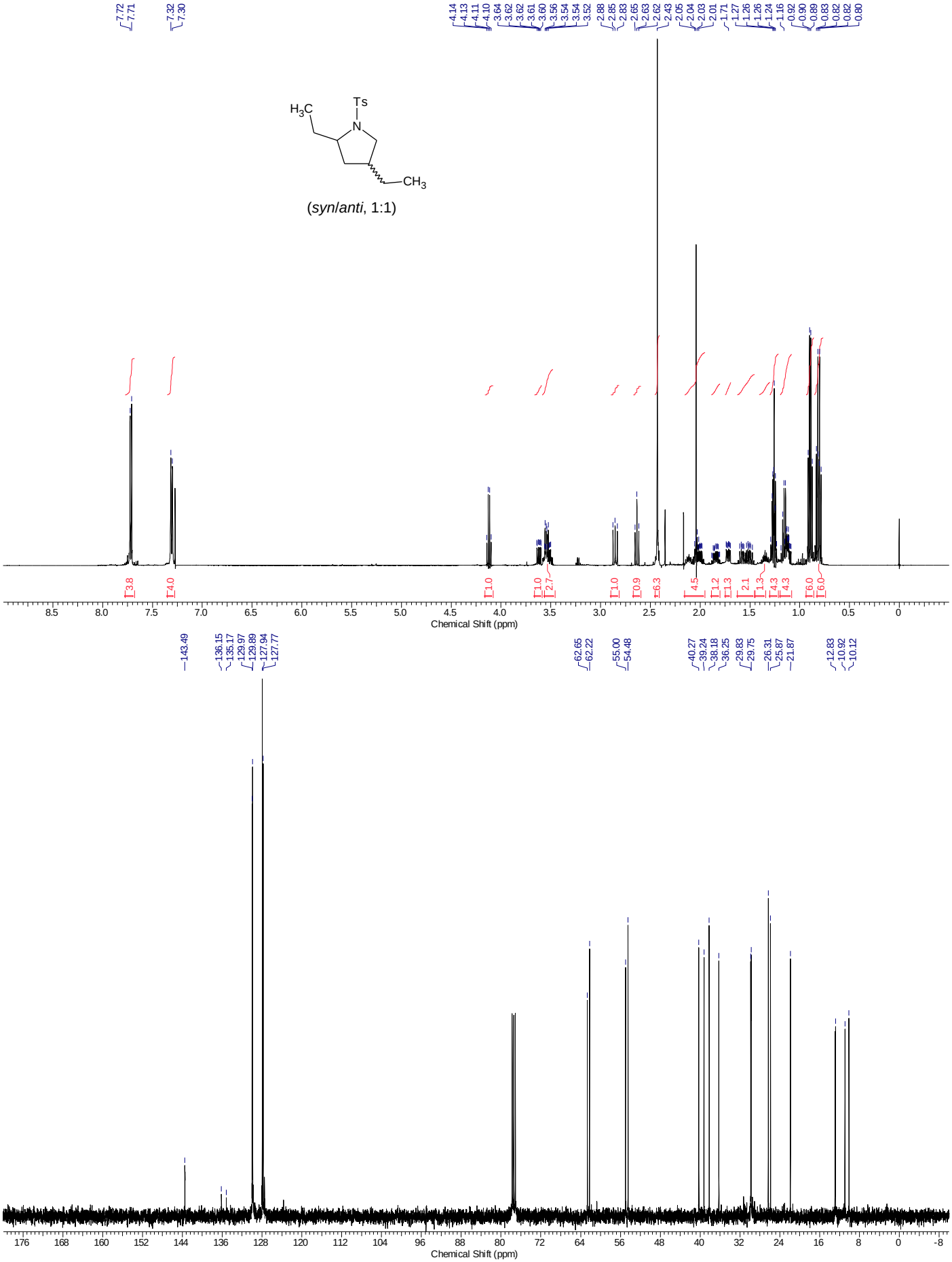


^{1}H NMR and ^{13}C NMR of *rac*-3:

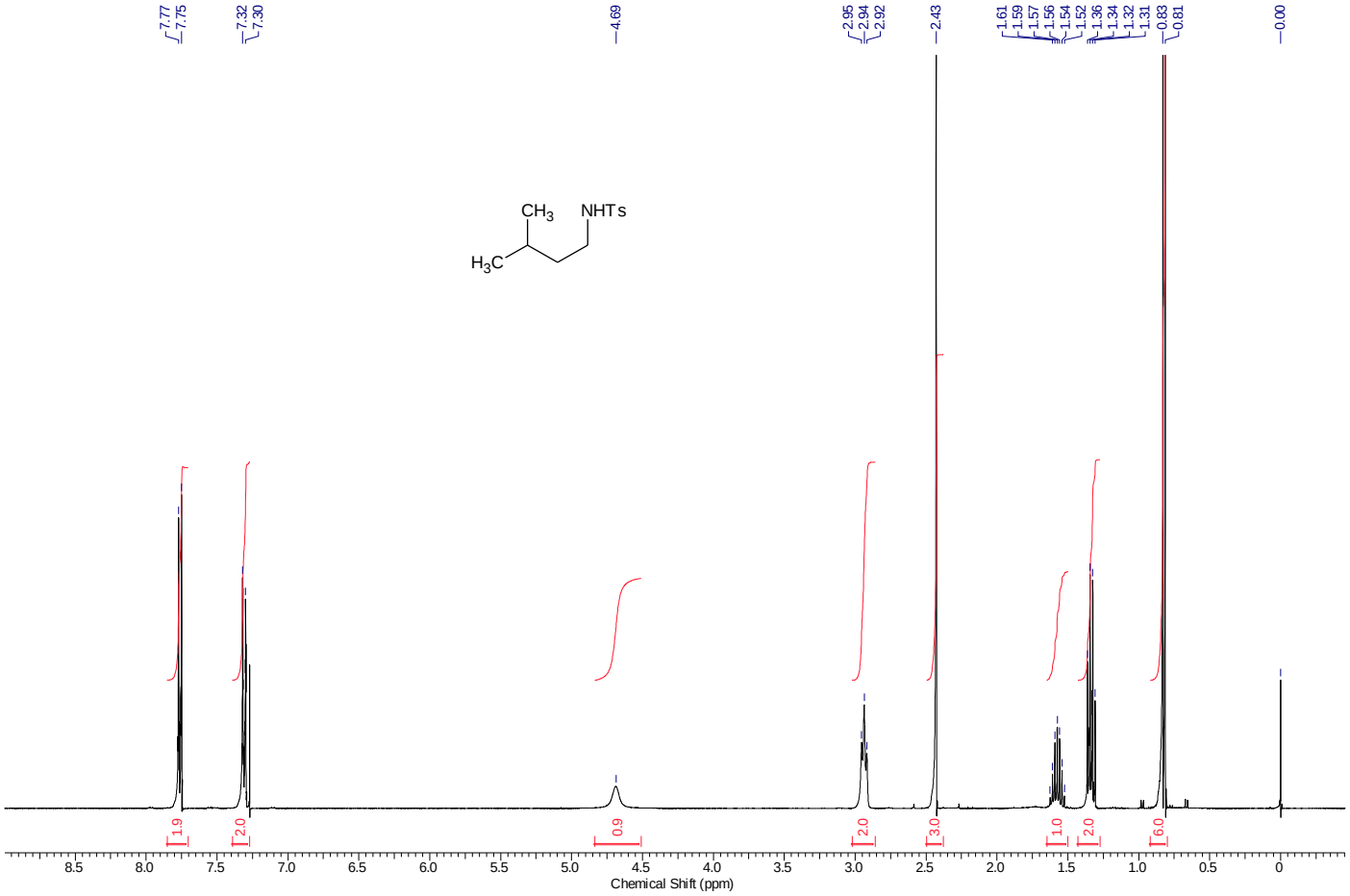


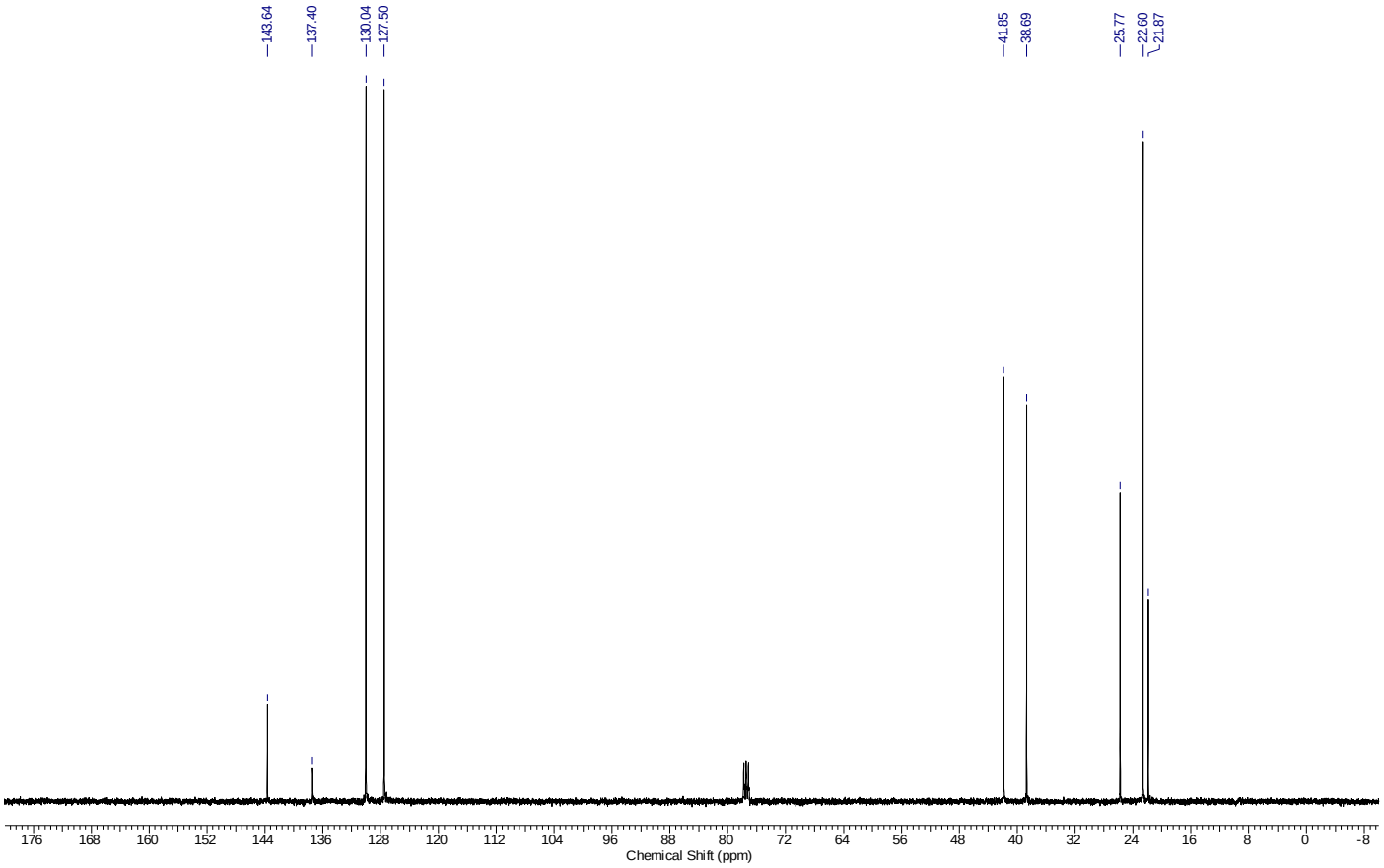


^{1}H NMR and ^{13}C NMR of *rac*-3a:

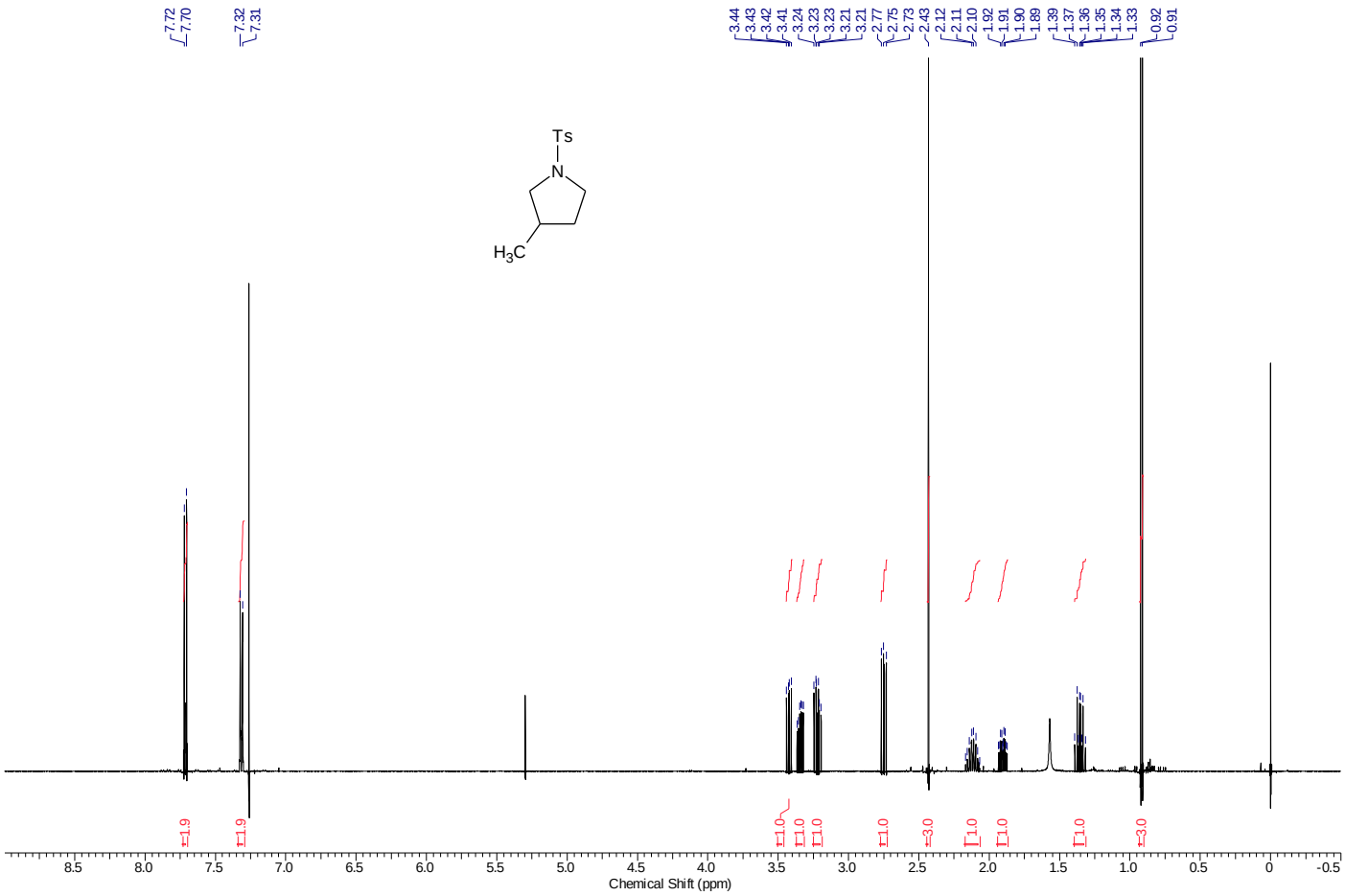


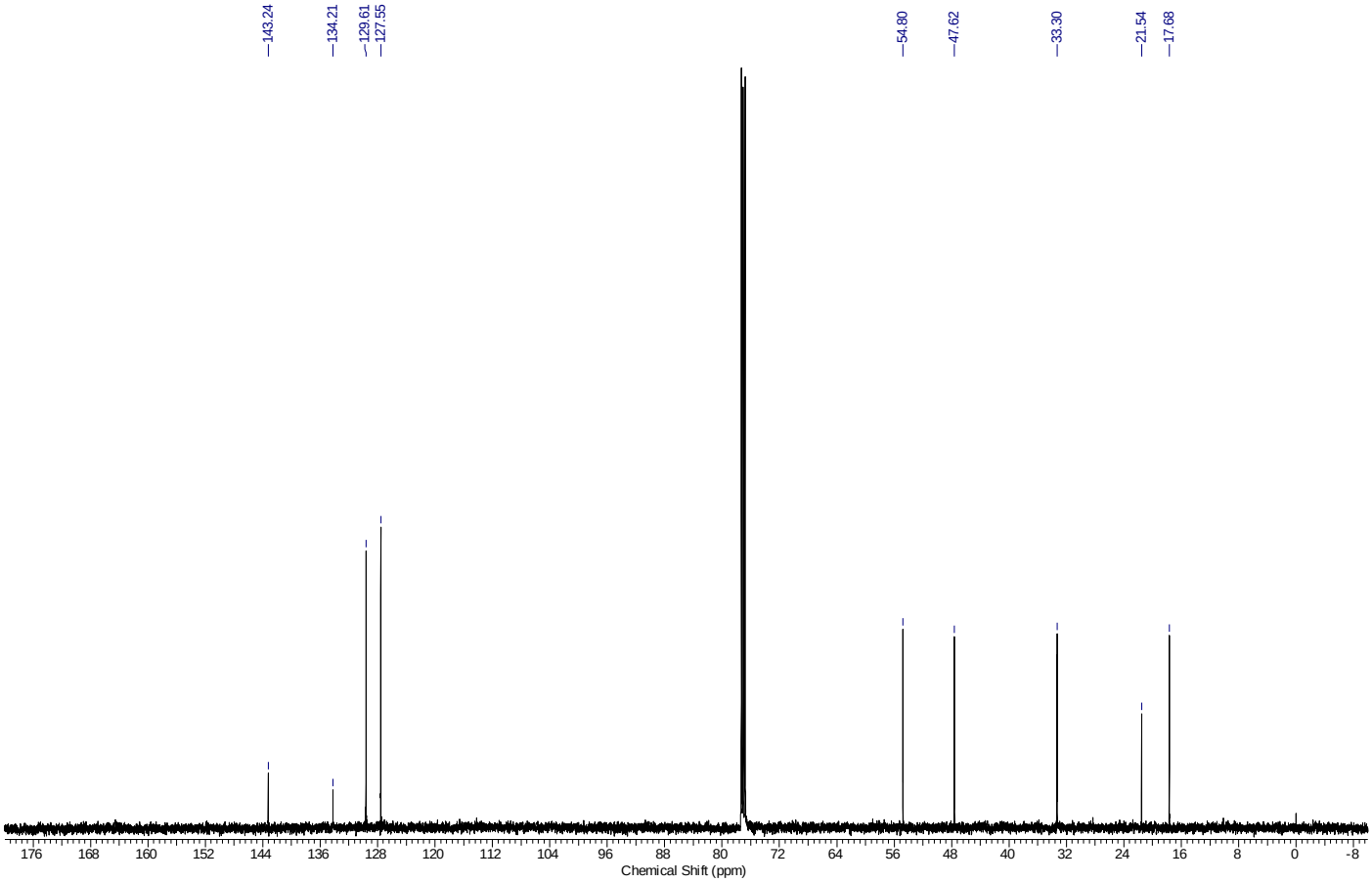
^{1}H NMR and ^{13}C NMR of 4:



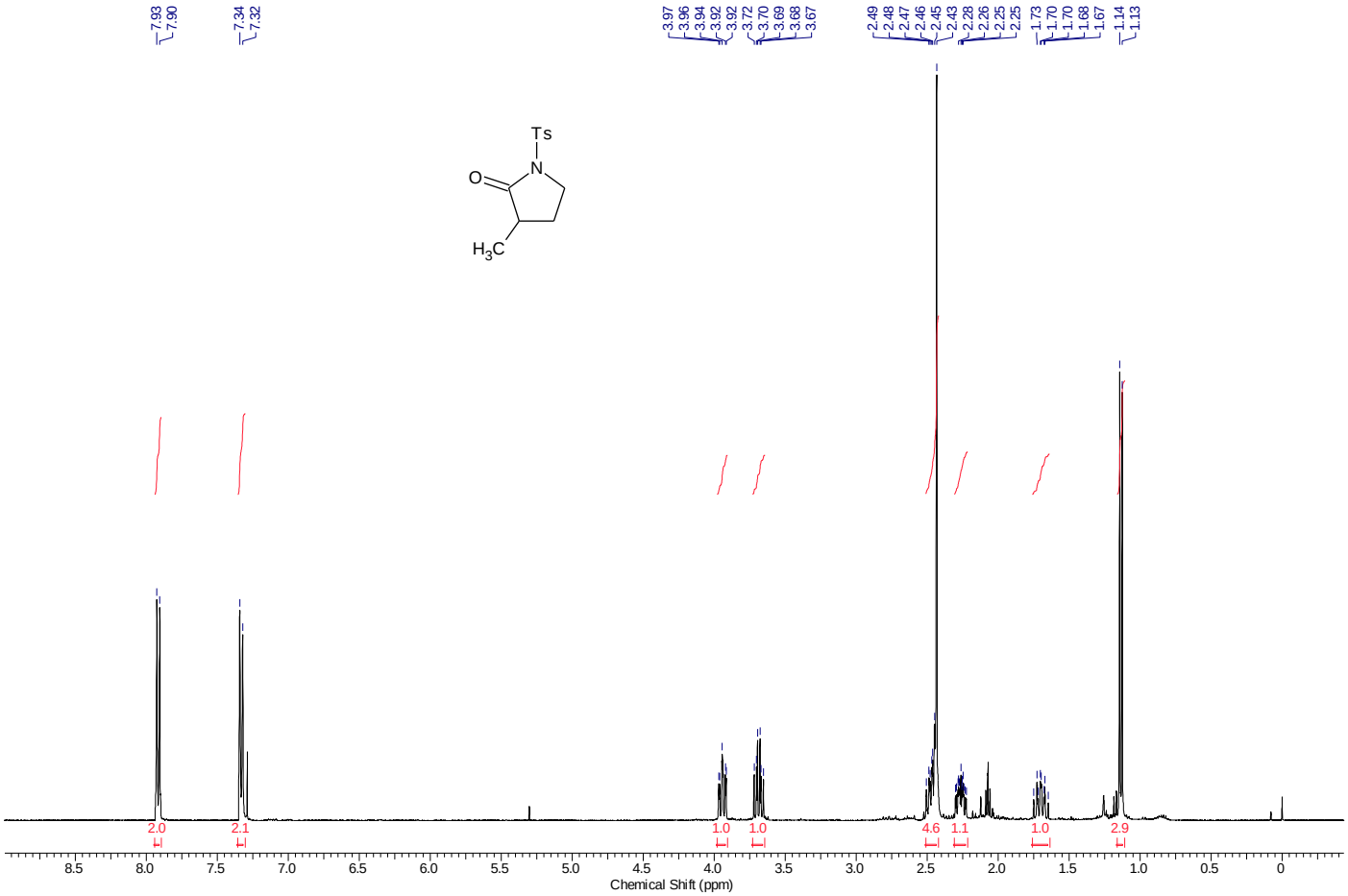


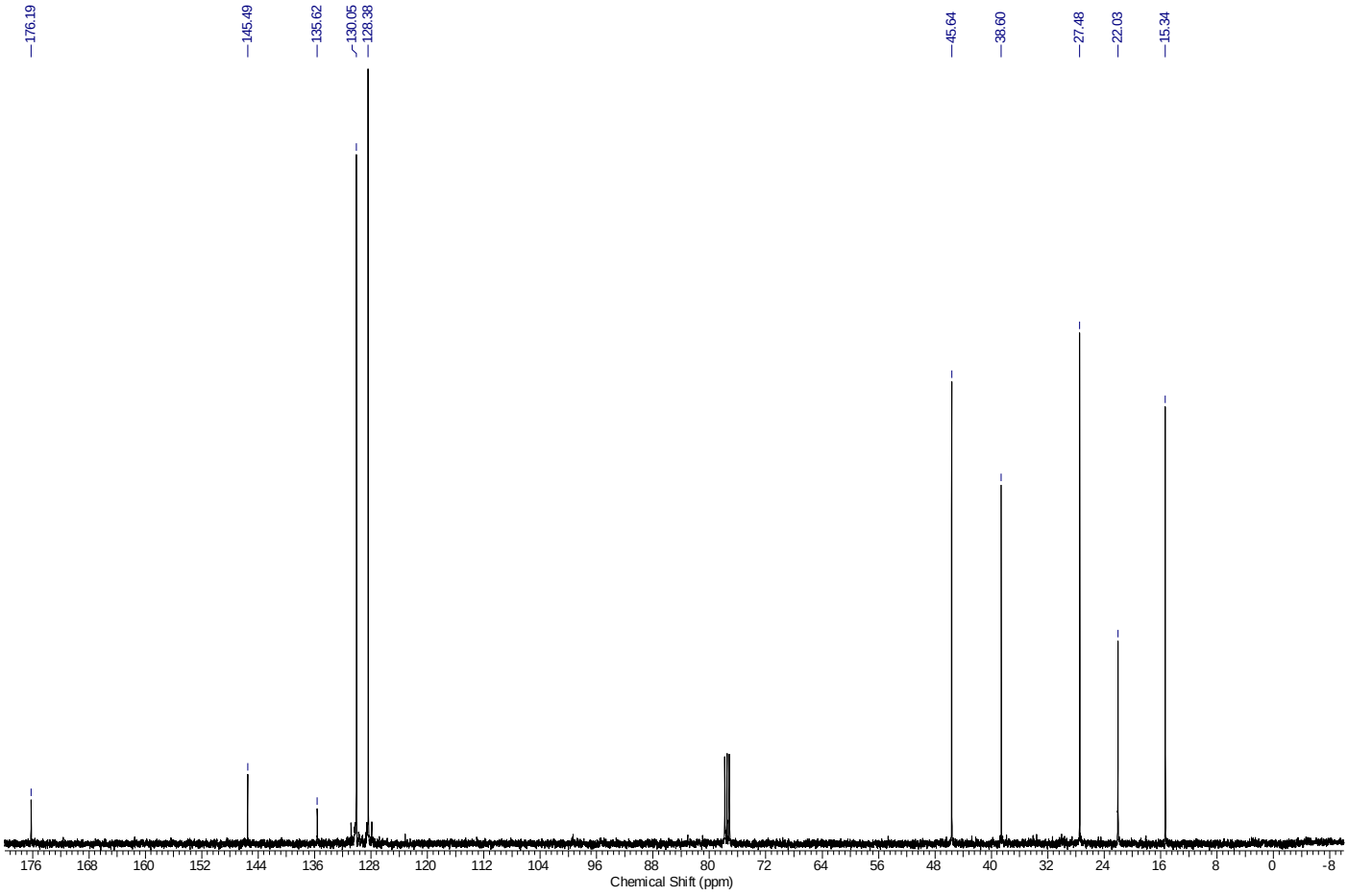
^{1}H NMR and ^{13}C NMR of *rac*-4a:



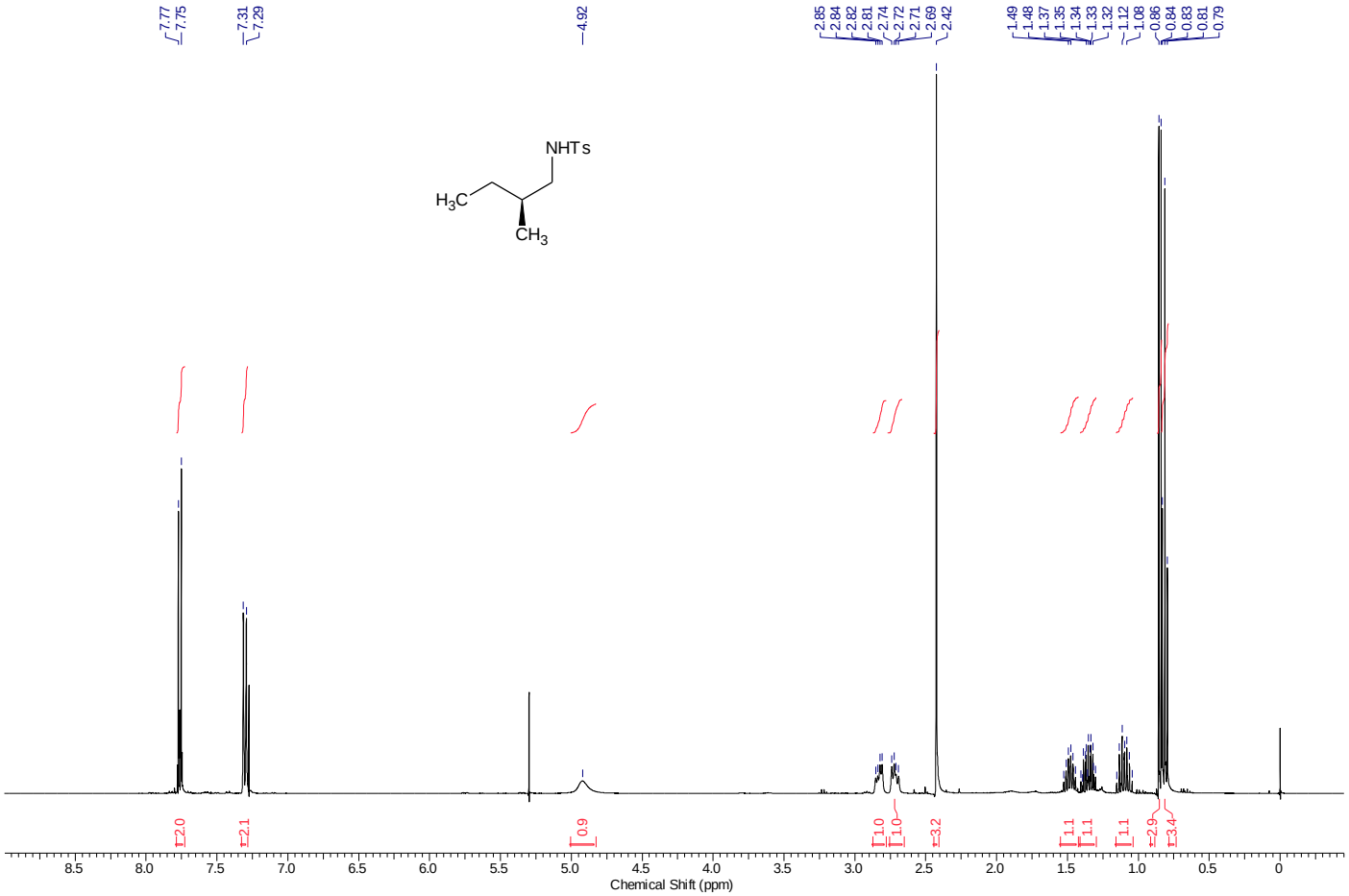


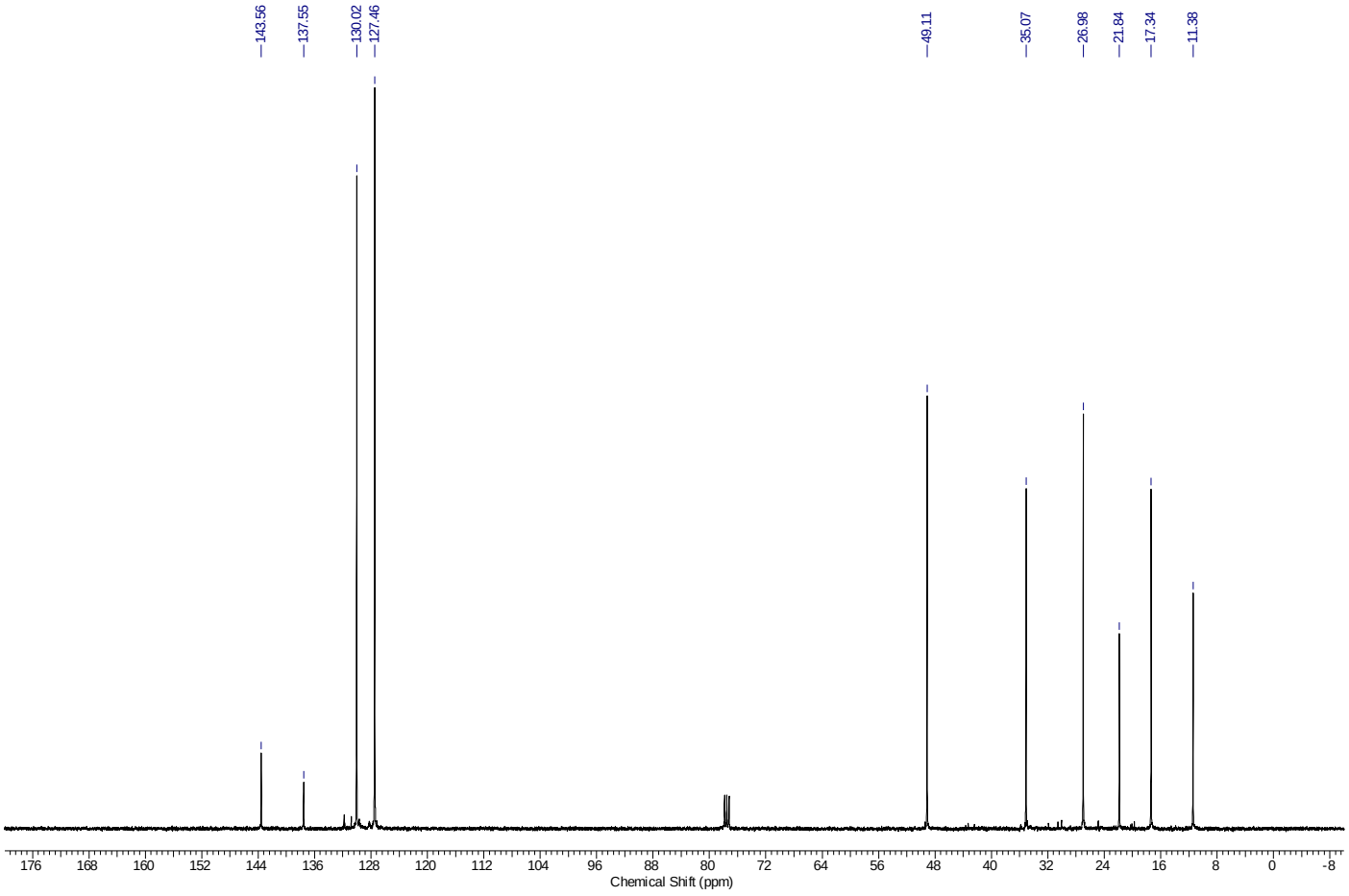
^{1}H NMR and ^{13}C NMR of *rac*-4c:



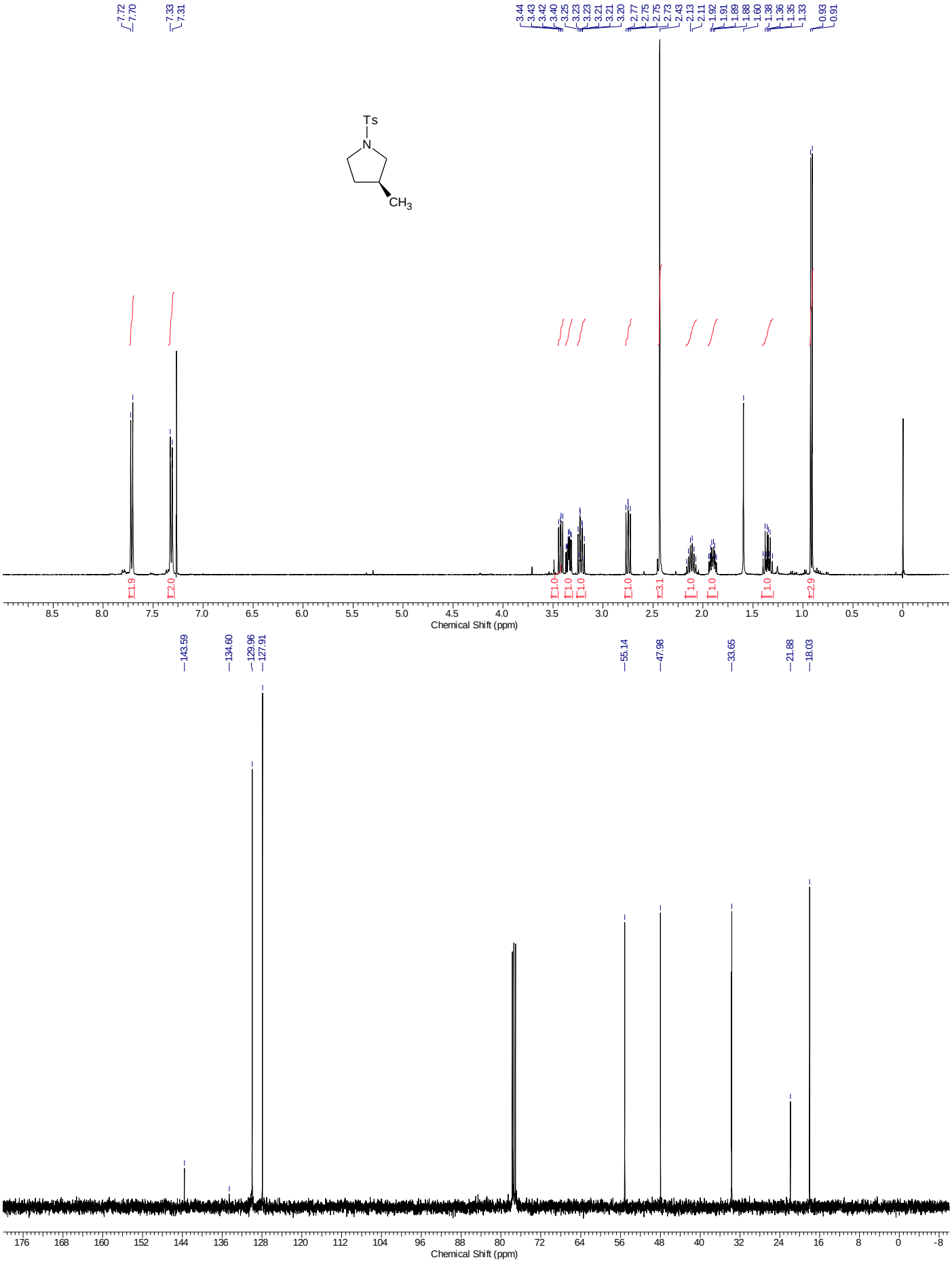


^{1}H NMR and ^{13}C NMR of 5:

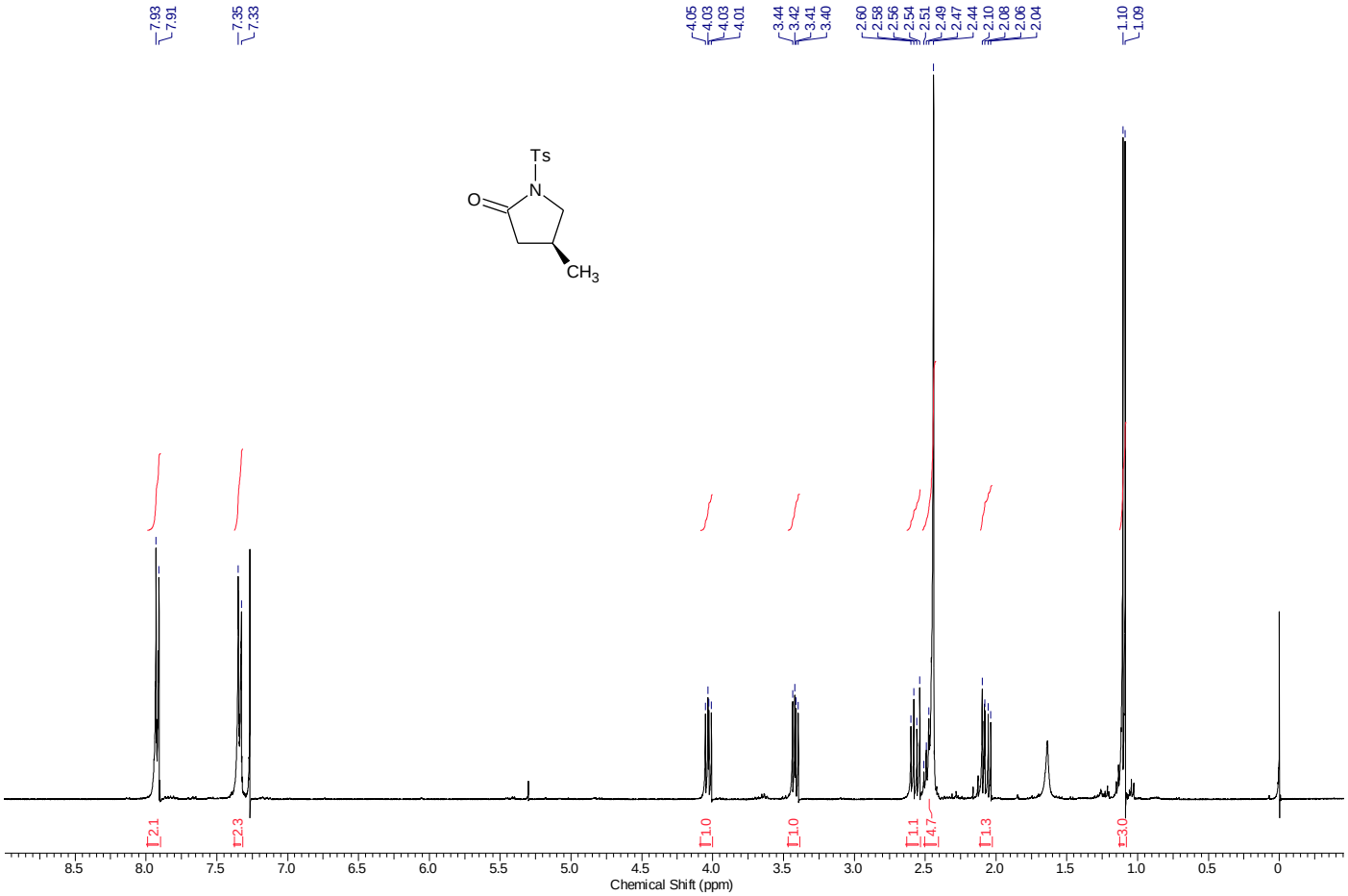


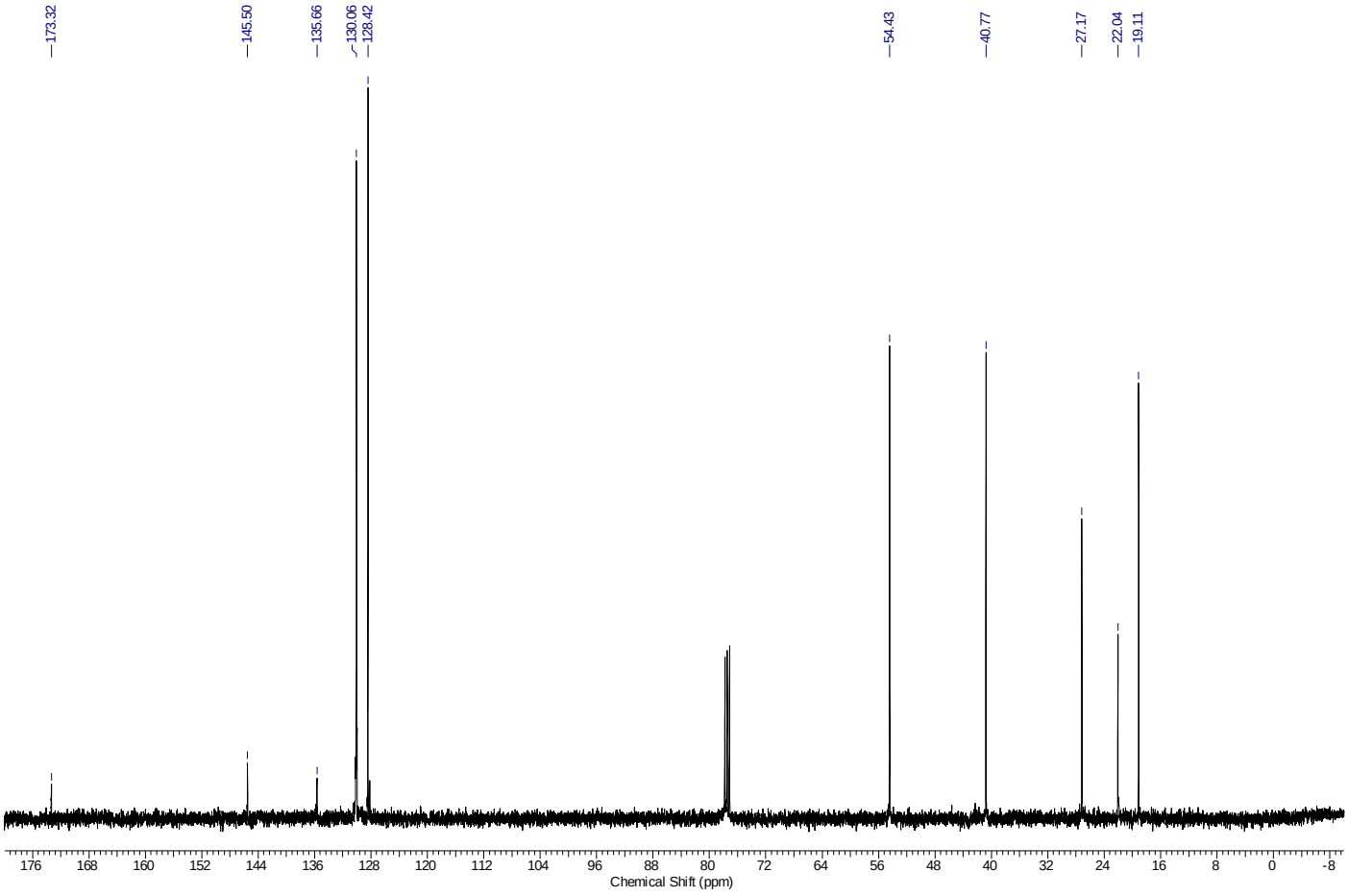


^{1}H NMR and ^{13}C NMR of 3*S*-5a:

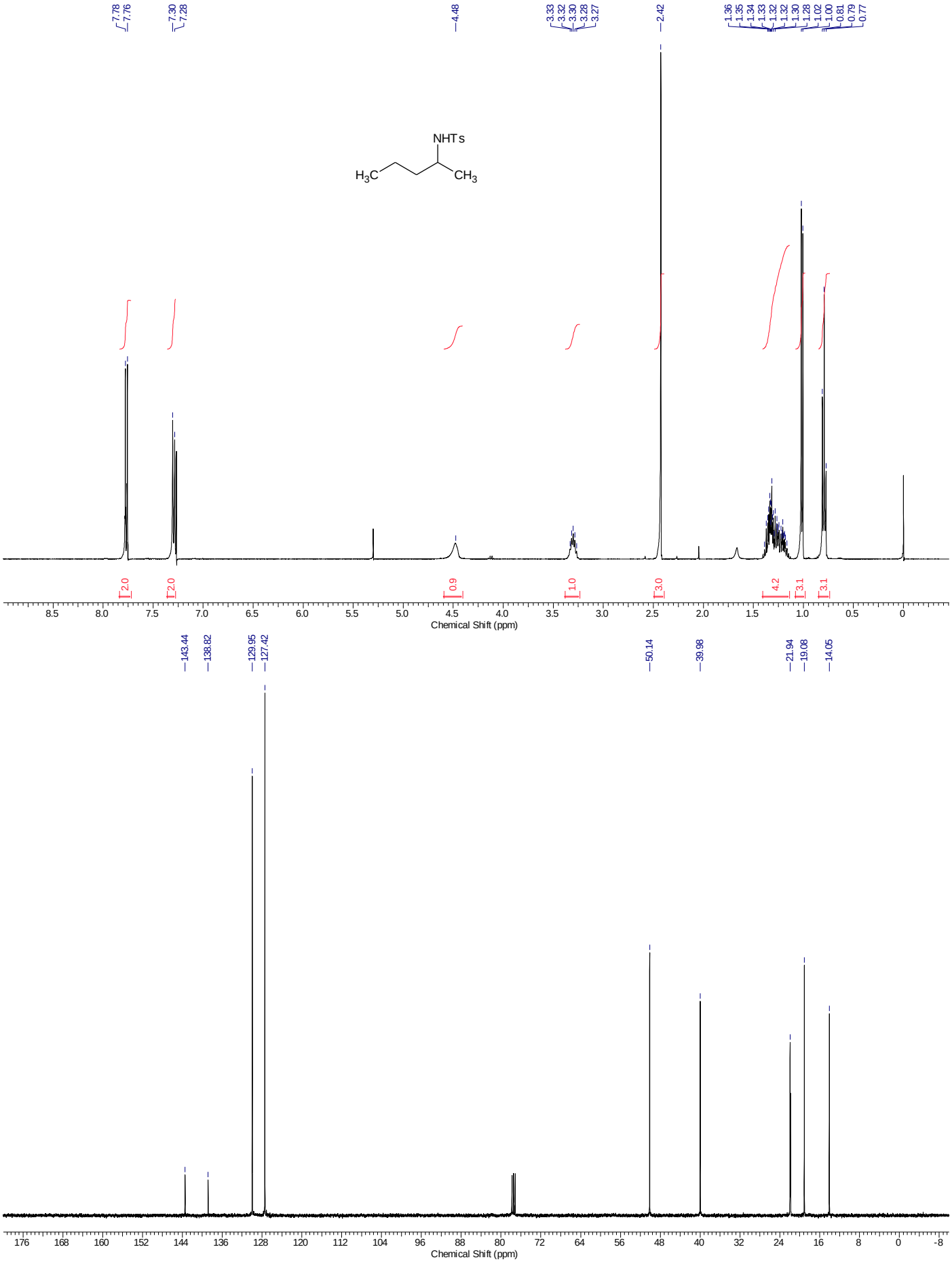


^{1}H NMR and ^{13}C NMR of 5c:

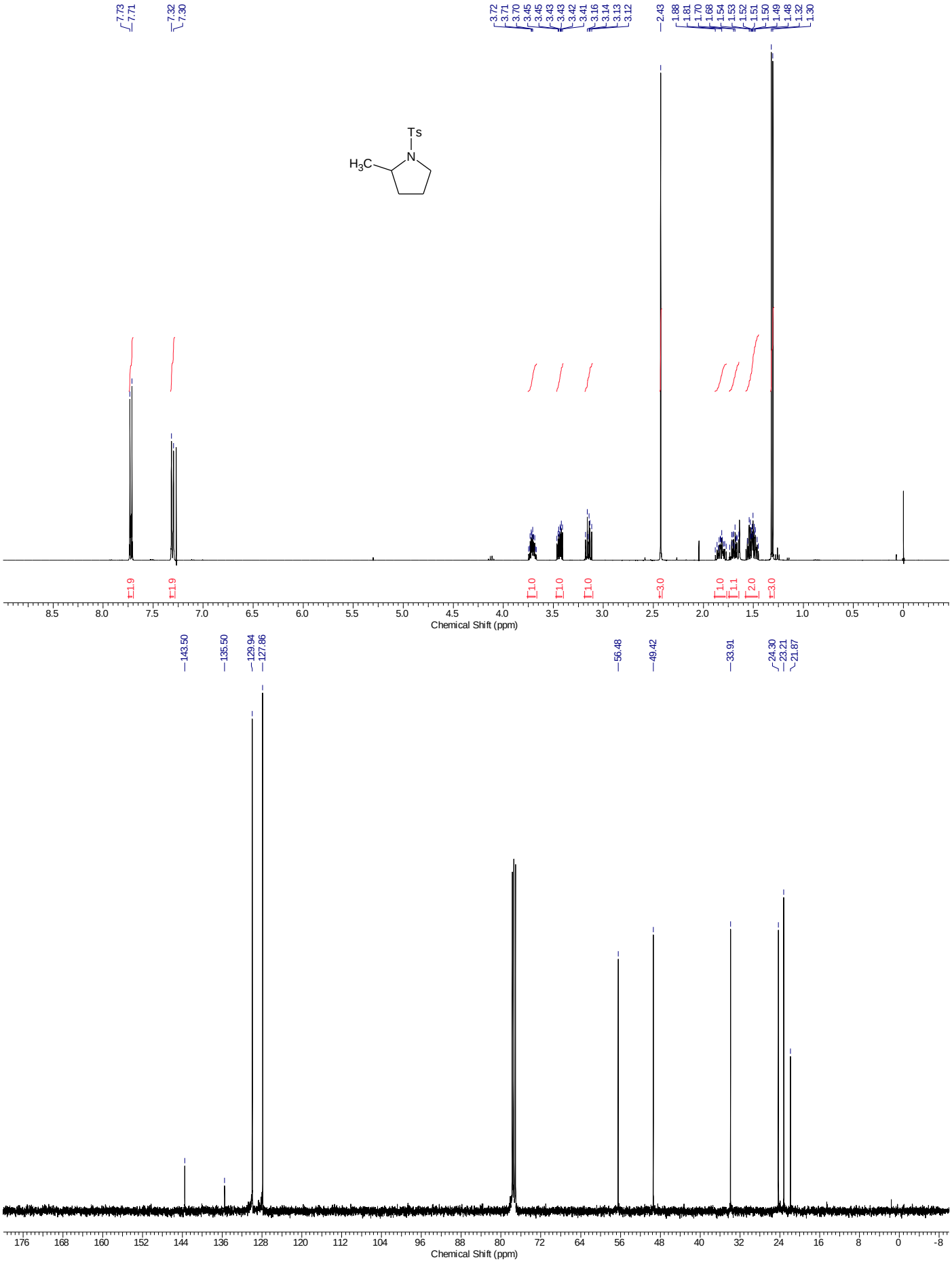




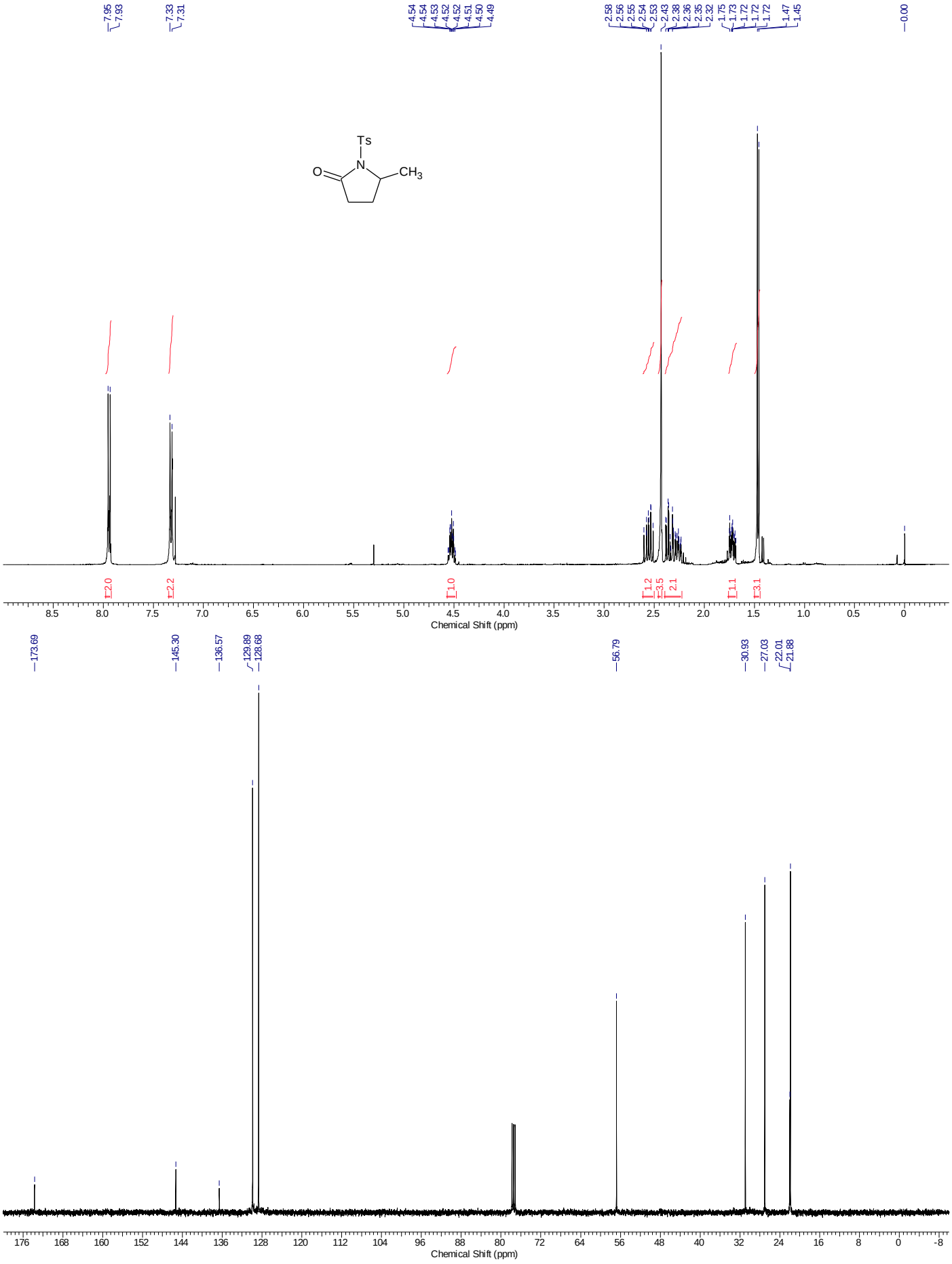
^{1}H NMR and ^{13}C NMR of *rac*-6:



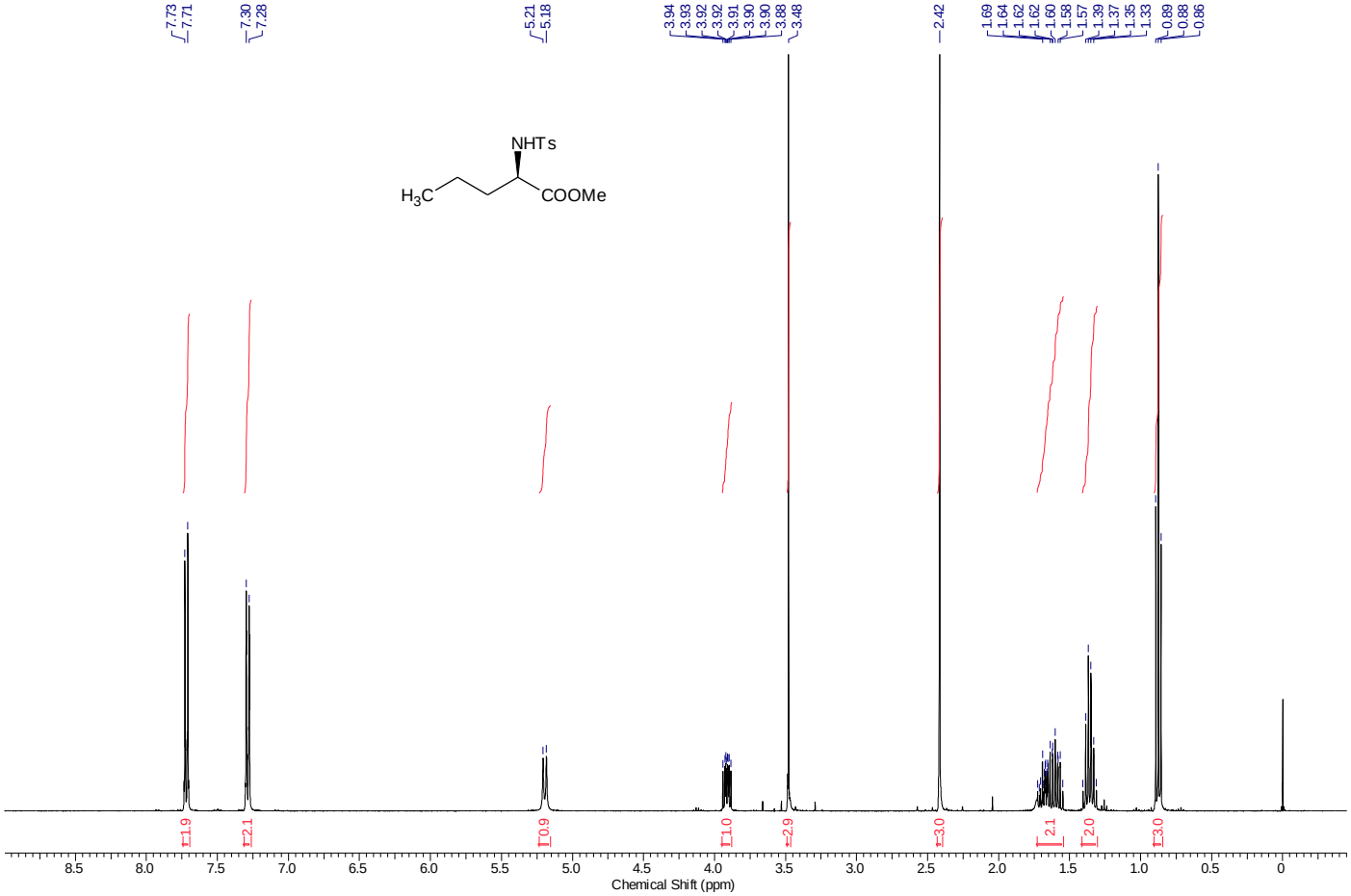
^{1}H NMR and ^{13}C NMR of *rac*-6a:

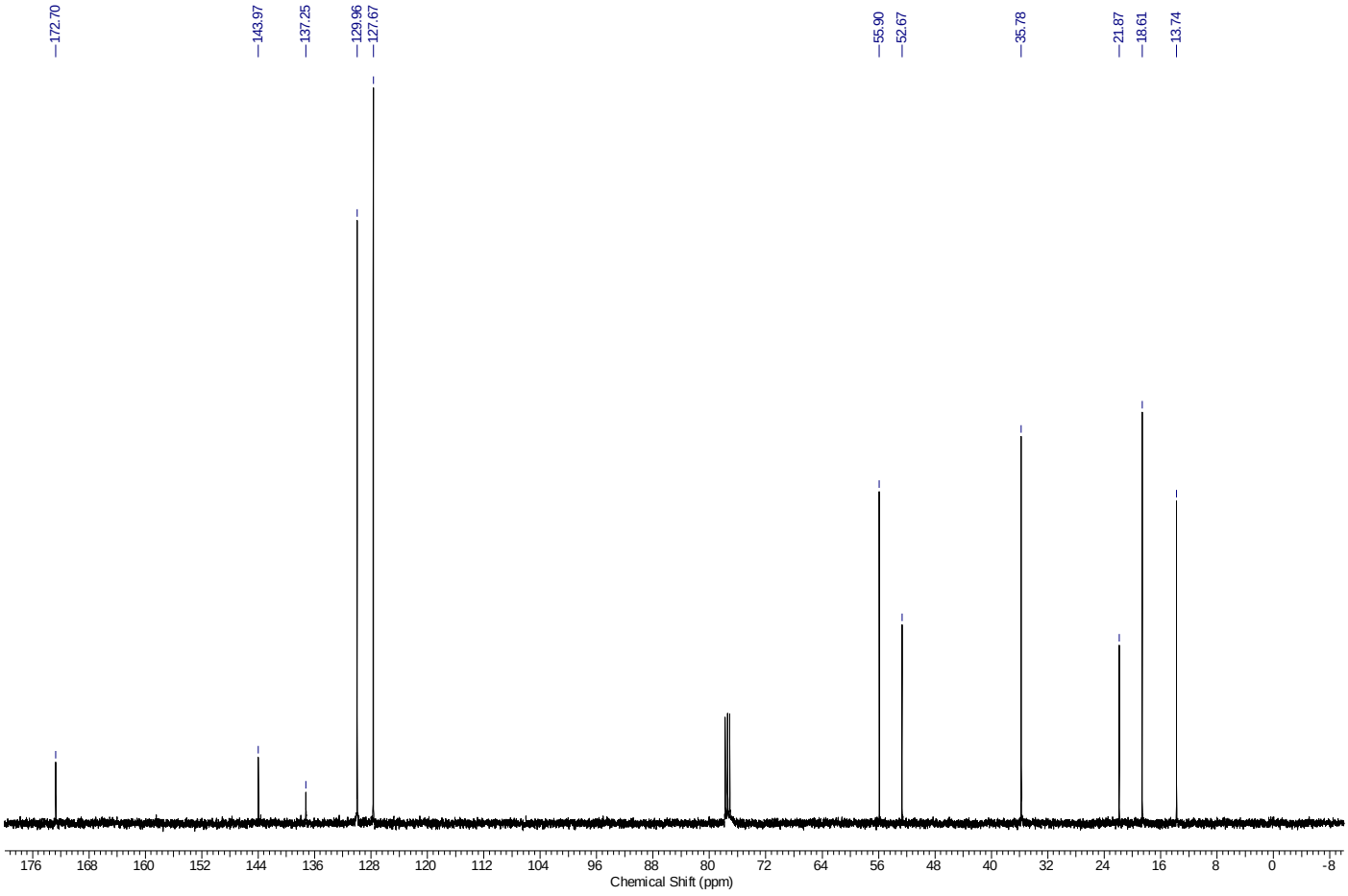


^{1}H NMR and ^{13}C NMR of *rac*-6c:

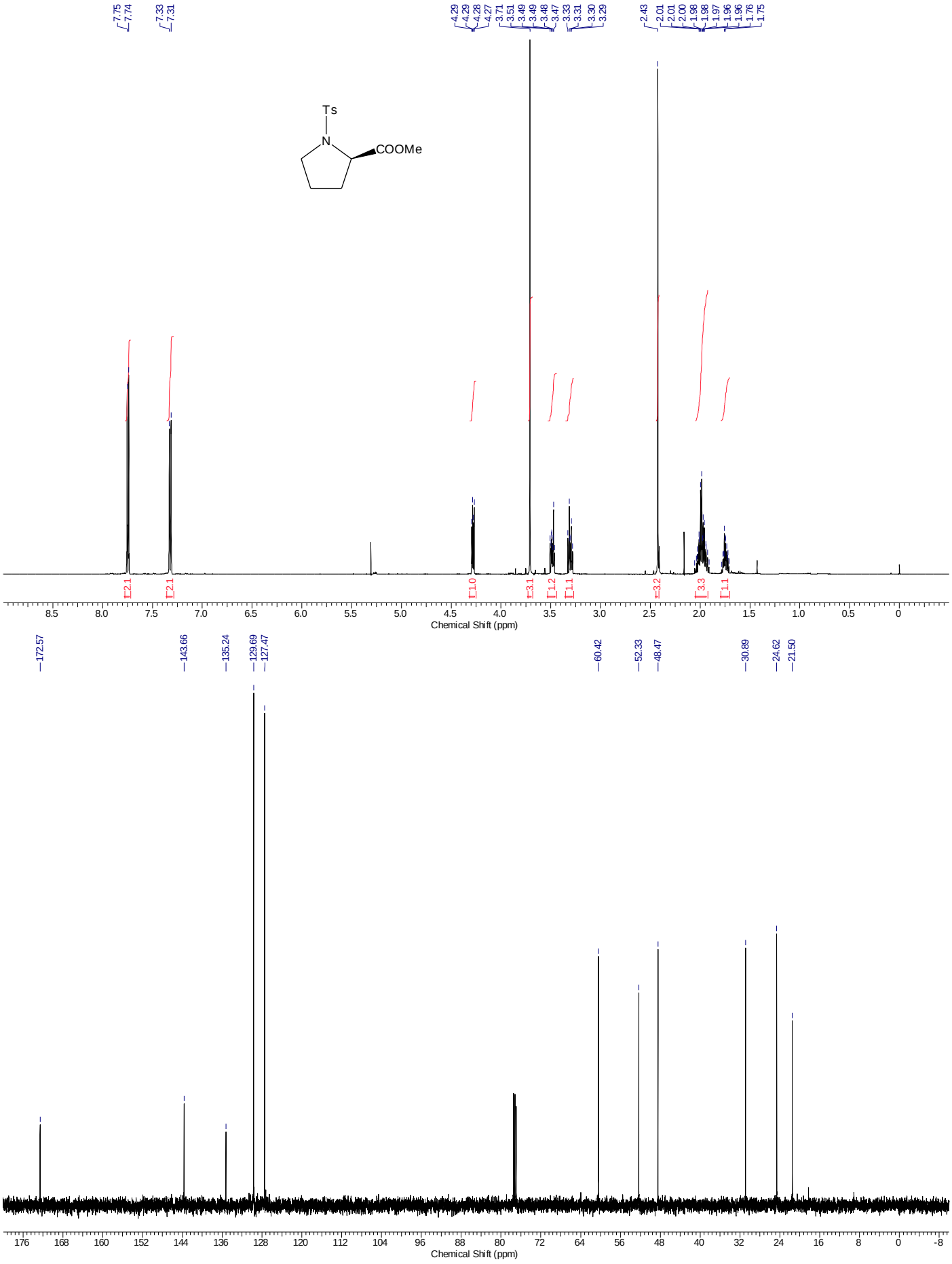


^{1}H NMR and ^{13}C NMR of 7:

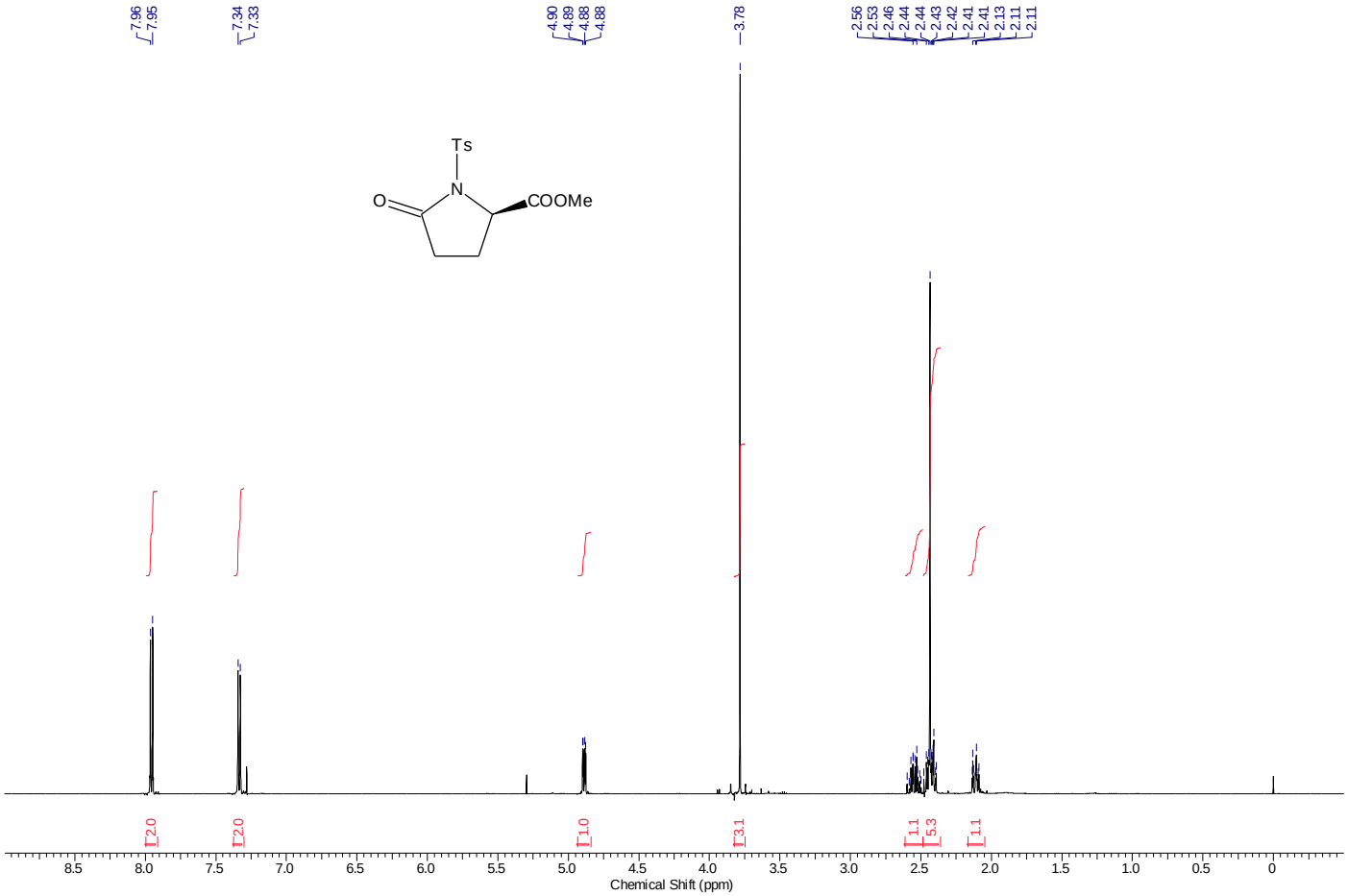


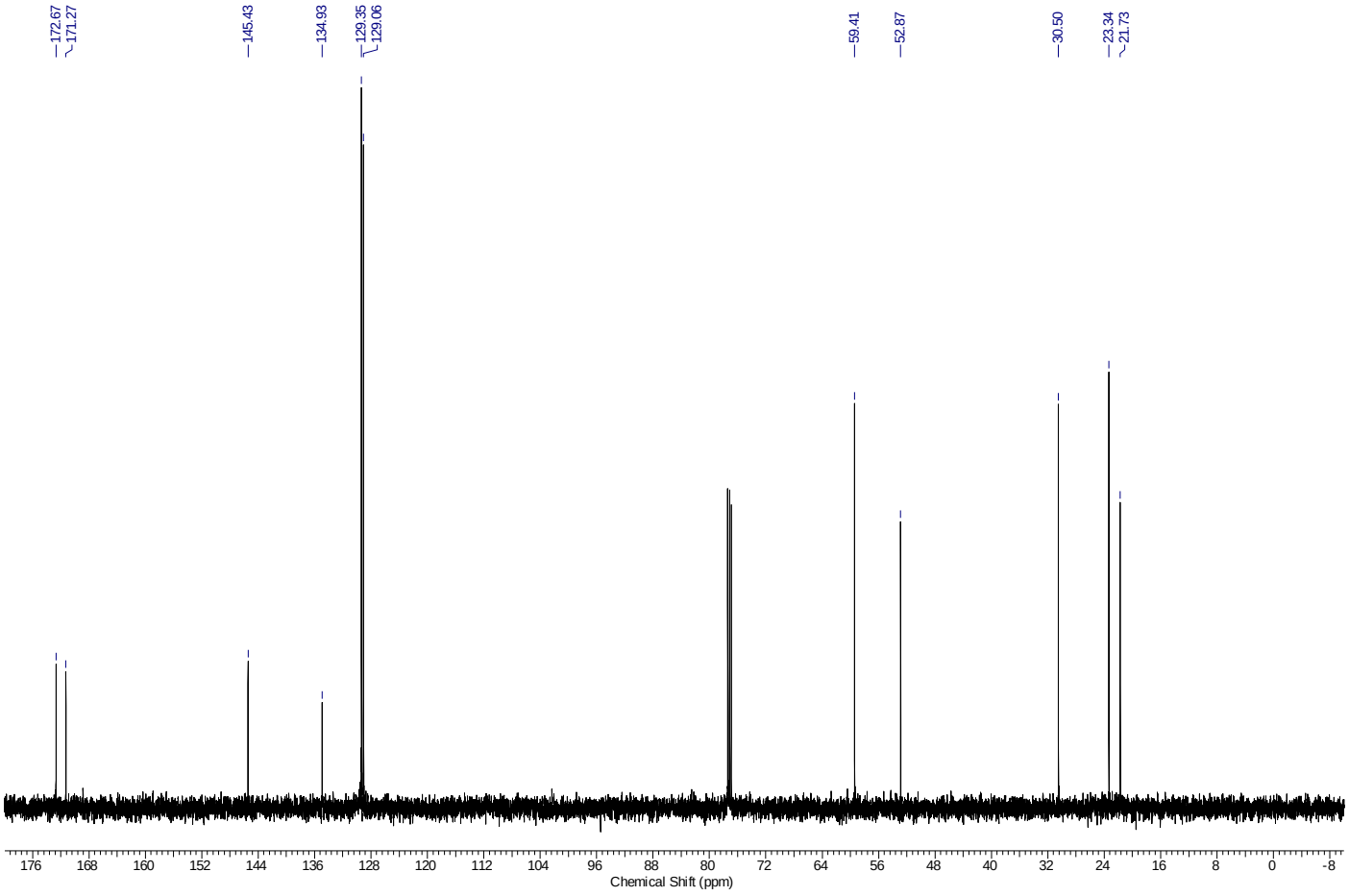


^{1}H NMR and ^{13}C NMR of 7a:

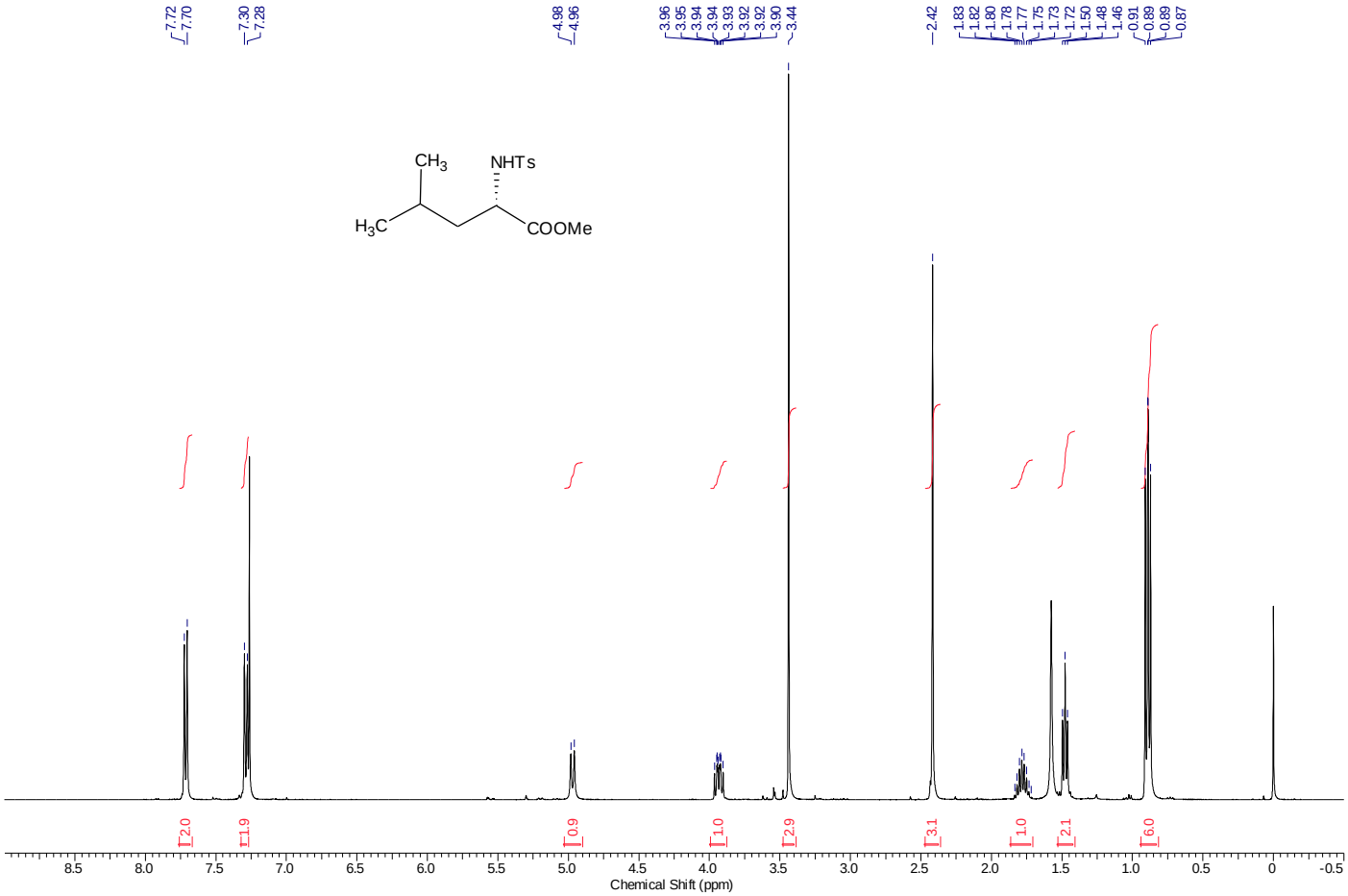


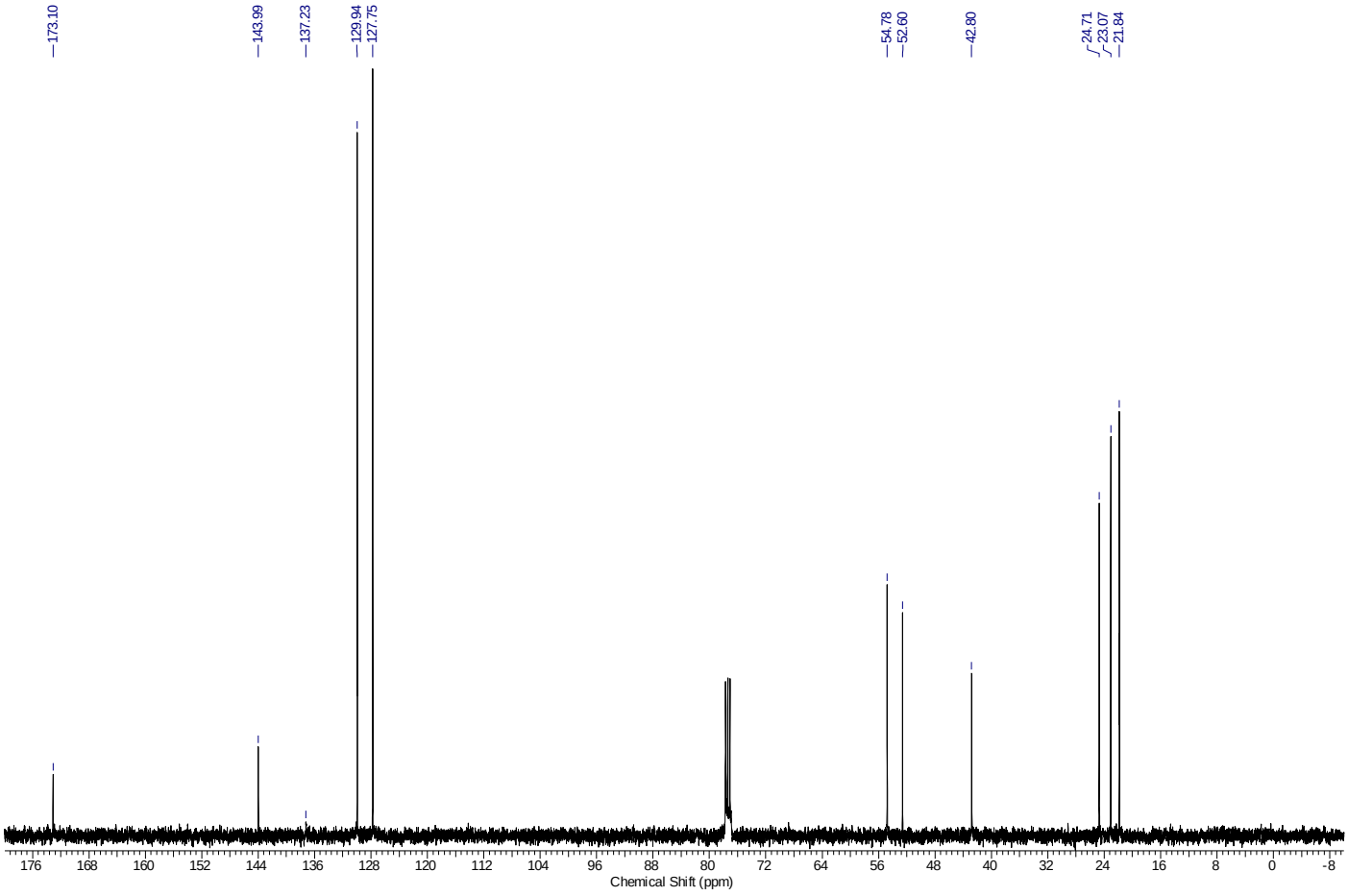
^{1}H NMR and ^{13}C NMR of 7c:



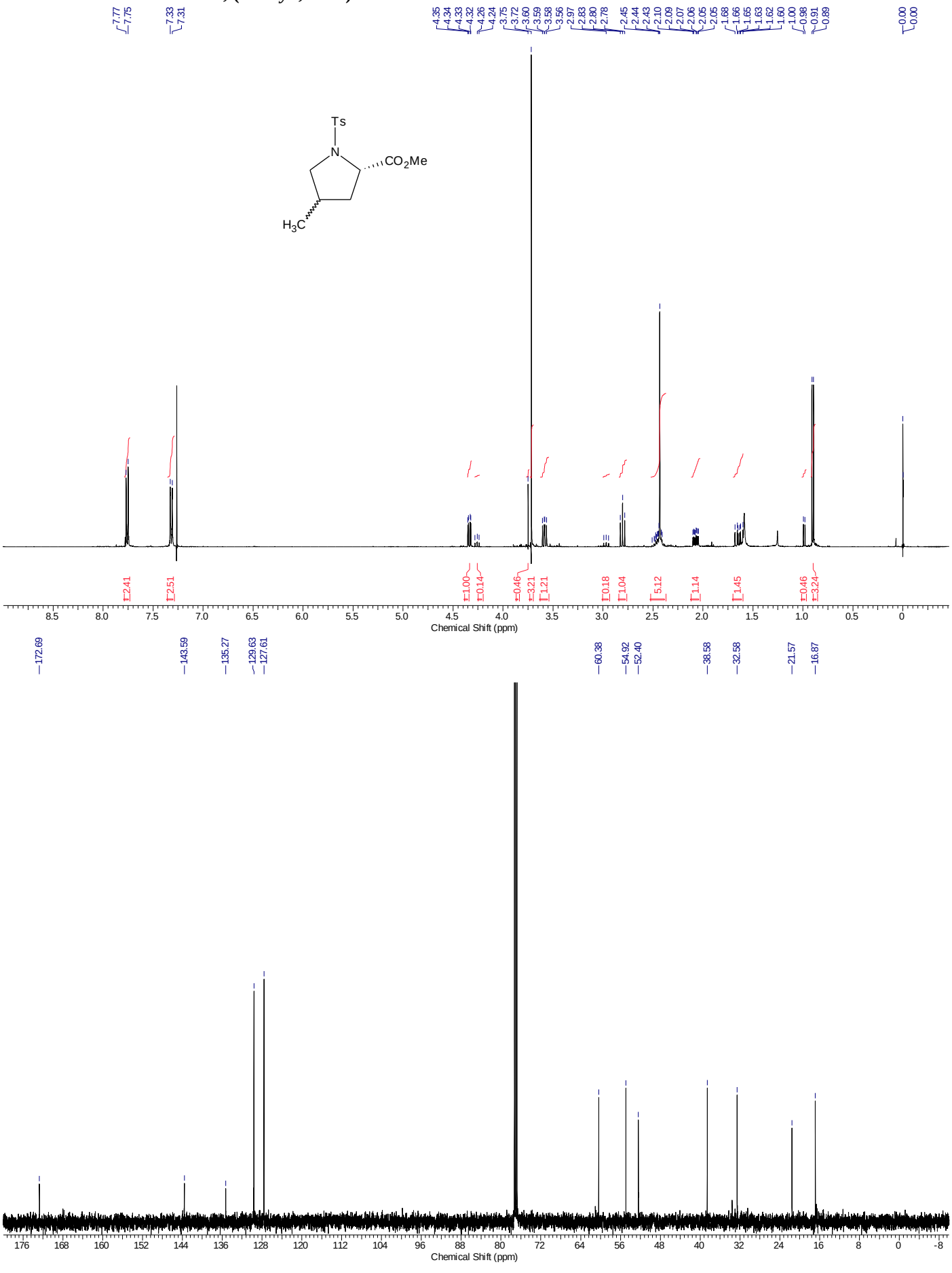


^{1}H NMR and ^{13}C NMR of 8:

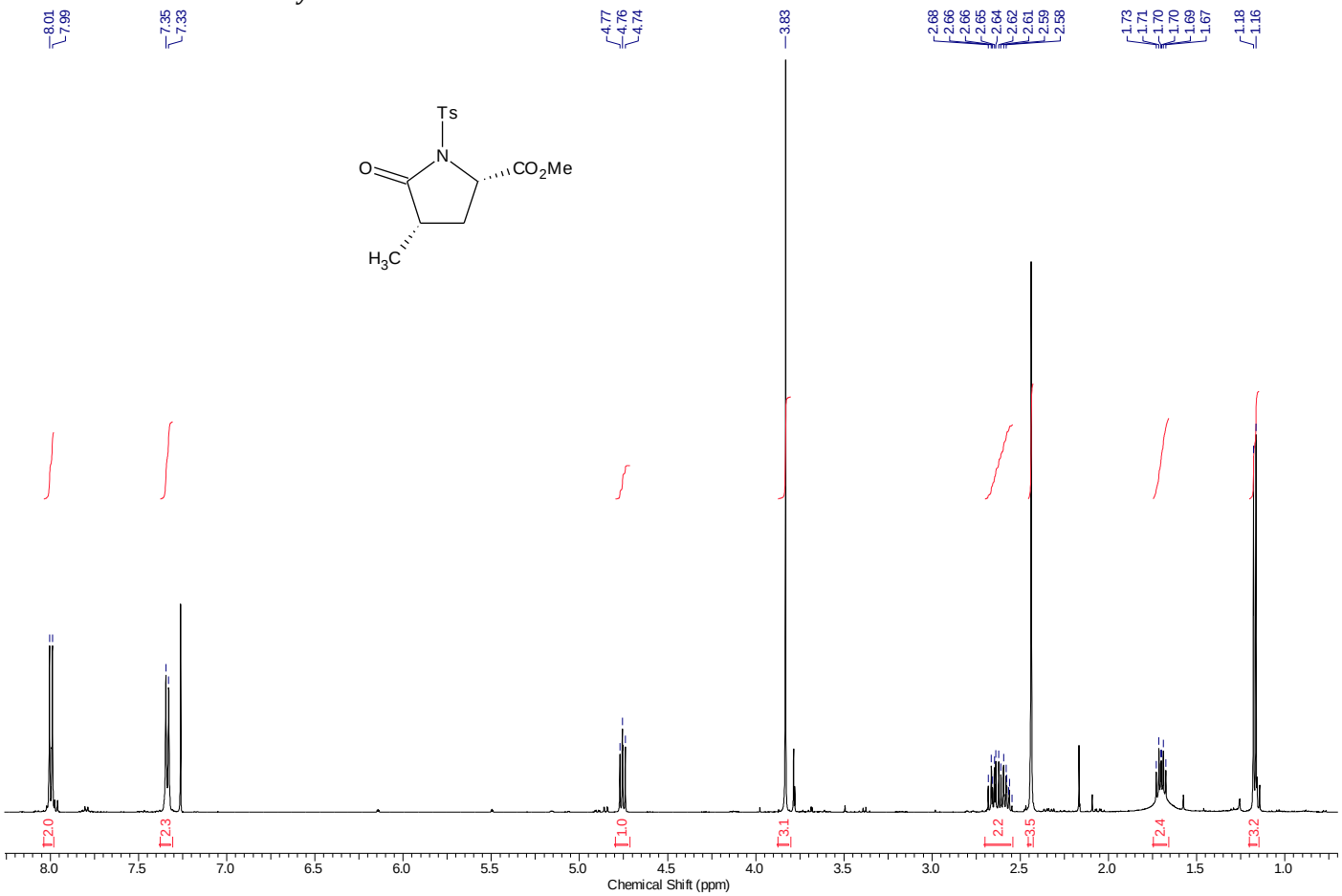


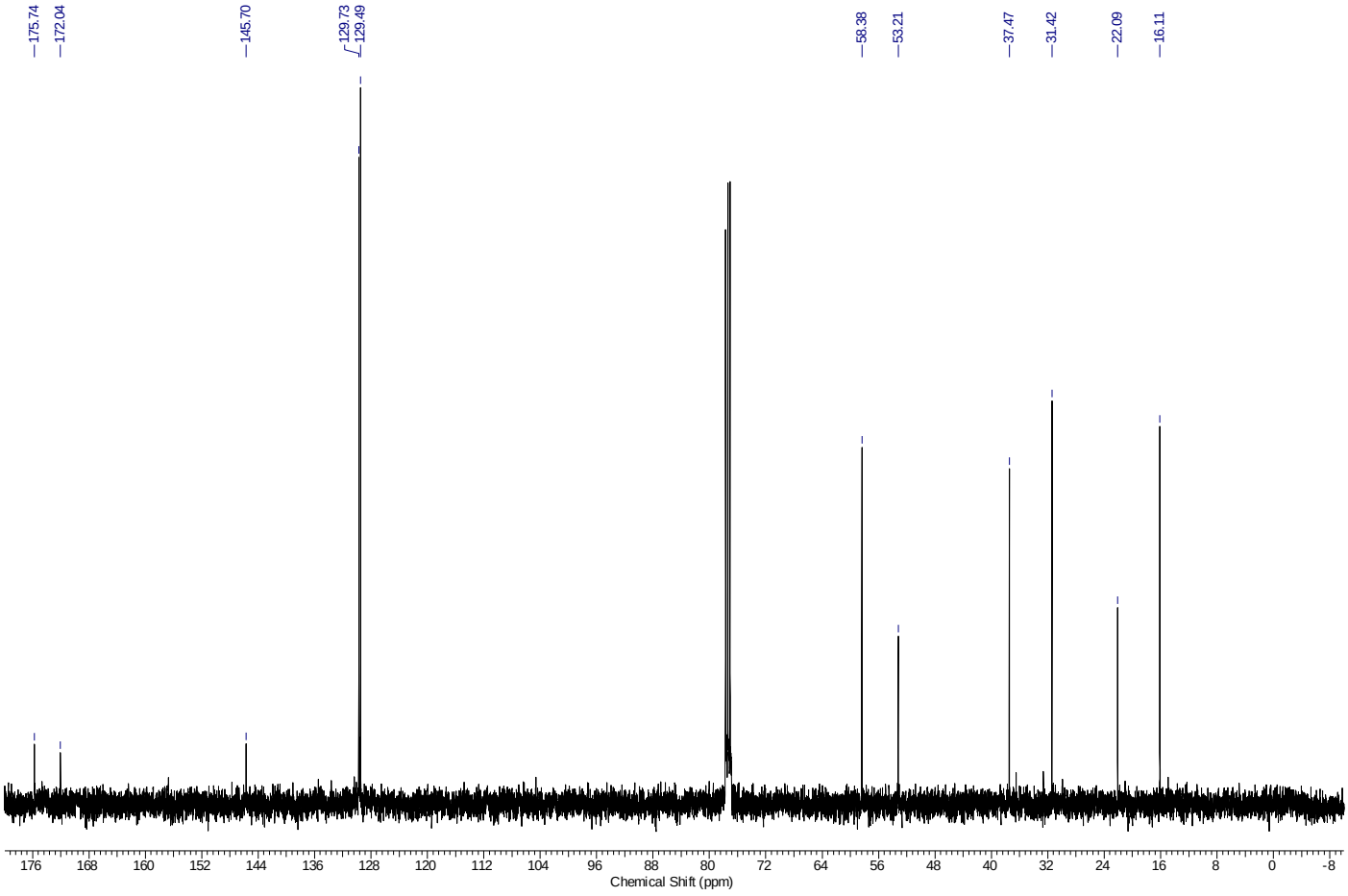


^{1}H NMR and ^{13}C NMR of 8a; (*anti*/*syn*, 7.2:1):

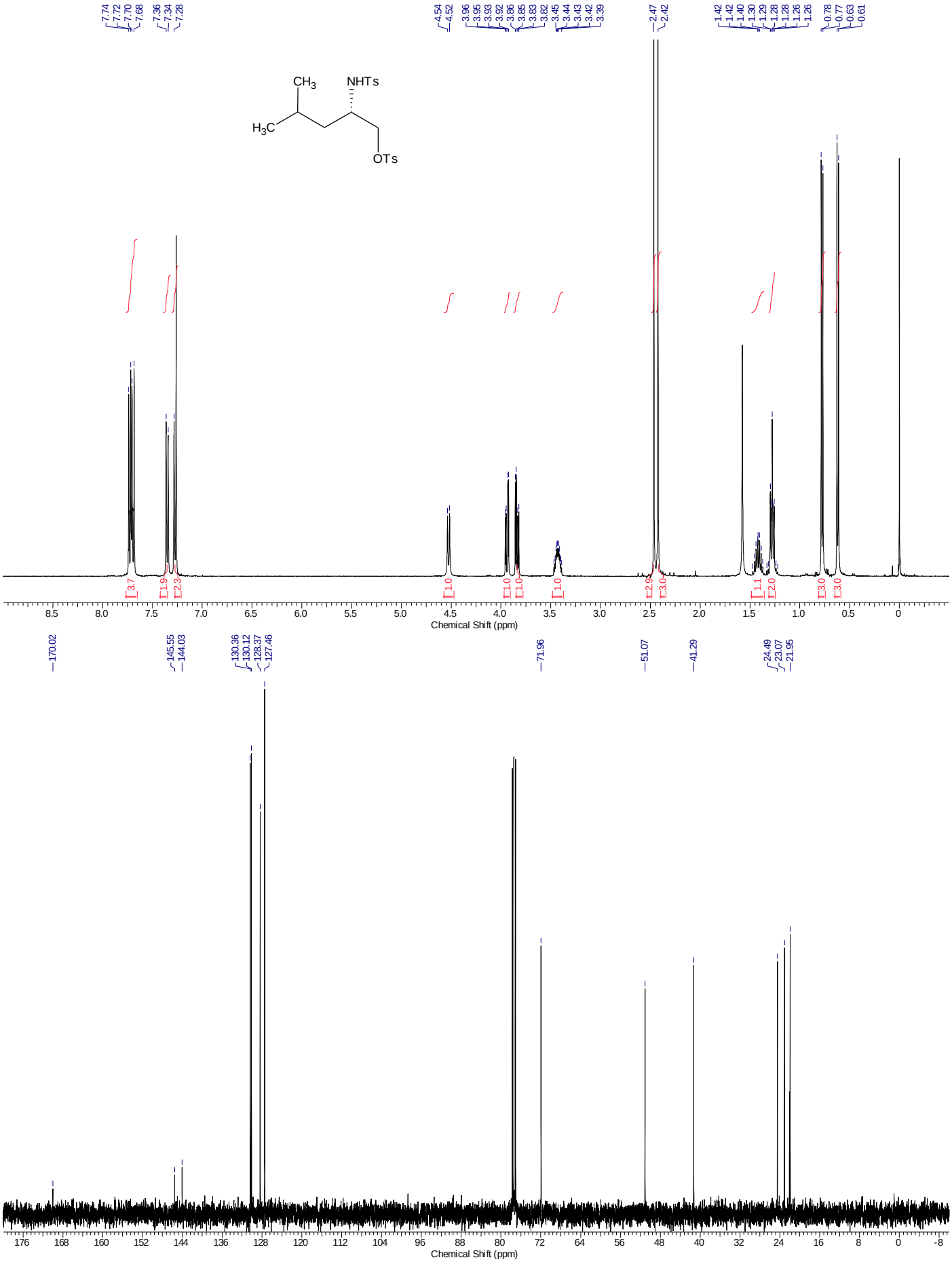


^{1}H NMR and ^{13}C NMR of *syn*-8c:

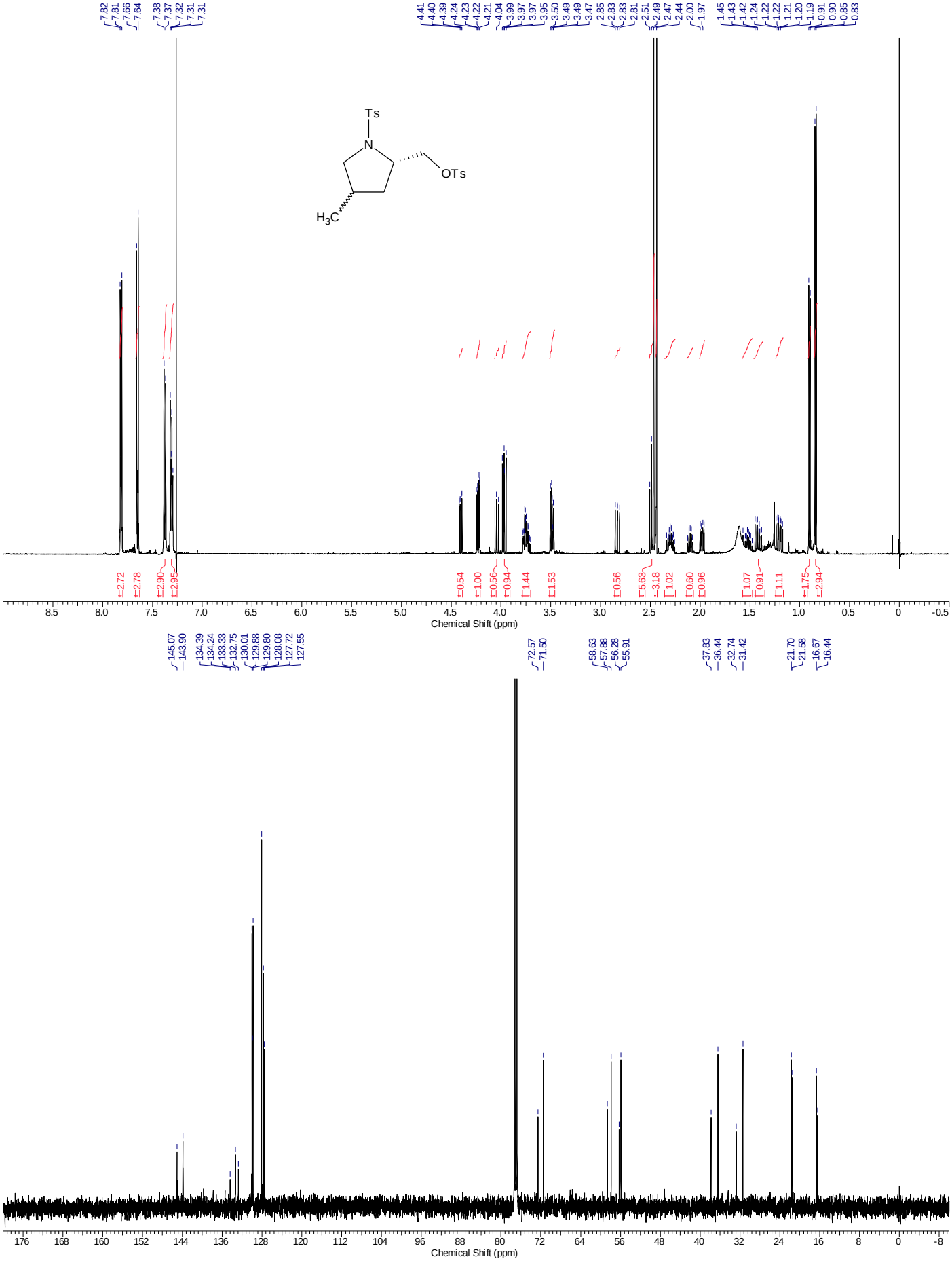




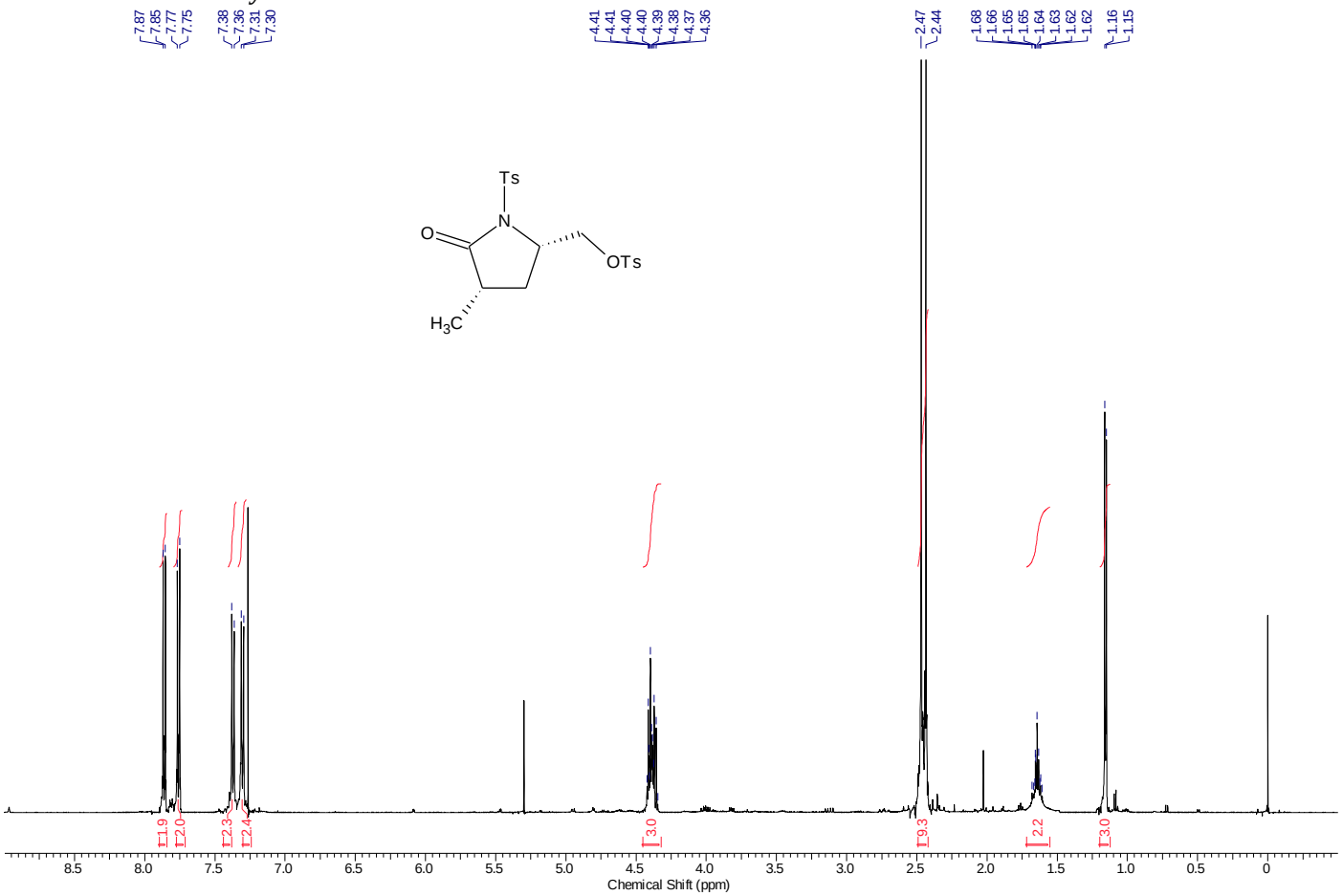
^{1}H NMR and ^{13}C NMR of 9:

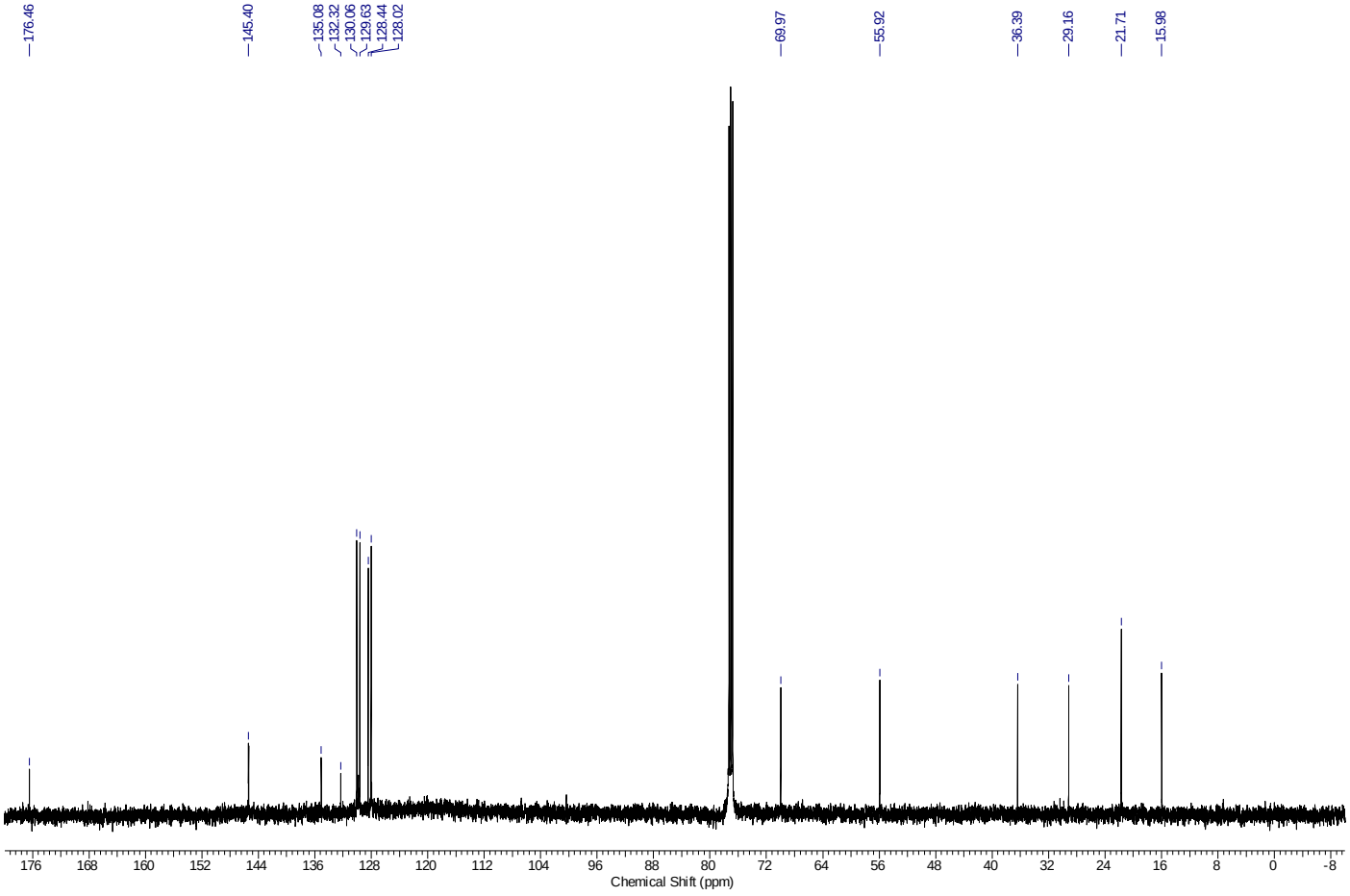


^{1}H NMR and ^{13}C NMR of 9a; (*anti*/*syn*, 1.7:1):

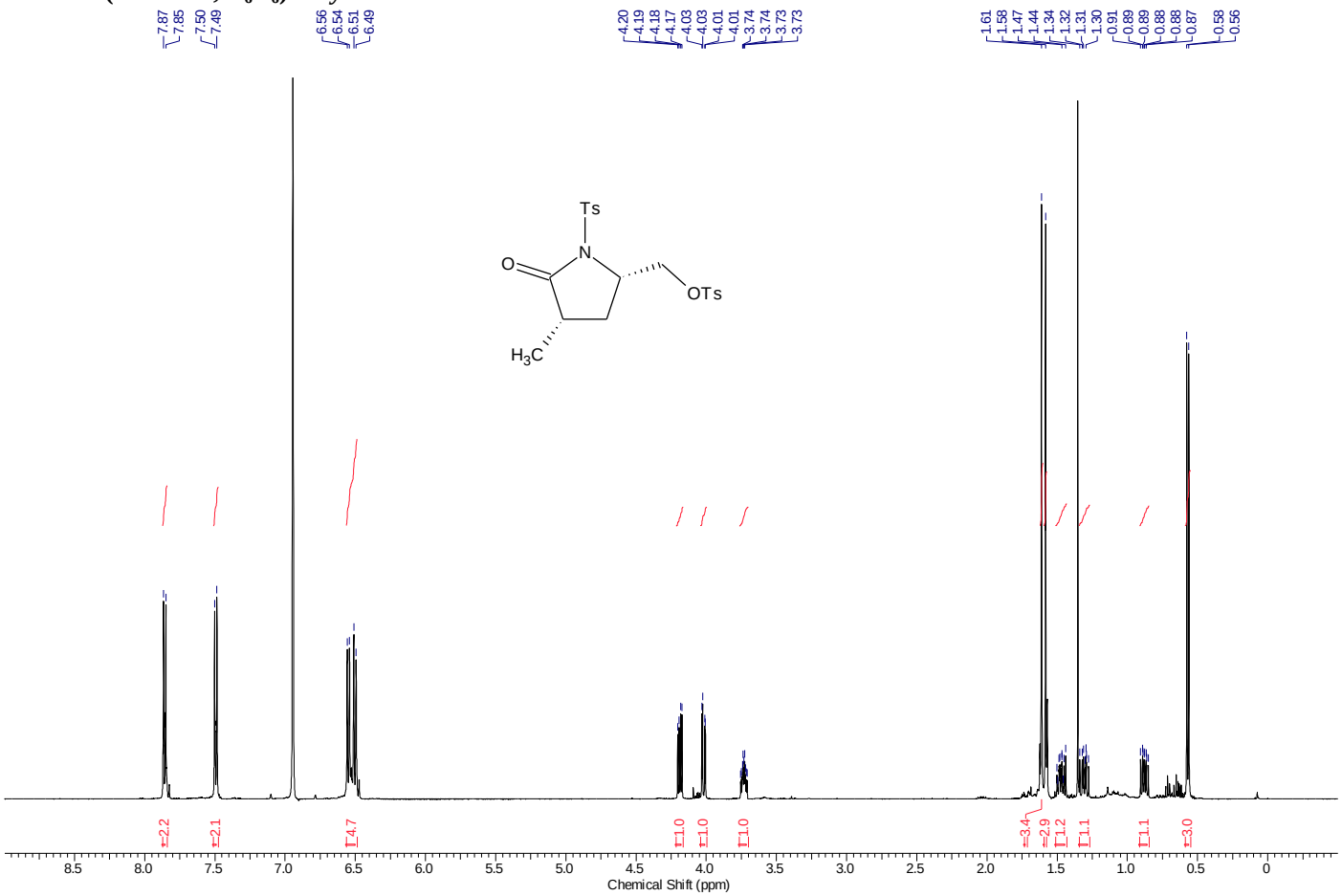


^{1}H NMR ^{13}C NMR of *syn*-9c:

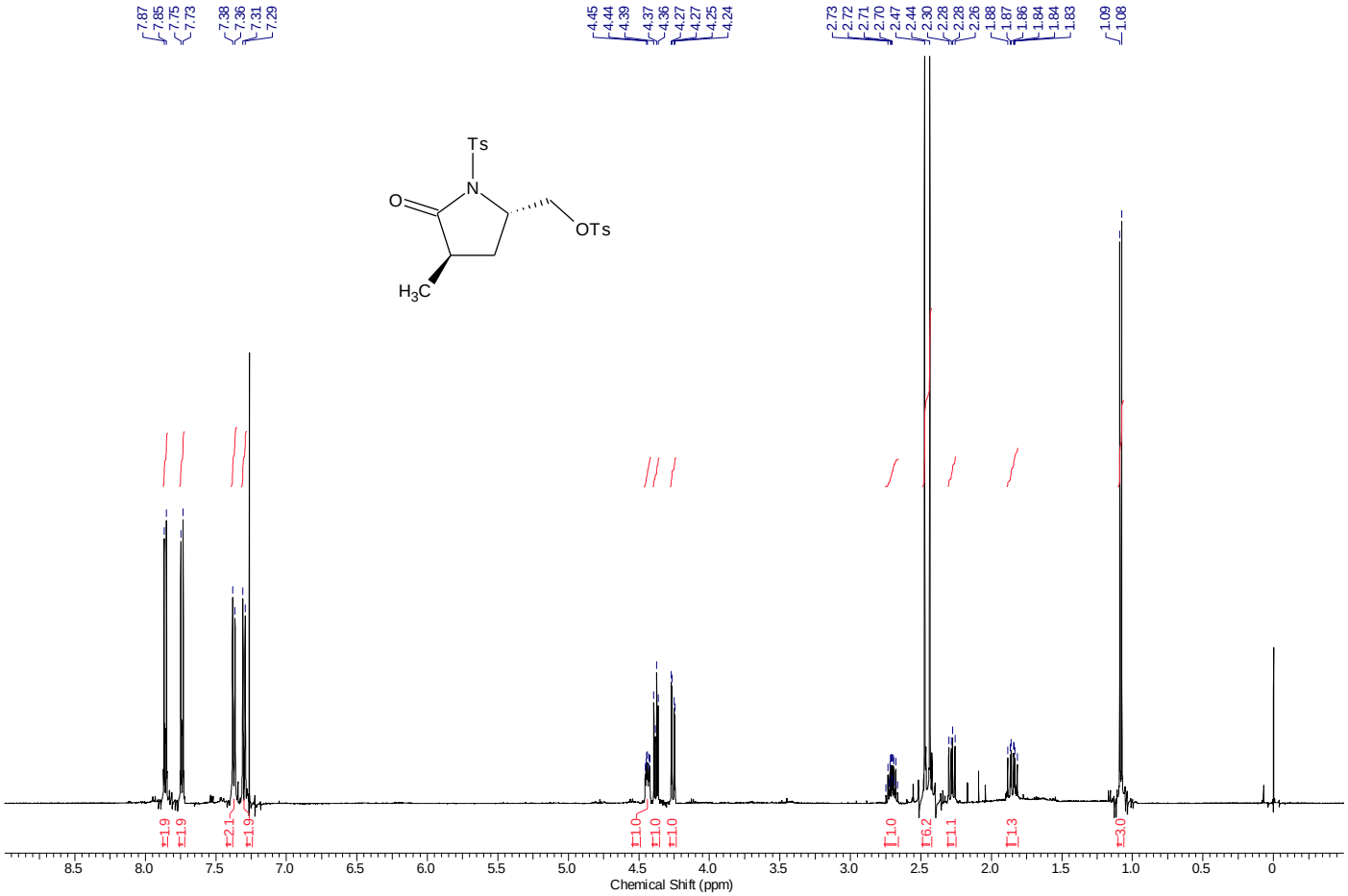


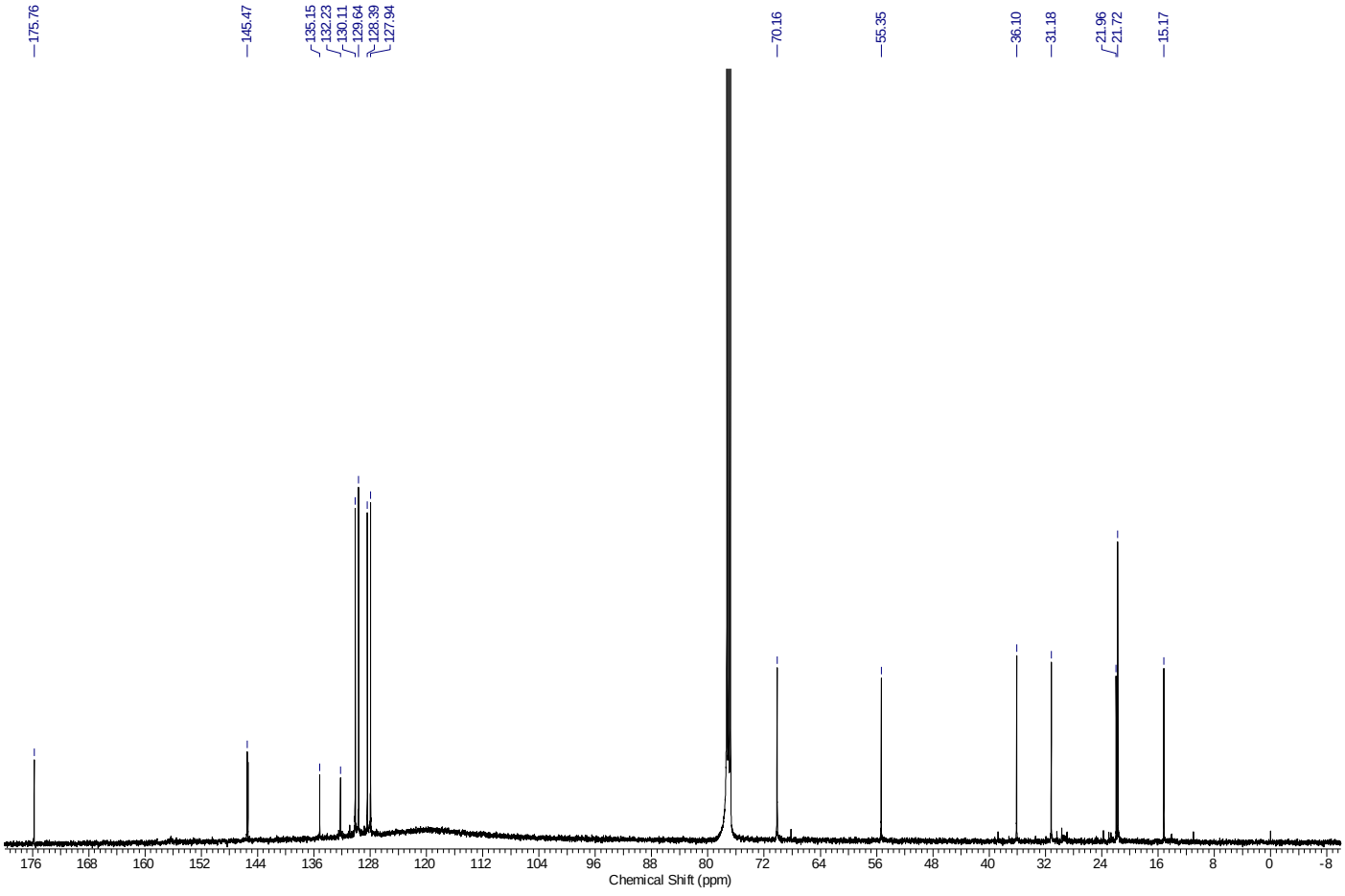


^{1}H NMR (500 MHz, C_6D_6) of *syn*-9c:

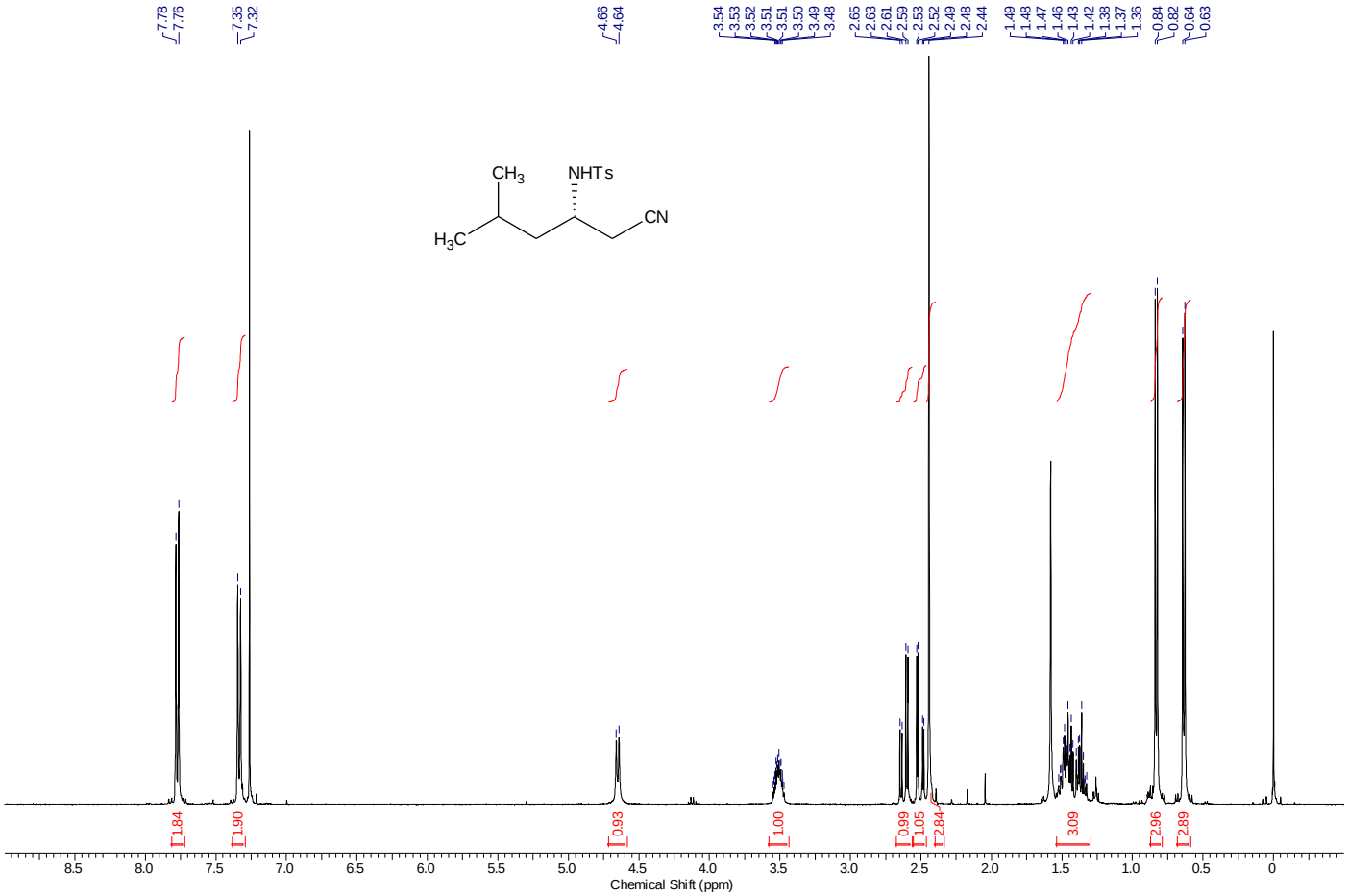


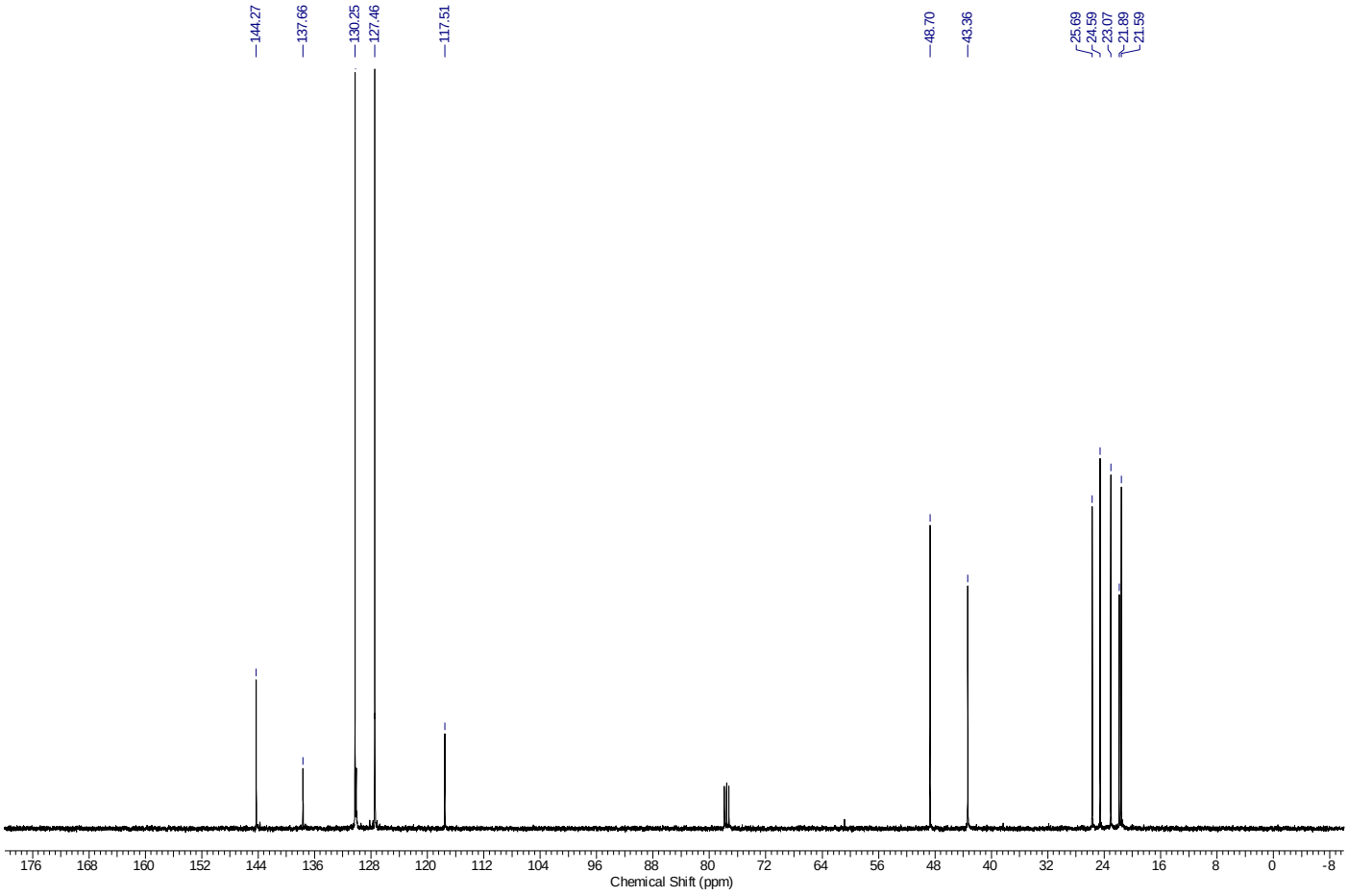
^{1}H NMR and ^{13}C NMR of *anti*-9c:



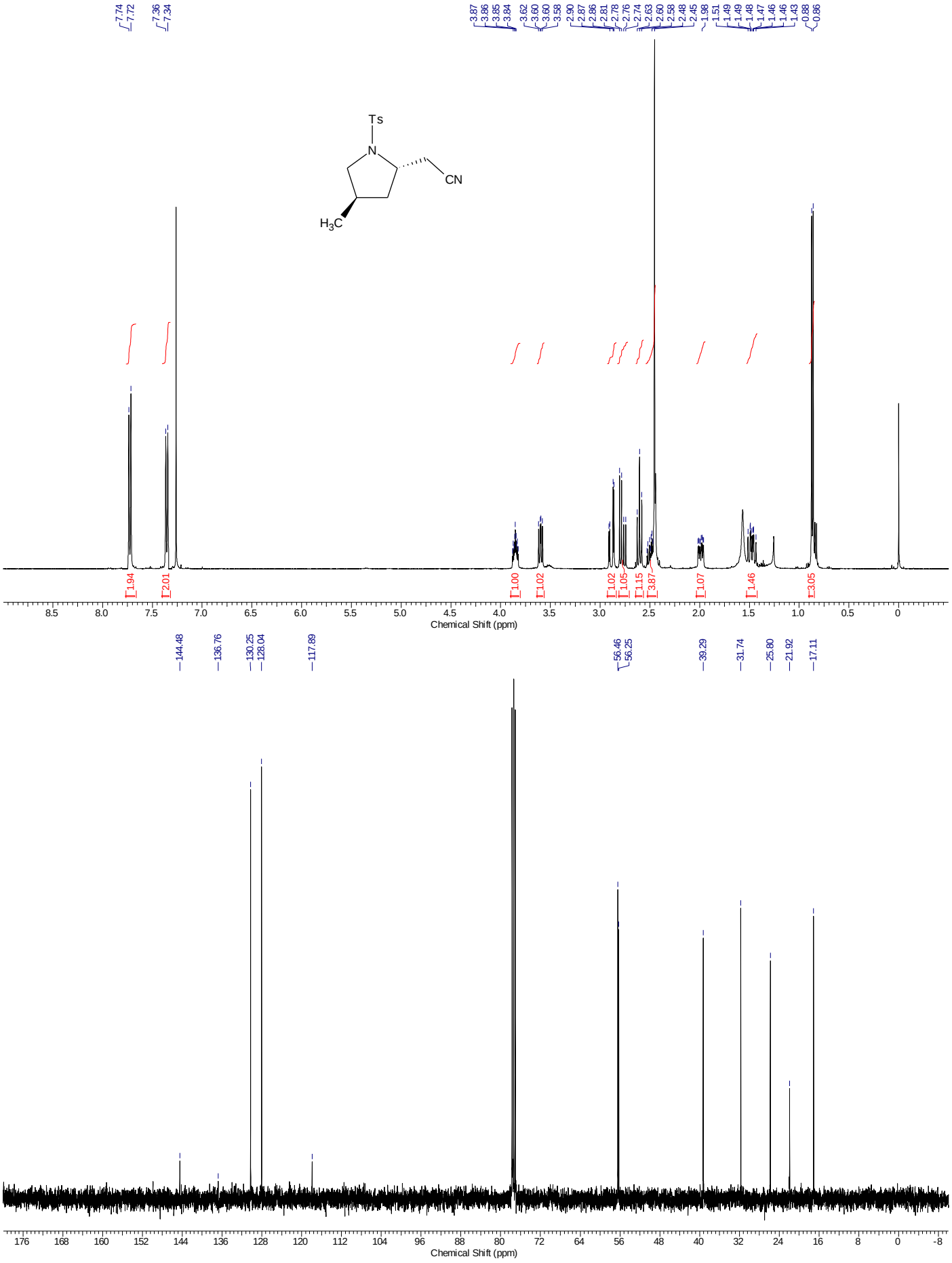


^{1}H NMR and ^{13}C NMR of 10:

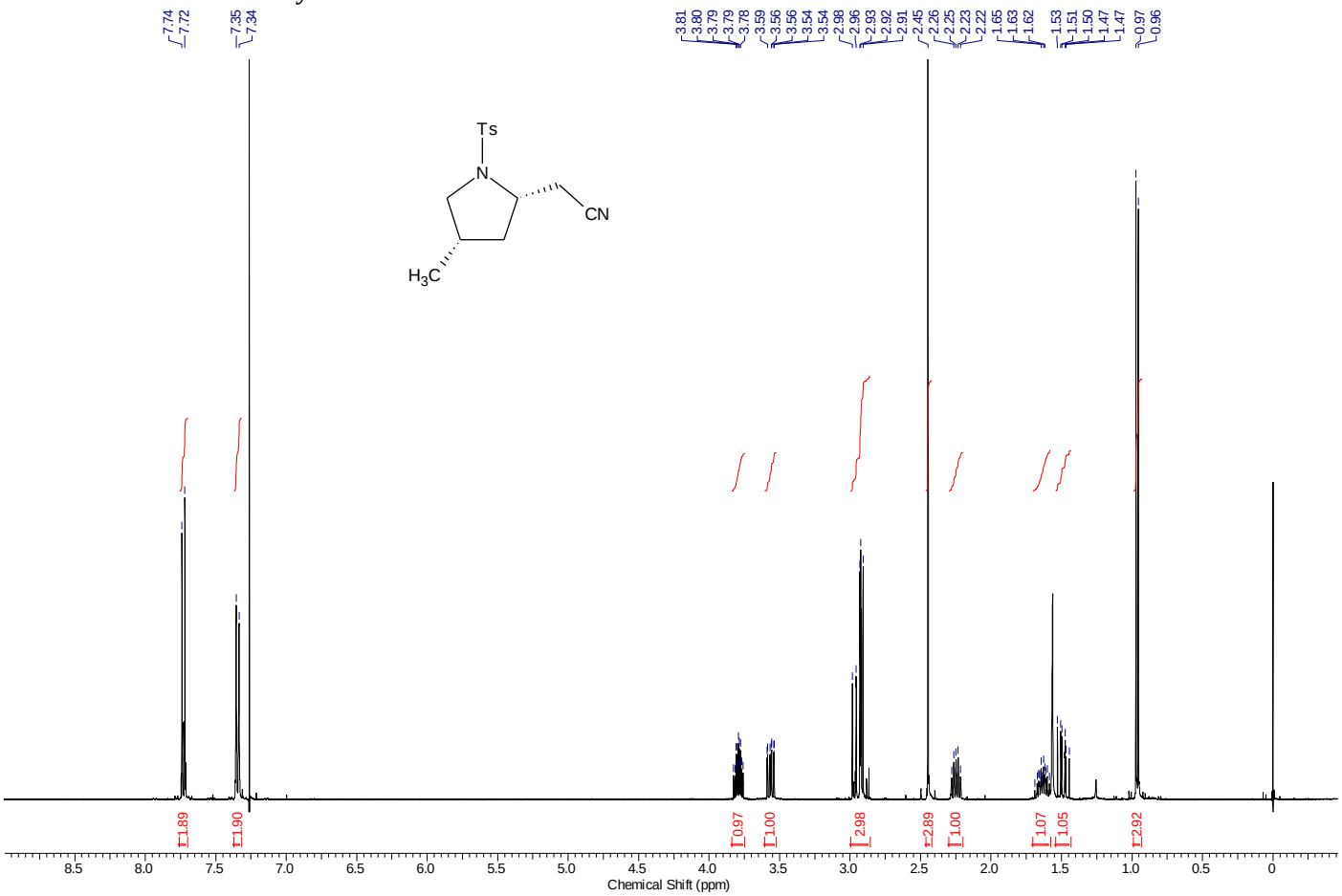


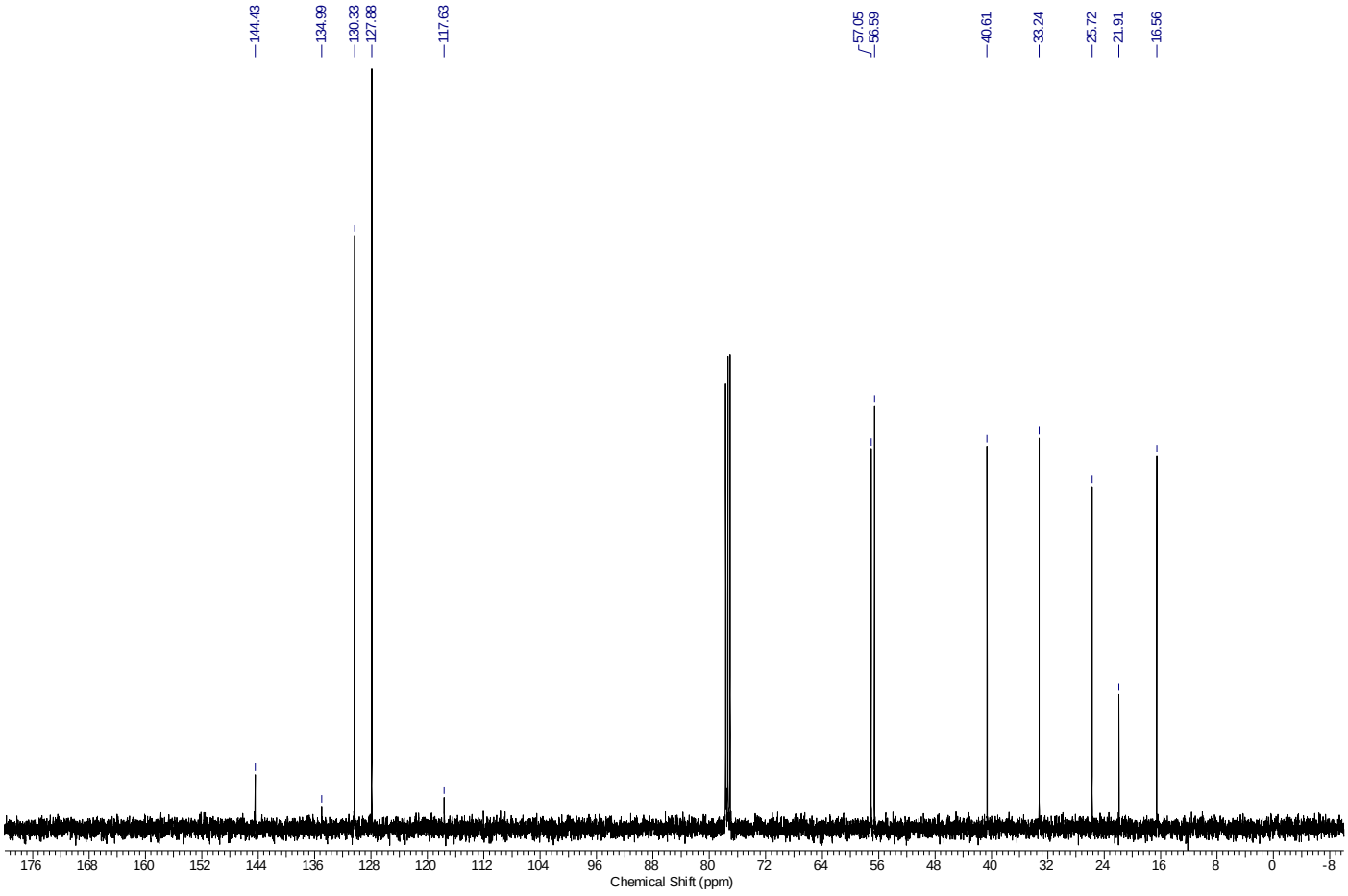


^{1}H NMR and ^{13}C NMR of *anti*-10a:

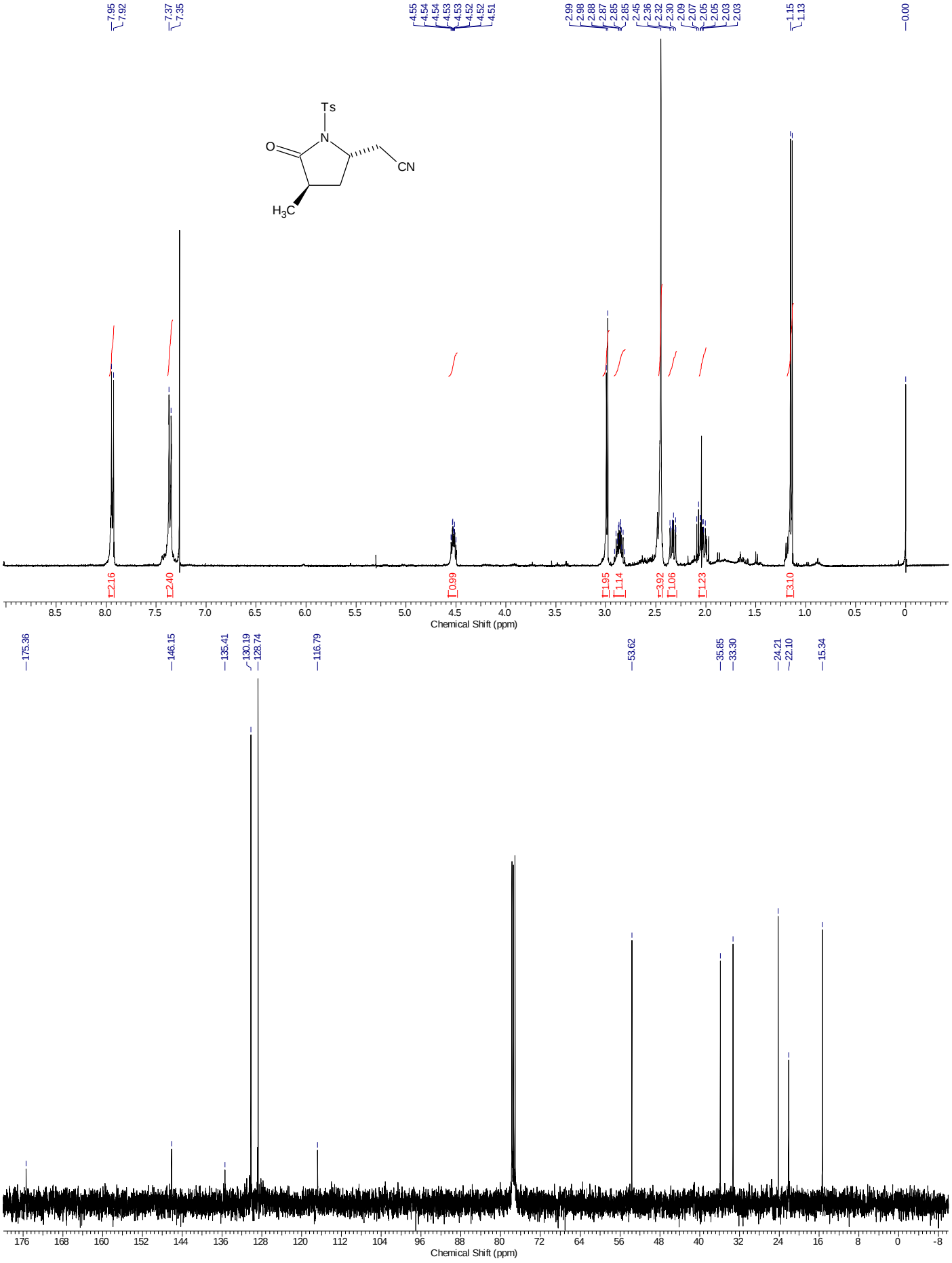


^{1}H NMR and ^{13}C NMR of *syn*-10a:

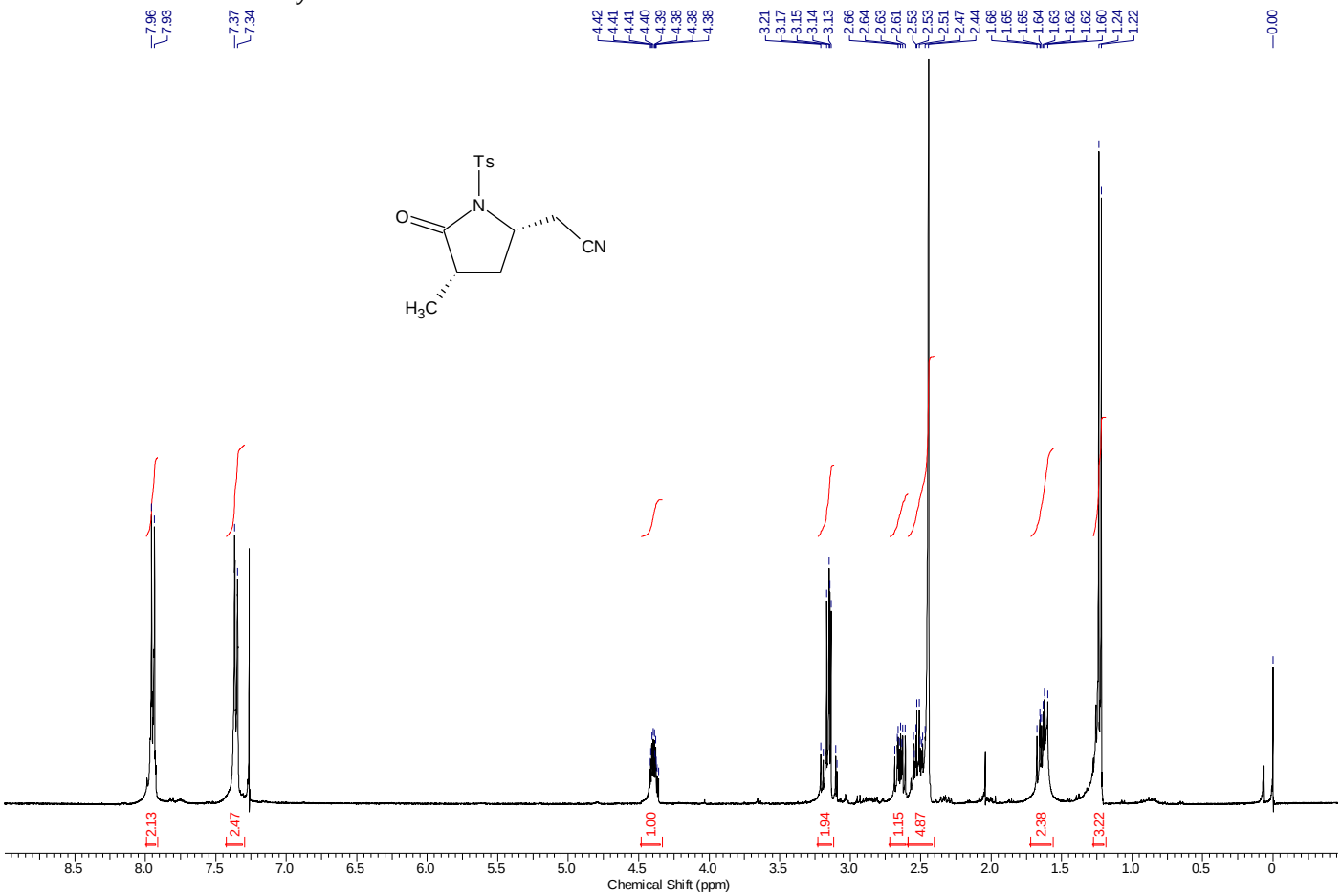


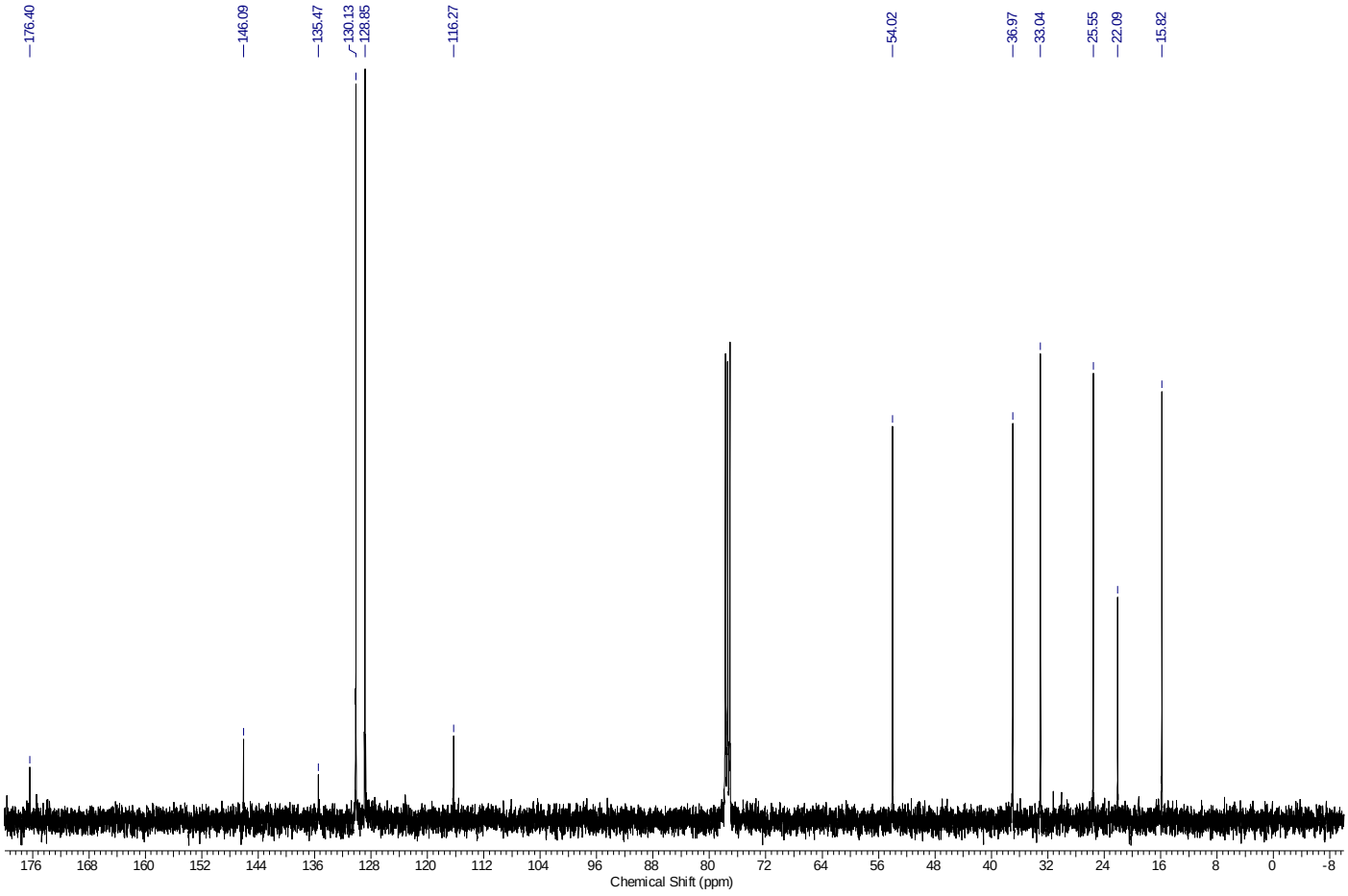


^{1}H NMR and ^{13}C NMR of *anti*-10c:

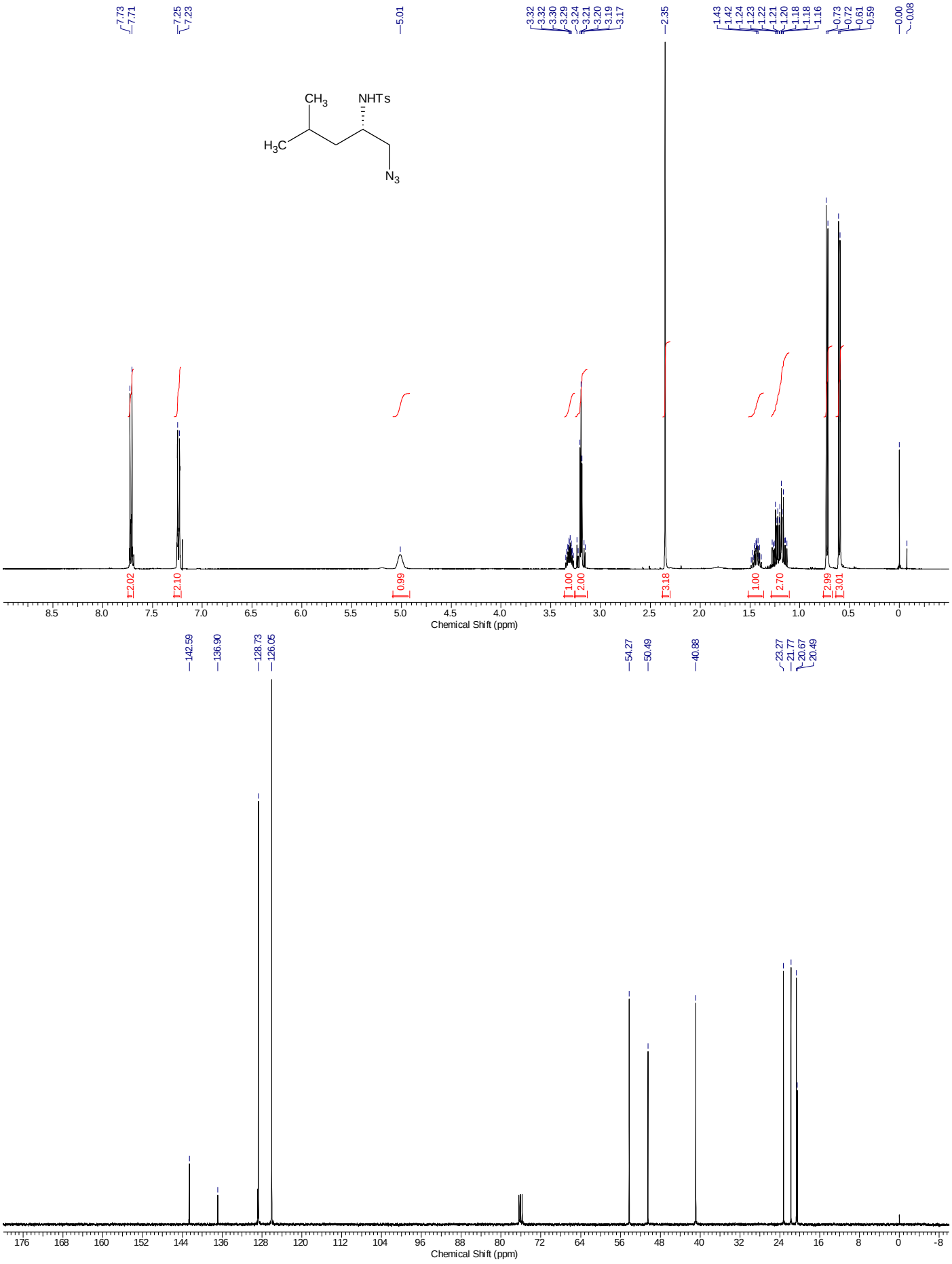


^{1}H NMR and ^{13}C NMR of *syn*-10c:

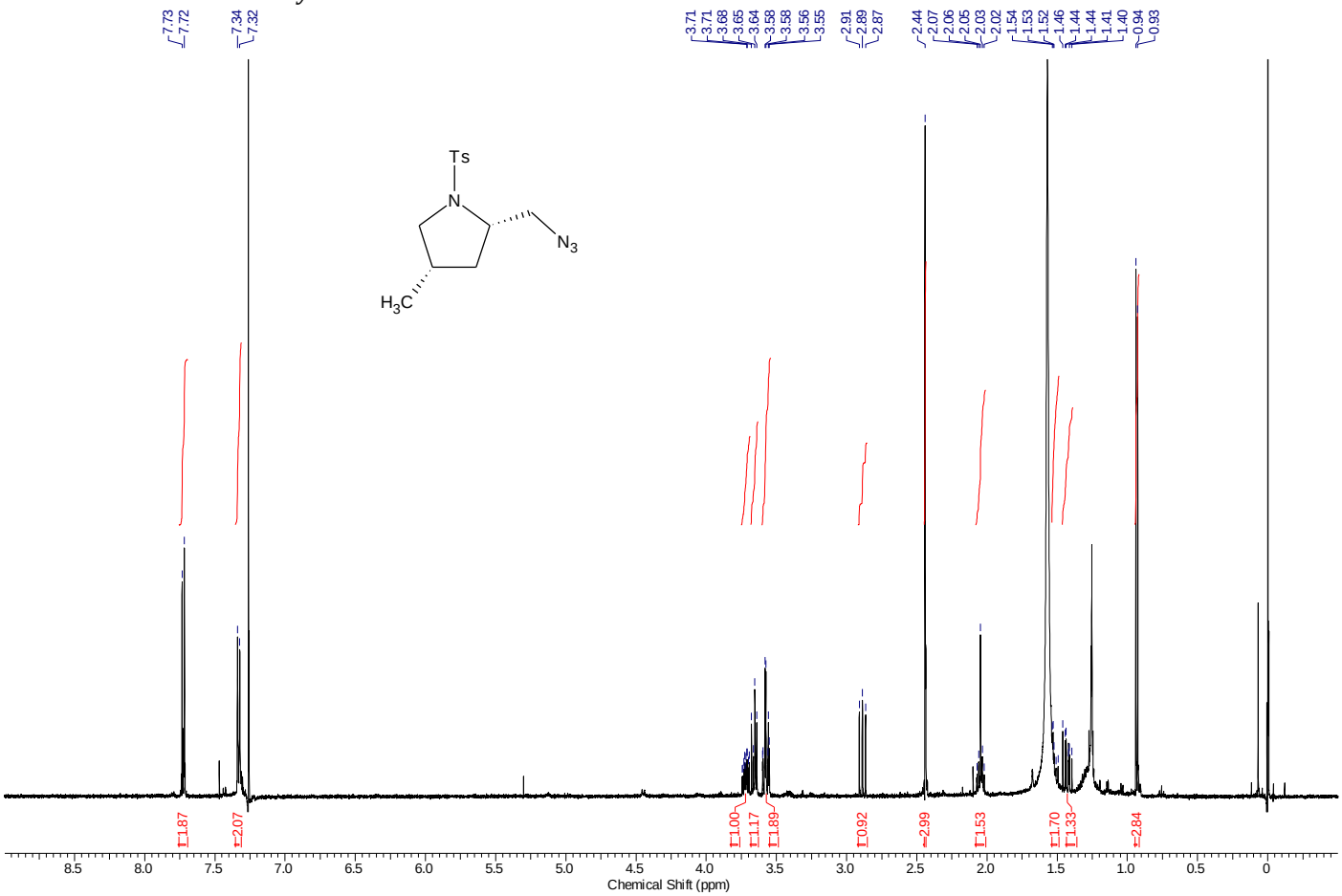


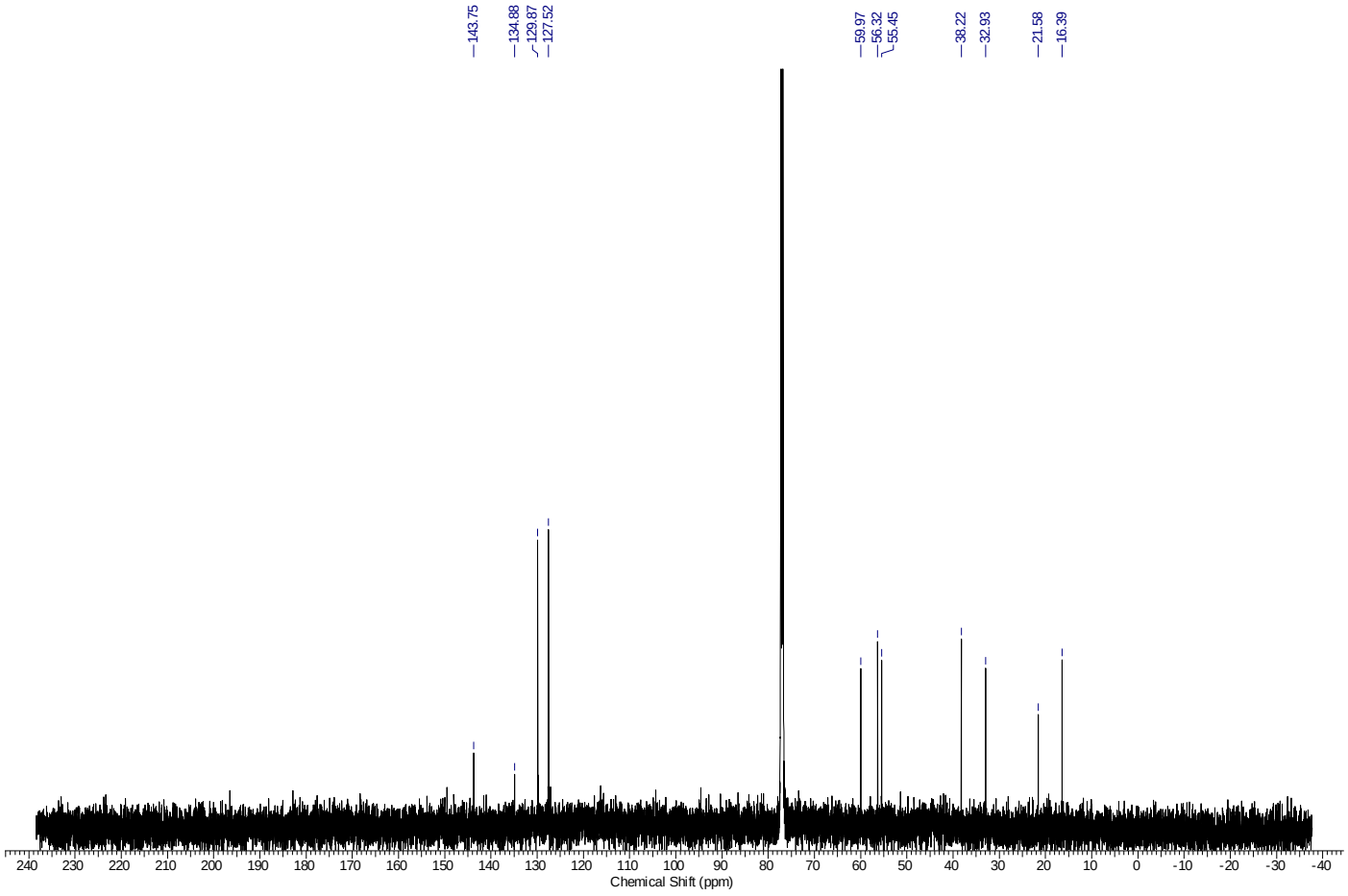


^{1}H NMR and ^{13}C NMR of 11:

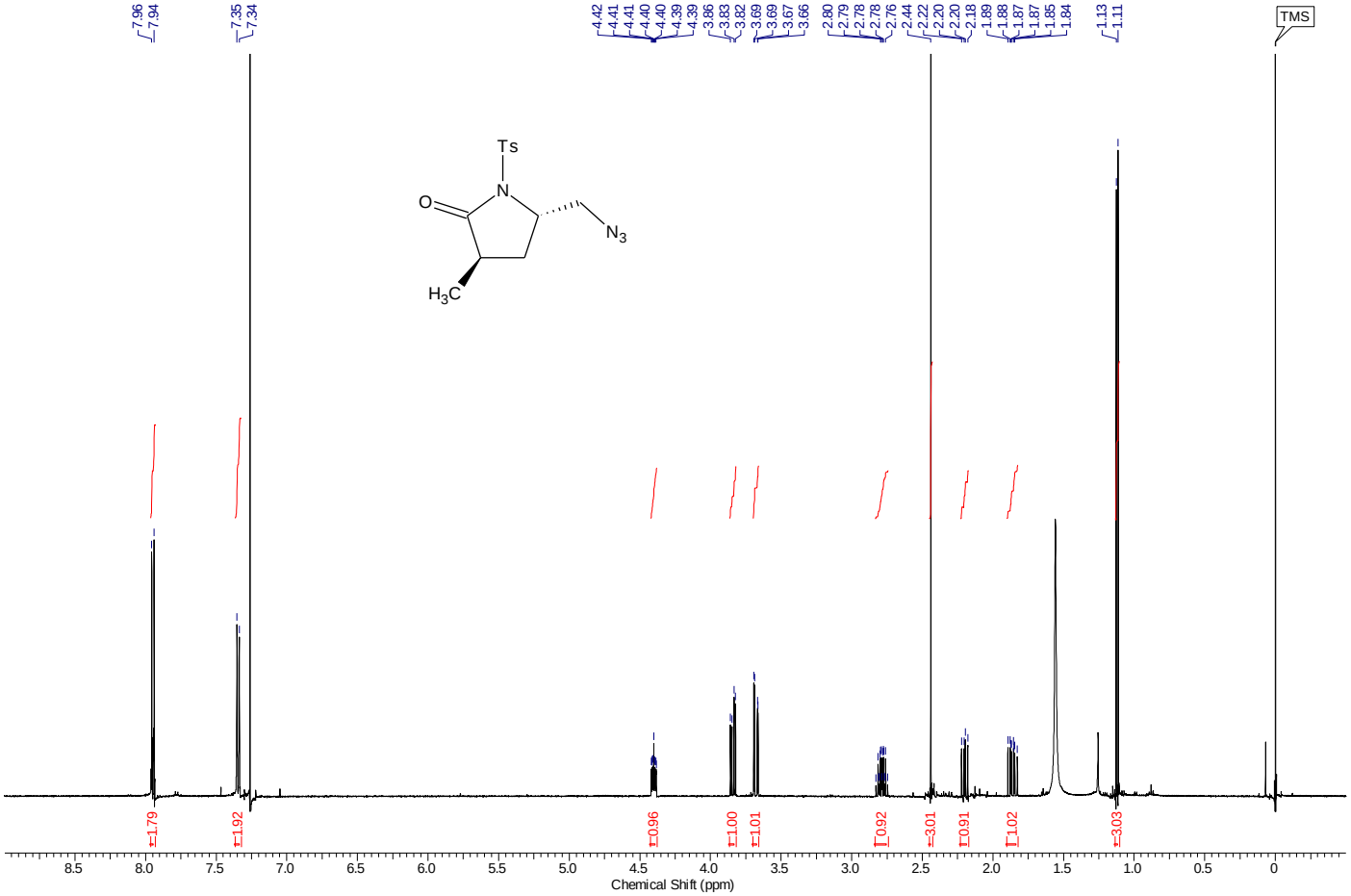


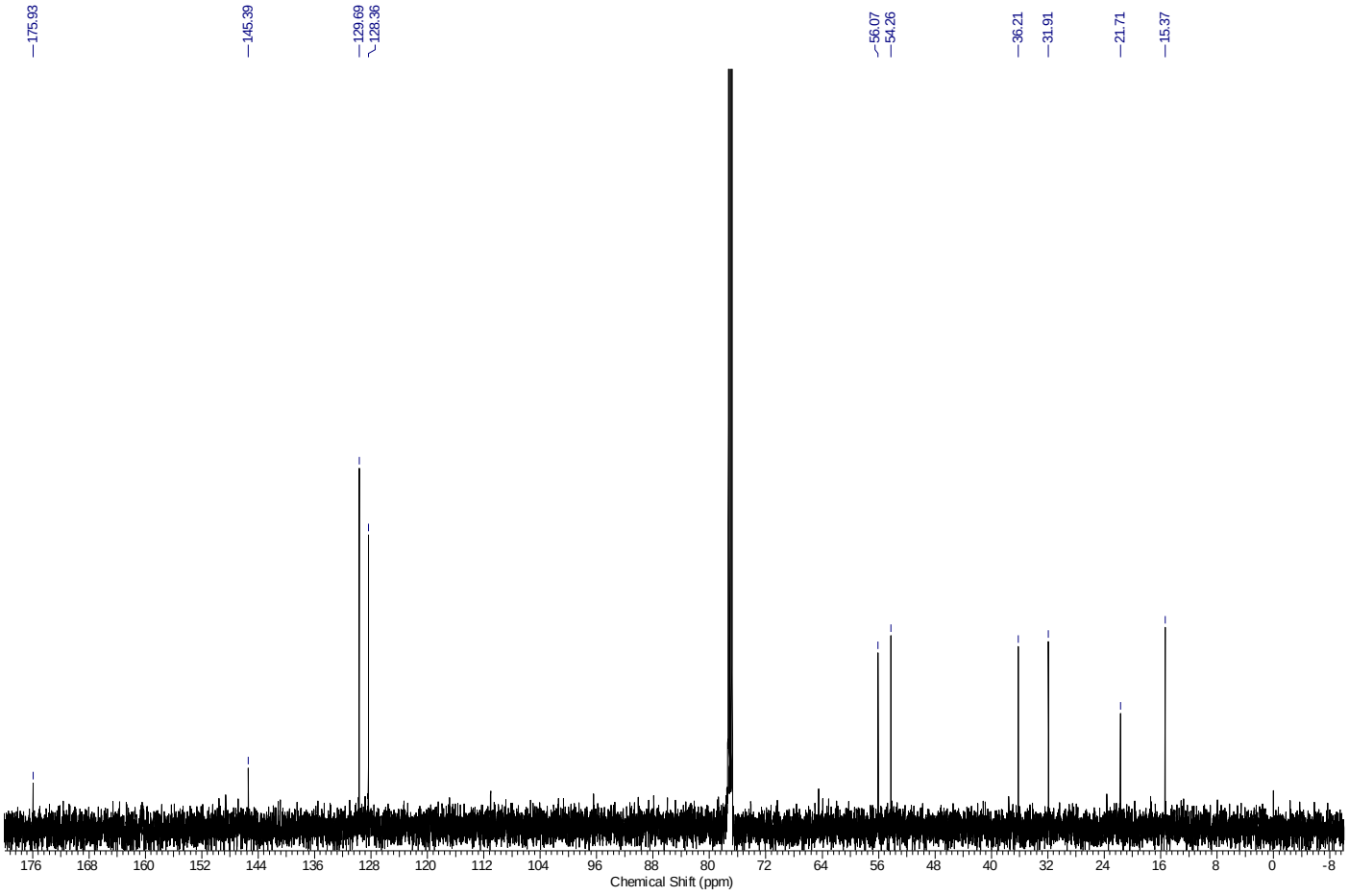
^{1}H NMR and ^{13}C NMR of *syn*-11a:



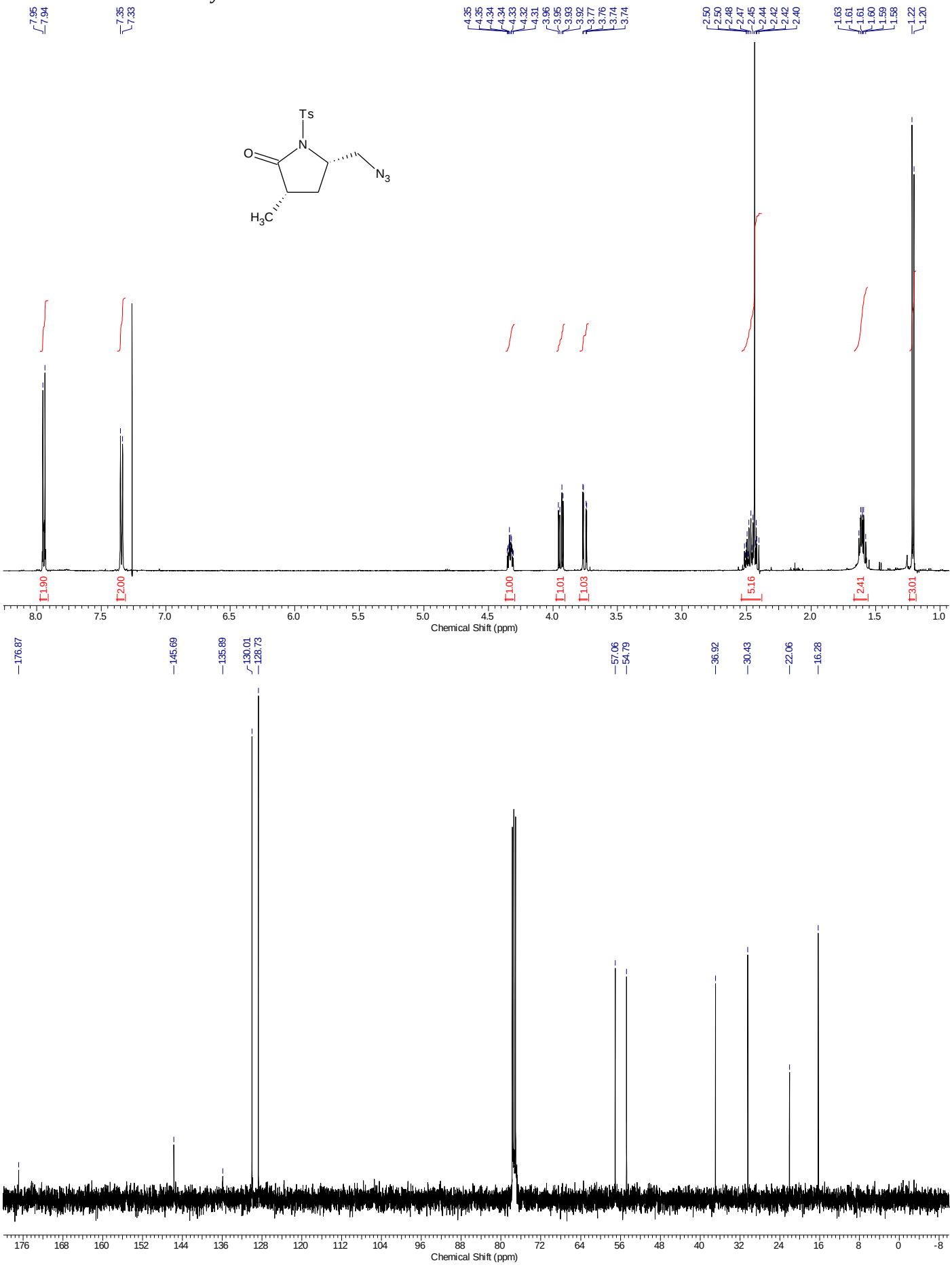


^{1}H NMR and ^{13}C NMR of *anti*-11c:

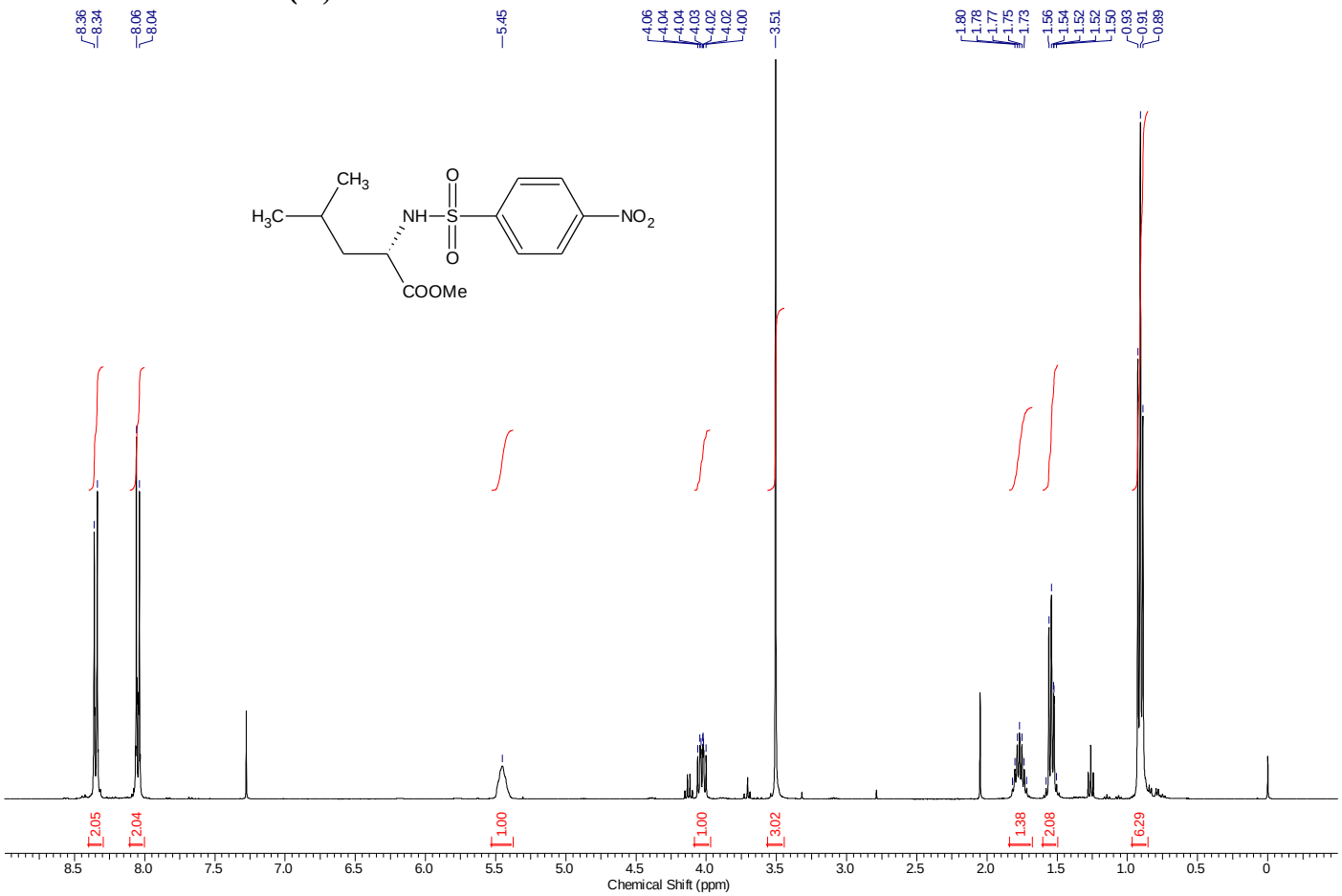


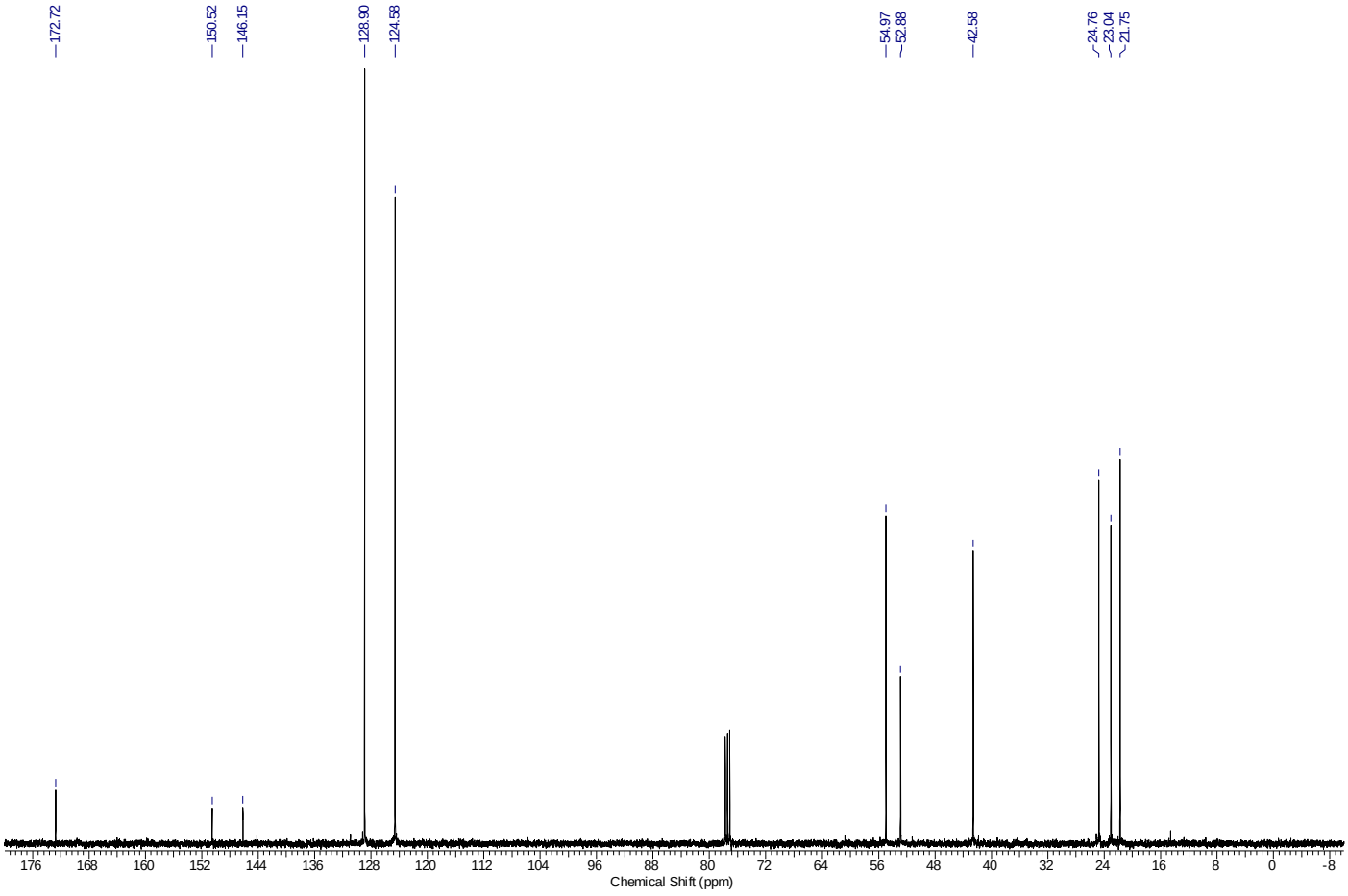


^{1}H NMR and ^{13}C NMR of *syn*-11c:

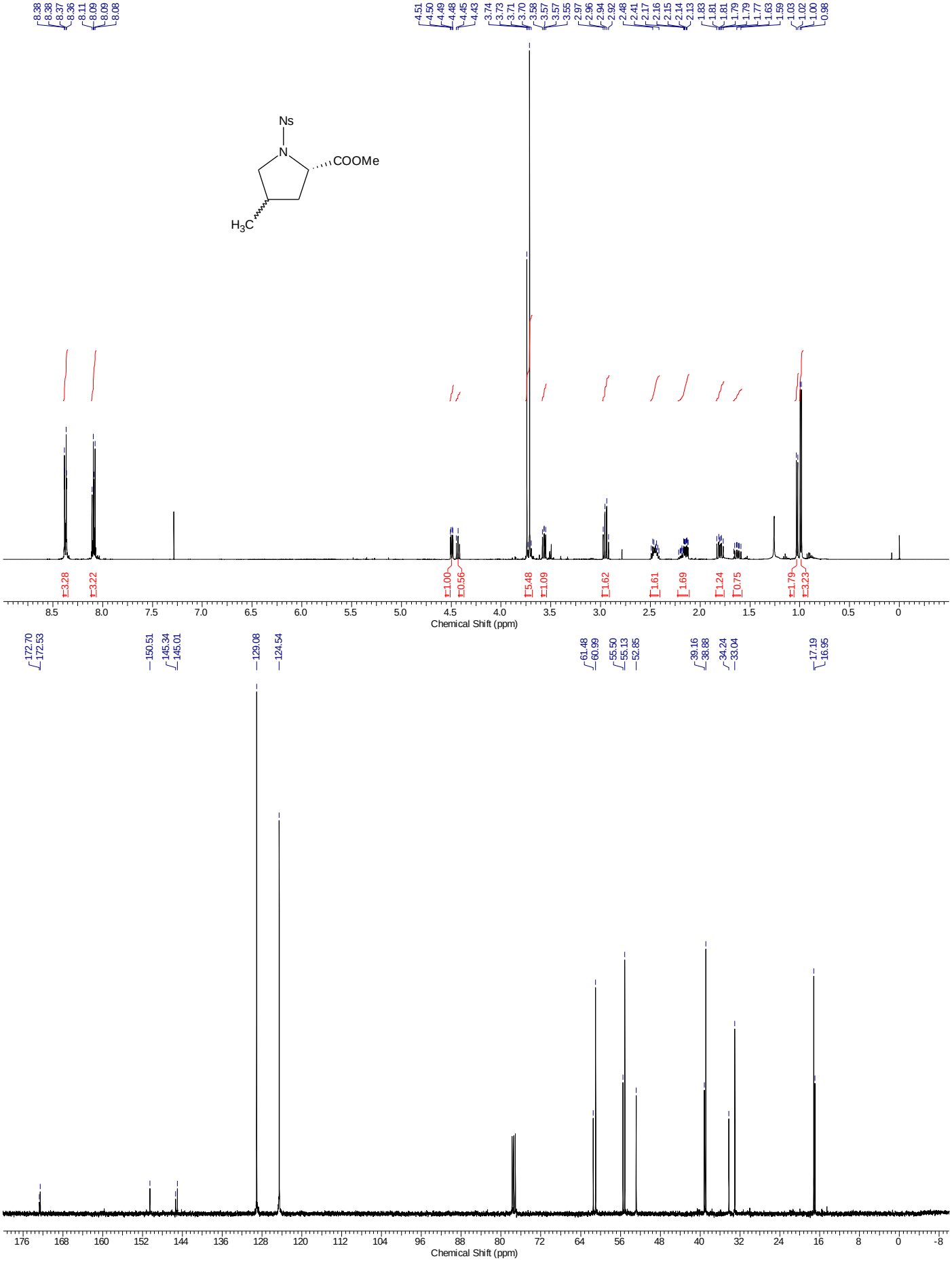


^{1}H NMR and ^{13}C NMR of (12):

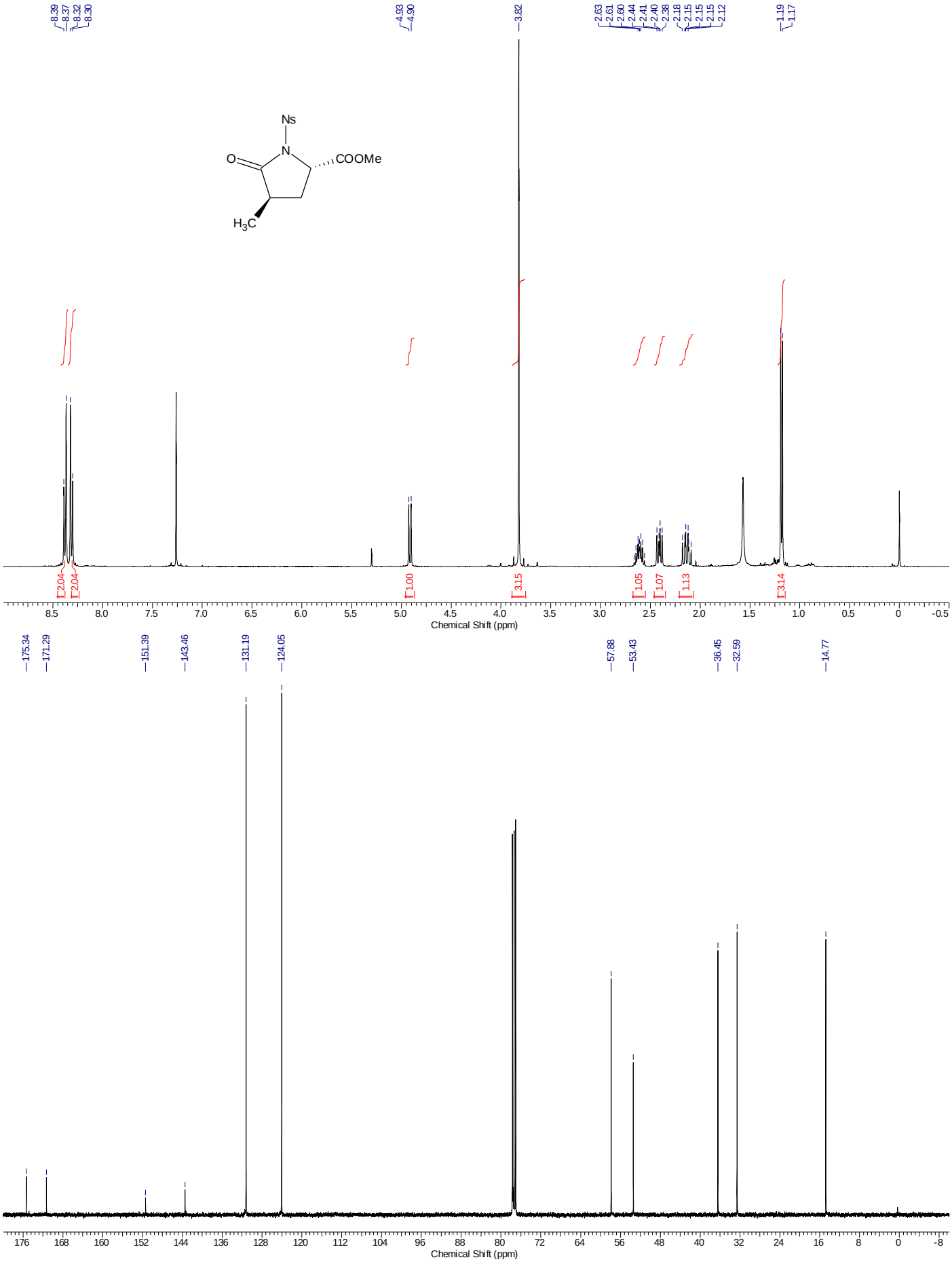




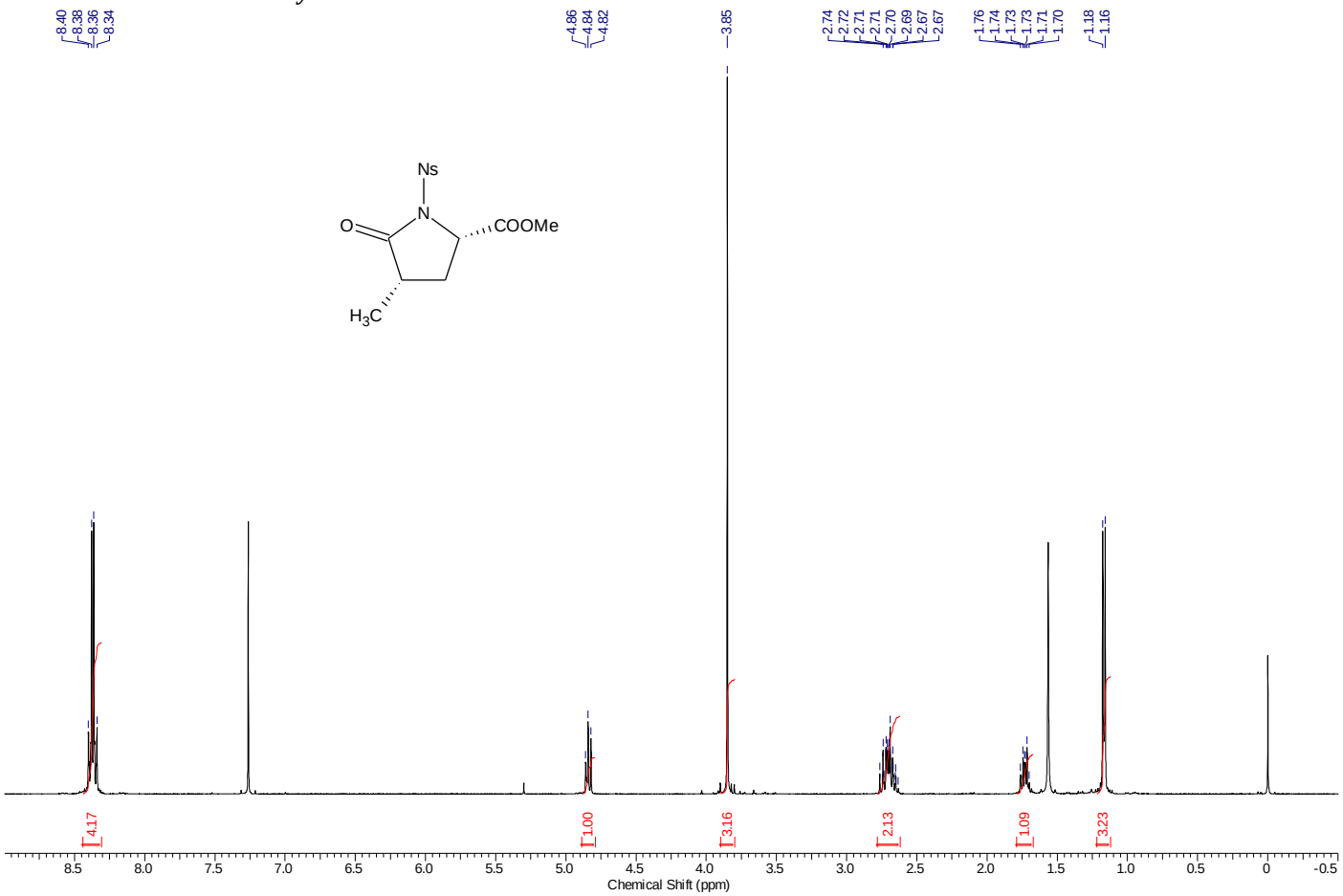
^{1}H NMR and ^{13}C NMR of 12a; (*anti*/*syn*, 1.8:1):

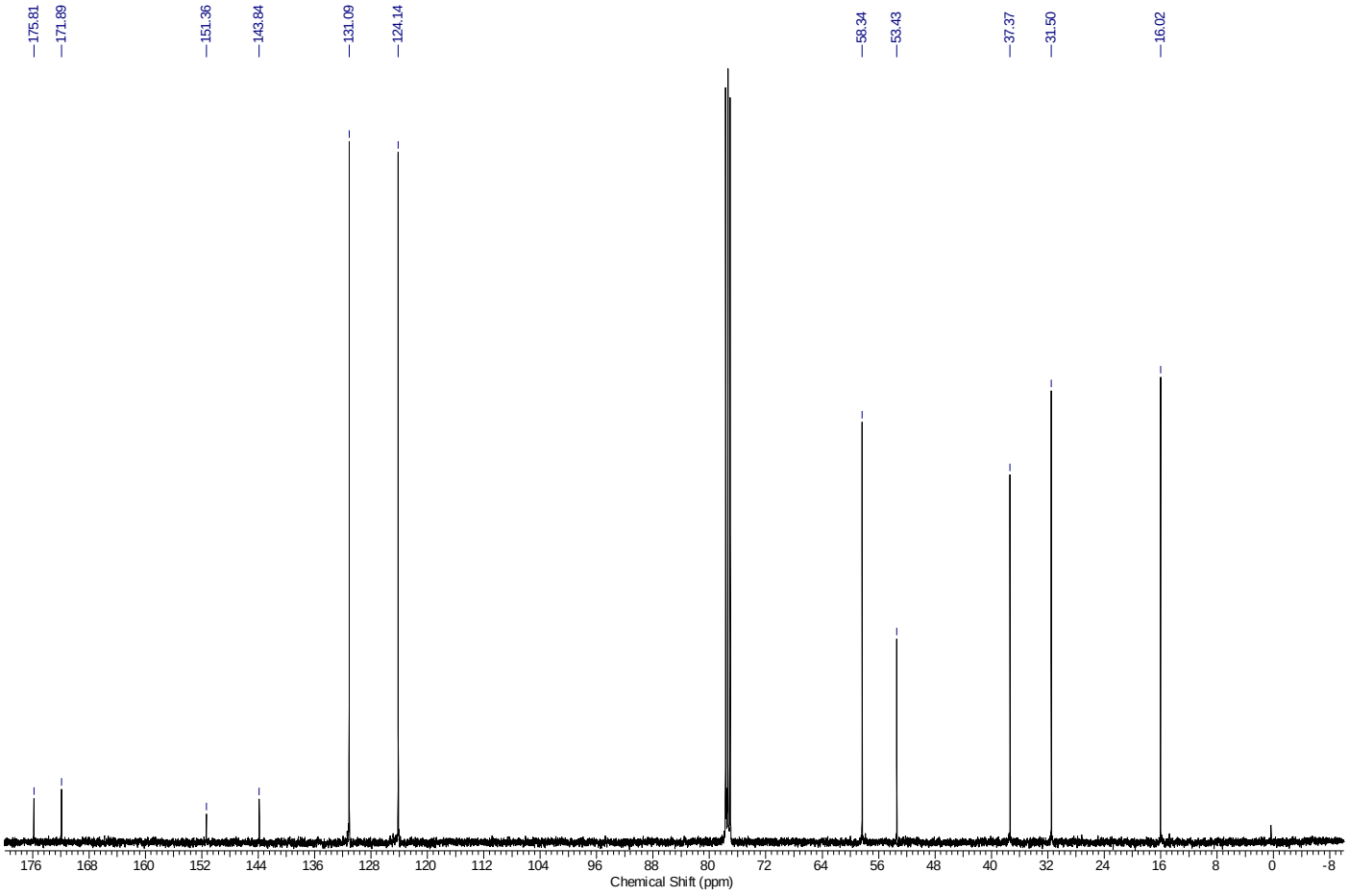


^{1}H NMR and ^{13}C NMR of *anti*-12c:

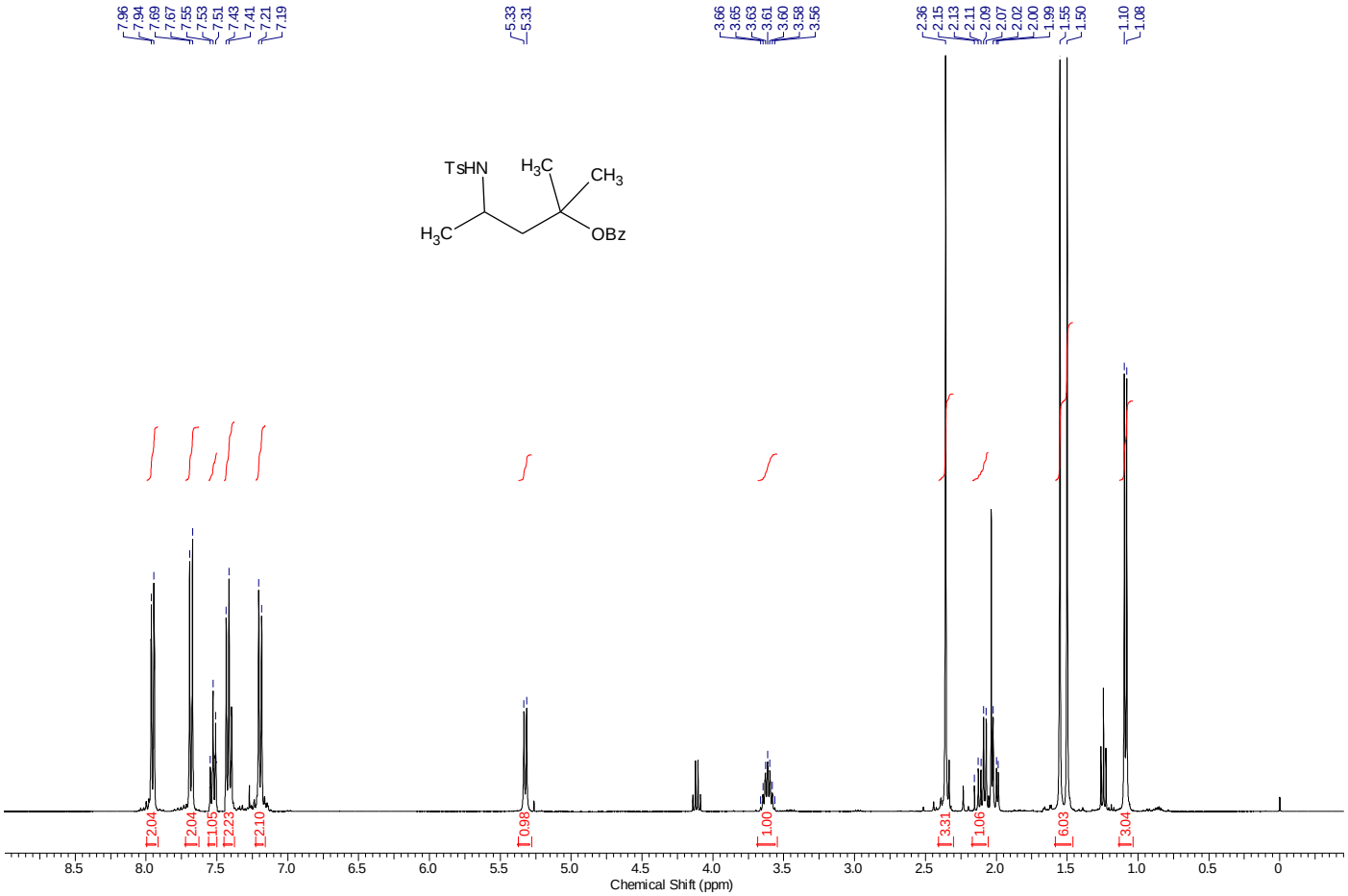


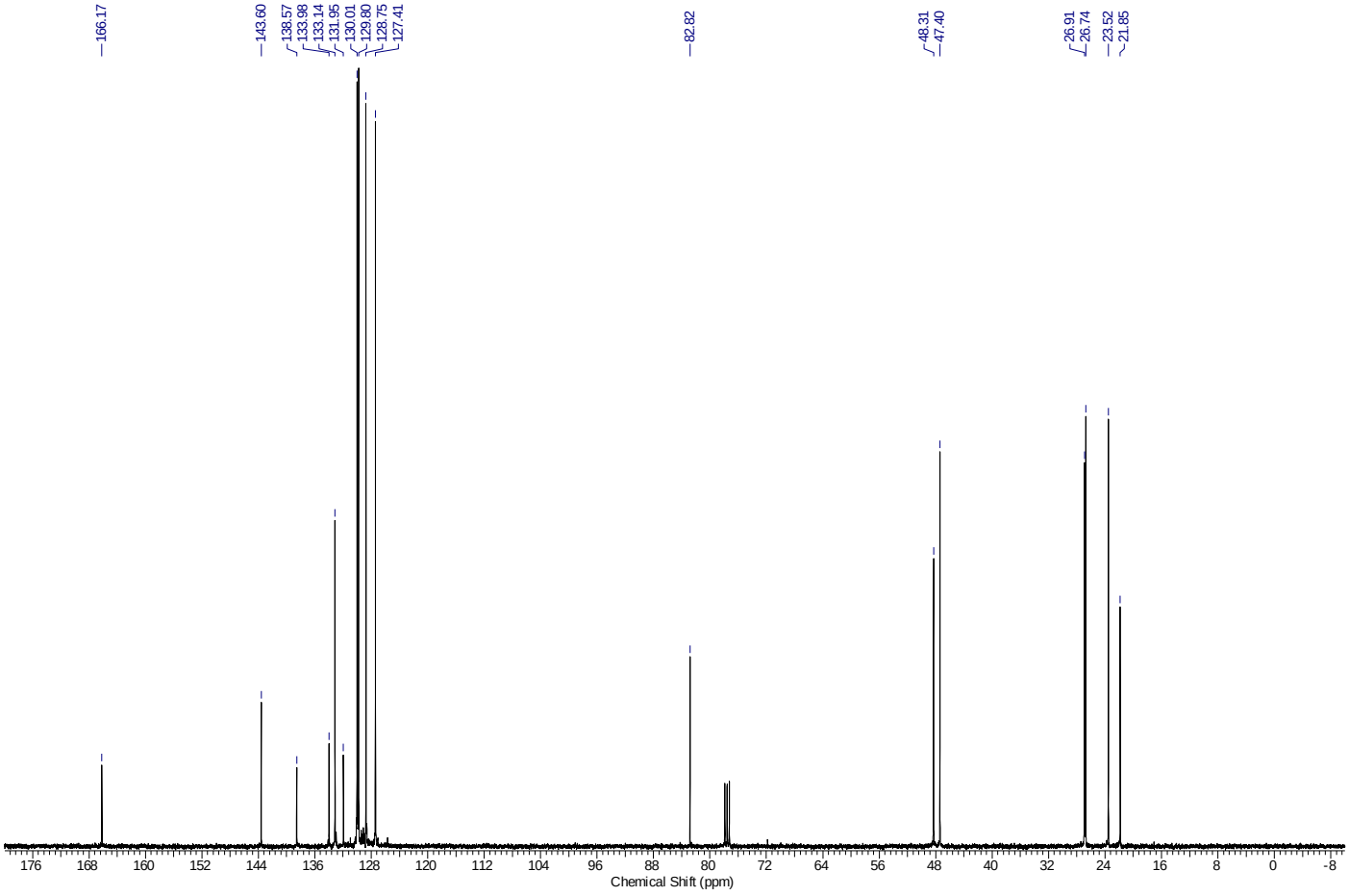
^{1}H NMR and ^{13}C NMR of *syn*-12c:



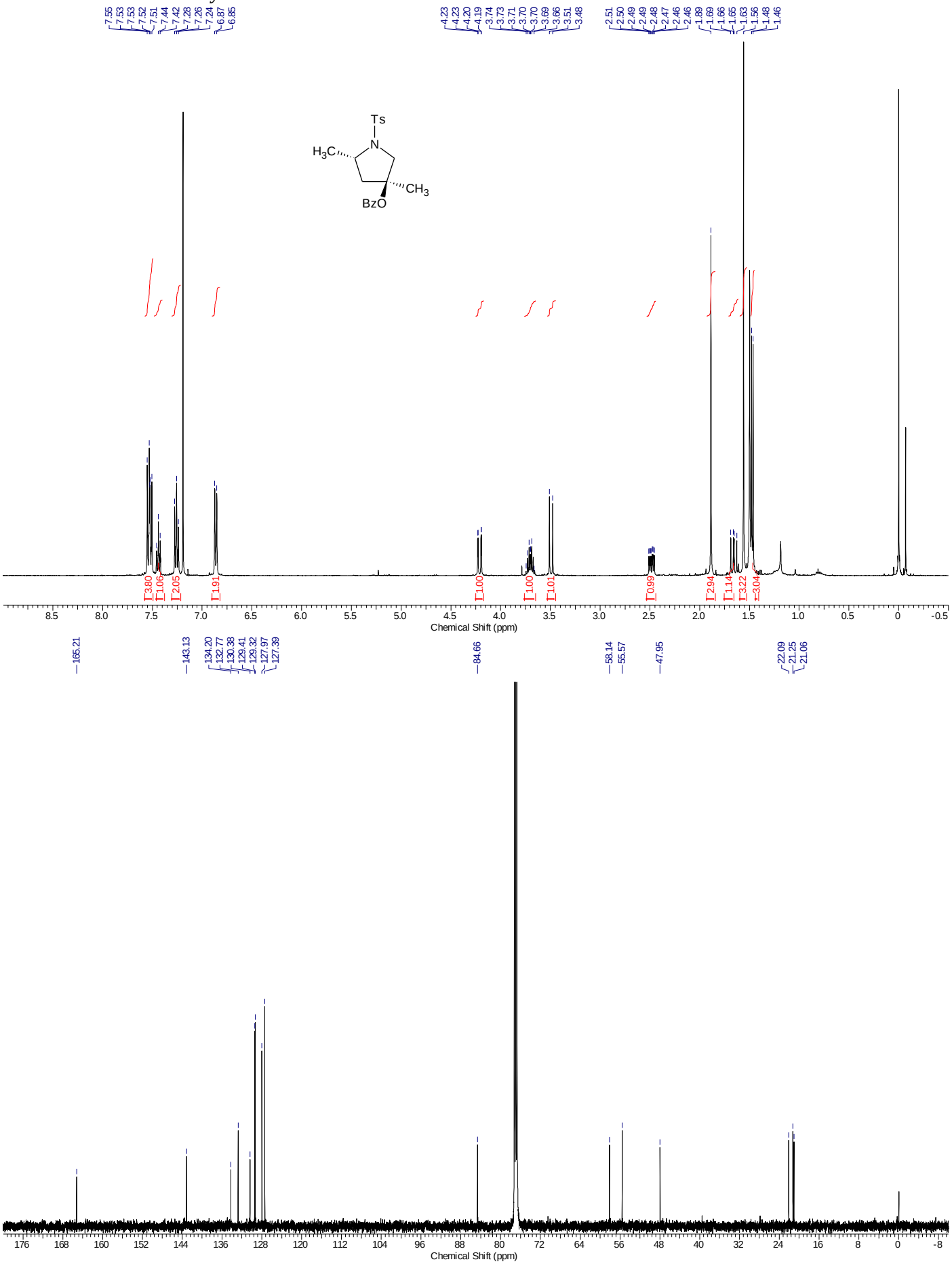


^{1}H NMR and ^{13}C NMR of 13:

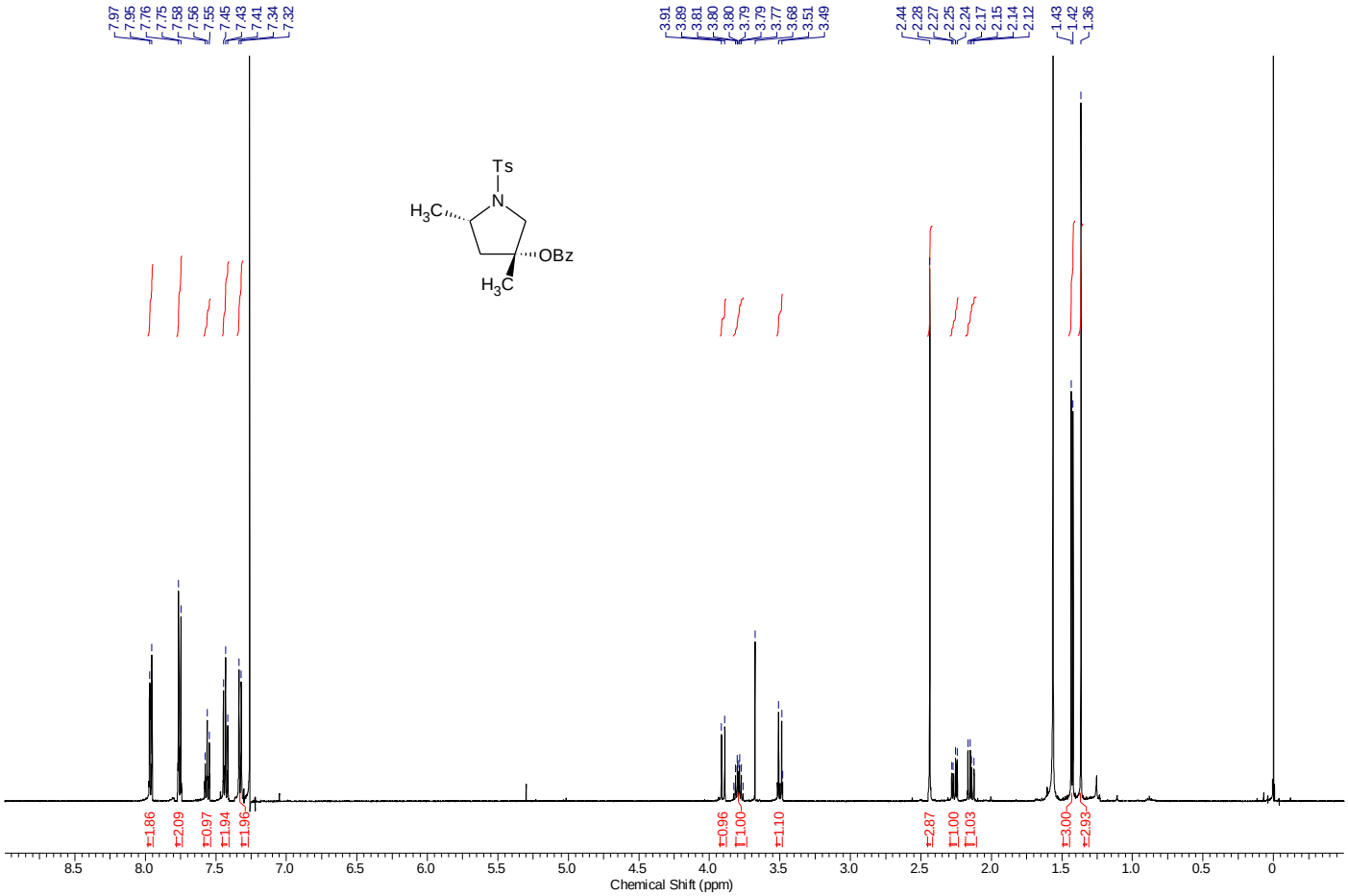


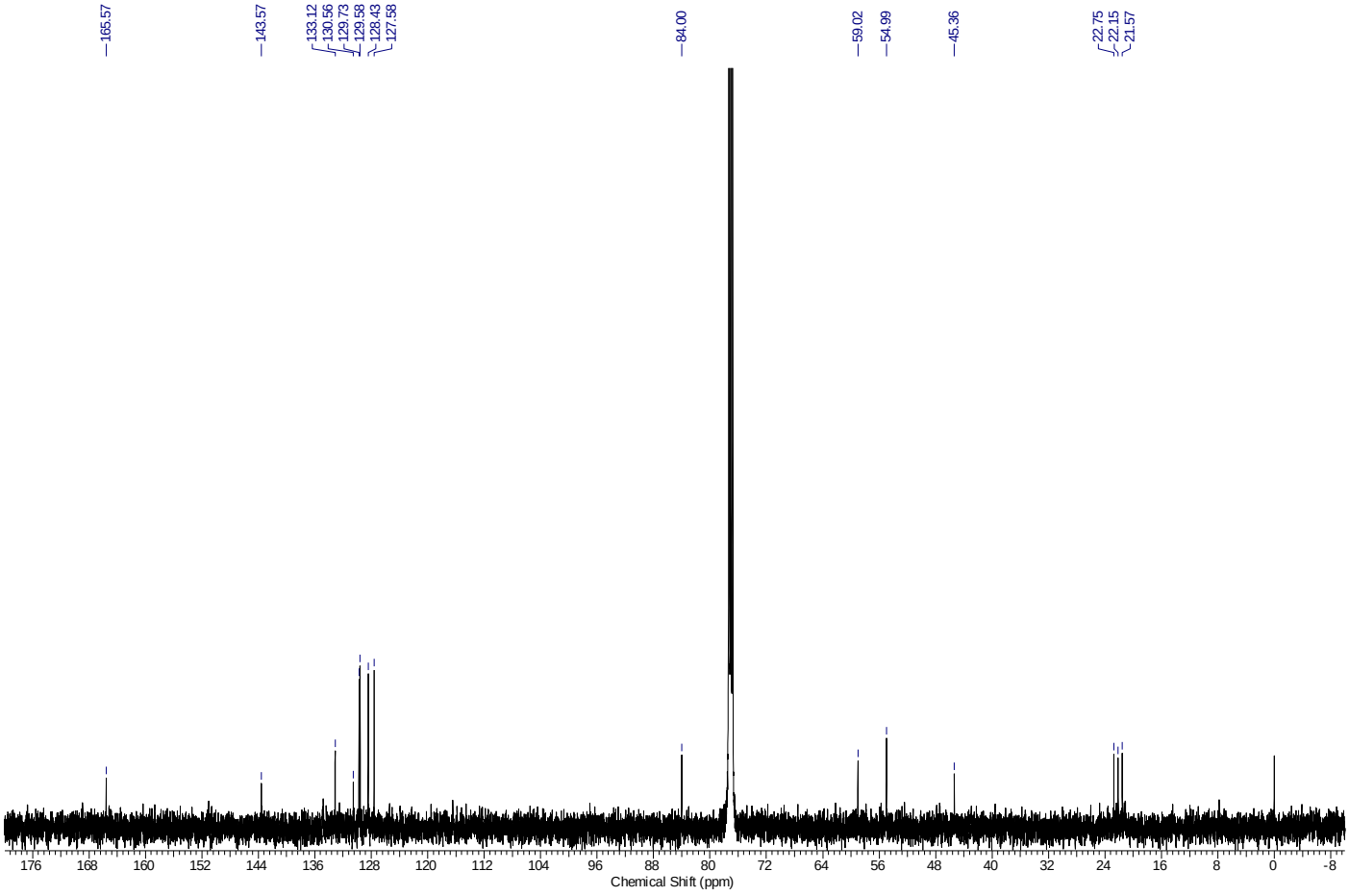


^{1}H NMR and ^{13}C NMR of *syn*-13a:

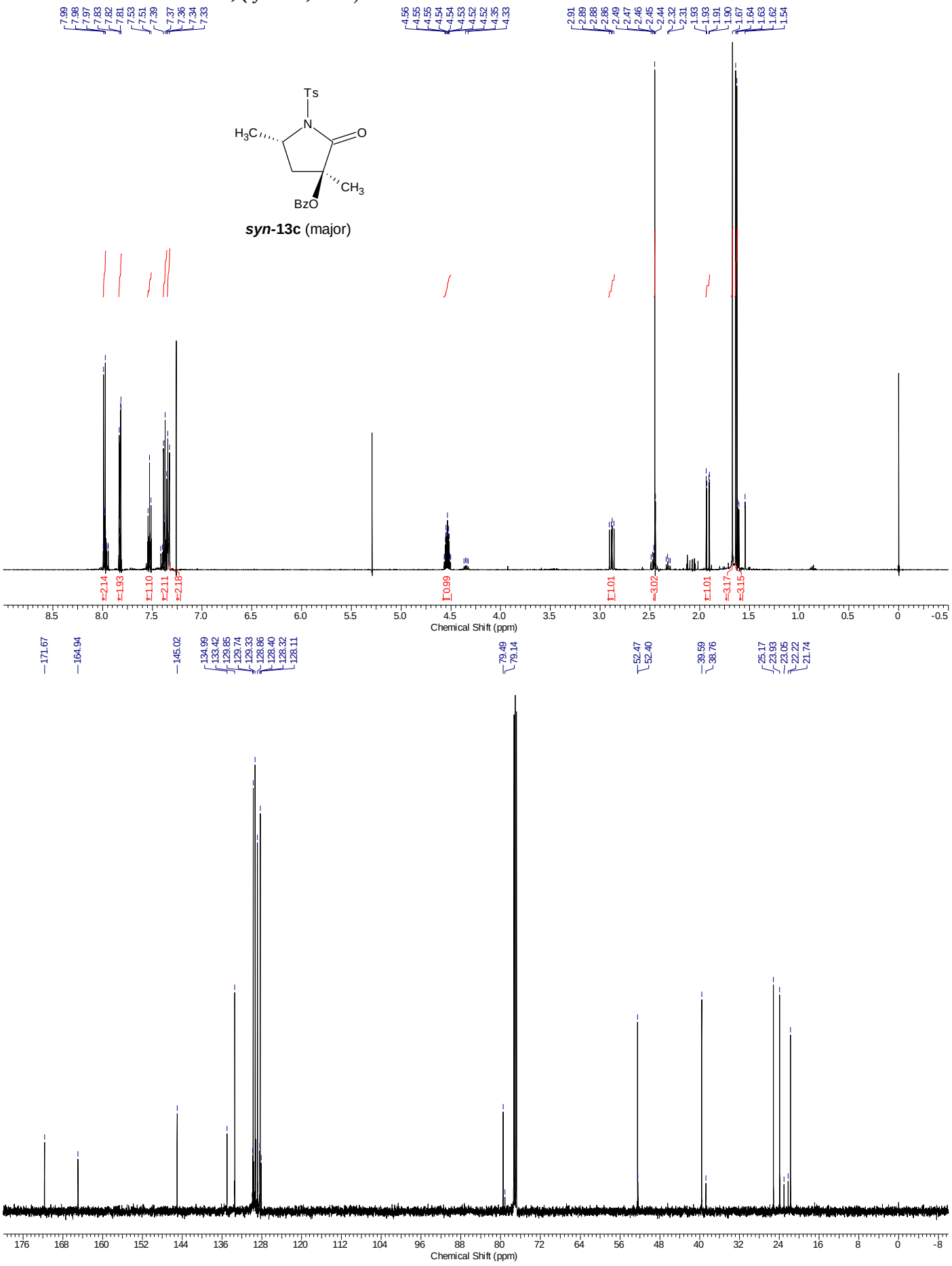


^{1}H NMR and ^{13}C NMR of *anti*-13a:



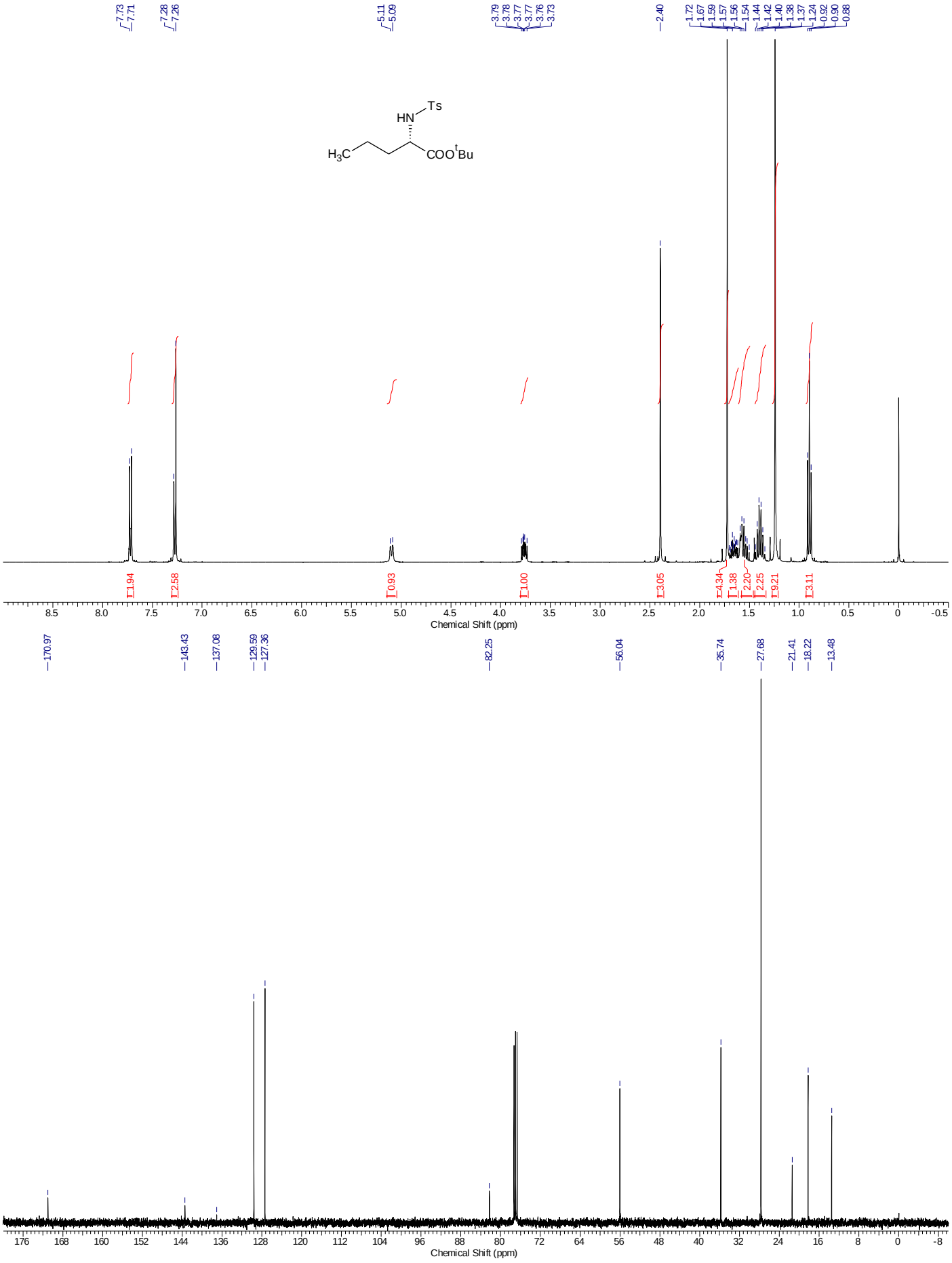


^{1}H NMR and ^{13}C NMR of 13c; (*syn/anti*, 7.5:1):

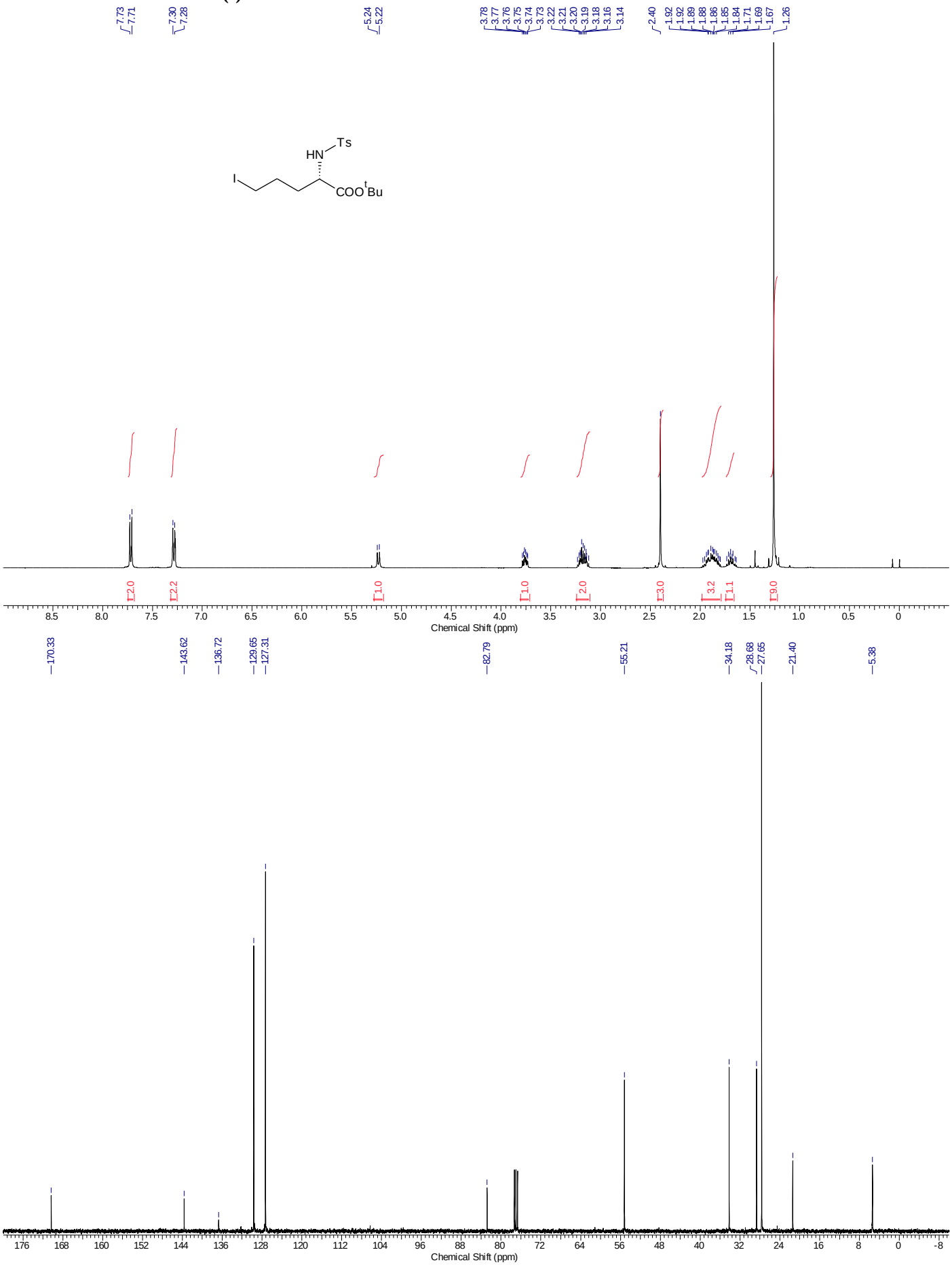


***syn*-13c** (major)

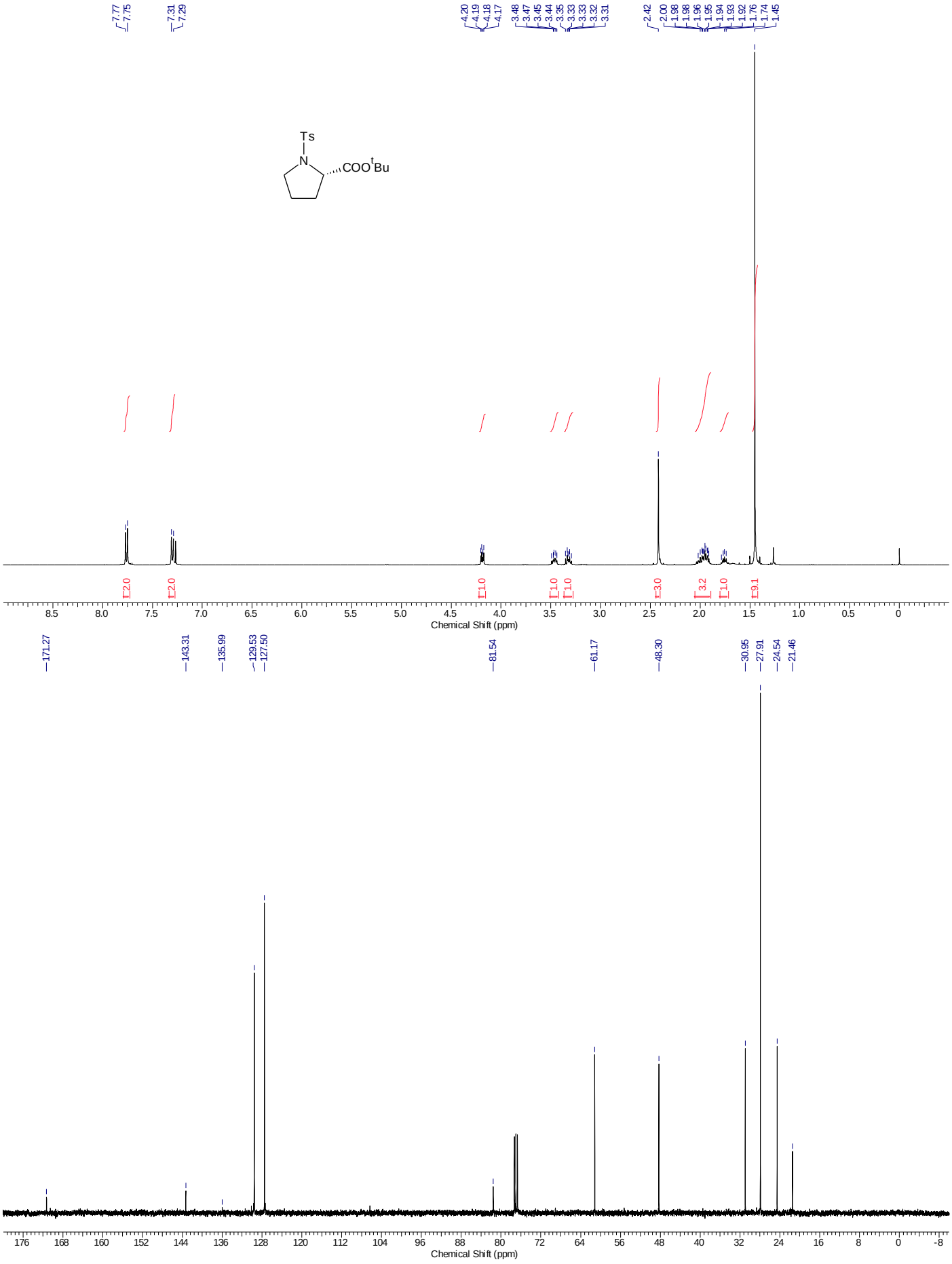
^{1}H NMR and ^{13}C NMR of 14:



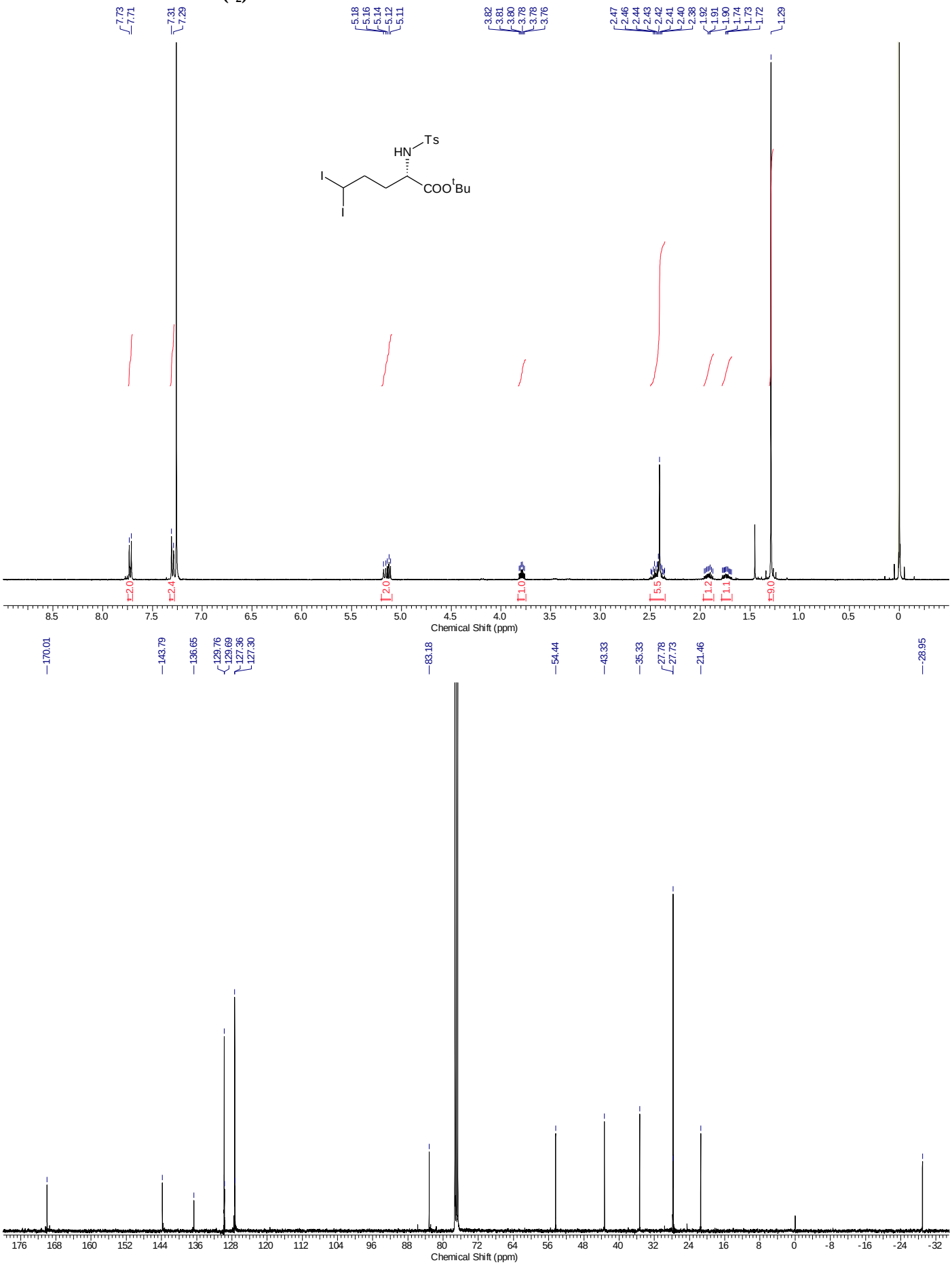
^{1}H NMR and ^{13}C NMR of 14(I):



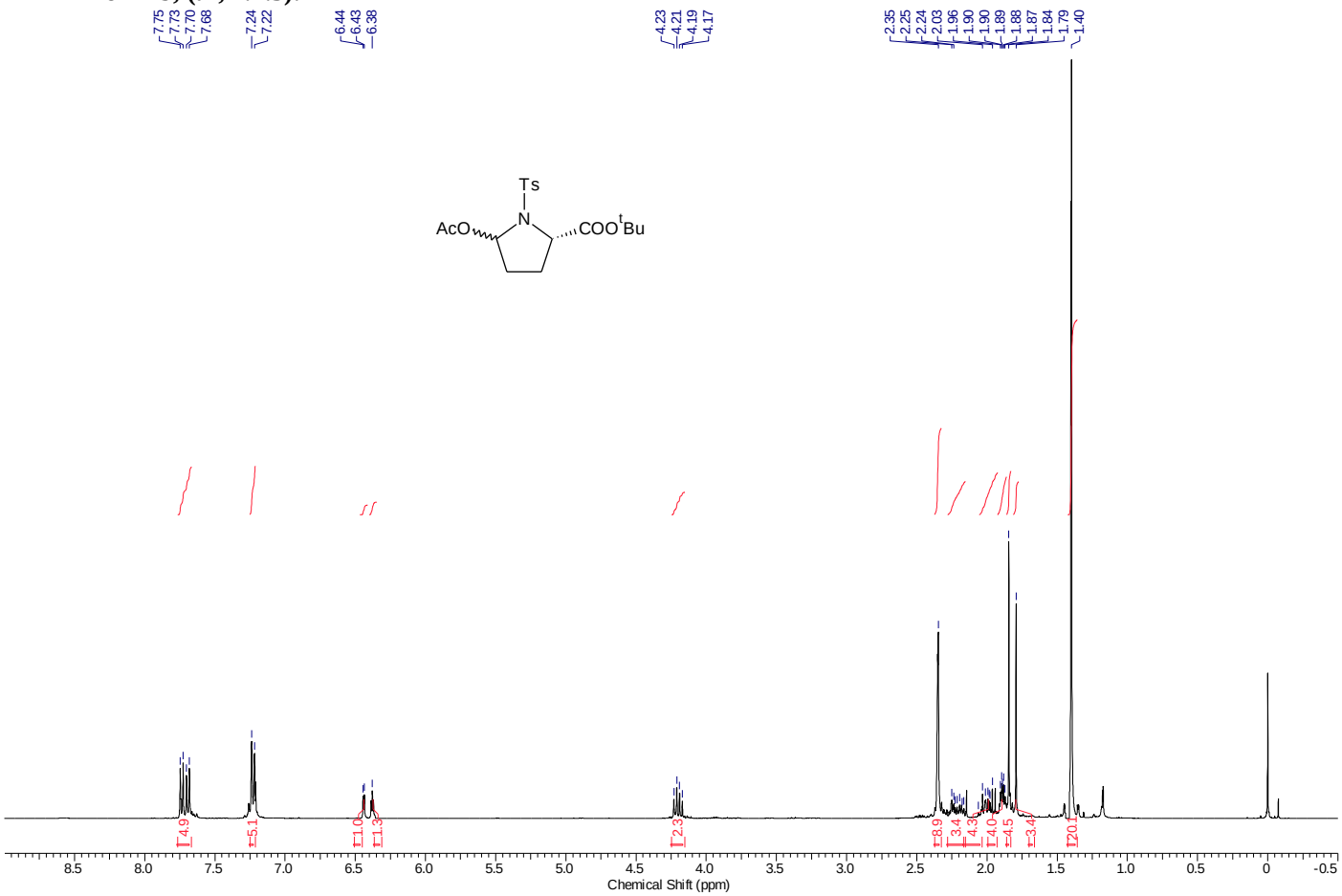
^{1}H NMR and ^{13}C NMR of 14a:



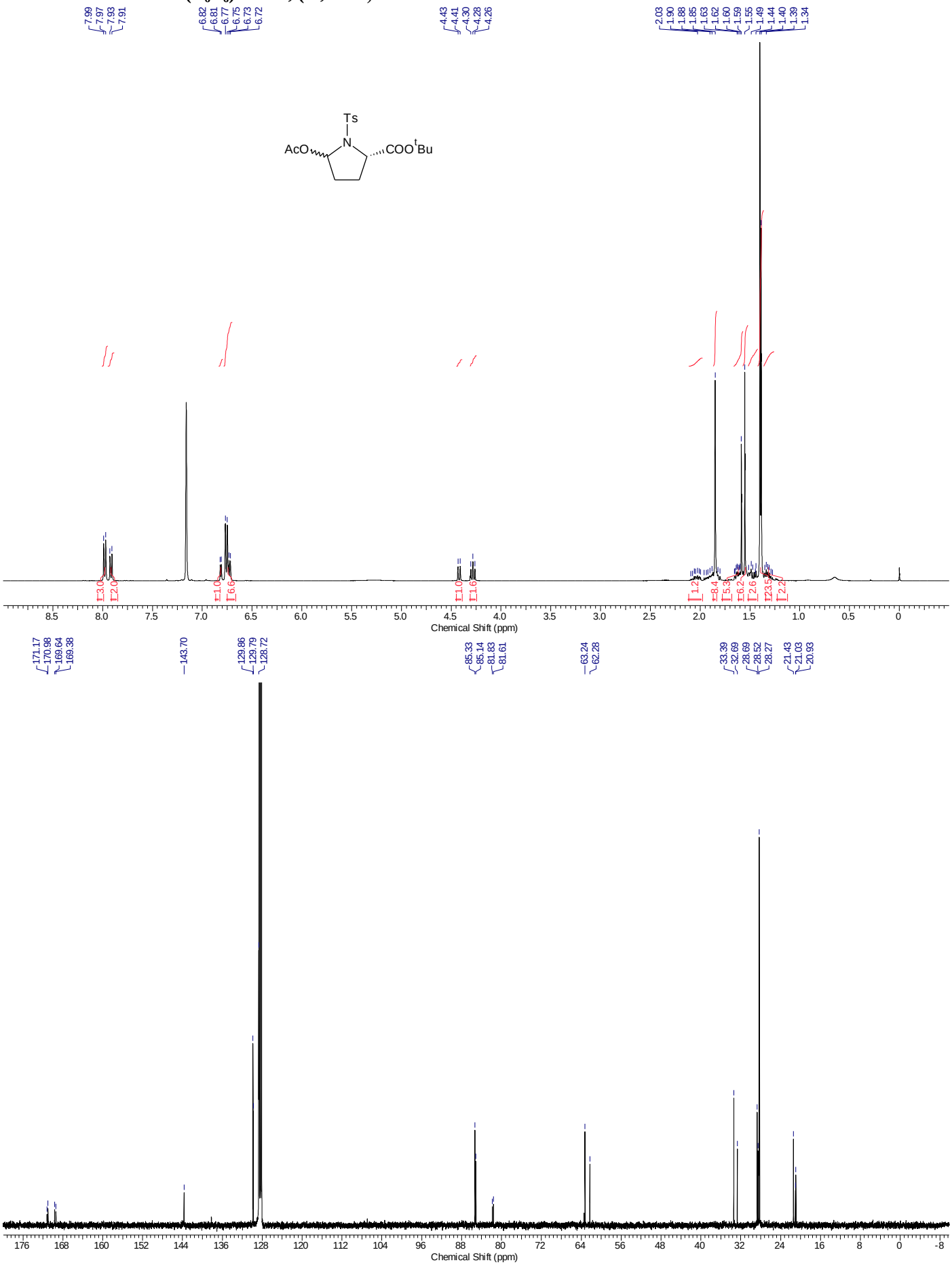
^{1}H NMR and ^{13}C NMR of 14(I_2):



^{1}H NMR of 14b; (*dr*, 1:1.3):



^{1}H NMR and ^{13}C NMR (C_6D_6) of 14b; (*dr*, 1:1.6):



^{1}H NMR and ^{13}C NMR of 14c: