A Telescoped Synthesis of Stereodefined Pyrrolidines

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Supporting information

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I) General Information

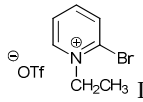
All reactions involving moisture sensitive reagents were performed under inert atmosphere (nitrogen or argon) *via* standard vacuum line techniques and with freshly dried solvents. All glassware was flame dried and allowed to cool under vacuum. Diethylether (Et_2O), tetrahydrofuran (THF), toluene (PhMe), hexane and dichloromethane (CH_2Cl_2) were obtained dry from a solvent purification system (MBraun, SPS-800). Petroleum ether is defined as 40–60 petrol. All solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Room temperature refers to 20–25 °C. Temperatures of 0 °C and −78 °C were achieved using ice/water and CO_2(s)/acetone baths respectively. Reduced pressure refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC_2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller. Analytic thin layer chromatography was performed on aluminium sheets coated with 60 F_{254} silica. TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining 1% aq. $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated. ^1H and ^{13}C NMR spectra were acquired on either a Bruker Avance 300 {δ_H (300 MHz), δ_C (75 MHz)}, a Bruker Avance II 400 {δ_H (400 MHz), δ_C (100 MHz)}, a Bruker Avance 500 {δ_H (500 MHz), δ_C (125 MHz)} or a Bruker Avance III 500 {δ_H (500 MHz), δ_C (125 MHz)} spectrometer at ambient temperature and in the deuterated solvent stated. Coupling constants (*J*) are reported in Hz. Data are expressed in chemical shifts in parts per million (ppm) relative to residual solvent as the internal standard. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sextet, sept (septet) and m (multiplet). Ar stands for aromatic, *app* for apparent and *br* for broad. Infrared spectra (ν_{max}) were recorded on a Shimadzu IRAffinity-1 fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50, characteristic peaks are reported. Melting points were recorded on an electrothermal apparatus and are uncorrected. HPLC analyses were obtained on two different machines: a Gilson HPLC consisting of a Gilson 305 pump, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118UV/Vis detector; secondly a Shimadzu HPLC consisting of a DGU-20A5 degasser, LX-20AT liquid chromatograph, SIL-20AHT autosampler, CMB-20A column oven with variable temperature setting (25–40 °C). Separation was achieved using Chiralcel OD-H and OJ-H columns or Chiralpak AD-H, AS-H, IA, IC, IB and ID columns. Mass spectrometric (*m/z*) data was acquired either at the University of St Andrews Mass

Spectrometry Facility or at the EPSRC National Mass Spectrometry Service Centre in Swansea. Low and high resolution MS (ES) and MS (CI) were carried out on a Micromass LCT spectrometer and on a Micromass GCT spectrometer, respectively. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell.

II) General experimental procedures and characterisation data:

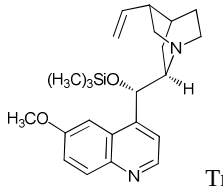
1) Synthesis of compound 29 and OTMS-quinidine

_N_-Ethyl-2-bromopyridinium triflate 29



In a flame dried resealable tube was added a solution of 2-bromopyridine (1.00 mL, 10.5 mmol, 1.0 eq) in DCM (2 mL) under Ar. The solution was cooled down to –78 °C and ethyl triflate (1.40 mL, 10.5 mmol, 1.0 eq) was slowly added as a white precipitate was formed. The cloudy mixture was stirred at rt for 5 h. The white precipitate was then washed with toluene (3×10 mL), and dried to afford **29** (3.45 g, 98%) as a white solid; **mp** 66-70 °C; $\boldsymbol{\nu_{max}}$ (KBr)/cm^{-1} 3052, 637, $\boldsymbol{\delta_H}$ ($CDCl_3$, 400 MHz) 1.68 (3H, t, *J* 7.31, CH_2CH_3), 4.95 (2H, q, *J* 7.31, CH_2CH_3), 8.15 (2H, m, C(5)*H*+C(3)*H*), 8.37 (1H, td, *J* 7.9, 1.6, C(4)*H*), 9.40 (1H, dd, *J* 6.2, 1.6, C(6)*H*); $\boldsymbol{\delta_c}$ ($CDCl_3$, 100 MHz) 15.8 (CH_2CH_3), 59.9 (CH_2CH_3), 118.9 (*C*), 128.6 *C*(5) , 134.8 *C*(3), 146.9 *C*(4), 149.2 *C*(6); $\boldsymbol{\delta_F}$ ($CDCl_3$, 282 MHz) 78.9 (CF_3); ***m/z*** (ES$^+$) 188 ([M(^{81}Br)+H]$^+$, 96%), 186 ([M(^{79}Br)+H]$^+$, 100%); HRMS (ES$^+$), $C_7H_9BrN^+$ ([M+H]$^+$) found 185.9913, requires 185.9910 (- 1.6 ppm).

(1*S*, 2*R*, 4*S*, 5*R*)-2-[(*S*)-(6-Methoxyquinolin-4-yl)((trimethylsilyl)oxy)methyl]-5-vinylquinuclidine (OTMS-Quinidine)



Trimethylsilyl chloride (0.37 mL, 3.67 mmol, 1.5 eq) was added to a solution of Quinidine (1.00 g, 3.08 mmol, 1.0 eq), in dry DCM (40 mL) and the reaction was stirred over night at rt. The reaction was quenched with sat. aq. $NaHCO_3$ (15 mL) and extracted with DCM (x3). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo.* Purification by chromatography column on silica gel (DCM : MeOH, 95 : 5) gave **OTMS-quinidine** as a viscous oil (918 mg, 75%); $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ + 181.9 (*c* 1.0 in $CHCl_3$); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1618 (C=C), 1505 (C=C), 1240 (Si-Me), 1007 (Si-OR); $\boldsymbol{\delta_H}$ ($CDCl_3$, 400MHz) 0.12 (9H, s, (Si(CH_3)$_3$), 1.04-1.14 (1H, broad m, CH_AH_B), 1.57-1.98 (3H, m, CH_AH_B+2xCH_2), 2.36-2.46 (1H, broad m, $CH_{quinuclidine}$), 2.48-2.57 (1H, broad m, $CHCH=CH_2$), 3.01-3.34 (4H, m, 2xCH_2), 3.84-3.89 (1H, m, $NCH_{quinuclidine}$), 4.07 (3H, s, OCH_3), 5.13-5.24 (2H, m, $CHCH=CH_2$), 5.98 (1H, ddd, *J* 17.3, 10.2, 7.2, $CHCH=CH_2$), 6.68-6.81 (1H, m, $Si(CH_3)_3OCH$), 7.34 (1H, d, *J* 9.2, Ar*H*), 7.43-7.48 (1H, m, Ar*H*), 7.55-7.65 (1H, m, Ar*H*), 7.94-8.00 (1H, d, *J* 9.2, Ar*H*), 8.69 (1H, d, *J* 4.5, Ar*H*); $\boldsymbol{\delta_c}$ ($CDCl_3$, 100MHz) 0.4 (Si(CH_3)$_3$), 18.2 (CH_2), 23.9 (CH_2), 27.7 ($CH_{quinuclidine}$), 37.8 ($CHCH=CH_2$), 48.0 (CH_2), 49.3 (OCH_3), 57.5 (CH_2), 60.3 ($NCH_{quinuclidine}$), 68.9 ($Si(CH_3)_3OCH$), 100.7 (*C*HAr5), 117.4 ($CHCH=CH_2$), 118.7 (*C*HAr), 123.0

(*C*HAr), 125.8 (*C*Ar4a), 131.8 (*C*HAr), 137.0 (CH*C*H=CH_2), 144.5 (*C*Ar8a), 146.8 (*C*ArCHO), 147.0 (*C*HAr2), 159.1 (*C*ArOCH$_3$); ***m/z*** (ES^+) 397 ($[M+H]^+$, 100 %); HRMS (ES^+) $C_{23}H_{33}N_2O_2Si^+$ ($[M+H]^+$) found 397.2308, requires 397.2306 (+ 0.6 ppm).

2) Synthesis of alkene-acids 4, 5, 10

General procedure 1: *Tosyl protection*

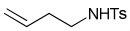
NEt_3 (2.2 eq) was added to a solution of the requisite amine (1.0 eq) in dry DCM (10 mL) and stirred for 10 min at rt. Toluenesulfonyl chloride (1.0 eq) was then slowly added to the solution under Ar at 0 °C. The reaction mixture was stirred at rt and monitored by TLC until completion then quenched with aq. citric acid (10%) and extracted with DCM (x3). The combined organic phases were washed with sat. aq. $NaHCO_3$ (x2), brine (x2) and concentrated *in vacuo* to give the corresponding tosyl amine.

General procedure 2: *Ester hydrolysis*

To a solution of the requisite ester (1.0 eq) in a mixture of H_2O/THF (1 : 3) was added LiOH (3.0 eq) in one portion at rt. The reaction was monitored by TLC until completion then quenched with 2M. aq. HCl (~pH 1) and extracted with Et_2O (x3). The organic phases were washed with brine (x2), dried ($MgSO_4$) and concentrated *in vacuo*, to give the corresponding carboxylic acids.

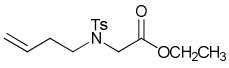
i. α-Amino series

***N*-(But-3-en-1-yl)-4-methylbenzenesulfonamide S1**



Following a modified literature procedure,[2] 4-bromobut-1-ene (10.0 mL, 98.5 mmol, 1.1 eq) and K_2CO_3 (24.7 g, 179 mmol, 2.0 eq) were added to a solution of tosylamine (15.3 g, 89.5 mmol, 1.0 eq) in acetone (90 mL). The reaction was stirred over night at 60 °C. The reaction was quenched with sat. aq. NH_4Cl, extracted with Et_2O (x3), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography column on silica gel (Pet.Ether : EtOAc; 90 : 10 to 80 : 20) gave **S1** (12 g, 60 %) as a clear oil; δ_H ($CDCl_3$, 300MHz) 2.22 (2H, br q, *J* 6.7, CH_2=CHCH_2), 2.45 (3H, s, CH_3), 3.04 (2H, q, *J* 6.4, CH_2NHTs), 4.39 (1H, br t, *J* 5.7, N*H*Ts), 5.03-5.12 (2H, m, CH_2=CHCH_2), 5.66 (1H, ddt, *J* 17.1, 10.3, 6.7, CH_2=C*H*CH_2), 7.33 (2H, d, *J* 8.1, $Ar_{Ts}H3$-5), 7.75 (2H, d, *J* 8.1, $Ar_{Ts}H2$-6). Data is in accordance with the literature.[3]

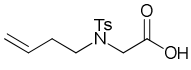
Ethyl 2-*N*-[(but-3-en-1-yl)-4-methylphenylsulfonamido]acetate S2



To a suspension of NaH (1.06 g, 26.6 mmol, 1.2 eq) in dry DMF (40 mL) was added **S1** portion-wise at 0 °C. After 10 min, bromoethylacetate (3.0 mL, 26.6 mmol, 1.2 eq) was added and the reaction was stirred for 2 h at rt. After completion, the reaction mixture was quenched with a mixture NH_4Cl/NH_4OH (2:1) and extracted with Et_2O (x3). The organic phases were washed with H_2O (x2), brine (x2), dried ($MgSO_4$) and concentrated *in vacuo*, to afford **S2** as a clear oil (5.6 g, 82%); δ_H ($CDCl_3$, 300MHz) 1.23 (3H, t, *J* 7.2, CH_2CH_3), 2.33 (2H, q, *J* 6.4, CH_2=CHCH_2), 2.44 (3H,

s, $Ar_{Ts}CH_3$), 3.34 (2H, t, *J* 6.4, CH_2NTs), 4.08 (2H, s, $CH_2CO_2CH_2CH_3$), 4.10 (2H, q, *J* 7.2, CH_2CH_3), 5.03-5.12 (2H, m, CH_2=$CHCH_2$), 5.72 (1H, ddt, *J* 17.2, 10.2, 6.6, CH_2=$CHCH_2$), 7.32 (2H, d, *J* 8.3, $Ar_{Ts}H3$-5), 7.68 (2H, d, *J* 8.3, $Ar_{Ts}H2$-6). Data is in accordance with the literature.[4]

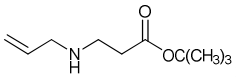
2-*N*-[(But-3-en-1-yl)-4-methylphenylsulfonamido]acetic acid 10



*Following general procedure **2***: ester **S2** (2.0 g, 6.42 mmol), H_2O/THF (1:3; 100 mL), LiOH (0.80 g, 41.9 mmol) gave **10** as a white solid in quantitative yield (1.8 g); **mp** 98 °C {lit[4] 97-99 °C}; $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 1.88 (2H, br q, *J* 7.3, CH_2=$CHCH_2$), 2.33 (3H, s, $Ar_{Ts}CH_3$), 3.34 (2H, t, *J* 6.4, CH_2NTs), 4.08 (2H, s, CH_2CO_2H), 5.05-5.12 (2H, m, CH_2=$CHCH_2$), 5.71 (1H, ddt, *J* 17.0, 10.4, 6.8, CH_2=$CHCH_2$), 7.32 (2H, d, *J* 8.2, $Ar_{Ts}H3$-5), 7.74 (2H, d, *J* 8.2, $Ar_{Ts}H2$-6). Data is in accordance with the literature.[4]

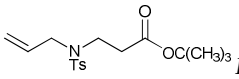
ii. β-Amino series

***tert*-Butyl-3-(allylamino)propanoate S3**



tert-Butyl acrylate (5.00 mL, 34.1 mmol, 1.0 eq) was added to a solution of allylamine (3.80 mL, 51.2 mmol, 1.5 eq) in MeOH (100 mL). The reaction mixture was stirred at 40 °C overnight and then concentrated *in vacuo*. Purification of the residue by chromatography column on silica gel (cyclohexane : Et_2O, 100 : 0 to 90 : 10) gave **S3** as a yellow oil (5.3 g, 83%); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.45 (9H, s, $C(CH_3)_3$), 2.44 (2H, t, *J* 6.4, $CH_2CO_2C(CH_3)_3$), 2.84 (2H, t, *J* 6.4, CH_2NH), 3.26 (2H, d, *J* 6.0 CH_2=$CHCH_2$), 5.09 (1H, dd, *J* 10.2, 1.1, CH_AH_B=$CHCH_2$), 5.18 (1H, d, *J* 17.0, 1.6, CH_AH_B=$CHCH_2$), 5.90 (1H, ddt, *J* 17.0, 10.2, 6.0, CH_2=$CHCH_2$). Data is in accordance with the literature.[5]

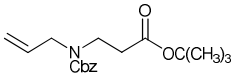
***tert*-Butyl-3-(*N*-allyl-4methylphenylsulfonamido)propanoate S4**



*Following general procedure **1***: Allylamine **S3** (1.00 g, 5.39 mmol), NEt_3 (1.66 mL, 11.9 mmol) in dry DCM (100 mL), toluenesulfonyl chloride (1.10 g, 5.90 mmol) under Ar for 2 h. Purification by chromatography column on silica gel (Pet.ether : EtOAc; 90 : 10) gave **S4** (1.6 g, 87%) as a clear oil; $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 2979 (C-H), 1731 (C=O), 1644 (C=C), 1367, (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 1.45 (9H, s, $C(CH_3)_3$), 2.45 (3H, s, $Ar_{Ts}CH_3$), 2.56 (2H, t, *J* 7.6, $CH_2CO_2C(CH_3)_3$), 3.38 (2H, t, *J* 7.6, CH_2NTs), 3.82 (2H, d, *J* 6.3, CH_2=$CHCH_2$), 5.15-5.25 (2H, m, CH_2=$CHCH_2$), 5.59-5.73 (1H, m, CH_2=$CHCH_2$), 7.30 (2H, d, *J* 8.0, $Ar_{Ts}H3$-5), 7.73 (2H, d, *J* 8.0, $Ar_{Ts}H2$-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 75MHz) 21.9 (CH_3), 28.5 ($C(CH_3)_3$), 35.7 ($CH_2CO_2C(CH_3)_3$), 43.7 (CH_2NTs), 51.8 (CH_2=$CHCH_2$), 81.4 $C(CH_3)_3$), 119.5 (CH_2=$CHCH_2$), 127.6 ($CHAr_{Ts}$2-6), 130.1 ($CHAr_{Ts}$3-5), 133.4 (CH_2=$CHCH_2$), 137.1 ($CAr_{Ts}SO_2$), 143.7 ($CAr_{Ts}CH_3$), 171.1 ($CO_2C(CH_3)_3$); ***m/z*** (ES^+) 696 ($[2M+NH_4]^+$, 100%), 284 ([(M-

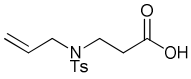
O^{t}Bu)+NH_4]$^+$, 95%), 340 ([M+H]$^+$, 65%); HRMS (ES^+) $C_{17}H_{26}SNO_4^+$ ([M+H]$^+$) found 340.1579, requires 340.1577 (+ 0.6 ppm).

***tert*-Butyl 3-(*N*-allyl-2-phenylacetamido)propanoate S5**



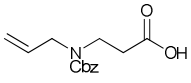
To a solution of allylamine **S3** (7.10 g, 38.3 mmol), and NEt_3 (11.4 mL, 84.3 mol) in dry DCM (100 mL) was added benzyl chloroformate (5.44 mL, 38.3 mmol) under Ar at rt. The reaction was stirred overnight at rt and then quenched with 0.1M aq. HCl and extracted with DCM (x3). The combined organic phases were washed with sat. aq. $NaHCO_3$ (x2), brine (x2) and concentrated *in vacuo*. Purification by chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20) gave **S5** (6.2 g, 50%) as a clear oil; $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 2979 (C-H), 1702 broad (C=O), $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) mixture of rotamers 1.45 (9H, s, C(CH_3)$_3$), 2.52 (2H, app dt, *J* 27.3, 7.3, CH_2CO$_2$C(CH$_3$)$_3$), 3.42-3.55 (2H, m, CH_2NCbz), 3.80-4.05 (2H, m, CH$_2$=CHCH_2), 4.87-5.28 (4H, m, NCO$_2$CH_2Ar +CH_2=CHCH$_2$), 5.77-5.81 (1H, m, CH$_2$=CHCH$_2$), 7.29-7.57 (5H, m, ArH); $\boldsymbol{\delta_C}$ ($CDCl_3$, 125MHz) mixture of rotamers 28.1 (C(*C*H$_3$)$_3$), 34.5, 35.1 (*C*H$_2$CO$_2$C(CH_3)$_3$), 42.6, 43.6 (*C*H$_2$NCbz), 50.1, 50.3 (CH$_2$=CH*C*H$_2$), 67.1 (NCO$_2$*C*H$_2$Ar), 80.7 ((*C*CH$_3$)$_3$), 116.6, 117.2 (*C*H$_2$=CHCH$_2$), 127.7 (3x*C*HAr), 127.9 (*C*HAr), 128.5 (*C*HAr), 133.5, 133.7 (CH$_2$=*C*HCH$_2$), 136.7 (*C*Ar), 155.9 (N*C*O$_2$CH$_2$Ar) 170.9, 171.1 (*C*O$_2$C(CH$_3$)$_3$); ***m/z*** (NSI$^+$) 320 ([M+H]$^+$, 100%); HRMS (ES^+) $C_{18}H_{26}NO_4^+$ ([M+H]$^+$) found 320.1859, requires 320.1856 (+ 0.8 ppm).

3-(*N*-Allyl-4-methylphenylsulfonamido)propanoic acid 4



Ester **S4** (5.00 g, 14.8 mmol, 1.0 eq) was stirred in DCM : TFA (1 : 1, 30 mL) at rt for 2 h. The reaction mixture was quenched with sat. aq. NH_4Cl (50 mL) and extracted with DCM (x3). The organic phases were washed with sat. aq. $NaHCO_3$ (x2), dried ($MgSO_4$) and concentrated *in vacuo* to afford **4** (4.7 g, 62 %) as a beige solid; **mp** 58 °C; $\boldsymbol{\nu_{max}}$ (KBr)/cm^{-1} 3100-2900 (O-H), 1703 (C=O), 1163 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 2.44 (3H, s, Ar$_{Ts}$CH_3), 2.70 (2H, t, *J* 7.5, CH_2CO$_2$H), 3.40 (2H, t, *J* 7.5, CH_2NTs), 3.82 (2H, d, *J* 6.4, CH$_2$=CHCH_2), 5.16-5.25 (2H, m, CH_2=CHCH$_2$), 5.59-5.74 (1H, m, CH$_2$=CHCH$_2$), 7.32 (2H, d, *J* 8.0, Ar$_{Ts}$*H*3-5), 7.71 (2H, d, *J* 8.0, Ar$_{Ts}$*H*2-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 75MHz) 21.9 (*C*H$_3$), 34.4 (*C*H$_2$CO$_2$H), 43.2 (*C*H$_2$NTs), 52.1 (CH$_2$=CH*C*H$_2$), 119.9 (*C*H$_2$=CHCH$_2$), 127.6 (*C*HAr$_{Ts}$2-6), 130.3 (*C*HAr$_{Ts}$3-5), 133.3 (CH$_2$=*C*HCH$_2$), 136.7 (*C*Ar$_{Ts}$SO$_2$), 143.9 (*C*Ar$_{Ts}$CH$_3$), 171.2 (*C*O$_2$H); ***m/z*** (ES^-) 565 ([2M-H]$^-$, 100%), 282 ([M-H]$^-$, 25%); HRMS (ES^-) $C_{13}H_{17}NO_4S^-$ ([M-H]$^-$) found 282.0801, requires 282.0806 (- 1.6 ppm).

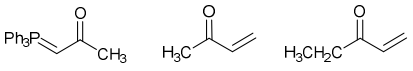
3-(Allyl((benzyloxy)carbonyl)amino)propanoic acid 5



Ester **S4** (2.35 g, 7.35 mmol, 1.0 eq) was stirred in DCM : TFA (1 : 1, 40 mL) at rt for 2 h. The reaction mixture was quenched with sat. aq. NH_4Cl (50 mL) and extracted with DCM (x3). The organic phases were washed with sat. aq. $NaHCO_3$ (x2), dried ($MgSO_4$) and concentrated *in vacuo* to afford **5** (1.9 g, 98 %) as a clear oil; $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 2.68 (2H, m, C*H*$_2$CO$_2$H), 3.57 (2H, t, *J* 6.9, C*H*$_2$NTs), 3.96 (2H, d, *J* 6.4, CH_2=CHC*H*$_2$), 5.17 (4H, broad s, NCO$_2$C*H*$_2$Ar+C*H*$_2$=CHCH$_2$), 5.76-5.80 (1H, m, CH_2=C*H*CH$_2$), 7.28-7.38 (5H, m, Ar*H*). Data is in accordance with the literature.[6]

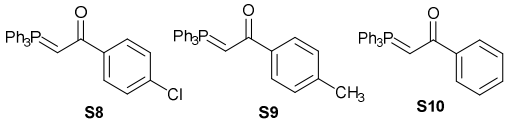
3) Synthesis of vinyl ketones and phosphoranes

1-(Triphenylphosphoranylidene)propan-2-one **S7**, methyl vinyl ketone **S14** and ethyl vinyl ketone **S15** were commercially available and purchase from Aldrich.



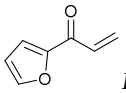
S7 **S14** **S15**

1-(4-Chlorophenyl) **S8**, 1-(p-tolyl)- **S9**, and 1-phenyl-2-(triphenylphosphoranylidene)ethanone **S10**, have previously been synthesized and characterized.[11]



S8 **S9** **S10**

1-(Furan-2-yl)prop-2-en-1-one S6



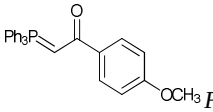
Following a modified literature procedure,[9] vinylmagnesium bromide (34.3 mL, 24.0 mmol, 2.0 eq; 0.7 M in THF) was slowly added to a solution of 2-furfuraldehyde (1.0 mL, 12.0 mmol, 1.0 eq) in dry THF (30 mL) at 0 °C under N_2. The reaction mixture was stirred for 15 min at 0 °C and then at rt for 3 h. The reaction was quenched with sat. aq. $NaHCO_3$, and then extracted with DCM (x3). The combined organic phases were washed with H_2O (x3), brine (x2), dried ($MgSO_4$) and concentrated *in vacuo* to afford 1-(furan-3-yl)prop-2-en-1-ol[10] as a brown oil and was used directly in the next step without any further purification; $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 5.23-5.29 (1H, m, C*H*OH), 5.32 (1H, dt, *J* 10.4, 1.3, CH=C*H*$_A$H$_B$), 5.45 (1H, dt, *J* 17.0, 1.3, CH=CH$_A$*H*$_B$), 6.15 (1H, ddd, *J* 17.0, 10.4, 5.7, C*H*=CH$_A$H$_B$), 6.28 (1H, d, *J* 3.3, C*H*Ar$_{furan}$3), 6.36 (1H, dd, *J* 3.3, 1.8, C*H*Ar$_{furan}$4), 7.42 (1H, dd, *J* 1.8, 0.9, C*H*Ar$_{furan}$5). To a solution of the vinyl alcohol in DMSO (10 mL) was slowly added IBX (5.0 g, 18.0 mmol, 1.5 eq) at rt. The reaction mixture was stirred for 3 h then quenched with H_2O : DCM (1 : 1; 10 mL). The mixture was filtered through Celite and the fíltrate was extracted with DCM (x3).

The combined organic phases were washed with H_2O (x2), brine (x2), dried ($MgSO_4$) and concentrated *in vacuo* to give vinyl ketone **S6** as a yellow oil (1.2 g, 79%); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1664 (C=O), 1463 (C=C); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 5.80 (1H, dd, *J* 10.5, 1.7, CH=CH_AH_B), 6.42-6.53 (2H, m, C*H*Ar_{furan}3+CH=CH_AH_B), 7.00 (1H, dd, *J* 17.2, 10.5, C*H*=CH_AH_B), 7.21 (1H, dd, *J* 3.6, 0.8, C*H*Ar_{furan}4), 7.52-7.62 (1H, dd, *J* 1.7, 0.8, C*H*Ar_{furan}5); $\boldsymbol{\delta_c}$ ($CDCl_3$, 75MHz) 112.9 (*C*HAr_{furan}4), 118.8 (*C*HAr_{furan}3), 129.9 (CH=*C*H_2), 131.7 (*C*H=CH_2), 147.4 (*C*HAr_{furan}5), 153.3 (*C*(2)Ar_{furan}), 178.5 (*C*O); ***m/z*** (ES^+) 123 ($[M+H]^+$, 100%); HRMS (ES^+) $C_7H_7O_2^+$ ($[M+H]^+$) found 123.0441, requires 123.0438 (- 2.1 ppm).

General procedure 3*: Phosphoranes synthesis*

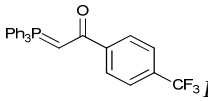
A solution of the corresponding 2-bromoethanone (1.0 eq) and triphenylphosphine (1.0 eq) were refluxed in dry solvent for 4 h. After completion, the reaction mixture was allowed to cool to rt and the phosphonium salt was filtered and washed with Et_2O (3×100 mL). The phosponium salt was then dissolved in H_2O : DCM (1.5 : 1) and 2M. aq. NaOH (100 mL) was added. The mixture was stirred for 2 h and then extracted with DCM (3×100 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to afford the corresponding phosphorane.

1-(4-Methoxyphenyl)-2-(triphenylphosphoranylidene)ethanone S11



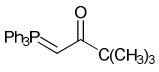
*Following general procedure **3***: 2-bromo-1-(4-methoxy)phenylethanone (15.0 g, 65.5 mmol), triphenylphosphine (17.2 g, 65.5 mmol), dry THF (200 mL), gave **S11** as an orange solid (17.7 g, 66%); **mp** 144-146 °C {litt.[12] 150-153 °C}; $\boldsymbol{\delta_H}$ (d^6-DMSO, 300MHz) 3.77 (3H, s, CH_3), 4.40 (1H, d, *J* 24.9, C*H*), 6.87-6.90 (2H, m, Ar*H*), 7.52-7.58 (6H, m, Ar*H*), 7.62-7.71 (9H, m, Ar*H*) 7.81-7.84 (2H, m, Ar*H*); $\boldsymbol{\delta_P}$ ($CDCl_3$, 121 MHz) 16.59. Data is in accordance with the literature.[12]

1-(4-(Trifluoromethyl)phenyl)-2-(triphenylphosphoranylidene)ethanone S12



*Following general procedure **3***: 2-bromo-1-(4-trifluoromethyl)phenylethanone (15.0 g, 56.2 mmol), triphenylphosphine (14.7 g, 56.2 mmol), dry THF (200 mL) gave **S12** as an orange solid (23.0 g, 92%); **mp** 158-160 °C; $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1716 (C=O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 400MHz) 4.57 (1H, d, *J* 24.6, C*H*), 7.67-7.70 (6H, m, Ar*H*), 7.71-7.73 (5H, m, Ar*H*), 7.74-7.77 (6H, m, Ar*H*), 8.06-8.10 (2H, m, Ar_{CF3}*H*2-6); $\boldsymbol{\delta_c}$ ($CDCl_3$, 125MHz) 52.3 (*C*H, d, *J* 111.0), 124.7 (*C*F_3, q, *J* 272.1), 124.8 (2x*C*HAr_{CF_3}, d, *J* 3.5), 126.5 (3x*C*Ar, d, *J* 90.0), 128.8 (2xCHAr_{CF_3}), 129.0 (6xCHAr, d, *J* 10.2), 130.9 (*C*CF_3, q, *J* 32.0), 132.3 (3x*C*HAr, d, *J* 2.4), 133.1 (6x*C*HAr, d, *J* 10.2), 144.7 (*C*ArCO) 183.0 (*C*O, d, *J* 3.2); $\boldsymbol{\delta_P}$ ($CDCl_3$, 282MHz) 1.37; $\boldsymbol{\delta_F}$ ($CDCl_3$, 121MHz) 15.99; ***m/z*** (ES^+) 449 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{27}H_{21}POF_3^+$ ($[M+H]^+$) found 449.1277, requires 449.1270 (- 1.5 ppm).

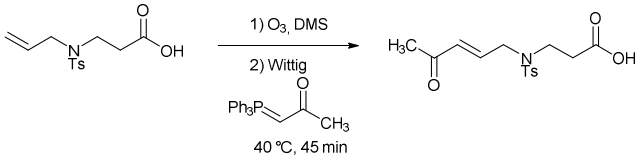
3,3-Dimethyl-1-(triphenylphosphoranylidene)butan-2-one S13



*Following general procedure **3***: 1-bromopinacolone (5.00 mL, 0.04 mol, 1.0 eq), triphenylphosphine (9.7 g, 0.04 mol, 1.0 eq), toluene (50 mL), gave **S13** as a white powder (10.3 g, 77%); **mp** 178 °C {lit[13]175-177 °C}; δ_H ($CDCl_3$, 500MHz) 1.23 (9H, s, C(C*H*$_3$)$_3$), 3.80 (1H, d, *J* 27.1 C*H*), 7.44-7.47 (6H, m, Ar*H*), 7.53-7.56 (3H, m, Ar*H*), 7.62-7.66 (6H, m, Ar*H*); δ_P ($CDCl_3$, 121MHz) 4.35. Data is in accordance with the literature. [14]

4) Synthesis of enone–acids 1 and 30

(*E*)-3-(4-Methyl-*N*-(4-oxopent-2-en-1-yl)phenylsulfonamido)propanoic acid 1

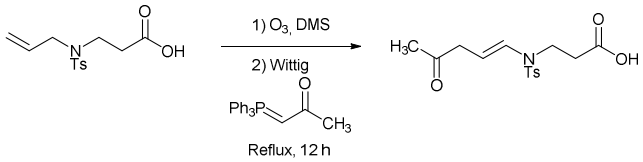


A stream of O_3 in O_2 was bubbled through a solution of alkene **4** (60.0 mg, 0.21 mmol, 1.0 eq), in dry DCM (0.3 mol/L) at - 78 °C. When the blue color persisted, dimethyl sulfide (2.0 eq) was added and the reaction was allowed to warm to rt. The solvent was evaporated *in vacuo* and aldehyde **S1a** was treated as an intermediate and used directly to the next step; (analytical data contains trace of DMS and DMSO); ν_{max} (film)/cm^{-1} 2922 (broad O-H), 1728 (broad C=O); δ_H ($CDCl_3$, 400MHz) 2.37 (3H, s, C*H*$_3$), 2.67 (2H, t, *J* 6.6, C*H*$_2$COH), 3.39 (2H, t, *J* 6.6, C*H*$_2$NTs), 3.92 (2H, d, *J* 1.1, C*H*$_2$CO$_2$H), 7.27 (2H, d, *J* 7.9, Ar$_{Ts}$*H*3-5), 7.63 (2H, d, *J* 8.0, Ar$_{Ts}$*H*2-6), 9.50 (1H, s, CO*H*); δ_c ($CDCl_3$, 75MHz) 21.9 (Ar$_{Ts}$*C*H$_3$), 35.0 (*C*H$_2$CO$_2$H), 46.3 (*C*H$_2$NTs), 59.0 (*C*H$_2$COH), 127.8 (*C*HAr$_{Ts}$2-6), 130.4 (*C*HAr$_{Ts}$3-5), 135.7 (*C*Ar$_{Ts}$SO$_2$), 144.5 (*C*Ar$_{Ts}$CH$_3$), 174.7 (*C*O$_2$H), 198.6 (*C*OH); ***m/z*** (ES$^-$) 284 ([M-H]$^-$, 100%) 242 ([M-CH$_2$COH]$^-$, 60%); HRMS (ES$^-$) $C_{12}H_{14}SNO_5^-$ ([M-H]$^-$); found 284.0595, requires 284.0598 (-1.1 ppm). Phosphorane **S7** (74.1 mg, 0.23 mmol, 1.1 eq) was added to a solution of the aldehyde in THF (8 mL) and acetic acid (0.05 mL). The reaction was stirred at 40 °C for 45 min (carefully monitored by NMR) and then concentrated *in vacuo*. The crude reaction mixture was dissolved in EtOAc and sat. aq. $NaHCO_3$ was added. The aqueous phase was washed with EtOAc (x3). The aqueous phase was acidified (pH ~2) with 2M aq. HCl and then extracted with EtOAc (x3). The combined organic phases were washed with brine (x2) and concentrated *in vacuo* to afford **1** as a yellow oil (43 mg, 63%); ν_{max} (film)/cm^{-1} 2923 (O-H), 1720 (C=O acid), 1667 (C=O ketone), 1160 (C-O); δ_H ($CDCl_3$, 400 MHz) 2.24 (3H, s, COC*H*$_3$), 2.46 (3H, s, Ar$_{Ts}$C*H*$_3$), 2.72 (2H, t, *J* 7.0, C*H*$_2$CO$_2$H), 3.44 (2H, t, *J* 7.0, C*H*$_2$NTs), 4.00 (2H, dd, *J* 5.8, 1.6, CH=CHC*H*$_2$), 6.15 (1H, dt, *J* 16.0, 1.6, C*H*=CHCH$_2$), 6.61 (1H, dt, *J* 16.0, 5.7, CH=C*H*CH$_2$), 7.36 (2H, d, *J* 8.3, Ar$_{Ts}$*H*3-5), 7.73 (2H, d, *J* 8.3, Ar$_{Ts}$*H*2-6); δ_c ($CDCl_3$, 100 MHz) 21.6 (Ar$_{Ts}$*C*H$_3$), 27.2 (CO*C*H$_3$), 34.1 (*C*H$_2$CO$_2$H), 44.2 (*C*H$_2$NTs), 50.1 (CH=CH$_2$*C*H$_2$), 127.3 (*C*HAr$_{Ts}$2-6), 129.9 (*C*HAr$_{Ts}$3-5), 132.7 (*C*H=CHCH$_2$), 135.9 (*C*Ar$_{Ts}$CH$_3$),

141.4 (CH=*C*HCH$_2$), 144.1 (*C*Ar$_{Ts}$SO$_2$), 175.6 (*C*O$_2$H), 197.9 (*C*OCH$_3$); ***m/z*** (ES$^-$) 649 ([2M-H]$^-$, 100%), 324 ([(M-H]$^-$, 60%); HRMS (ES$^-$) $C_{15}H_{18}SNO_5^-$ ([M-H]$^-$); found 324.0902, requires 324.0911 (- 2.8 ppm).

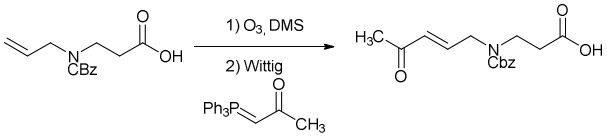
Isomerisation product S16

The isomerisation product **S16** was observed only in this *N*-tosylated series when the Wittig reaction was performed for a longer period of time, or/and at higher temperature.



A stream of O_3 in O_2 was bubbled through a solution of alkene **4** (132 mg, 0.46 mmol, 1.0 eq), in dry DCM (0.3 mol/L) at - 78 °C. When the blue color persisted, dimethyl sulfide (2.0 eq) was added and the reaction was allowed to warm to rt. The solvent was evaporated *in vacuo* and aldehyde **S30a** was treated as an intermediate and used directly for the next step; Phosphorane **S7** (163 mg, 0.51 mmol, 1.1 eq) was added to a solution of the aldehyde in $CHCl_3$ (50 mL) and the reaction was stirred at 70 °C overnight. The mixture was concentrated *in vacuo* and the residue was purified by chromatography column (DCM : MeOH, 99.9 : 0.1) to give **S16** as a yellow oil. Chromatography column unabled a clean purification of this compound and **S16** was isolated as a mixture with triphenylphosphine oxide. $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 3059-2850 (O-H), 1712 (C=O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500 MHz) contaminated with PPh_3O; 2.15 (3H, s, COC*H*$_3$), 2.42 (5H, m, Ar$_{Ts}$C*H*$_3$+C*H*$_2$CO$_2$H), 3.10 (2H, d, *J* 7.3, C*H*$_2$CH=CH), 3.58 (2H, dd, *J* 9.7, 6.6, NTsC*H*$_2$), 4.90 (1H, dt, *J* 14.4, 7.3, CH$_2$CH=C*H*), 6.67 (1H, d, *J* 14.3, CH$_2$C*H*=CH), 7.21-7.75 (4H, m, Ar$_{Ts}$*H*); $\boldsymbol{\delta_C}$ ($CDCl_3$, 500 MHz) contaminated with PPh_3O 21.5 (Ar$_{Ts}$*C*H$_3$), 27.4 (COCH3), 32.7 (*C*H$_2$CO$_2$H), 41.7 (NTsC*H*$_2$), 45.0 (*C*H$_2$CH=CH), 102.4 (CH$_2$*C*H=CH), 127.6 (*C*HAr$_{Ts}$2-6), 128.5 (CH$_2$CH=*C*H), 129.9 (*C*HAr$_{Ts}$3-5), 135.9 (*C*Ar$_{Ts}$CH$_3$), 143.7 (*C*Ar$_{Ts}$SO$_2$), 173.9 (*C*O$_2$H), 206.9 (*C*OCH$_3$); ***m/z*** (ES$^+$) 348.0867 ([M+Na]$^+$, 50%).

(*E*)-3-[((Benzyloxy)carbonyl)(4-oxopent-2-en-1-yl)amino]propanoic acid 30

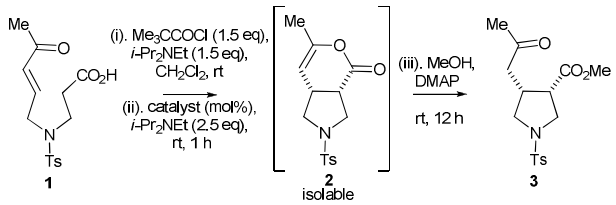


A stream of O_3 in O_2 was bubbled through a solution of alkene **5** (150 mg, 0.56 mmol, 1.0 eq), in dry DCM (0.3 mol/L) at – 78 °C. When the blue color persisted, dimethyl sulfide (2.0 eq) was added and the reaction was allowed to warm to rt. The solvent was evaporated *in vacuo* and the aldehyde was treated as an intermediate and used directly to the next step; (analytical data contains trace of DMS and DMSO); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 3338-2576 (broad O-H), 1695 (broad C=O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) mixture of rotamers 2.61 (2H, t, *J* 6.4, C*H*$_2$CO$_2$H), 3.60 (2H, app q, *J* 6.7, C*H*$_2$NCbz), 4.16, 4.19 (2H, s

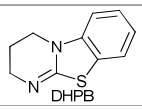
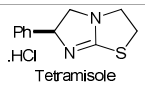
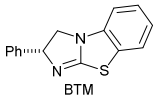
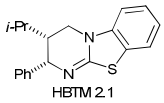
C*H*$_2$COH), 5.10, 5.17 (2H, m, NCO$_2$C*H*$_2$Ar), 7.27-7.37 (5H, m, Ar*H*), 9.51, 9.55 (1H, s, CO*H*); **δ$_c$** (CDCl$_3$, 75MHz) 33.5, 34.0 (*C*H$_2$CO$_2$H), 44.7, 45.6 (*C*H$_2$NCbz), 58.9, 59.1 (*C*H$_2$COH), 67.7, 67.8 (NCO$_2$*C*H$_2$Ar), 127.9 (3X*C*HAr), 128.2 (*C*HAr), 128.6 (*C*HAr), 136.1 (*C*Ar), 155.7, 156.4, (NCO$_2$CH$_2$Ar), 175.0, 175.5 (*C*O$_2$H), 198.2 (*C*OH); ***m/z*** (AS$^+$) 266 ([M+H]$^+$, 100%); HRMS (AS$^+$) C$_{13}$H$_{16}$NO$_5^+$ ([M+H$^+$); found 266.1024, requires 266.1023 (+ 0.4 ppm).

Phosphorane **S7** (196 mg, 0.62 mmol, 1.1 eq) was added to a solution of the aldehyde in CHCl$_3$ (8 mL) and the mixture was stirred at 40 °C for 2 h. The solvent was evaporated and the residue dissolved in EtOAc. H$_2$O was added and the pH was adjusted by addition of 1M aq. NaOH to pH~11. The aqueous layer was washed with EtOAc (x3). The aqueous layer was acidified with 2M aq. HCl and extracted with EtOAc (x3). The combined organic layers were washed with brine (x2), dried (MgSO$_4$) and concentrated *in vacuo*, to give **30** (150 mg, 88%) as a clear oil; **ν$_{max}$** (film)/cm^{-1} 3064-2927 (O-H), 1728 (C=O acid), 1674 (C=O ketone), 1118 (C-O); **δ$_H$** (CDCl$_3$, 300MHz) mixture of rotamers 2.13-2.18 (3H, m, COC*H*$_3$), 2.54-2.61 (2H, m, C*H*$_2$CO$_2$H), 3.45-3.48 (2H, m, C*H*$_2$NCBz), 4.05 (2H, app broad s, CH=CHC*H*$_2$), 5.05-5.08 (2H, m, NCO$_2$C*H*$_2$Ph), 5.95-6.04 (1H, m, C*H*=CHCH$_2$), 6.55-6.64 (1H, m, CH=C*H*CH$_2$), 7.25-7.28 (5H, m, Ar$_{CBz}$*H*),10.8 (1H, braod s, CO$_2$*H*); **δ$_c$** (CDCl$_3$, 75MHz) 27.5, 27.8 (*C*H$_3$), 33.6, 34.1 (*C*H$_2$CO$_2$H), 43.6, 44.5 (*C*H$_2$NTs), 49.6 (CH=CH$_2$*C*H$_2$), 68.1, 68.2 (NCO$_2$*C*H$_2$Ph), 128.4 (*C*HAr$_{CBz}$2-6), 128.7 (*C*HAr$_{CBz}$4), 128.9 (*C*HAr$_{CBz}$3-5), 131.3, 131.8 (*C*H=CHCH$_2$), 136.5 (*C*(1)Ar$_{CBz}$), 142.7 (CH=*C*HCH$_2$), 156.3 (*C*O$_2$CH$_2$Ph), 176.9, 177.3 (*C*O$_2$H), 198.7, 198.9 (*C*OCH$_3$); ***m/z*** (ES$^-$) 304 ([M-H]$^-$, 100%); HRMS (ES$^-$) C$_{16}$H$_{18}$NO$_5^-$ ([M-H]$^-$); found 304.1191, requires 304.1190 (+ 0.2 ppm).

5) Reaction optimisation



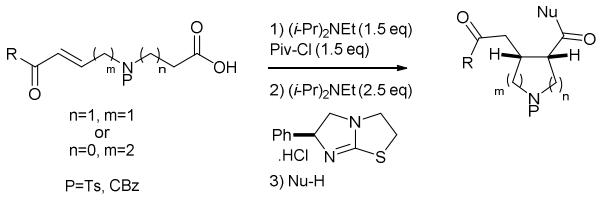
To a solution of the enone-acid **1** (50.0 mg, 0.15 mmol, 1.0 eq) in DCM was added pivaloylchloride (28.0 µL, 0.23 mmol, 1.5 eq) and (i-Pr)$_2$NEt (39.5 µL, 0.23 mmol, 1.5 eq) at rt. After 10 min (i-Pr)$_2$NEt (65.7 µL, 0.38 mmol, 2.5 eq) and the corresponding catalyst (20 mol%) were added. The reaction was monitored by TLC until completion and then was either purified by chomatography column on silica gel (Pet.ether : EtOAc, 90 : 10 to 80 : 20) to yield lactone **2**, or quenched with MeOH and DMAP (cat) at rt to afford the pyrrolidine **3**.

Entry	Catalyst	mol %	dr[a]	Lactone 2 Yield(%)	ee(%)[b]	Ester 3 Yield(%)	ee(%)[c]
1	 DHPB	20	99:1	40	--	70	--
2	 DABCO	20	80:20	--	--	88	--
3	 Tetramisole	20	99:1	48	97	70	99
4		5	99:1	--	--	67	99
5	 BTM	20	99:1	45	99 (*ent*)	70	99 (*ent*)
6	 HBTM 2.1	20	99:1	54	75 (*ent*)	--	--

[a] Diastereomeric ratio determined by 1H NMR spectroscopic analysis of the unpurified reaction mixture; [b] Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 40 % i-PrOH : hexane, 0.1 mL/min tr maj = 39.9 min, tr min = 36.1 min; 211 nm, 30 °C); [c] Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 30 % i-PrOH : hexane, 1.0 mL/min tr maj = 19.1 min, tr min = 16.2 min; 254 nm, 30 °C).

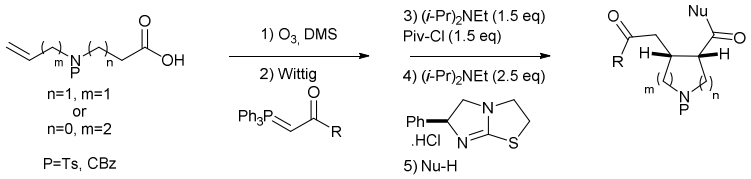
6) General procedures: *Syn* pyrrolidines synthesis

General procedure 4: *from enone-acids starting material*



To a solution of the corresponding enone-acid (1.0 eq) in DCM (final concentration c=0.03 mol/L) was added pivaloylchloride (1.5 eq) and $(i\text{-Pr})_2$NEt (1.5 eq) at rt. After 10 min (−)-tetramisole.HCl and $(i\text{-Pr})_2$NEt (2.5 eq) were added. The reaction was monitored by TLC until completion then quenched with the corresponding nucleophile. The solvent was evaporated and the residue was purified by chomatography column on silica gel (Pet.ether : EtOAc) to yield the corresponding pyrrolidines.

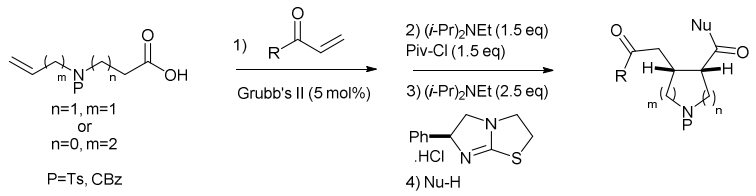
General procedure 5: *via tandem Wittig/organocatalysis*



A stream of O_3 in O_2 was bubbled through a solution of the corresponding alkene in dry DCM (0.3 mol/L) at - 78 °C. When the blue colore persisted, dimethyl sulfide (2.0 eq) was added and the reaction was allowed to warm to rt. After concentration *in vacuo* the corresponding aldehyde was disolved in $CHCl_3$ and the corresponding phosphorane (1.1 eq) was added. The reaction was refluxed overnight, unless otherwise stetted, and then concentrated *in vacuo*. The crude reaction mixture was dissolved in DCM (final concentration c=0.03 mol/L) and pivaloylchloride (1.5 eq) and $(i\text{-Pr})_2$NEt (1.5 eq) were added at rt. After 10 min, (−)-tetramisole.HCl (mol%) and $(i\text{-Pr})_2$NEt (2.5 eq) were added. The reaction was monitored by TLC until completion then quenched with the corresponding nucleophile. The solvent was evaporated and the residue was purified by chomatography column (Pet.ether : EtOAc) to yield the corresponding pyrrolidines.

Racemic *syn* products were obtained using commercially available (±) tetramisole (5 mol%) as a racemic catalyst following general procedures 4, 5 or 6

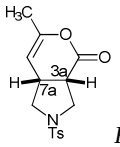
General procedure 6: *via tandem metathesis/organocatalysis*



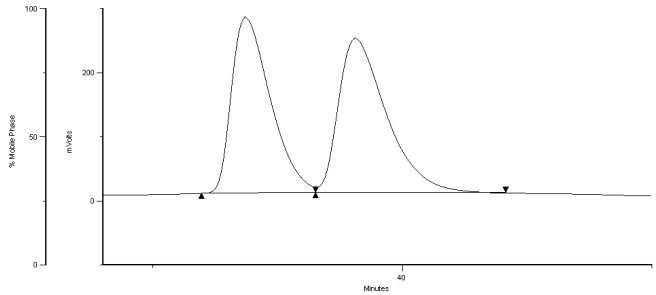
Grubbs II (5 mol%) and the corresponding alkene (1.0 eq) were added into a flame dry microwave tube under N_2. The tube was then sealed. Dry DCM (0.3 mol/L) and the corresponding ketone (5.0 eq) were added and the solution was heated at 40 °C. After completion, the mixture was cooled to rt and pivaloylchloride (1.5 eq), (i-Pr)$_2$NEt (1.5 eq) and DCM (final concentration c=0.03 mol/L) were added. After 10 min (−)-tetramisole.HCl and (i-Pr)$_2$NEt (2.5 eq) were added. The reaction was monitored by TLC until completion then quenched with the corresponding nucleophile. The solvent was evaporated and the residue was purified by chomatography column on silica gel (Pet.ether : EtOAc) to yield the corresponding pyrrolidines.

7) Characterisation of 3, 4 substituted lactone 2 and pyrrolidine derivatives 3, 6-9, 22, 23

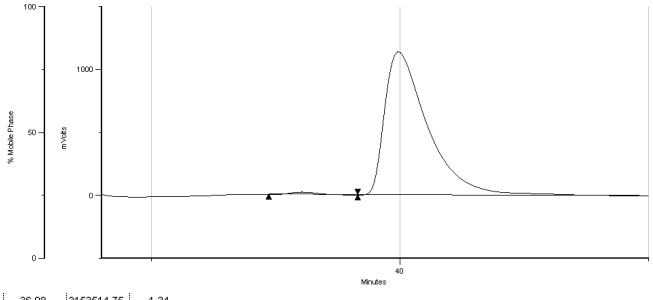
(3a*S*,7a*R*)-6-Methyl-2-tosyl-1,3,3a,7a-tetrahydropyrano[3,4-c]pyrrol-4(2*H*)-one 2



*Following general procedure **4** without addition of nucleophile*: enone-acid **1** (50.0 mg, 0.15 mmol), pivaloylchloride (28.0 µL, 0.23 mmol), (*i*-Pr)$_2$NEt (39.5 µL, 0.23 mmol), DCM (5 mL), (−)-tetramisole.HCl (7.2 mg, 0.03 mmol), (*i*-Pr)$_2$NEt (65.7 µL, 0.38 mmol). Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 90 : 10 to 80 : 20) gave **2** as an oil (52 mg, 48%) in 97% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ +7.7 (*c* 0.3 in $CHCl_3$); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1732 (C=O), 1465 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 400MHz) 1.73 (3H, s, CH_3), 2.37 (3H, s, Ar$_{Ts}$CH_3), 2.87-2.90 (3H, m, C(7a)*H*+C(3a)*H*+C(1)H_AH$_B$), 3.52-3.64 (3H, m, C(1)H$_A$$H_B$+C(3)$H_2$), 4.63-4.65 (1H, m, C(7)*H*), 7.27 (2H, d, *J* 8.3, Ar$_{Ts}$*H*3-5), 7.64 (2H, d, *J* 8.3, Ar$_{Ts}$*H*2-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 100MHz) 19.2 (*C*H$_3$), 22.0 (Ar$_{Ts}$*C*H$_3$), 36.3 (*C*(3a)H), 41.3 (*C*(7a)H), 49.6 (*C*(3)H$_2$), 53.9 (*C*(1)H$_2$), 99.3 (*C*(7)H), 128.0 (*C*HAr$_{Ts}$2-6), 130.2 (*C*HAr$_{Ts}$3-5), 133.6 (*C*Ar$_{Ts}$SO$_2$), 144.4 (*C*Ar$_{Ts}$CH$_3$), 150.3 (*C*(6)-CH$_3$), 167.7 (*C*O); ***m/z*** (APCI$^+$) 308 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{15}H_{18}SNO_4^+$ ([M+H]$^+$); found 308.0948, requires 308.0951 (- 1.0 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 40 % *i*-PrOH : hexane, 0.1 mL/min $t_{r\ maj}$ = 39.9 min, $t_{r\ min}$ = 36.1 min; 211 nm, 30 °C).

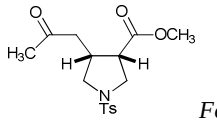


33.71	49794588.00	47.91
38.12	54139268.00	52.09

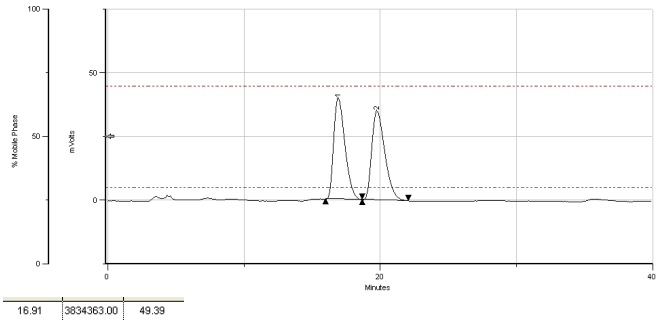


36.08	3153514.75	1.34
39.94	32439328.00	98.66

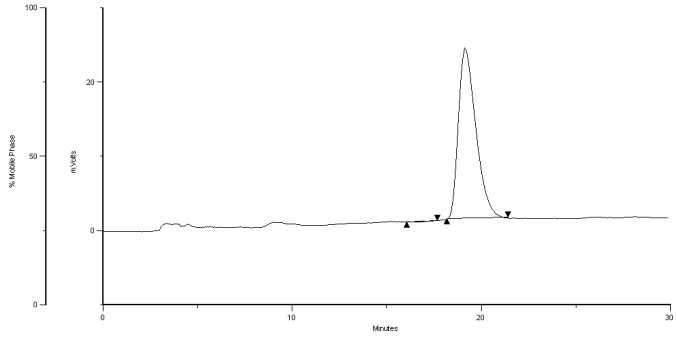
(3*S*,4*R*)-Methyl 4-(2-oxopropyl)-1-tosylpyrrolidine-3-carboxylate 3



*Following general procedure **4***: enone-acid **1** (50.0 mg, 0.15 mmol), pivaloylchloride (28.0 µL, 0.23 mmol), (*i*-Pr)$_2$NEt (39.5 µL, 0.23 mmol), DCM (6 mL), (−)-tetramisole.HCl (1.8 mg, 0.008 mmol), (*i*-Pr)$_2$NEt (65.7 µL, 0.38 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**3** as a white solid (34 mg, 67%) in 99% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ - 0 (*c* 0.3 in DCM); **mp** 92-94 °C; $\boldsymbol{\nu}_{\mathbf{max}}$ (KBr)/cm^{-1} 1726 (C=O ester), 1705 (C=O ketone), 1160 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 300MHz) 1.98 (3H, s, COCH_3), 2.19 (1H, dd, *J* 18.3, 7.9, CH_AH$_B$), 2.35-2.43 (4H, m, Ar$_{Ts}$CH_3+CH$_A$$H_B$), 2.72 (1H, m, C(3)*H*), 2.99 (2H, m, C(2)H_AH$_B$+C(4)*H*), 3.42-3.46 (3H, m, C(2)H$_A$$H_B$+C(5)$H_2$), 3.49 (3H, s, CO$_2CH_3$), 7.27 (2H, d, *J* 8.3, Ar$_{Ts}$*H*3-5), 7.65 (2H, d, *J* 8.3, Ar$_{Ts}$*H*2-6); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 75MHz) 21.9 (Ar$_{Ts}$CH_3), 30.5 (CO*C*H$_3$), 36.2 (*C*(3)H), 42.5 (*C*H$_2$CO), 45.8 (*C*(4)H), 49.3 (*C*(5)H$_2$), 52.3 (CO$_2$*C*H$_3$), 52.5 (*C*(2)H$_2$), 127.9 (*C*HAr$_{Ts}$2-6), 130.1 (*C*HAr$_{Ts}$3-5), 134.2 (*C*Ar$_{Ts}$SO$_2$), 144.0 (*C*Ar$_{Ts}$CH$_3$), 172.1 (*C*O$_2$CH$_3$), 206.3 (*C*OCH$_3$); ***m/z*** (NSI$^+$) 340 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{16}H_{22}SNO_5^+$ ([M+H]$^+$); found 340.1217, requires 354.1213 (+ 1.1 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak OD-H 30 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 19.1 min, $t_{r\ min}$ = 16.2 min; 254 nm, 30 °C).



16.91	3834363.00	49.39
19.76	3929570.50	50.61



16.17	10534.89	0.42
19.14	2472303.50	99.58

***Syn*-3** was also synthesised using (−)-tetramisole.HCl (7.2 mg, 0.03 mmol, 0.2 eq) following the same procedure and was obtained after chromatography column purification as a white solid (36 mg, 70 %) in 99 % ee.

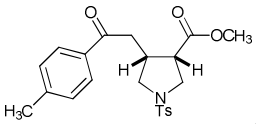
*Compound **3** was also synthesized via tandem Wittig/organocatalysis route:*

*Following general procedure **5***: ozonolysis of alkene **4** (60.0 mg, 0.22 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S7** (95.6 mg, 0.24 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (*i*-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (95.8 µL, 0.55 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**3** as a white solid (40 mg, 52%) in 99% ee.

*Compound **3** was also synthesized via tandem metathesis/organocatalysis route:*

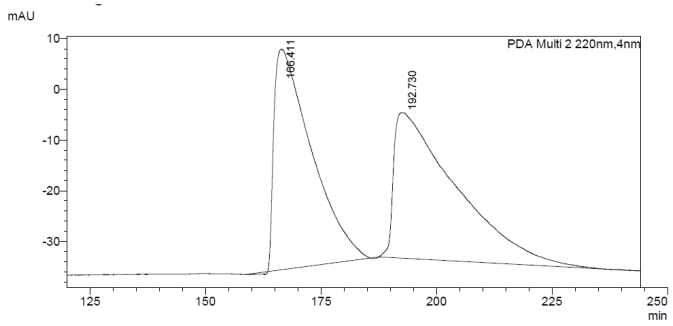
*Following general procedure **6***: alkene **4** (100 mg, 0.35 mmol), Grubb's II (14.8 mg, 0.02 mmol), dry DCM (1.2 mL), methyl vinyl ketone **S14** (146 µL, 1.76 mmol), stirred for 1 h at 40 °C. Organocatalysis with pivaloylchloride (64.6 µL, 0.53 mmol), (*i*-Pr)$_2$NEt (92.3 µL, 0.53 mmol), DCM (5 mL), (−)-tetramisole.HCl (4.2 mg, 0.017 mmol), (*i*-Pr)$_2$NEt (1.78 mL, 0.88 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**3** as a white solid (84 mg, 71%) in 98% ee.

(3*S*,4*R*)-Methyl 4-(2-oxo-2-(p-tolyl)ethyl)-1-tosylpyrrolidine-3-carboxylate 6



*Following general procedure **5***: ozonolysis of alkene **4** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S9** (112 mg, 0.31 mmol), AcOH (0.05 mL) in $CHCl_3$ (50 mL) heated at 40 °C for 2 h. Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122.0 µL, 0.70 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 90 : 10 to 80 : 20) gave *syn*-**6** as a yellow oil (68 mg, 57%) in 96% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ - 11.5 (*c* 0.3 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm^{-1} 1732 (C=O ester), 1680 (C=O ketone), 1172 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 2.40 (3H, s, $Ar_{Ts}CH_3$), 2.44 (3H, s, $Ar_{CH3}CH_3$), 2.68 (1H, dd, *J* 17.4, 7.6 CH_AH_B), 2.86-3.10 (2H, m, CH_AH_B+C(3)*H*), 3.15-3.31 (2H, m, C(2)H_AH_B+C(4)*H*), 3.56 (3H, s, CO_2CH_3), 3.56-3.75 (3H, m, C(2)H_AH_B+C(5)H_2), 7.27-7.34 (4H, m, $Ar_{Ts}H3$-5+$Ar_{CH3}H3$-5), 7.72-7.76 (4H, m, $Ar_{Ts}H2$-6+$Ar_{CH3}H2$-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 75MHz) 21.5 ($Ar_{Ts}CH_3$), 21.6 ($Ar_{CH3}CH_3$), 36.2 (*C*(3)H), 37.2 (CH_2CO), 45.6 (*C*(4)H), 48.9 (*C*(5)H_2), 51.9 (CO_2CH_3), 52.4 (*C*(2)H_2), 127.5 (*C*HAr_{Ts}2-6), 127.9 (*C*HAr_{CH3}2-6), 129.3 (*C*HAr_{Ts}3-5), 129.7 (*C*HAr_{CH3}3-5), 133.7 (*C*(1)Ar_{CH3}), 133.9 (*C*$Ar_{Ts}SO_2$), 143.6 (*C*$Ar_{Ts}CH_3$), 144.3 (*C*$Ar_{CH3}CH_3$), 171.8

(CO_2CH_3), 196.9 ($COAr_{CH3}$); ***m/z*** (NSI$^+$) 416 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{22}H_{26}SNO_5^+$ ([M+H]$^+$); found 416.1528, requires 416.1526 (+ 0.4 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak OD-H 1 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 182.2 min, $t_{r\ min}$ = 172.5 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch2 220nm

Peak#	Ret. Time	Area%
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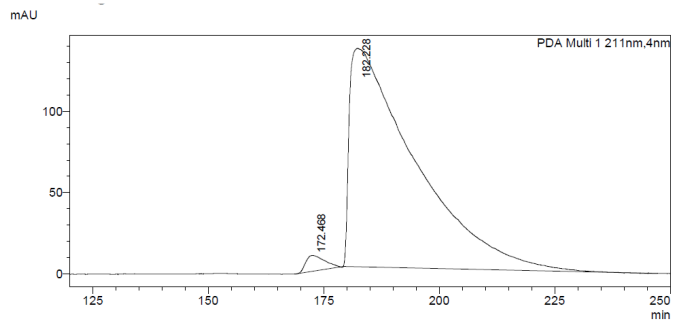
2	192.730	52.483
Total		100.000

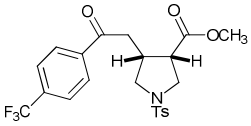


<Peak Table>

PDA Ch1 211nm

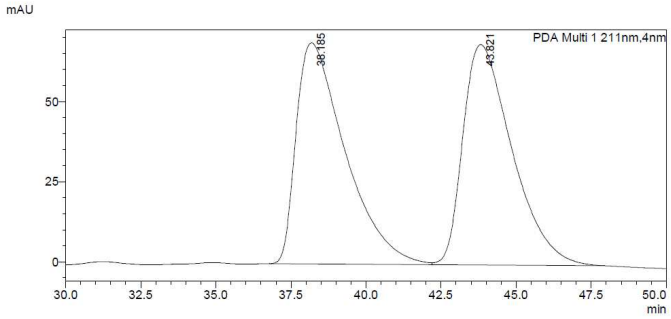
Peak#	Ret. Time	Area%
1	172.468	2.002
2	182.228	97.998
Total		100.000

(3*S*,4*R*)-Methyl-4-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-1-tosylpyrrolidine-3-carboxylate 7



Following general procedure 5: ozonolysis of alkene **4** (60.0 mg, 0.22 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S12** (99.3 mg, 0.24 mmol), in $CHCl_3$ (50 mL) heated at 65 °C for 12 h. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (*i*-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (95.8 µL, 0.55 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 70 : 30) gave *syn*-**7** as a yellow oil (51 mg, 49%) in 90% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ - 5.2 (*c* 0.3 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm^{-1} 1734 (C=O ester), 1683 (C=O ketone), 1321 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 400MHz) 2.30 (3H, s, $Ar_{Ts}CH_3$), 2.60-2.75

(1H, m, CH_AH$_B$), 2.89-2.99 (2H, m, CH$_A$$H_B$+C(3)*H*), 3.07-3.23 (2H, m, C(2)H_AH$_B$+C(4)*H*), 3.46 (3H, s, CO$_2$CH_3), 3.53-3.57 (3H, m, C(2)H$_A$$H_B$+C(5)$H_2$), 7.19-7.22 (2H, m, Ar$_{Ts}$*H*3-5), 7.63-7.66 (4H, m, Ar$_{Ts}$*H*2-6+Ar$_{CF3}$*H*3-5), 7.84-7.87 (2H, m, Ar$_{CF3}$*H*2-6); **δ$_C$** ($CDCl_3$, 125MHz) 21.5 (Ar$_{Ts}$$CH_3$), 35.9 (*C*(3)H), 37.5 (*C*H$_2$CO), 45.5 (*C*(4)H), 48.9 (*C*(5)H$_2$), 52.0 (*C*O$_2$CH$_3$), 52.4 (*C*(2)H$_2$), 124.5 (q, *J* 33.0 *C*(4)Ar$_{CF3}$), 125.7 (m, *C*HAr$_{CF3}$3-5), 127.8 (*C*HAr$_{Ts}$2-6), 127.9 (*C*HAr$_{CF3}$2-6), 128.3 (q, $J_{C\text{-}F}$ 272.7, *C*F$_3$), 129.8 (*C*HAr$_{Ts}$3-5), 133.6 (*C*Ar$_{Ts}$SO$_2$), 138.9 (*C*(1)Ar$_{CF3}$), 143.7 (*C*Ar$_{Ts}$CH$_3$), 171.8 (*C*O$_2$CH$_3$), 196.5 (*C*OAr$_{CF3}$); ***m/z*** (ES$^+$) 492 ([M+Na]$^+$, 100%); HRMS (ES$^+$) $C_{22}H_{22}F_3SNO_5Na^+$ ([M+Na]$^+$); found 492.1067, requires 492.1068 (- 0.2 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak OD-H 15 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 38.1 min, $t_{r\ min}$ = 45.9 min; 220 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
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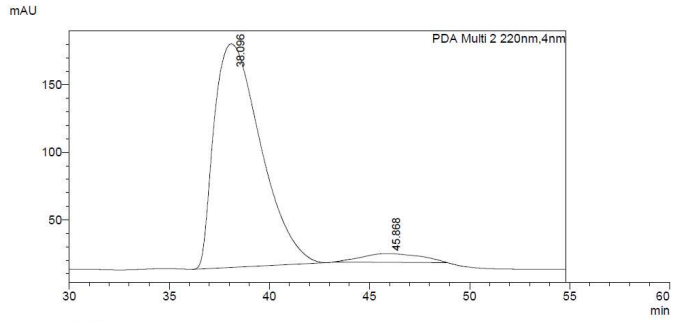
2	43.821	49.998
Total		100.000

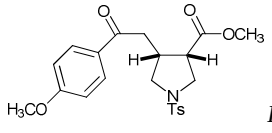


<Peak Table>

PDA Ch2 220nm

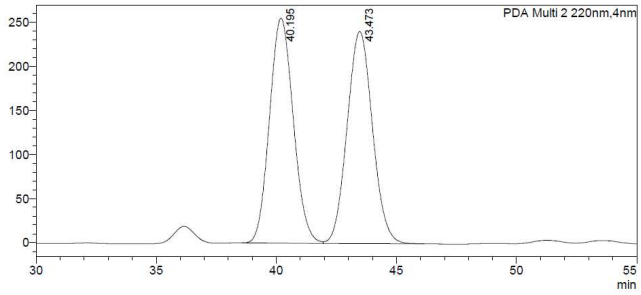
Peak#	Ret. Time	Area%
1	38.096	95.151
2	45.868	4.849
Total		100.000

(3*S*,4*R*)-Methyl 4-(2-(4-methoxyphenyl)-2-oxoethyl)-1-tosylpyrrolidine-3-carboxylate 8



*Following general procedure **5***: ozonolysis of alkene **4** (60.0 mg, 0.22 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S11** (99.3 mg, 0.24 mmol), in $CHCl_3$

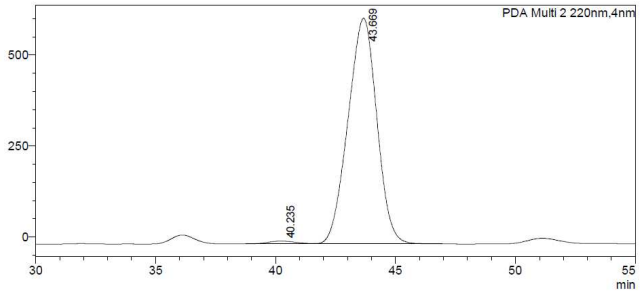
(80 mL) heated at 65 °C for 3 h. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (*i*-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (95.8 µL, 0.55 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 70 : 30) gave *syn*-**8** as a yellow oil (60 mg, 64%) in 98% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ - 9.2 (*c* 0.3 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$ **(**film)/cm^{-1} 1732 (C=O ester), 1674 (C=O ketone), 1160 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ (CDCl$_3$, 500MHz) 2.31 (3H, s, Ar$_{Ts}$C*H*$_3$), 2.57 (1H, dd, *J* 17.7, 8.1, C*H*$_A$H$_B$), 2.83 (1H, dd, *J* 17.7, 6.0, CH$_A$*H*$_B$), 2.88-2.97 (1H, m, C(3)*H*), 3.08-3.17 (2H, m, C(2)*H*$_A$H$_B$+C(4)*H*), 3.45 (3H, s, CO$_2$C*H*$_3$), 3.47-3.58 (3H, m, C(2)H$_A$*H*$_B$+C(5)*H*$_2$), 3.80 (3H, s, Ar$_{OCH3}$OC*H*$_3$), 6.84 (2H, d, *J* 8.8, Ar$_{OCH3}$*H*3-5), 7.18-7.22 (2H, d, *J* 8.1, Ar$_{Ts}$*H*3-5), 7.65 (2H, d, *J* 8.1, Ar$_{Ts}$*H*2-6), 7.72 (2H, d, *J* 8.8, Ar$_{OCH3}$*H*2-6); $\boldsymbol{\delta}_{\mathbf{C}}$ (CDCl$_3$, 100MHz) 21.6 (Ar$_{Ts}$*C*H$_3$), 36.7 (*C*(3)H), 37.2 (*C*H$_2$CO), 46.1 (*C*(4)H), 49.4 (*C*(5)H$_2$), 52.3 (CO$_2$*C*H$_3$), 52.9 (*C*(2)H$_2$), 55.9 (Ar$_{OCH3}$O*C*H$_3$), 114.2 (*C*HAr$_{OCH3}$3-5), 127.9 (*C*HAr$_{Ts}$2-6), 129.9 (*C*(1)Ar$_{OCH3}$), 130.1 (*C*HAr$_{Ts}$3-5), 130.6 (*C*HAr$_{OCH3}$2-6), 134.1 (*C*Ar$_{Ts}$SO$_2$), 143.9 (*C*Ar$_{Ts}$CH$_3$), 164.1 (*C*(4)Ar$_{OCH3}$), 172.3 (*C*O$_2$CH$_3$), 196.3 (*C*OAr$_{OCH3}$); ***m/z*** (NSI$^+$) 432 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{22}H_{26}SNO_6^+$ ([M+H]$^+$); found 432.1475, requires 432.1475 (- 0.1 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 43.7 min, $t_{r\ min}$ = 40.2 min; 220 nm, 30 °C).



<Peak Table>

PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	40.195	49.906
2	43.473	50.094
Total		100.000

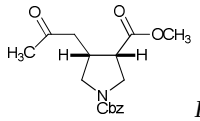


<Peak Table>

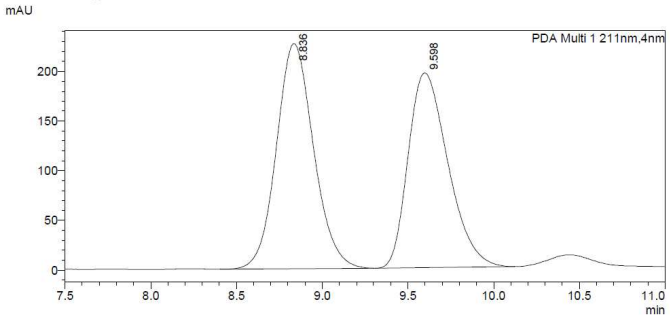
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	40.235	1.187
2	43.669	98.813
Total		100.000

(3*S*,4*R*)-1-Benzyl 3-methyl 4-(2-oxopropyl)pyrrolidine-1,3-dicarboxylate 9



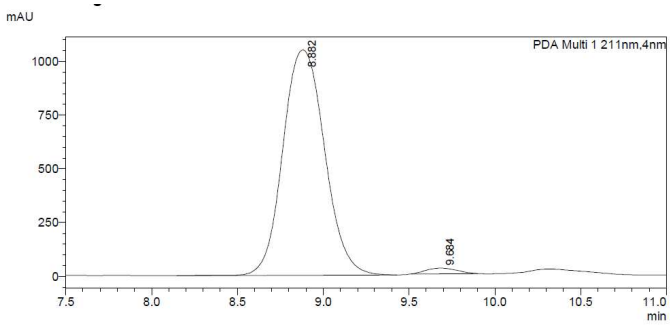
*Following general procedure **5***: ozonolysis of alkene **5** (117.2 mg, 0.44 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S7** (156 mg, 0.49 mmol), in $CHCl_3$ (100 mL). Organocatalysis with pivaloylchloride (81.2 µL, 0.66 mmol), $(i\text{-Pr})_2NEt$ (114 µL, 0.66 mmol), DCM (10 mL), (−)-tetramisole.HCl (10.5 mg, 0.044 mmol), $(i\text{-Pr})_2NEt$ (190.8 µL, 1.10 mmol), stirred 1 h at rt. Ring opening MeOH and DMAP 1 h at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column (Pet.ether : EtOAc, 90 : 10 to 70 : 30) gave *syn*-**9** as a clear oil (119 mg, 85%) in 96% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ 0 (*c* 0.3 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$ **(**film)/cm^{-1} 1701 broad (C=O), 1168 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 500MHz) mixture of rotamers 2.16, 2.17 (3H, s, $COCH_3$), 2.51-2.64 (1H, m, $CH_AH_BCOCH_3$), 2.64 (1H, td, *J* 17.8, 17.2, 7.0, $CH_AH_BCOCH_3$), 2.94-3.19 (1H, m, C(4)*H*), 3.20-3.24 (2H, m, C(3)*H*+$C(2)H_AH_B$), 3.60-3.62 (1H, m, $C(2)H_AH_B$), 3.66-3.76 (5H, m, $C(5)H_2$+$COCH_3$), 5.11-5.18 (2H, m, $PhCH_2OCO$), 7.31-7.44 (5H, m, Ar*H*); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 75MHz) 50:50 mixture of rotamers 30.6 (CH_3), 35.7, 36.5 (*C*(4)H), 43.0 (CH_2CO), 45.2, 45.9 (*C*(3)H), 47.8, 48.4 (*C*$(5)H_2$), 50.3, 50.8 (*C*$(2)H_2$), 52.3 (OCH_3), 67.3 ($ArCH_2OCO$), 128.3 (*C*HAr), 128.3 (*C*HAr), 128.4 (*C*HAr), 128.9 (2X*C*HAr), 137.1 (*C*(1)$ArCH_2OCO$), 155.0 155.1 ($ArCH_2OCO$), 172.9, 173.0 (CO_2CH_3), 206.4, 206.6 ($COCH_3$); ***m/z*** (ES^+) 342 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{17}H_{21}SNO_5Na^+$ ($[M+Na]^+$); found 342.1326, requires 342.1317 (+ 0.9 ppm); Enantiomeric excess determined by chiral HPLC (ChiralPak AD-H 30% *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 8.8 min, $t_{r\ min}$ = 9.7 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

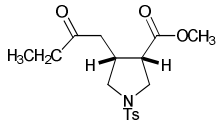
Peak#	Ret. Time	Area%
1	8.836	51.926
2	9.598	48.074
Total		100.000



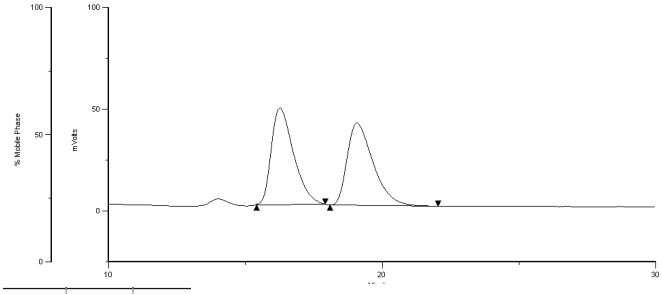
<Peak Table>
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	8.882	98.185
2	9.684	1.815
Total		100.000

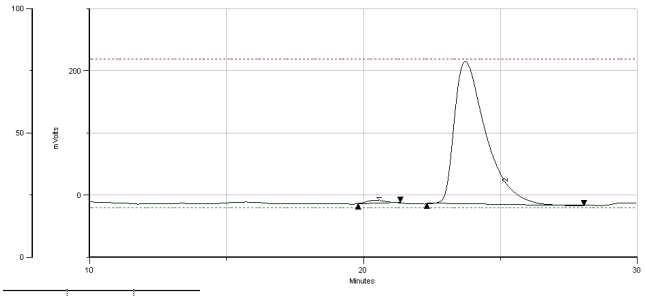
(3*S*,4*R*)-Methyl 4-(2-oxobutyl)-1-tosylpyrrolidine-3-carboxylate 22



*Following general procedure **6***: alkene **4** (100.0 mg, 0.35 mmol), Grubb's II (14.8 mg, 0.02 mmol), dry DCM (1.2 mL), ethyl vinyl ketone **S15** (148 µL, 1.76 mmol), stirred 1 h at 40 °C. Organocatalysis with pivaloylchloride (64.6 µL, 0.53 mmol), (*i*-Pr)$_2$NEt (92.3 µL, 0.53 mmol), DCM (5 mL), (−)-tetramisole.HCl (4.2 mg, 0.017 mmol), (*i*-Pr)$_2$NEt (1.78 mL, 0.88 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20) gave *syn*-**22** as a white solid (99 mg, 80%) in 97% ee; **mp** 56-58 °C; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ – 0.93 (*c* 0.8 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$ (film)/cm^{-1} 1724 (C=O ester), 1707 (C=O ketone), 1160 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 300MHz) 0.93 (3H, s, CH_2CH_3), 2.12-2.27 (3H, m, $COCH_2CH_3$+CH_AH_B), 2.32-2.40 (4H, m, $Ar_{Ts}CH_3$+CH_AH_B), 2.66-2.80 (1H, m, C(3)*H*), 2.94-3.05 (2H, m, C(2)H_AH_B+C(4)*H*), 3.42-3.49 (6H, m, C(2)H_AH_B+C(5)H_2+CO_2CH_3) 7.27 (2H, d, *J* 8.3, $Ar_{Ts}H$3-5), 7.65 (2H, d, *J* 8.3, $Ar_{Ts}H$2-6); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 75MHz) 7.67 ($COCH_2CH_3$), 21.6 ($Ar_{Ts}CH_3$), 35.9 ($COCH_2CH_3$), 36.1(*C*(3)H), 40.7 (CH_2CO), 45.5 (*C*(4)H), 48.9 (*C*(5)H_2), 51.9 (CO_2CH_3), 52.3 (*C*(2)H_2), 127.6 ($CHAr_{Ts}$2-6), 129.7 ($CHAr_{Ts}$3-5), 133.9 ($CAr_{Ts}SO_2$), 143.6 ($CAr_{Ts}CH_3$), 171.8 (CO_2CH_3), 208.7 ($COCH_2CH_3$); ***m/z*** (NSI$^+$) 354 ([M+H]$^+$, 100%); HRMS (ES$^+$) $C_{17}H_{24}SNO_5^+$ ([M+H]$^+$); found 354.1373, requires 354.1370 (+ 0.9 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 23.7 min, $t_{r\ min}$ = 20.4 min; 254 nm, 30 °C).

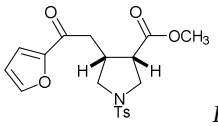


16.26	4556992.00	50.00
19.08	4556707.00	50.00



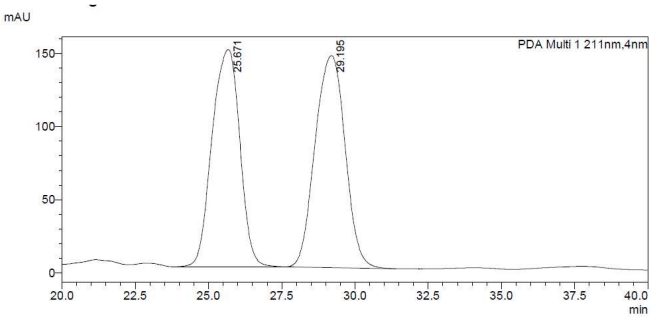
20.44	518394.91	1.63
23.72	31306228.00	98.37

(3*S*,4*R*)-1-(benzenesulfonyl)-4-[2-furan-2-yl)-2-oxoethyl] pyrrolidine-3-carboxylate 23



*Following general procedure **6***: alkene **4** (60 mg, 0.22 mmol), Grubb's II (9.3 mg, 0.11 mmol), dry DCM (1.2 mL), vinyl ketone **S6** (129 µL, 1.06 mmol), stirred at 40 °C overnight. Grubb's II (9.3 mg, 0.11 mmol), was added again and stirred for 6 h at 40 °C. Organocatalysis with pivaloylchloride (54.8 µL, 0.31 mmol), (*i*-Pr)$_2$NEt (40.6 µL, 0.31 mmol), DCM (3 mL), (−)-tetramisole.HCl (2.7 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (67.7 µL, 0.55 mmol). Quenched with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**23** as a yellow oil (54 mg, 63%) in 84% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ - 2.1 (*c* 1.2 in DCM); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1732 (C=O ester), 1672 (C=O ketone), 1154 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 2.43 (3H, s, $Ar_{Ts}CH_3$), 2.68 (1H, dd, *J* 17.6, 8.3, CH_AH_B), 2.88 (1H, dd, *J* 17.6, 6.2, CH_AH_B), 2.93-3.03 (1H, m, C(4)*H*), 3.12-3.22 (2H, m, C(2)H_AH_B+C(3)*H*), 3.56-3.62 (6H, m, CO_2CH_3+C(2)H_AH_B+C(5)H_2), 6.56 (1H, dd, *J* 3.6, 1.7, $Ar_{Furan}H4$), 7.15 (1H, dd, *J* 3.6, 0.8, $Ar_{Furan}H3$), 7.31-7.36 (2H, m, $Ar_{Ts}H3$-5), 7.58 (1H, dd, *J* 1.7, 0.8, $Ar_{Furan}H5$), 7.74 (2H, d, *J* 8.2, $Ar_{Ts}H2$-6). $\boldsymbol{\delta_C}$ ($CDCl_3$, 125MHz) 21.5 ($Ar_{Ts}CH_3$), 35.8 (*C*(4)H), 36.9 (CH_2CO), 45.6 (*C*(3)H), 48.9 (*C*(5)H_2), 51.9 (CO_2CH_3), 52.2 (*C*(2)H_2), 112.4 ($CHAr_{furan}4$), 117.2 ($CHAr_{furan}3$), 127.5 ($CHAr_{Ts}2$-6), 129.8 ($CHAr_{Ts}3$-5), 133.7 ($CAr_{Ts}SO_2$), 143.6 ($CAr_{Ts}CH_3$), 146.5 ($CHAr_{furan}5$), 152.3 (*C*(2)Ar_{furan}), 171.7 (CO_2CH_3), 186.5 ($COAr_{Furan}$); ***m/z*** (NSI$^+$) 392 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{19}H_{22}SNO_6^+$

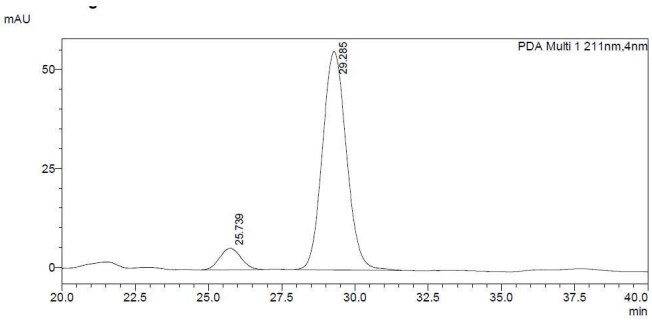
([M+H]$^+$); found 392.1162, requires 392.1162 (- 0.1 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak AD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 29.3 min, $t_{r\ min}$ = 25.7 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	25.671	48.595
2	29.195	51.405
Total		100.000



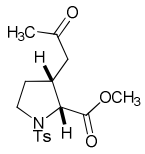
<Peak Table>

PDA Ch1 211nm

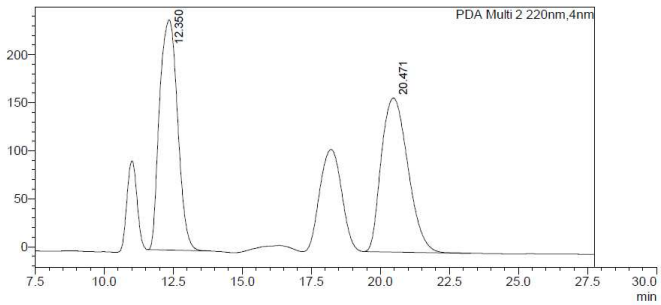
Peak#	Ret. Time	Area%
1	25.739	7.913
2	29.285	92.087
Total		100.000

8) Characterisation of 2,3 substituted pyrrolidine derivatives 11-21

(2*R*,3*R*)-Methyl 3-(2-oxopropyl)-1-tosylpyrrolidine-2-carboxylate 11



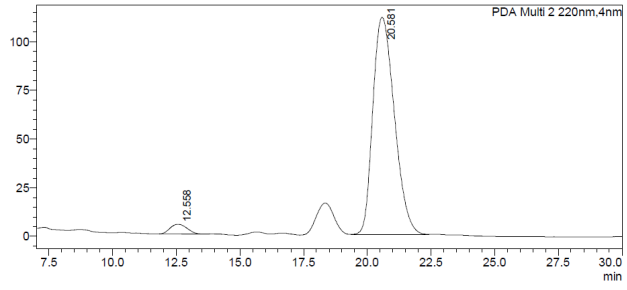
*Following general procedure **5***: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S7** (98.6 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30 to 60 : 40) gave *syn*-**11** as a clear oil (67 mg, 70%) in 93% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 38.4 (*c* 0.8 in $CHCl_3$); $\boldsymbol{\nu}_{\mathbf{max}}$ (film)/cm^{-1} 1747 (C=O ester), 1714 (C=O ketone), 1340 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 300 MHz) 1.64-1.74 (1H, m, C(4)H_AH_B), 1.89-1.92 (1H, m, C(4)H_AH_B), 2.04 (3H, s, COCH_3), 2.24-2.31 (1H, m, CH_AH_B), 2.37 (3H, s, Ar$_{Ts}$CH_3), 2.40-2.51 (2H, m, C(3)H+CH_AH_B), 3.13 (1H, ddd, *J* 10.1, 9.2, 6.7, C(5)H_AH_B), 3.53-3.59 (1H, m, C(5)H_AH_B), 3.64 (3H, s, CO$_2$CH_3), 4.27 (1H, d, *J* 8.1, C(2)H), 7.25 (2H, d, *J* 8.0, Ar$_{Ts}$$H$3-5), 7.65 (2H, d, *J* 8.0, Ar$_{Ts}$$H$2-6); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 75MHz) 21.9 (Ar$_{Ts}$$CH_3$), 30.2 ($C$(4)H$_2$), 30.5 (CO$CH_3$), 37.9 ($C$(3)H), 43.7 ($CH_2$CO), 47.7 ($C$(5)H$_2$), 52.5 (CO$_2$$CH_3$), 62.8 ($C$(2)H), 127.7 ($CHAr_{Ts}$2-6), 130.1 ($C$HAr3-5), 135.3 ($CAr_{Ts}SO_2$), 144.1 ($CAr_{Ts}CH_3$), 171.6 ($CO_2CH_3$), 206.0 ($COCH_3$); ***m/z*** (ES$^+$) 362 ([M+Na]$^+$, 100%); HRMS (ES$^+$) $C_{16}H_{21}SNO_5Na^+$ ([M+Na]$^+$); found 362.1030, requires 362.1030; Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 20.6 min, $t_{r\ min}$ = 12.6 min; 220 nm, 30 °C).



<Peak Table>

PDA Ch2 220nm

Peak#	Ret. Time	Name	Area%
1	12.350		50.294
2	20.471		49.706
Total			100.000



<Peak Table>
PDA Ch2 220nm

Peak#	Ret. Time	Name	Area%
1	12.558		3.367
2	20.581		96.633
Total			100.000

Preparative scale wittig/organocatalysis route

Following general procedure 5: ozonolysis of alkene **10** (1.00 g, 3.50 mmol), dry DCM (250 mL). Wittig reaction with phosphorane **S7** (1.20 g, 3.85 mmol), in $CHCl_3$ (150 mL). Organocatalysis with pivaloylchloride (0.64 mL, 5.25 mmol), (*i*-Pr)$_2$NEt (0.91 mL, 5.25 mmol), DCM (30 mL), (−)-tetramisole.HCl (8.4 mg, 0.035 mmol), (*i*-Pr)$_2$NEt (1.50 mL, 8.75 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30 to 60 : 40) gave *syn*-**11** as a clear oil (772 mg, 65%) in 93% ee.

Catalyst loading screen

Catalsyt stock solution: (−)-tetramisole (63.0 mg) was disolved in DCM (10 mL) to prepare a solution (0.053 M) of the free based catalyst.

1 mol % procedure

Following general procedure **5**: ozonolysis of alkene **10** (150 mg, 0.53 mmol), dry DCM (180 mL). Wittig reaction with phosphorane **S7** (184 mg, 0.58 mmol), in $CHCl_3$ (100 mL). Organocatalysis with pivaloylchloride (98 µL, 0.80 mmol), (*i*-Pr)$_2$NEt (138 µL, 0.79 mmol), DCM (18 mL), (−)-tetramisole.HCl (2 mL of the stock solution, 0.0053 mmol), (*i*-Pr)$_2$NEt (92.3 µL, 0.53 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30 to 60 : 40) gave *syn*-**11** as a clear oil (90 mg, 50%) in 93% ee.

0.1 mol % procedure

Following general procedure **5**: ozonolysis of alkene **10** (150 mg, 0.53 mmol), dry DCM (180 mL). Wittig reaction with phosphorane **S7** (184.5 mg, 0.58 mmol), in $CHCl_3$ (100 mL). Organocatalysis with pivaloylchloride (98.0 µL, 0.80 mmol), (*i*-Pr)$_2$NEt (138 µL, 0.79 mmol), DCM (18 mL), (−)-tetramisole.HCl (0.2 mL of the stock solution, 0.00053 mmol), (*i*-Pr)$_2$NEt (92.3 µL, 0.53 mmol) rt for 12 h. Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1

$dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30 to 60 : 40) gave *syn*-**11** as a clear oil (53 mg, 30%) in 92% ee.

Metathesis/organocatalysis route

*Following general procedure **6**:* Alkene **10** (60.0 mg, 0.22 mmol), Grubb's II (8.9 mg, 0.01 mmol), dry DCM (0.72 mL), methyl vinyl ketone **S14** (91.8 µL, 1.10 mmol), stirred 2 h at 40 °C. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), $(i\text{-Pr})_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), $(i\text{-Pr})_2$NEt (95.8 µL, 0.55 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**11** as a clear oil (56 mg, 75%) in 97% ee.

Catalyst loading screen

Catalsyt stock solution: (−)-tetramisole (63.0 mg) was disolved in DCM (10 mL) to prepare a solution (0.053 M) of the free basedcatalyst.

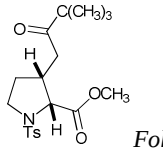
1 mol% procedure

*Following general procedure **6**:* alkene**10** (150 mg, 0.53 mmol), Grubb's II (4.5 mg, 0.01 mmol), dry DCM (1.85 mL), methyl vinyl ketone **S14** (220 µL, 2.65 mmol), stirred 4 h at 40 °C. Organocatalysis with pivaloylchloride (98.0 µL, 0.80 mmol), $(i\text{-Pr})_2$NEt (138.5 µL, 0.79 mmol), DCM (6 mL), (−)-tetramisole.HCl (2 mL of the stock solution, 0.0053 mmol), $(i\text{-Pr})_2$NEt (92.3 µL, 0.53 mmol) 1 h at rt. Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**11** as a clear oil (134 mg, 75%) in 97% ee.

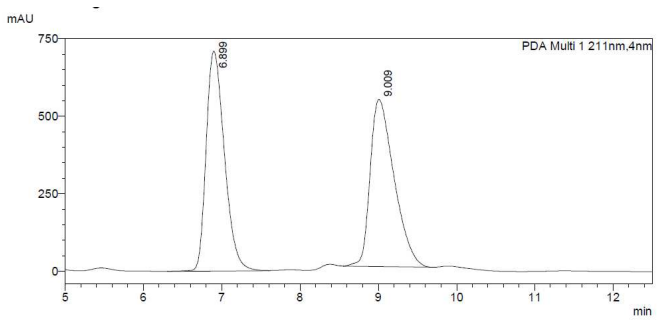
0.1 mol% procedure

*Following general procedure **6**:* alkene **10** (150 mg, 0.53 mmol), Grubb's II (4.5 mg, 0.01 mmol), dry DCM (1.85 mL), methyl vinyl ketone **S14** (220.1 µL, 2.65 mmol), stirred 4 h at 40 °C. Organocatalysis with pivaloylchloride (98.0 µL, 0.80 mmol), $(i\text{-Pr})_2$NEt (138 µL, 0.79 mmol), DCM (6 mL), (−)-tetramisole.HCl (0.2 mL of the stock solution, 0.00053 mmol), $(i\text{-Pr})_2$NEt (92.3 µL, 0.53 mmol) 1 h at rt. Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**11** as a clear oil (131 mg, 73%) in 98% ee.

(2*R*,3*R*)-Methyl 3-(3,3-dimethyl-2-oxobutyl)-1-tosylpyrrolidine-2-carboxylate 12



*Following general procedure **5***: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S13** (112 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 90 : 10 to 80 : 20) gave *syn*-**12** as an oil (66 mg, 61%) in 98% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 49.6 (*c* 0.7 in DCM); $\boldsymbol{\nu_{max}}$ (film)/cm$^{-1:}$ 1739 (C=O ester), 1705 (C=O ketone), 1344 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.02 (9H, s, C(CH_3)$_3$), 1.66-1.75 (1H, m, C(4)H_AH_B), 1.86-1.92 (1H, m, C(4)H_AH_B), 2.36 (3H, s, $Ar_{Ts}CH_3$), 2.36-2.43 (3H, m, C(3)*H*+CH_2), 3.10 (1H, td, *J* 9.7, 6.6, C(5)H_AH_B,), 3.58 (1H, m, C(5)H_AH_B), 3.62 (3H, s, CO_2CH_3), 4.32 (1H, d, *J* 8.0, C(2)*H*), 7.26 (2H, d, *J* 8.0, $Ar_{Ts}H$3-5), 7.78 (2H, d, *J* 8.0, $Ar_{Ts}H$2-6); $\boldsymbol{\delta_c}$ ($CDCl_3$, 125MHz) 21.6 ($Ar_{Ts}CH_3$), 26.5 (C(CH_3)$_3$), 29.8 (*C*(4)H_2), 36.6 (CH_2CO), 37.6 (*C*(3)H), 43.9 (*C*(CH_3)$_3$), 47.8 (*C*(5)H_2), 52.1 (CO_2CH_3), 62.5 (*C*(2)H), 127.3 ($CHAr_{Ts}$2-6), 129.7 ($CHAr_{Ts}$3-5), 134.5 ($CAr_{Ts}SO_2$), 143.6 ($CAr_{Ts}CH_3$), 171.3 (CO_2CH_3), 213.3 (*C*O); ***m/z*** (ES$^+$) 382 ([M+H]$^+$, 100%); HRMS (ES$^+$) $C_{19}H_{28}SNO_5^+$ ([M+H]$^+$); found 382.1686, requires 382.1683 (+ 0.9 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 8.97 min, $t_{r\ min}$ = 6.95 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

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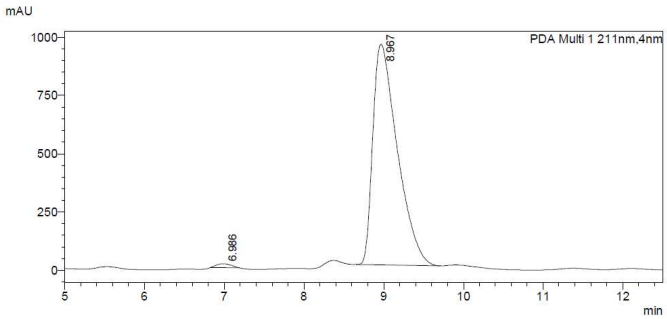
2	9.009	49.954
Total		100.000

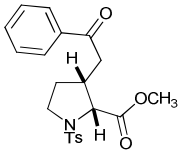


<Peak Table>

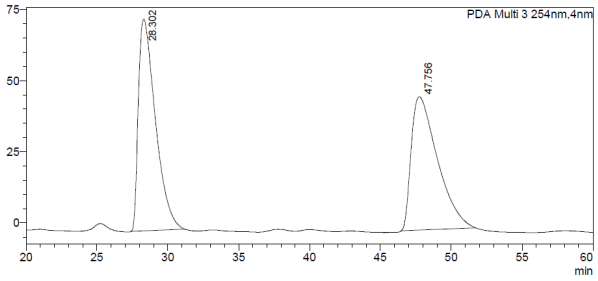
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	6.986	1.056
2	8.967	98.944
Total		100.000

(2*R*,3*R*)-Methyl-3-(2-oxo-2-phenylethyl)-1-tosylpyrrolidine-2-carboxylate 13



*Following general procedure **5***: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S10** (117 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (0.73 mL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column (Pet.ether : EtOAc, 80 : 20 to 70 : 30) gave *syn*-**13** as a clear oil (72 mg, 61%) in 93% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ + 55.5 (*c* 0.5 in $CHCl_3$); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1743 (C=O ester), 1683 (C=O ketone), 1340 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 1.81 (1H, tdd, *J* 12.0, 10.4, 8.3, C(4)H_AH_B), 2.00-2.06 (1H, m, C(4)H_AH_B), 2.05 (3H, s, $Ar_{Ts}CH_3$), 2.68-2.74 (1H, m, C(3)*H*), 2.79 (1H, dd, ABX system, J_{AB} 17.6, J_{AX} 6.7, CH_AH$_B$), 2.99 (1H, dd, ABX system, J_{BA} 17.6, J_{BX} 7.2, CH$_A$$H_B$), 3.17 (1H, ddd, *J* 10.2, 9.1, 6.6, C(5)H_AH_B), 3.49 (3H, s, CO_2CH_3), 3.61 (1H, td, *J* 8.6, 1.2, C(5)H$_A$$H_B$), 4.41 (1H, d, *J* 8.3, C(2)*H*), 7.26 (2H, d, *J* 7.9, $Ar_{Ts}H$2-6), 7.38 (2H, t, *J* 7.6, Ar*H*3-5), 7.50 (1H, m, Ar*H*4), 7.66-7.70 (2H, d, *J* 8.6, $Ar_{Ts}H$3-5), 7.81 (2H, d, *J* 8.6, Ar*H*2-6); $\boldsymbol{\delta_c}$ ($CDCl_3$, 75MHz) 21.6 ($Ar_{Ts}CH_3$), 30.0 (*C*(4)H$_2$), 37.9 (*C*(3)H), 38.6 (*C*H$_2$CO), 47.4 (*C*(5)H$_2$), 52.0 (CO_2CH_3), 62.6 (*C*(2)H), 127.4 (*C*HAr_{Ts}2-6), 127.9 (*C*HAr2-6), 128.8 (*C*HAr3-5), 129.8 (*C*HAr_{Ts}3-5), 129.8 (*C*HAr4), 133.5 (*C*(1)Ar), 136.5 (*C*$Ar_{Ts}SO_2$), 143.7 (*C*$Ar_{Ts}CH_3$), 171.3 (*C*O_2CH_3), 197.2 (*C*OAr); ***m/z*** (ES$^+$) 402 ([M+H]$^+$, 100%); HRMS (ES+) $C_{21}H_{24}SNO_5^+$ ([M+H]$^+$); found 402.1372, requires 402.1370 (+ 0.6 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 10 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 46.9 min, $t_{r\ min}$ = 29.0 min; 254 nm, 30 °C).



<Peak Table>
PDA Ch3 254nm

Peak#	Ret. Time	Name	Area%
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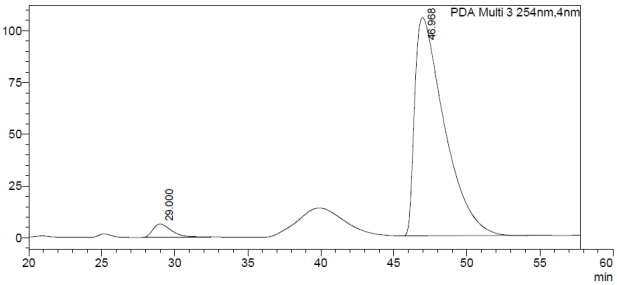
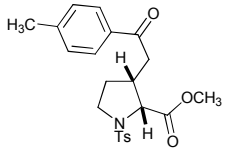
2	47.756	RT:47.756	49.251
Total			100.000



<Peak Table>
PDA Ch3 254nm

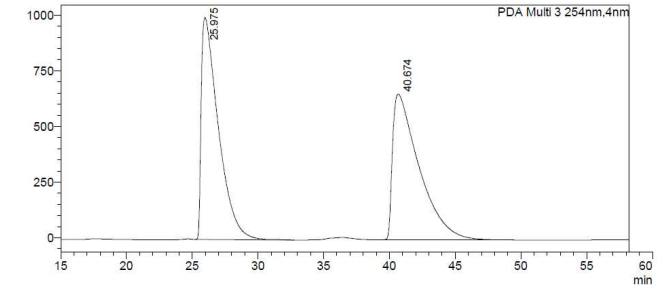
Peak#	Ret. Time	Name	Area%
1	29.000	RT:29.000	3.641
2	46.968	RT:46.968	96.359
Total			100.000

(2*R*,3*R*)-Methyl-3-(2-oxo-2-(9-tolyl)ethyl))-1-tosylpyrrolidine-2-carboxylate 14



*Following general procedure **5***: ozonolysis of alkene **10** (150 mg, 0.53 mmol), dry DCM (180 mL). Wittig reaction with phosphorane **S9** (230 mg, 0.58 mmol), in $CHCl_3$ (100 mL). Organocatalysis with pivaloylchloride (98.0 µL, 0.80 mmol), (*i*-Pr)$_2$NEt (0.23 mL, 1.32 mmol), DCM (18 mL), (−)-tetramisole.HCl (6.4 mg, 0.027 mmol), (*i*-Pr)$_2$NEt (0.23 mL, 1.32 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30 to 60 : 40) gave *syn*-**14** as a clear oil (135 mg, 64%) in 91% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 56.7 (*c* 0.5 in $CHCl_3$); $\boldsymbol{\nu}_{\mathbf{max}}$ (film)/cm^{-1} 1737 (C=O ester), 1681 (C=O ketone), 1342 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 300MHz) 1.80 (1H, tdd, *J* 12.1, 10.3, 8.1, C(4)H_AH_B), 1.97-2.05 (1H, m, C(4)H_AH_B), 2.33 (3H, s, $Ar_{CH3}CH_3$), 2.36 (3H, s, $Ar_{Ts}CH_3$), 2.64-2.80 (2H, m, C(3)*H*+CH_AH_B), 3.02 (1H, dd, *J* 17.7, 6.9, CH_AH_B), 3.15 (1H, ddd, *J* 10.2, 9.1, 6.6, C(5)H_AH_B), 3.49 (3H, s, CO_2CH_3), 3.61 (1H, m, C(5)H_AH_B), 4.40 (1H, d, *J* 8.3, C(2)*H*), 7.17 (2H, d, *J* 8.0, $Ar_{CH3}H$3-5), 7.26 (2H, d, *J* 7.8, $Ar_{Ts}H$3-5), 7.72-7.79 (4H, m, $Ar_{CH3}H$2-6+$Ar_{Ts}H$2-6); $\boldsymbol{\delta}_{\mathbf{c}}$ ($CDCl_3$, 75MHz) 21.9

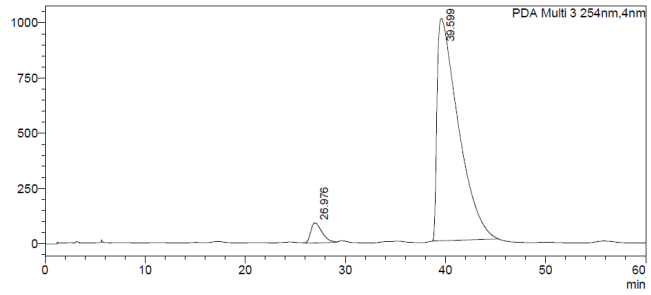
($Ar_{CH3}CH_3$), 22.1 ($Ar_{Ts}CH_3$), 30.4 (*C*(4)H_2), 38.4 (*C*(3)H), 38.8 (CH_2CO), 47.8 (*C*(5)H_2), 52.4 (CO_2CH_3), 63.0 (*C*(2)H), 127.7 (*C*HAr_{Ts}2-6), 128.3 (*C*HAr_{CH3}2-6), 129.8 (*C*HAr_{CH3}3-5), 130.1 (*C*HAr_{Ts}3-5), 134.4 (*C*(1)Ar_{CH3}) 135.3 (*C*$Ar_{Ts}SO_2$), 144.1 (*C*$Ar_{Ts}CH_3$), 144.8 (*C*(4)$Ar_{CH3}CH_3$), 171.4 (CO_2CH_3), 197.3 (*CO*Ar); ***m/z*** (ES^+) 416 ($[M+H]^+$, 100%); HRMS (ES+) $C_{22}H_{26}SNO_5^+$ ($[M+H]^+$); found 416.1527, requires 416.1526 (+ 0.2 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 10 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 39.6 min, $t_{r\ min}$ = 26.9 min; 254 nm, 30 °C).



<Peak Table>

PDA Ch3 254nm

Peak#	Ret. Time	Name	Area%
1	25.975		49.563
2	40.674		50.437
Total			100.000

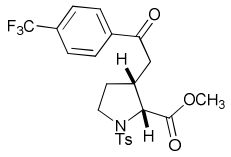


<Peak Table>

PDA Ch3 254nm

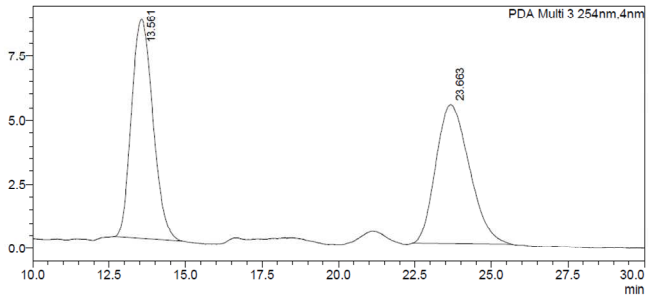
Peak#	Ret. Time	Name	Area%
1	26.976	RT:26.976	4.572
2	39.599	RT:39.599	95.428
Total			100.000

(2*R*,3*R*)-Methyl 3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-1-tosylpyrrolidine-2-carboxylate 15



Following general procedure 5: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S12** (138 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122.0 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$;

Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**15** as a white solid (100 mg, 76%) in 93% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 50.9 (*c* 0.5 in $CHCl_3$); **mp** 136 °C; $\boldsymbol{\nu}_{\mathbf{max}}$ (KBr)/cm^{-1} 1749 (C=O ester), 1693 (C=O ketone), 1321 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 500MHz) 1.85-1.92 (1H, m, C(4)H_AH_B), 2.09-2.14 (1H, m, C(4)H_AH_B), 2.44 (3H, s, $Ar_{Ts}CH_3$), 2.75-2.84 (1H, m, C(3)*H*), 2.91 (1H, dd, ABX system, J_{AB} 18.1, J_{AX} 6.4, CH_AH$_B$), 3.09 (1H, dd, ABX system, J_{BA} 18.1, J_{BX} 7.7, CH$_A$$H_B$), 3.27 (1H, td, *J* 9.6, 6.7, C(5)H_AH$_B$), 3.58 (3H, s, CO_2CH_3), 3.67-3.71 (1H, m, C(5)H$_A$$H_B$), 4.52 (1H, d, *J* 8.5, C(2)*H*), 7.36 (2H, d, *J* 8.3, $Ar_{Ts}H3$-5), 7.73-7.77 (4H, m, $Ar_{Ts}H2$-6+$Ar_{CF3}H3$-5), 7.99 (2H, d, *J* 8.1, $Ar_{CF3}H2$-6); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 125MHz) 21.6 ($Ar_{Ts}CH_3$), 29.9 (*C*(4)H_2), 37.7 (*C*(3)H), 38.9 (*C*H_2CO), 47.2 (*C*(5)H_2), 52.1 (CO_2CH_3), 62.4 (*C*(2)H), 123.0 (q, *J* 272.7, *C*F_3), 124.6 (q, *J* 33.0 *C*(4)$Ar_{CF3}CF_3$), 125.7 (*C*HAr_{CF3}3), 125.8 (*C*HAr_{CF3}5), 127.4 (*C*HAr_{Ts}2-6), 128.2 (*C*HAr_{CF3}2-6), 129.8 (*C*HAr_{Ts}3-5), 134.9 (*C*$Ar_{Ts}SO_2$), 139.0 (*C*(1)Ar_{CF3}), 143.7 (*C*$Ar_{Ts}CH_3$), 171.2 (*C*O_2CH_3), 196.3 (*C*OAr); ***m/z*** (ES^+) 470 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{22}H_{23}F_3SNO_5^+$ ($[M+H]^+$); found 470.1240, requires 470.1244 (- 0.8 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 15 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 23.4 min, $t_{r\ min}$ = 13.6 min, 254 nm, 30 °C).



<Peak Table>

PDA Ch3 254nm

Peak#	Ret. Time	Area%
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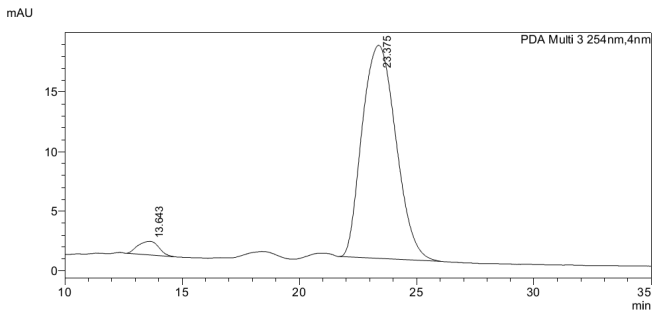
2	23.663	49.656
Total		100.000

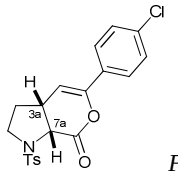


<Peak Table>

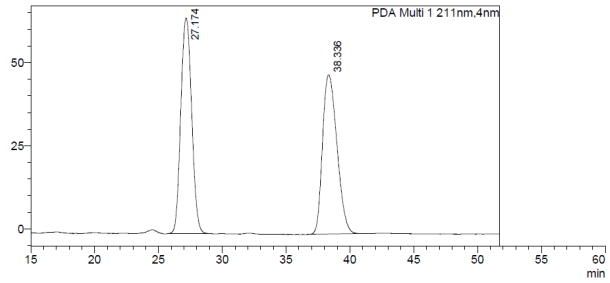
PDA Ch3 254nm

Peak#	Ret. Time	Area%
1	13.643	3.746
2	23.375	96.254
Total		100.000

(3a*R*,7a*R*)-5-(4-Chlorophenyl)-1-tosyl-1,3,3a,7a-tetrahydropyrano[3,4-b]pyrrol-7(2H)-one S17



*Following general procedure **5** without addition of nucleophile*: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S8** (128 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), $(i\text{-Pr})_2NEt$ (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), $(i\text{-Pr})_2NEt$ (122 µL, 0.70 mmol). Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 70 : 30) gave *syn*-**S17** as a white solid (50 mg, 45%) in 93% ee; **mp** 180 °C; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 70.0 (*c* 0.1 in $CHCl_3$); $\boldsymbol{\nu_{max}}$ (KBr)/cm^{-1} 1770 (C=O) 1342 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.73-1.82 (1H, m, C(3)H_AH_B), 2.27 (1H, dtd, *J* 12.8, 6.5, 3.1, C(3)H_AH_B), 2.47 (3H, s, $Ar_{Ts}CH_3$), 3.02 (1H, ddt, *J* 10.6, 8.2, 5.6, C(3a)*H*), 3.41-3.50 (2H, m, C(2)H_2), 4.66 (1H, d, *J* 8.2, C(7a)*H*), 5.67 (1H, d, *J* 5.6, C(4)*H*), 7.36 (4H, app d, $Ar_{Ts}H3$-5+$Ar_{Cl}H3$-5), 7.53 (2H, d, *J* 8.6, $Ar_{Cl}H2$-6), 7.91 (2H, d, *J* 8.2, $Ar_{Ts}H2$-6); $\boldsymbol{\delta_c}$ ($CDCl_3$, 125MHz) 21.6 ($Ar_{Ts}CH_3$), 31.9 (*C*(3)H_2), 37.9 (*C*(3a)H), 46.6 (*C*(2)H_2), 58.3 (*C*(7a)H), 99.3 (*C*(4)H), 126.1 (*C*HAr_{Cl}2-6), 127.9 (*C*HAr_{Ts}2-6), 128.8 (*C*HAr_{Cl}3-5), 129.7 (*C*HAr_{Ts}3-5), 130.1 (*C*(1)Ar_{Cl}), 135.4 (*C*$Ar_{Ts}SO_2$+*C*(4)Ar_{Cl}Cl), 143.9 (*C*$Ar_{Ts}CH_3$), 149.2 (*C*(5)-Ar_{Cl}), 165.9 (*C*O); ***m/z*** (ES^+) 404 ($[M+H]^+$, 100%), HRMS (ES^+) $C_{20}H_{19}SNO_4Cl^+$ ($[M+H]^+$); found 404.0716, requires 404.0718 (- 0.5 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak AD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 27.1 min, $t_{r\ min}$ = 38.6 min; 220 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Name	Area%
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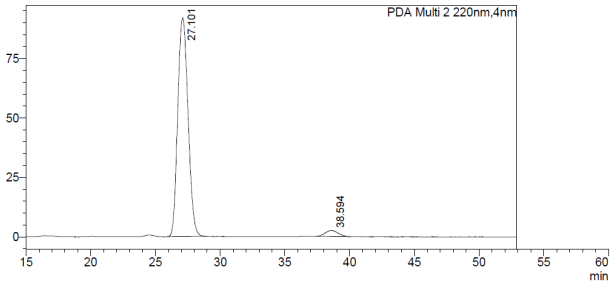
Total			100.000

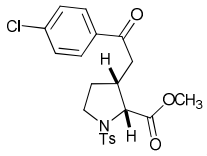


<Peak Table>

PDA Ch2 220nm

Peak#	Ret. Time	Name	Area%
1	27.101		96.679
2	38.594		3.321
Total			100.000

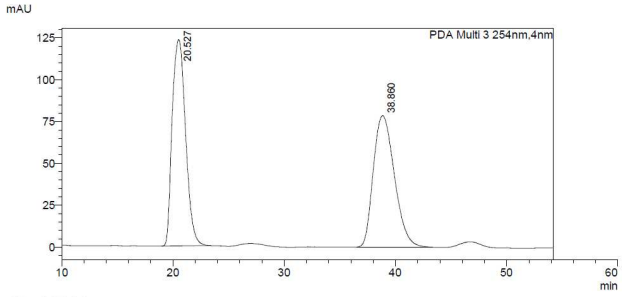
(2*R*,3*R*)-Methyl 3-(2-(4-chlorophenyl)-2-oxoethyl)-1-tosylpyrrolidine-2-carboxylate 16



Following general procedure ***5***: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S8** (129 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), $(i\text{-Pr})_2NEt$ (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), $(i\text{-Pr})_2NEt$ (122 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 60 : 40) gave *syn*-**16** as a clear oil (95 mg, 78%) in 94% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ + 31.7 (*c* 0.5 in DCM); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1749 (C=O ester), 1685 (C=O ketone); 1340 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.89 (1H, tdd, *J* 12.1, 10.2, 8.3, C(4)H_AH_B), 2.07-2.15 (1H, m, C(4)H_AH_B), 2.46 (3H, s, $Ar_{Ts}CH_3$), 2.73-2.82 (1H, m, C(3)*H*), 2.86 (1H, dd, ABX system, J_{AB} 17.8, J_{AX} 6.6, CH_AH_B), 3.04 (1H, dd ABX system, J_{BA} 17.8, J_{BX} 7.4, CH_AH_B), 3.23-3.31 (1H, m, C(5)H_AH_B,), 3.60 (3H, s, CO_2CH_3), 3.67-3.73 (1H, m, C(5)H_AH_B), 4.50 (1H, d, *J* 8.3, C(2)*H*), 7.36 (2H, d, *J* 8.0, $Ar_{Ts}H$3-5), 7.46 (2H, d, *J* 8.6, $Ar_{Cl}H$3-5), 7.78 (2H, d, *J* 8.0, $Ar_{Ts}H$2-6), 7.84 (2H, d, *J* 8.6, $Ar_{Cl}H$2-6); $\boldsymbol{\delta_c}$ ($CDCl_3$, 125MHz) 21.6 ($Ar_{Ts}CH_3$), 29.9 (*C*(4)H_2), 37.9 (*C*(3)H), 38.6 (*C*H_2CO), 47.3 (*C*(5)H_2), 52.1 (CO_2CH_3), 62.5 (*C*(2)H), 127.4 (*C*HAr_{Ts}2-6), 128.9 (*C*HAr_{Cl}3-5), 129.1 (*C*HAr_{Cl}2-6), 129.2 (*C*HAr_{Ts}3-5), 129.7 (*C*(4)Ar_{Cl}Cl), 129.8 (*C*$Ar_{Ts}CH_3$), 134.7 (*C*(1)Ar_{Cl}), 139.9 (*C*$Ar_{Ts}SO_2$), 171.2 (CO_2CH_3), 195.9 (*C*OAr); ***m/z*** (ES^+) 436 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{21}H_{23}SNO_5Cl^+$ ($[M+H]^+$); found 436.0981, requires 436.0980 (+ 0.2 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 10 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 36.1 min, $t_{r\ min}$ = 20.0; 211 nm, 30 °C).

Mis en forme : Non Exposant/ Indice

Supprimé: Cl



<Peak Table>
PDA Ch3 254nm

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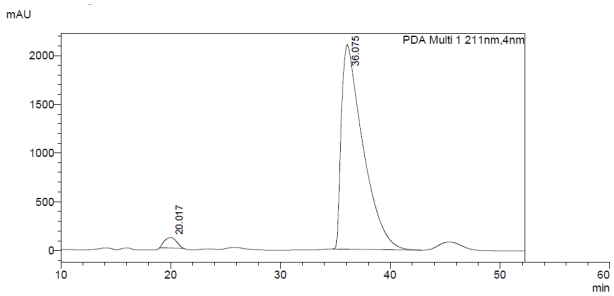
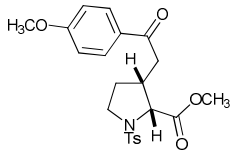


<Peak Table>
PDA Ch1 211nm

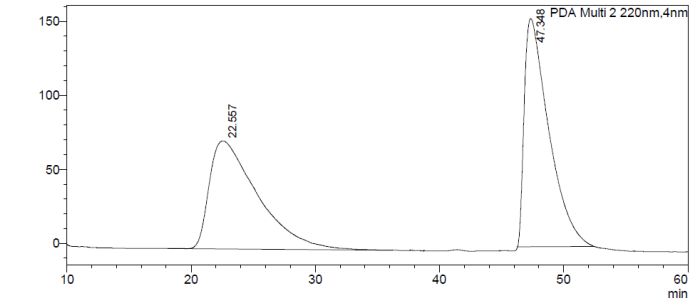
Peak#	Ret. Time	Area%
1	20.017	2.832
2	36.075	97.168
Total		100.000

(2*R*,3*R*)-Methyl 3-(2-(4-methoxyphenyl)-2-oxoethyl)-1-tosylpyrrolidine-2-carboxylate 17



*Following general procedure **5***: ozonolysis of alkene **10** (80.0 mg, 0.28 mmol), dry DCM (100 mL). Wittig reaction with phosphorane **S11** (127 mg, 0.31 mmol), in $CHCl_3$ (80 mL). Organocatalysis with pivaloylchloride (51.7 µL, 0.42 mmol), (*i*-Pr)$_2$NEt (73.1 µL, 0.42 mmol), DCM (10 mL), (−)-tetramisole.HCl (3.3 mg, 0.014 mmol), (*i*-Pr)$_2$NEt (122.0 µL, 0.70 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 70 : 30) gave *syn*-**17** as a yellow oil (96 mg, 80%) in 99% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 67.0 (*c* 0.4 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$ (film)/cm^{-1} 1743 (C=O ester), 1676 (C=O ketone) 1342 (C-O), 1115 (C-O-C); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 300MHz) 1.75-1.87 (1H, m, C(4)H_AH$_B$), 1.97-2.05 (1H, m, C(4)H$_A$$H_B$), 2.37 (3H, s, Ar$_{Ts}CH_3$), 2.69-2.75 (2H, m, C(3)H+CH_AH$_B$), 2.89-2.98 (1H, m, CH$_A$$H_B$), 3.16 (1H, ddd, *J* 10.2, 9.2, 6.6, C(5)H_AH$_B$), 3.51 (3H, s, CO$_2$CH_3), 3.58-3.64 (1H, m, C(5)H$_A$$H_B$), 3.80 (3H, s, OC$H_3$), 4.39 (1H, d, *J* 8.1, C(2)H), 6.85 (2H, d, *J* 9.0, Ar$_{OCH3}$$H$3-5), 7.26 (2H, d, *J* 8.0, Ar$_{Ts}$$H$3-5), 7.68 (2H, d, *J* 8.0, Ar$_{Ts}$$H$2-6), 7.79 (2H, d, *J* 9.0, Ar$_{OCH3}$$H$2-6); $\boldsymbol{\delta}_{\mathbf{c}}$ ($CDCl_3$, 75MHz) 21.9 (Ar$_{Ts}$$CH_3$), 30.4 ($C$(4)H$_2$), 38.5 ($C$(3)H), 38.6 ($CH_2$CO), 47.8 ($C$(5)H$_2$), 52.4 (O$CH_3$), 55.9

(OCH_3), 63.0 (*C*(2)H), 114.3 ($CHAr_{OCH3}$3-5), 127.8 ($CHAr_{Ts}$2-6), 130.0 (C(1)Ar_{OCH3}), 130.2 ($CHAr_{Ts}$3-5), 130.5 ($CHAr_{OCH3}$2-6), 135.3 ($CAr_{Ts}SO_2$), 144.1 ($CAr_{Ts}CH_3$), 164.1 (C(4)$Ar_{OCH3}OCH_3$) 171.7 (CO_2CH_3), 196.1 (*C*OAr); ***m/z*** (ES^+) 432 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{22}H_{26}SNO_6^+$ ($[M+H]^+$); found 432.1476, requires 432.1475 (+ 0.2 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 16.1 min, $t_{r\ min}$ = 49.9 min; 220 nm, 30 °C).



<Peak Table>

PDA Ch2 220nm

Peak#	Ret. Time	Area%
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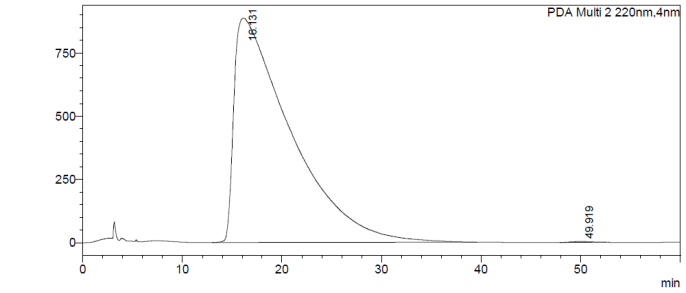
2	47.348	51.807
Total		100.000

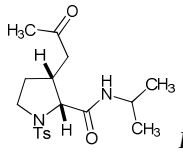


<Peak Table>

PDA Ch2 220nm

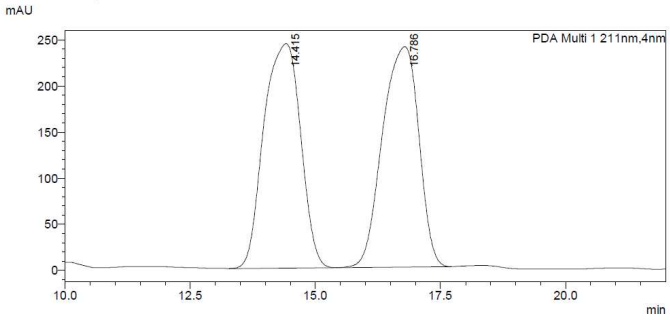
Peak#	Ret. Time	Area%
1	16.131	99.856
2	49.919	0.144
Total		100.000

(2*R*,3*R*)-*N*-Isopropyl-3-(2-oxopropyl)-1-tosylpyrrolidine-2-carboxamide 18



*Following general procedure **5**:* alkene **10** (60.0 mg, 0.22 mmol), Grubb's II (8.9 mg, 0.01 mmol), dry DCM (0.72 mL), methyl vinyl ketone **S14** (88.3 µL, 1.06 mmol), stirred 1 h at 40 °C. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (i-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM(6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (i-Pr)$_2$NEt (95.8 µL, 0.55 mmol). The mixture was evaporated *in vacuo* and the residue was disolved in DMF (3 mL) and isopropylamine (37.5 µL, 0.44 mmol) was added. The reaction was stirred at 50 °C for 2 h and then quenched with

0.1M HCl and extracted with EtOAc (x3). The combined organic phases were washed with H_2O (x4), brine (x2), dried ($MgSO_4$) and concentrated *in vacuo*. Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (DCM : MeOH, 99.9 : 0.1 to 99.5 : 0.5) gave *syn*-**18** as an oil (55 mg, 68%) in 92% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 94.6 (*c* 0.5 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm^{-1} 3365 (N-H), 1714 (C=O), 1653 (N-C=O amide), 1259 (C-N); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300 MHz) 1.12 (6H, app t, *J* 6.4, $CH(CH_3)_2$), 1.38-1.53 (1H, m, C(4)H_AH_B), 1.80-1.88 (1H, m, C(4)H_AH_B), 2.05 (3H, s, $COCH_3$), 2.11-2.27 (2H, m, C(3)*H*+CH_AH_B), 2.38 (3H, s, $Ar_{Ts}CH_3$), 2.74 (1H, m, CH_AH_B), 2.98 (1H, ddd, *J* 11.2, 9.5, 6.2, C(5)H_AH_B), 3.56 (1H, ddd, *J* 9.5, 7.5, 1.2, C(5)H_AH_B), 3.94-4.04 (2H, m, C(2)*H*+$CH(CH_3)_2$), 6.38 (1H, d, *J* 8.2, N*H*), 7.29 (2H, d, *J* 8.3, $Ar_{Ts}H3$-5), 7.67 (2H, d, *J* 8.3, $Ar_{Ts}H2$-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 75MHz) 22.0 ($Ar_{Ts}CH_3$), 22.8 ($CH_{isopropyl}(CH_3)$), 23.4 ($CH_{isopropyl}(CH_3)$), 30.2 (*C*(4)H_2), 30.6 ($COCH_3$), 37.6 (*C*(3)H), 41.9 ($CH(CH_3)_2$), 43.6 (CH_2CO), 48.6 (*C*(5)H_2), 63.5 (*C*(2)H), 128.3 ($CHAr_{Ts}$2-6), 130.4 ($CHAr_{Ts}$3-5), 132.9 ($CAr_{Ts}SO_2$), 144.8 ($CAr_{Ts}CH_3$), 168.9 (*C*ONH), 207.4 ($COCH_3$); ***m/z*** (NSI^+) 367 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{18}H_{27}SN_2O_4^+$ ($[M+H]^+$); found 367.1692, requires 367.1686 (+1.6 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 15 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 16.9 min, $t_{r\ min}$ = 14.3 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
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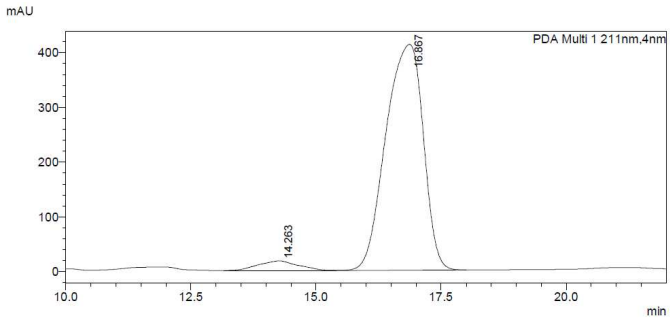
2	16.786	49.257
Total		100.000

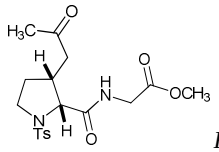


<Peak Table>

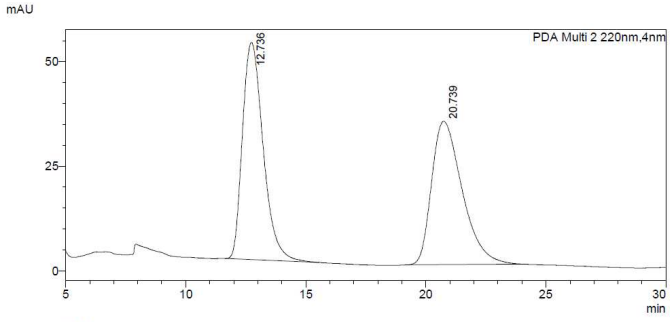
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.263	4.282
2	16.867	95.718
Total		100.000

Methyl 2-[(2*R*,3*R*)-3-(2-oxopropyl)-1-tosylpyrrolidine-2-carboxamido]acetate 19



*Following general procedure **6:*** alkene **10** (60.0 mg, 0.22 mmol), Grubb's II (8.9 mg, 0.01 mmol), dry DCM (0.72 mL), methyl vinyl ketone **S14** (88.3 µL, 1.06 mmol), stirred 2 h at 40 °C. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (*i*-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (95.8 µL, 0.55 mmol), quenched with glycinemethyl ester. HCl[15] (75.4 mg 0.88 mmol), (*i*-Pr)$_2$NEt (1.47 mL, 0.88 mmol), in DMF (3 mL), stirred 3 h at 65 °C. After completion the reaction mixture was quenched with brine and extracted with EtOAc (x3). The combined organic phases were washed with H_2O (x4), brine (x2), dried ($MgSO_4$) and concentrated *in vacuo.* Crude reaction mixture 99 : 1 $dr_{syn/anti}$; Chromatography column on silica gel (DCM : MeOH, 99.9 : 0.1) gave *syn*-**19** as a clear oil (63 mg, 72%) in 97% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 41.5 (*c* 0.4 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm$^{-1:}$ 3286 (N-H), 1747 (C=O ester), 1712 (C=O ketone), 1658 (N-C=O amide), 1338 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.72 (1H, m, C(4)H_AH_B), 1.93-2.02 (1H, m, C(4)H_AH_B), 2.13 (3H, s, COCH_3), 2.29 (1H, dddd, *J* 16.0, 12.9, 8.1, 6.4, C(3)*H*), 2.40 (1H, dd, *J* 18.4, 6.8, CH_AH_B), 2.47 (3H, s, $Ar_{Ts}CH_3$), 2.84 (1H, dd, *J* 18.4, 7.5, CH_AH_B), 3.06 (1H, ddd, *J* 11.3, 9.4, 6.2, C(5)H_AH_B), 3.69 (1H, m, C(5)H_AH_B), 3.79 (3H, s, CO_2CH_3), 3.89 (1H, dd, *J* 18.0, 4.9, NHC$H_AH_BCO_2CH_3$), 4.20 (1H, d, *J* 8.9, C(2)*H*), 4.29 (1H, dd, *J* 18.0, 6.9, NHC$H_AH_BCO_2CH_3$), 7.08 (1H, t, *J* 6.0, N*H*), 7.37 (2H, dd, *J* 8.6, 0.8, $Ar_{Ts}H3$-5), 7.76 (2H, d, *J* 8.3, $Ar_{Ts}H2$-6); $\boldsymbol{\delta_C}$ ($CDCl_3$, 100MHz) 21.6 ($Ar_{Ts}CH_3$), 29.6 (*C*(4)H_2), 30.2 (CO*C*H_3), 37.5 (*C*(3)H), 40.9 (NH*C*$H_2CO_2CH_3$), 42.9 (*C*H_2CO), 48.2 (*C*(5)H_2), 52.4 (CO_2CH_3), 63.1 (*C*(2)H), 127.3 (*C*HAr_{Ts}2-6), 130.4 (*C*HAr3-5), 132.4 (*C*$Ar_{Ts}SO_2$), 144.5 (*C*$Ar_{Ts}CH_3$), 168.3 (*C*ONH), 170.1 (CO_2CH_3), 207.2 (*C*OCH_3); ***m/z*** (ES^+) 397 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{18}H_{25}SN_2O_6^+$ ($[M+H]^+$); found 397.1431, requires 397.1428 (+0.8 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 19.4 min, $t_{r\ min}$ = 12.7 min; 220 nm, 30 °C).



<Peak Table>
PDA Ch2 220nm

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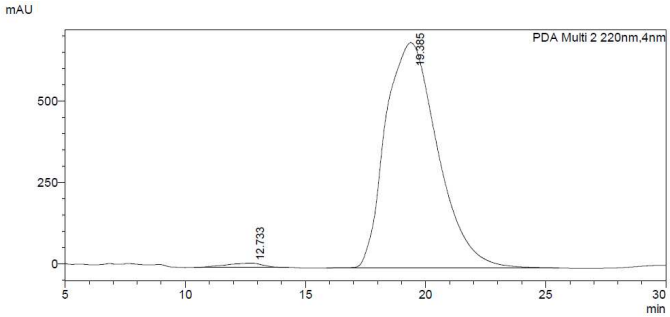
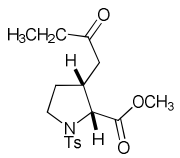
Total		100.000



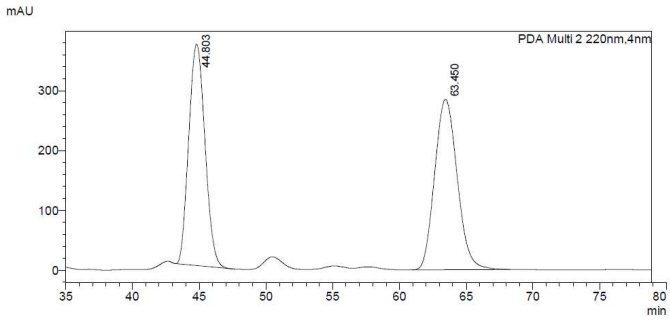
<Peak Table>
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	12.733	1.372
2	19.385	98.628
Total		100.000

(2*R*,3*R*)-Methyl 3-(2-oxobutyl)-1-tosylpyrrolidine-2-carboxylate 20



*Following general procedure **6**:* alkene **10** (60.0 mg, 0.22 mmol), Grubb's II (8.9 mg, 0.01 mmol), dry DCM (0.72 mL), ethyl vinyl ketone **S15** (109 µL, 1.06 mmol), stirred for 2 h at 40 °C. Organocatalysis with pivaloylchloride (39.1 µL, 0.33 mmol), (*i*-Pr)$_2$NEt (55.7 µL, 0.33 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (95.8 µL, 0.55 mmol). Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80 : 20 to 60 : 40) gave *syn*-**20** as a brown oil (62 mg, 80%) in 99% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 52.9 (*c* 0.6 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$ **(**film)/cm^{-1} 1739 (C=O ester), 1714 (C=O ketone), 1342 (C-O); $\boldsymbol{\delta}_{\mathbf{H}}$ ($CDCl_3$, 500MHz) 0.95 (3H, t, *J* 7.3, CH_2CH_3), 1.66-1.70 (1H, m, C(4)H_AH_B), 1.93 (1H, dt, *J* 12.5, 6.3, C(4)H_AH_B), 2.26-2.29 (3H, m, CH_2CH_3+CH_AH_B), 2.30-2.36 (4H, m, $Ar_{Ts}CH_3$+CH_AH_B), 2.36-2.45 (1H, m, C(3)*H*), 3.12 (1H, td, *J* 9.6, 6.7, C(5)H_AH_B), 3.56 (1H, t, *J* 8.7, C(5)H_AH_B), 3.63 (3H, s, $COCH_3$), 4.23 (1H, d, *J* 8.5, C(2)*H*), 7.25 (2H, d, *J* 8.0, $Ar_{Ts}H$3-5), 7.65 (2H, d, *J* 8.0, $Ar_{Ts}H$2-6); $\boldsymbol{\delta}_{\mathbf{C}}$ ($CDCl_3$, 100MHz) 7.7 (CH_2CH_3), 21.6 ($Ar_{Ts}CH_3$), 29.8 (*C*(4)H_2), 36.2 (CH_2CO), 37.6 (*C*(3)H), 42.1 (CH_2CH_3), 47.4 (*C*(5)H_2), 52.2 (CO_2CH_3), 62.5 (*C*(2)H), 127.4 ($CHAr_{Ts}$2-6), 129.8 (*C*HAr3-5), 134.9 ($CAr_{Ts}SO_2$), 143.7 ($CAr_{Ts}CH_3$), 171.3 ($CO_2CH_2CH_3$), 208.5 ($COCH_3$); ***m/z*** (ES$^-$) 354 ([M-H]$^-$, 100%); HRMS (ES) $C_{17}H_{24}SNO_5^+$ ([M+H]$^+$); found 354.1374, requires 354.1370 (+ 1.2 ppm); Enantiomeric excess determined by chiral HPLC new (ChiralPak AD-H 5 % *i*-PrOH, 1.0 mL/min $t_{r\ maj}$ = 63.3 min, $t_{r\ min}$ = 44.6 min; 220 nm, 30 °C).



<Peak Table>
PDA Ch2 220nm

Peak#	Ret. Time	Area%
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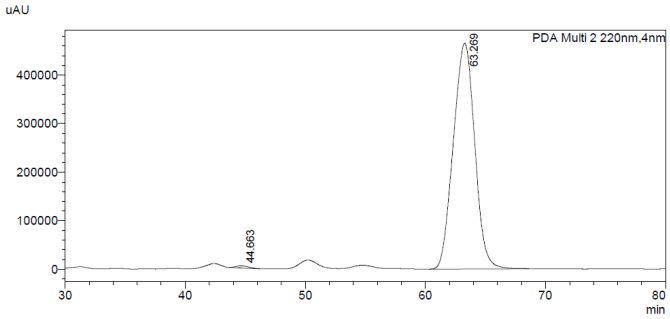
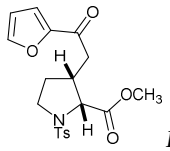
2	63.450	51.593
Total		100.000



<Peak Table>
PDA Ch2 220nm

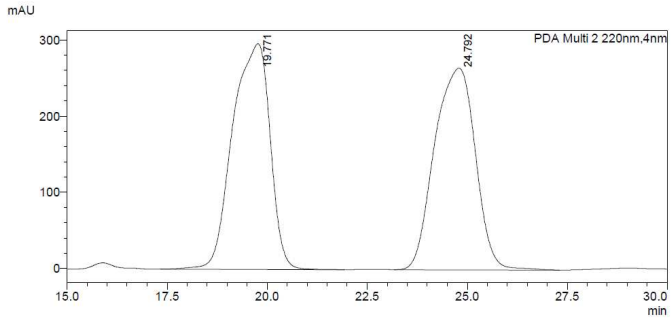
Peak#	Ret. Time	Area%
1	44.663	0.546
2	63.269	99.454
Total		100.000

(2*R*,3*R*)-Methyl 3-[2-(furan-2-yl)-2-oxoethyl]-1-[(4-methylbenzene)sulfonyl]pyrrolidine-2-carboxylate 21



*Following general procedure **6***: alkene **10** (60.0 mg, 0.21 mmol), Grubb's II (8.9 mg, 0.01 mmol), dry DCM (0.72 mL), vinyl ketone **S6** (129.3 mg, 1.06 mmol), stirred 12 h at 40 °C. Organocatalysis with pivaloylchloride (38.9 µL, 0.31 mmol), (*i*-Pr)$_2$NEt (54.8 µL, 0.31 mmol), DCM (6 mL), (−)-tetramisole.HCl (2.6 mg, 0.01 mmol), (*i*-Pr)$_2$NEt (91.5 µL, 0.53 mmol) 1 h at rt. Ring opening with MeOH and DMAP, stirred overnight at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (DCM : MeOH, 99.9 : 0.1) gave *syn*-**21** as a yellow oil (62 mg, 75%) in 96% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 41.1 (*c* 2.6 in DCM); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 1734 (C=O ester), 1674 (C=O ketone), 1340 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.76-1.84 (1H, m, C(4)H_AH_B), 1.96-2.01 (1H, m, C(4)H_AH_B), 2.37 (3H, s, Ar$_{Ts}$CH_3), 2.64-2.67 (2H, m, C(3)H+CH_AH_B), 2.84-2.89 (1H, m, CH_AH_B), 3.15 (1H, td, *J* 9.5, 6.6, C(5)H_AH_B), 3.55 (3H, s, CO_2CH_3), 3.58-3.64 (1H, m, C(5)H_AH_B), 4.35 (1H, d, *J* 7.9, C(2)H), 6.47 (1H, dd, *J* 3.6, 1.7, Ar$_{Furan}$*H*4), 7.10 (1H, dd, *J* 3.6, 0.9, Ar$_{Furan}$*H*3), 7.26 (2H, d, *J* 8.0, Ar$_{Ts}$*H*3-5), 7.50

(1H, dd, *J* 1.8, 0.9, $Ar_{Furan}H5$), 7.67 (2H, d, *J* 8.0, $Ar_{Ts}H2$-6); **δ_c** ($CDCl_3$, 125MHz) 21.6 ($Ar_{Ts}CH_3$), 29.9 (*C*(4)H_2), 37.5 (*C*(3)H), 38.2 (CH_2CO), 47.4 (*C*(5)H_2), 52.1 (CO_2CH_3), 62.5 (*C*(2)H), 112.5 ($CHAr_{furan}4$), 117.1 ($CHAr_{furan}3$), 127.4 ($CHAr_{Ts}2$-6), 129.8 ($CHAr_{Ts}3$-5), 134.8 ($CAr_{Ts}SO_2$), 143.7 ($CAr_{Ts}CH_3$), 146.5 ($CHAr_{furan}5$), 152.3 (*C*(2)Ar_{furan}), 171.2 (CO_2CH_3), 186.4 (*C*O); ***m/z*** (ES^+) 413 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{19}H_{21}SNO_6Na^+$ ($[M+Na]^+$); found 414.0985, requires 414.0987 (-0.2 ppm). Enantiomeric excess determined by chiral HPLC new (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 24.9 min, $t_{r\ min}$ = 19.9 min; 270 nm, 30 °C).



<Peak Table>

PDA Ch2 220nm

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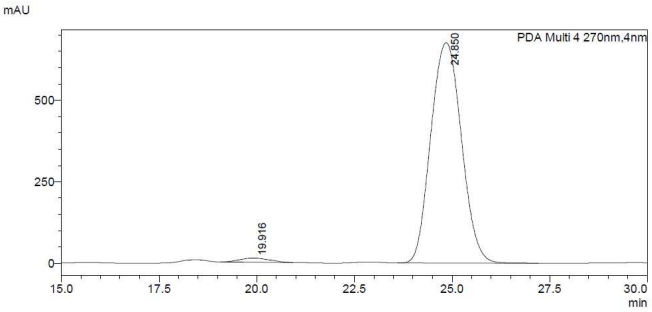
2	24.792	49.366
Total		100.000



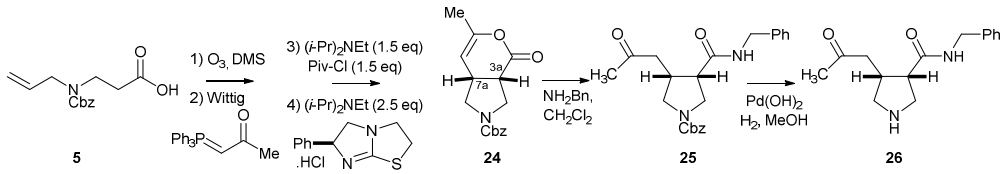
<Peak Table>

PDA Ch4 270nm

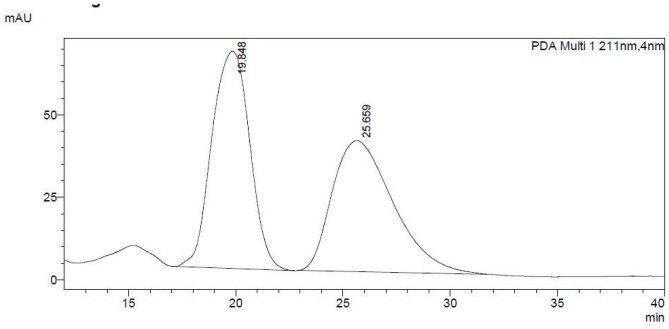
Peak#	Ret. Time	Area%
1	19.916	1.850
2	24.850	98.150
Total		100.000

9) Telescoped olefination/asymmetric Michael addition-lactonisation/ring opening

i. Tandem Wittig



*Following general procedure **5***: ozonolysis of alkene **5** (150 mg, 0.57 mmol), dry DCM (200 mL). Wittig reaction with **S7** (199 mg, 0.63 mmol), in $CHCl_3$ (100 mL). Organocatalysis with pivaloylchloride (106 µL, 0.86 mmol), (*i*-Pr)$_2$NEt (148.3µL, 0.86 mmol), DCM (10 mL), (−)-tetramisole.HCl (13.7 mg, 0.06 mmol), (*i*-Pr)$_2$NEt (247 µL, 1.43 mmol), stirred for 1 h at rt. Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30) gave (3a*S*,7a*R*)-*syn* **24** as a yellow oil (114 mg, 71%); $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ + 43.9 (*c* 1.2 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm^{-1} 1773 (C=O lactone), 1695 (C=O), 1425 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) mixture of rotamers 1.83 (3H, s, CH_3), 2.70-3.14 (2H, m, C(3a)*H*+C(7a)*H*),), 3.17-3.21 (1H, m, C(1)H_AH$_B$), 3.63-3.67 (2H, m, C(1)H$_A$$H_B$+C(3)$H_AH_B$), 3.68-3.83 (1H, m, C(3)H$_A$$H_B$), 4.75- 4.92 (1H, m, C(7)*H*), 5.06 (2H, m, PhCH_2OCO), 7.23-7.39 (5H, m, Ar*H*); $\boldsymbol{\delta_C}$ ($CDCl_3$, 75MHz,) 18.8 (Ar$_{Ts}$CH_3), 35.2, 36.0 (*C*(3a)H), 40.6, 41.4 (*C*(7a)H), 47.2, 47.7 (*C*(3)H$_2$), 51.5, 51.9 (*C*(1)H$_2$), 67.1 (PhCH_2OCO), 100.1 (*C*(7)H), 127.9 (*C*HAr), 128.1 (*C*HAr), 128.5 (2X*C*HAr), 136.5 (*C*(1)Ar), 150.1 (*C*(6)CH$_3$), 154.4 (PhCH$_2$O*C*O), 167.9 (*C*O) ***m/z*** (ES$^+$) 288 ([M+H]$^+$, 100%); HRMS (ES$^+$) $C_{16}H_{18}NO_4^+$ ([M+H]$^+$); found 288.1229, requires 288.1226 (- 0.5 ppm). Ring opening of *syn*-**24** with benzylamine (47.7 µL, 0.44 mmol) in DCM (7 mL) 1 h at rt. The reaction was quenched with 0.1M aq. HCl, extracted with DCM (x3), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give (3*S*,4*R*)-*syn* **25** as a clear oil (124 mg, 79%) in 99% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ - 0.12 (*c* 6.3 in DCM); $\boldsymbol{\nu_{max}}$ **(**film)/cm$^{-1:}$ 3307 (N-H), 1699 (N-C=O), 1666 (C=O ester), 1651 (C=O ketone); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 1.97 (3H, s, COCH_3), 2.53-2.57 (2H, m, CH_2COCH$_3$), 2.58-2.77 (1H, m, C(3)*H*), 3.11 (1H, dtd, *J* 13.7, 7.1, 3.4, C(4)*H*), 3.28 (1H, td, *J* 10.1, 9.6, 2.9, C(2)H_AH$_B$), 3.58-3.66 (2H, m, C(2)H$_A$$H_B$+C(5)$H_AH_B$), 3.76-3.80 (1H, m, C(5)H$_A$$H_B$), 4.30 (1H, dt, *J* 14.4, 5.2, NHCH_AH$_B$Ph), 4.48 (1H, dd, *J* 14.4, 6.3, NHCH$_A$$H_B$Ph), 5.05-5.22 (2H, m, PhCH_2OCO), 5.96 (1H, t, *J* 5.9, N*H*), 7.24-7.42 (10H, m, Ar*H*); $\boldsymbol{\delta_C}$ ($CDCl_3$, 125MHz) 50:50 mixture of rotamers 30.1 (*C*H$_3$), 35.9, 36.8 (*C*(3)H), 42.3, 42.4 (*C*H$_2$CO), 43.4, 43.5 (NH*C*H$_2$Ph), 45.6, 46.5 (*C*(4)H), 48.1, 48.8 (*C*(5)H$_2$), 50.0, 50.6 (*C*(2)H$_2$), 66.8, 66.9 (Ar*C*H$_2$OCO), 127.7, 127.8 (*C*HAr), 127.8, 127.9 (2X*C*HAr), 128.0, 128.1 (*C*HAr), 128.5(3X*C*HAr), 128.8, 128.8 (3X*C*HAr), 136.8 (NHCH$_2$*C*(1)Ar), 138.1 (*C*(1)ArCH$_2$OCO), 154.6, 154.6 (ArCH$_2$O*C*O), 171.5, 171.6 (*C*ONH), 207.9, 208.0 (*C*OCH$_3$)**;** ***m/z*** (ES$^+$) 417([M+Na]$^+$, 100%); HRMS (ES$^+$) $C_{23}H_{26}SN_2O_4Na^+$ ([M+Na]$^+$); found 417.1797, requires 417.1790 (+ 0.7 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 23.3 min, $t_{r\ min}$ = 19.8 min; 211 nm, 30 °C).



<Peak Table>
PDA Ch1 211nm

Peak#	Area%	Ret. Time
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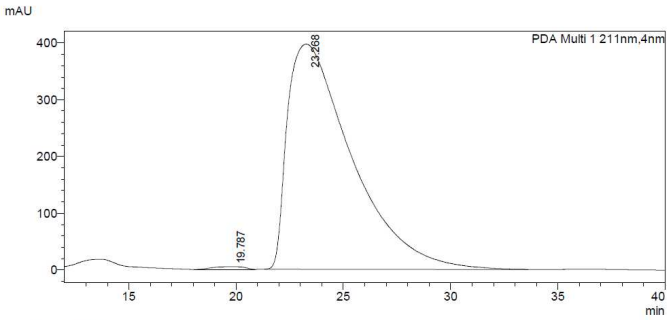
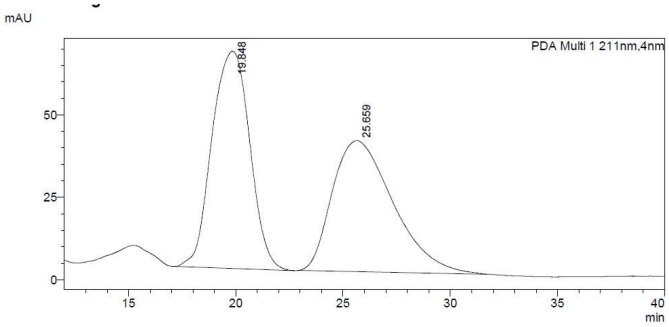
2	49.252	25.659
Total	100.000	



<Peak Table>
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	19.787	0.615
2	23.268	99.385
Total		100.000

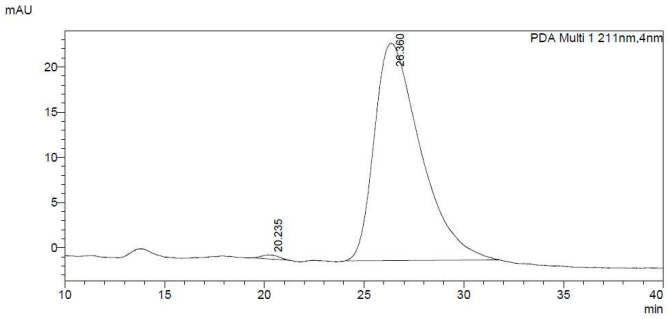
To a solution of *syn*-**25** (121 mg, 0.30 mmol, 1.0 eq) in MeOH (5 mL) was added $Pd(OH)_2/C$ (60.5 mg, 50%w/w). The resultant mixture was stirred under hydrogen (1 atm) for 20 min at rt. After completion the reaction was filtered through celite and washed with MeOH. The fíltrate was concentrated *in vacuo* to give the corresponding amine *syn*-**26** as a clear oil (59 mg, 71%) in 99% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ - 1.9 (*c* 0.3 in DCM); $\boldsymbol{\nu_{max}}$ (film)/cm^{-1} 3271 (N-H), 1719 (C=O ester), 1647 (C=O amide); $\boldsymbol{\delta_H}$ ($CDCl_3$, 500MHz) 2.01, (3H, s, $COCH_3$), 2.48 (1H, dd, *J* 18.0, 6.2, $CH_AH_BCOCH_3$), 2.59-2.68 (1H, m, $CH_AH_BCOCH_3$), 2.68-2.78 (2H, m, C(4)*H*+C(5)H_AH_B), 2.88 (1H, ddd, *J* 8.3, 6.1, 2.6, C(3)*H*), 3.04 (1H, dd, *J* 10.8, 6.1, C(2)H_AH_B), 3.14-3.30 (2H, m, C(2)H_AH_B+C(5)H_AH_B), 4.36 (1H, dd, *J* 14.5, 5.7, $NHCH_AH_BAr$), 4.43 (1H, dd, *J* 14.5, 6.0, $NHCH_AH_BAr$), 6.94 (1H, t, *J* 6.0, N*H*CO), 7.23-7.39 (5H, m, Ar*H*); $\boldsymbol{\delta_C}$ ($CDCl_3$, 125MHz) 30.1 (CH_3), 37.4 (*C*(4)H), 43.4 ($NHCH_2Ar$), 43.5 (CH_2COCH_3), 47.3 (*C*(3)H), 49.9 (*C*(2)H_2), 50.5 (*C*(5)H_2), 127.5 (*C*HAr4), 127.9 (*C*HAr2-6), 128.7 (*C*HAr3-5), 138.4 (*C*(1)Ar), 172.8 (*C*ONH), 208.2 ($COCH_3$); HRMS (ES^+) 283 ($[M+Na]^+$; 100%); 261 ($[M+H]^+$; 90%); $C_{15}H_{21}N_2O_2^+$ ($[M+H]^+$); found 261.1601, requires 261.1598 (+ 1.3 ppm). Enantiomeric excess determined by chiral HPLC of the corresponding Cbz protected compound (ChiralPak OD-H 20 % *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 26.4 min, $t_{r\ min}$ = 20.2 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Area%	Ret. Time
1	50.748	19.848
2	49.252	25.659
Total	100.000	

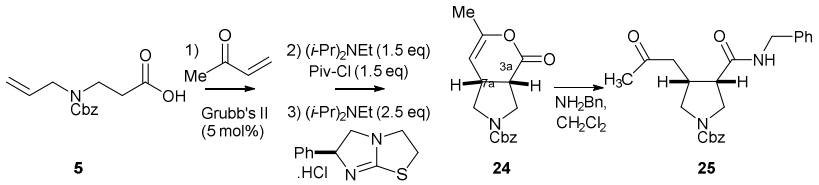


<Peak Table>

PDA Ch1 211nm

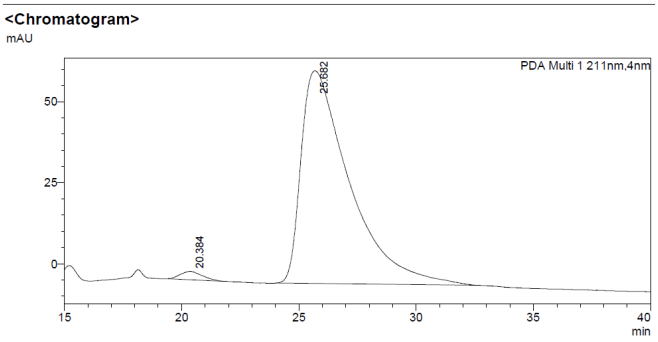
Peak#	Ret. Time	Area%
1	20.235	0.659
2	26.360	99.341
Total		100.000

ii. Tandem Metathesis



*Following general procedure **6***: alkene **5** (60 mg, 0.23 mmol), Grubb's II (9.3 mg, 0.11 mmol), dry DCM (1.2 mL), methyl vinyl ketone **S14** (95 µL, 1.06 mmol), stirred at 40 °C over night. Organocatalysis with pivaloylchloride (42.1 µL, 0.34 mmol), (*i*-Pr)$_2$NEt (59.0 µL, 0.34 mmol), DCM (3 mL), (−)-tetramisole.HCl (2.7 mg, 0.011 mmol), (*i*-Pr)$_2$NEt (98.8 µL, 0.55 mmol). Crude reaction mixture 99 : 1 dr$_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 70 : 30) gave (3a*S*,7a*R*)-*syn* **24** as a yellow oil (42 mg, 65%); Ring opening of *syn*-**24** with benzylamine (22.2 µL, 0.21 mmol) in DCM (7 mL) 1 h at rt. The reaction was quenched with 0.1M aq. HCl, extracted with DCM (x3), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give (3*S*,4*R*)-*syn* **25** as a

yellow oil (34 mg, 60%) in 99% ee. Other analytical data were identical to the one previously described for this compound.



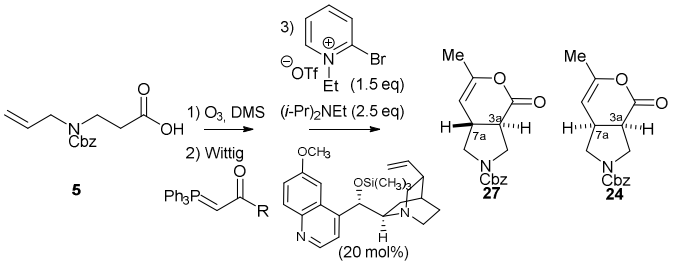
<Peak Table>
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.384	1.718
2	25.682	98.282
Total		100.000

10) Stereodivergent telescoped olefination/asymmetric Michael addition-lactonisation/ring opening

Racemic *anti* products were obtained using DABCO (20 mol%) as a achiral catalyst.

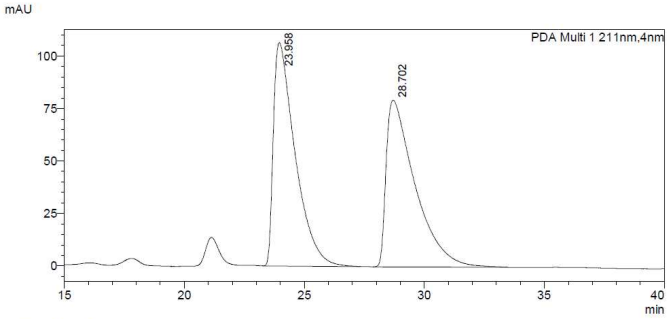
iii. Tandem Wittig



A stream of O_3 in O_2 was bubbled through a solution of **5** (200 mg, 0.76 mmol) in dry DCM (200 mL) at - 78 °C. When the blue color persisted (1 min), dimethyl sulfide (2.0 eq) was added and the reaction was allowed to warm to rt. After concentration *in vacuo* the aldehyde was disolved in $CHCl_3$ (50 mL) and phosphorane **S7** (242 mg, 0.84 mmol) was added. The reaction was stirred overnight at 65 °C and then concentrated *in vacuo*. The crude mixture was dissolved in DCM and was slowly added to a solution of Mukayaima derivative **29** (383 mg, 1.14 mmol), (*i*-Pr)$_2$NEt (329 µL, 1.90 mmol) and OTMS-quinidine (60.0 mg, 0.15 mmol) in dry DCM (10 mL). After 2 h at rt the reaction was concentrated *in vacuo* and the residue was purified by chomatography column. Crude reaction mixture 33 : 67 $dr_{syn/anti}$; Chromatography column in silica gel (Pet.ether : EtOAc, 80:20) gave (3a*R*, 7a*R*)-*anti* **27** and (3a*R*, 7a*S*)-*syn* **24** (203 mg, 93% combined yield);

Anti-**27**: was obtained as a white solid (130.0 mg, 60%) in 97% ee; **mp**: 100-102 °C $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ - 1.8 (*c* 1.1 in DCM); $\boldsymbol{\nu_{max}}$ **(**KBr)/cm^{-1} 1774 (C=O lactone), 1695 (C=O), 1423 (C-O); $\boldsymbol{\delta_H}$ ($CDCl_3$, 300MHz) 1.97

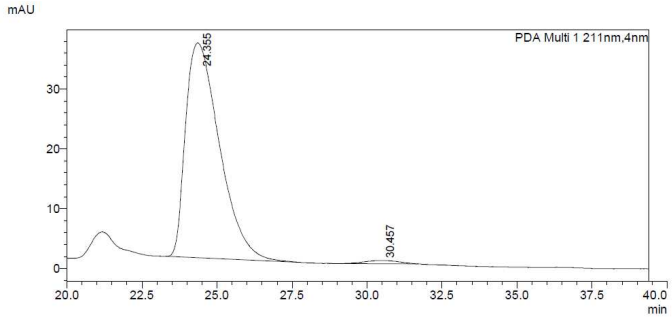
(3H, s, CH_3), 2.70-3.14 (1H, m, C(3a)*H*), 2.58-2.81 (1H, m, C(7a)*H*), 3.11-3.18 (1H, m, C(1)H_AH_B), 3.53-3.56 (1H, m, C(3)H_AH_B), 3.83-3.92 (2H, m, C(1)H_AH_B+C(3)H_AH_B), 5.17 (2H, s, PhCH_2OCO), 5.28-5.35 (1H, m, C(7)*H*), 7.37-7.40 (5H, m, Ar*H*); δ_C ($CDCl_3$, 125MHz) mixture of rotameres 18.5 (CH_3), 36.8, 37.5 (*C*(7a)H), 44.5, 44.9 (*C*(3a)H), 44.7, 45.2 (*C*(3)H_2), 48.9, 49.1 (*C*(1)H_2), 67.1 (Ph*C*H_2OCO), 102.5, 102.7 (*C*(7)H), 127.9 (*C*HAr), 128.1 (*C*HAr), 128.1 (*C*HAr), 128.5 (2X*C*HAr), 136.4, 136.5 (*C*(1)Ar), 152.7, 152.8 (*C*(6)-CH_3), 154.7, 154.8 (PhCH_2O*C*O), 167.7, 167.9 (*C*O); ***m/z*** (ES^+) 310 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{16}H_{17}NO_4Na^+$ ($[M+Na]^+$); found 310.1047, requires 310.1055 (- 2.8 ppm); Enantiomeric excess determined by chiral HPLC (ChiralPak OD-H 15% *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 24.3 min, $t_{r\ min}$ = 30.5 min; 211 nm, 30 °C).



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	23.958	50.179
2	28.702	49.821
Total		100.000

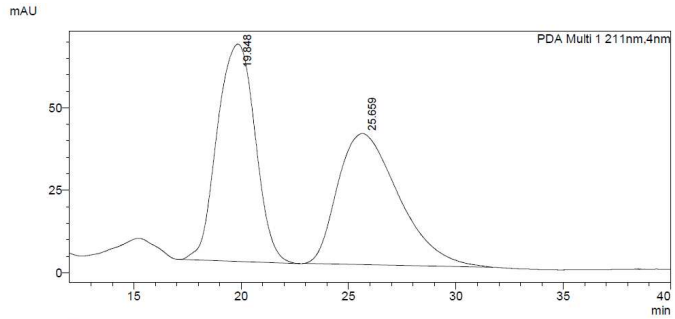


<Peak Table>

PDA Ch1 211nm

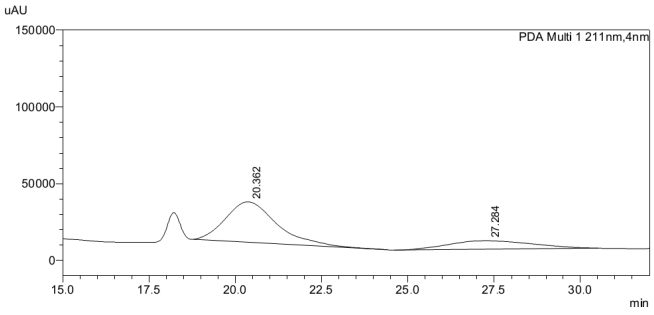
Peak#	Ret. Time	Area%
1	24.355	98.492
2	30.457	1.508
Total		100.000

Ent syn-**24:** was obtained as an oil (72 mg, 33%) in 50% ee; Analytical data were indentical to *syn*-**24;** Enantiomeric excess of *ent syn*-**24** was determined *via* ring opening with benzylamine; analytical data were indentical to *syn*-**25.** Determined by chiral HPLC (ChiralPak OD-H 20% *i*-PrOH : hexane, 1.0 mL/min $t_{r\ maj}$ = 20.4 min, $t_{r\ min}$ = 27.3 min; 211 nm, 30 °C)



<Peak Table>
PDA Ch1 211nm

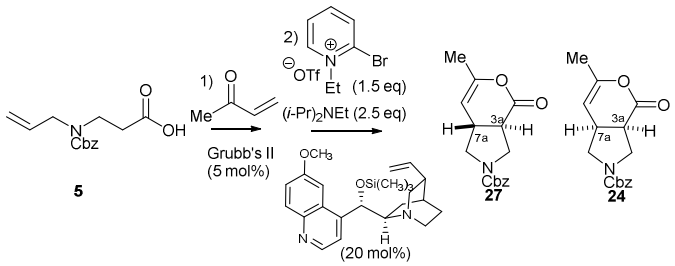
Peak#	Area%	Ret. Time
1	50.748	19.848
2	49.252	25.659
Total	100.000	



<Peak Table>
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.362	74.627
2	27.284	25.373
Total		100.000

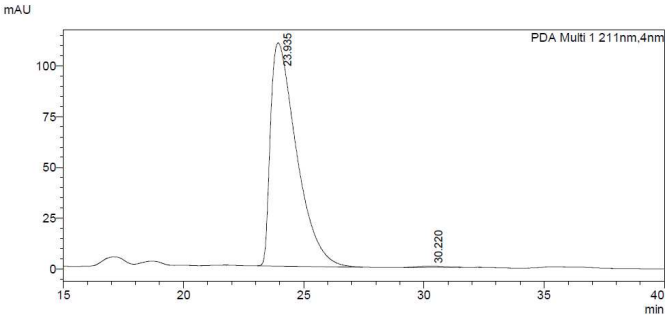
iv. Tandem Metathesis



Grubbs II (6.8 mg, 0.01 mmol) and alkene **5** (42.0 mg, 0.16 mmol, 1.0 eq), were added into a flame dry microwave tube under N_2. The tube was then sealed deagsed and purged with N_2. Dry DCM (0.72 mL) and methyl vinyl ketone **S14** (66.6 µL, 0.79 mmol, 5.0 eq) were added and the solution was heated at 40 °C for 4 h. The mixture was then cooled to rt and was slowly added to a solution of Mukaiyama derivative **29** (80.5 mg, 0.23 mmol, 1.5 eq), (i-Pr)$_2$NEt (69.2 µL, 0.40 mmol, 2.5 eq), and OTMS-Quinidine (12.6 mg, 0.032 mmol, 0.2 eq) in DCM (3 mL). After 2 h at rt the solvent was evaporated *in vacuo* and the residue was purified by chomatography column; Crude reaction mixture

33 : 67 $dr_{syn/anti}$; Chromatography column on silica gel (Pet.ether : EtOAc, 80:20) gave *anti*-**27** and *syn*-**24** lactones (44.2 mg, 96% combined yield;) in 99% ee for *anti*-**27**.

Anti-**27**: was obtained as a white solid (30 mg, 66%) in 99% ee; other analytical data were indentical to the one previously described for this compound.

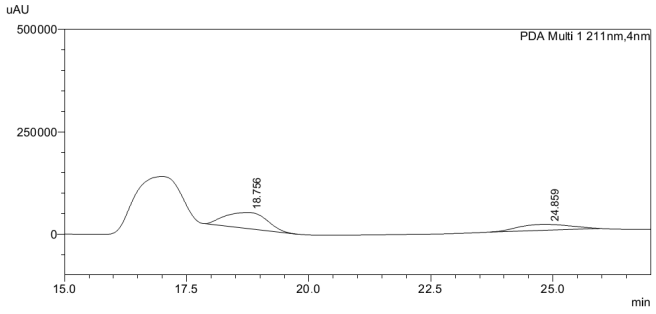


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	23.935	99.449
2	30.220	0.551
Total		100.000

Ent syn-**24:** was obtained as an oil (14 mg, 30%) in 37% ee. Enantiomeric excess of *ent syn*-**24** was determined *via* ring opening with benzylamine; analytical data were indentical to *syn*-**25** previously described.

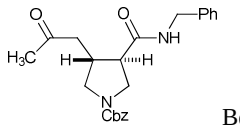


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	18.756	68.398
2	24.859	31.602
Total		100.000

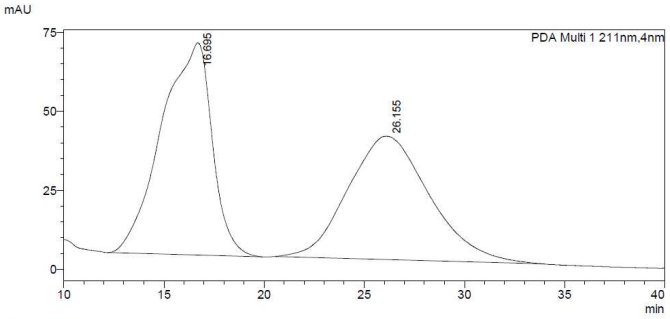
(3*R*,4*R*)-Benzyl-3-(benzylcarbamoyl)-4-(2-oxopropyl)pyrrolidine-1-carboxylate 28



Benzylamine (54.4 µL, 0.49 mmol, 1.1 eq) was added to a solution of lactone *anti*-**27** (130 mg, 0.45 mmol, 1.0 eq) in DCM. The reaction was stirred 1 h at rt and then quenched with 1M aq. HCl, extracted with DCM (x3), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give *anti*-**28** as a clear oil (142 mg, 80%) in 95% ee; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 3.0 (*c* 0.5 in DCM); $\boldsymbol{\nu}_{\mathbf{max}}$

(film)/cm$^{-1:}$ 3275 (N-H), 1697 (N-C=O), 1660 (C=O ester), 1651 (C=O ketone); δ_H ($CDCl_3$, 500 MHz) mixture of rotamers 2.16-2.18 (3H, m, COC*H*$_3$), 2.60-2.76 (4H, m, C*H*$_2$COCH$_3$+C(3)*H*)+C(4)*H*), 3.05-3.17 (1H, m, C(2)*H*$_A$H$_B$), 3.71-3.81 (3H, m, C(2)H$_A$*H*$_B$+C(5)*H*$_2$), 4.47-4.49 (2H, m, NHC*H*$_2$Ph), 5.14-5.15 (2H, m, PhC*H*$_2$OCO), 6.21-6.40 (1H, m, N*H*), 7.29-7.39 (10H, m, Ar*H*); δ_C ($CDCl_3$, 125MHz) 50:50 mixture of rotamers 30.2, 30.3 (*C*H$_3$), 37.8, 38.3 (*C*(3)H),43.8 (NH*C*H$_2$Ph), 46.5, 46.9 (*C*H$_2$CO), 47.8 (*C*(5)H$_2$), 48.6, 49.3 (*C*(4)H), 50.4, 50.6 (*C*(2)H$_2$), 66.9 (PhCH$_2$OCO), 127.7, 127.9 (3X*C*HAr), 128.0 (2X*C*HAr), 128.5 (3X*C*HAr), 128.8 (2X*C*HAr), 136.7 (*C*(1)ArCH$_2$OCO), 138.1 (NHCH$_2$*C*(1)Ar), 154.6 (PhCH$_2$O*C*ON), 171.2, 171.3 (*C*ONH), 207.4, 207.8 (*C*OCH$_3$)**; *m/z*** (ES$^+$) 417 ([M+Na]$^+$, 100%); HRMS (ES$^+$) $C_{23}H_{26}N_2O_4Na^+$ ([M+Na]$^+$); found 417.1786, requires 417.1790 (-0.4 ppm). Enantiomeric excess determined by chiral HPLC (ChiralPak AS-H 20 % *i*-PrOH, 1.0 mL/min t_r $_{maj}$ = 24.3 min, $t_{r\,min}$ = 15.1 min; 211 nm).

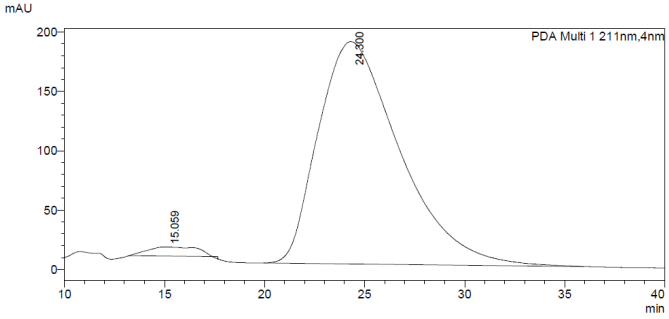
Supprimé: S



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	16.695	51.697
2	26.155	48.303
Total		100.000

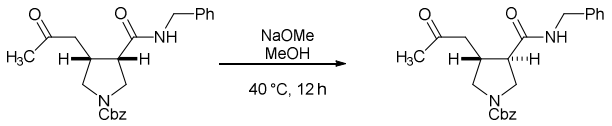


<Peak Table>

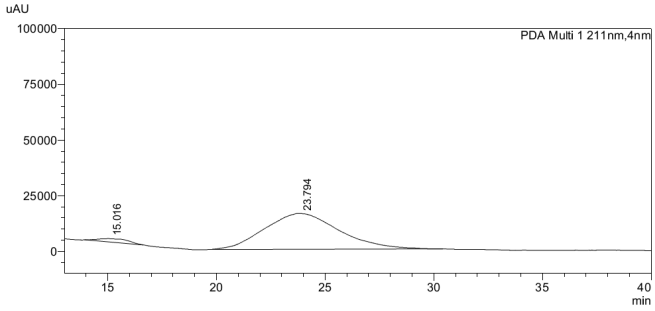
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	15.059	2.483
2	24.300	97.517
Total		100.000

11) Epimerisation procedure



To a freshly made solution of NaOMe in MeOH was added *syn*-**25** (92 mg, 0.23 mmol). The mixture was heated at 40 °C overnight then quenched with 0.1M aq. HCl, extracted with EtOAc (x3), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give *anti*-**28** as a clear oil (64 mg, 70%) in 93% ee. Other analytical data were indentical to the one previously described for *anti*-**28**

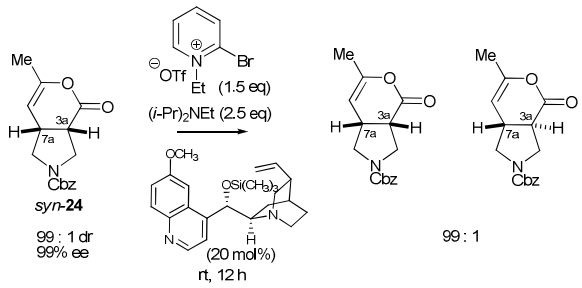


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	15.016	3.857
2	23.794	96.143
Total		100.000

12) Control experiment



Syn-**24** (20.0 mg, 0.07 mmol, 1.0 eq) was added to a solution of Mukaiyama derivative **29** (35.0 mg, 0.10 mmol, 1.5 eq), (*i*-Pr)$_2$NEt (30.2 µL, 0.17 mmol, 2.5 eq), and OTMS-Quinidine (5.6 mg, 0.014 mmol, 0.2 eq) in DCM (3 mL). After 12 h at rt ,the reaction was quenched with 0.1 M HCl and extracted with DCM (x3). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Crude reaction mixture 99 : 1 $dr_{syn/anti}$.

II) References

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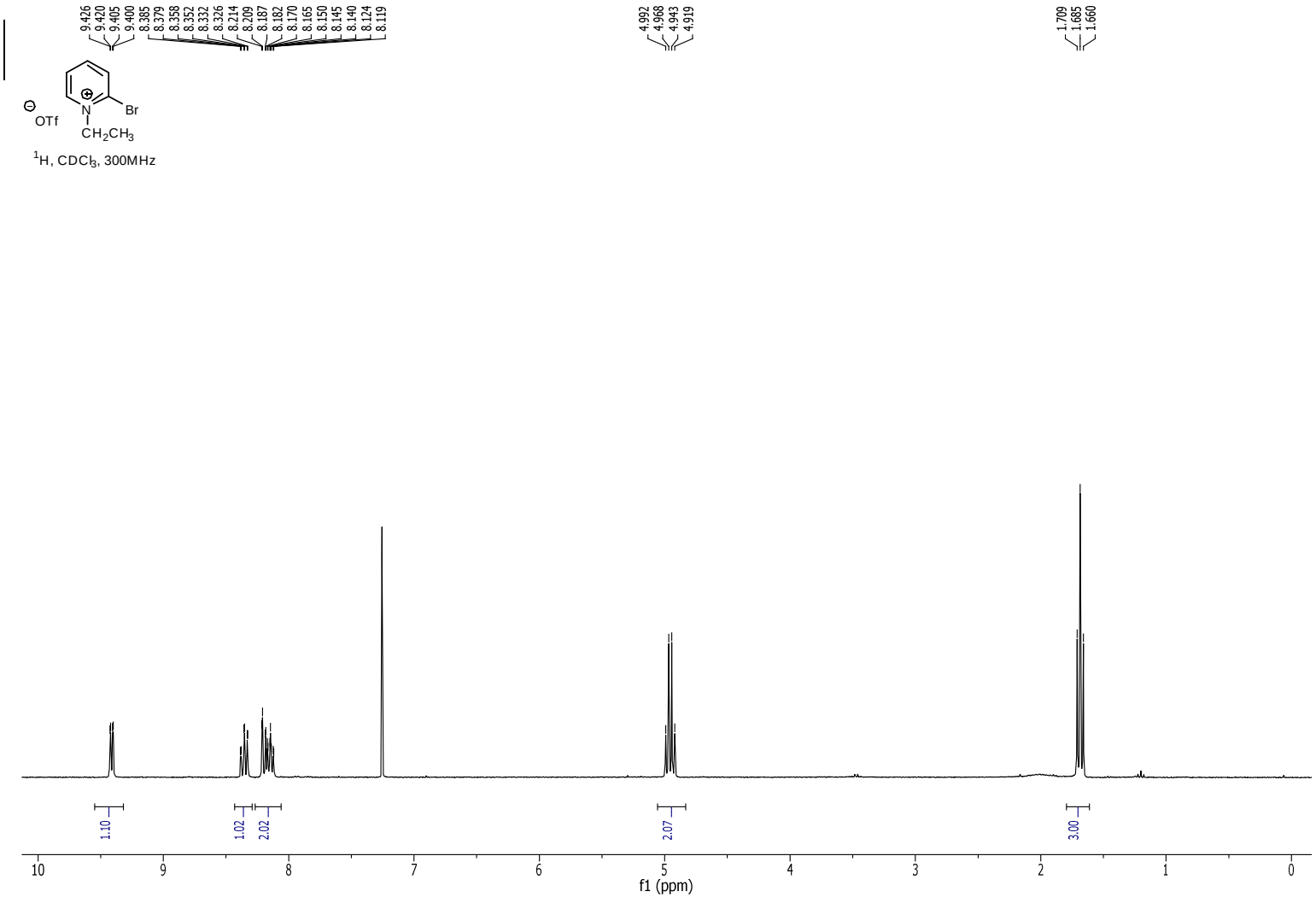
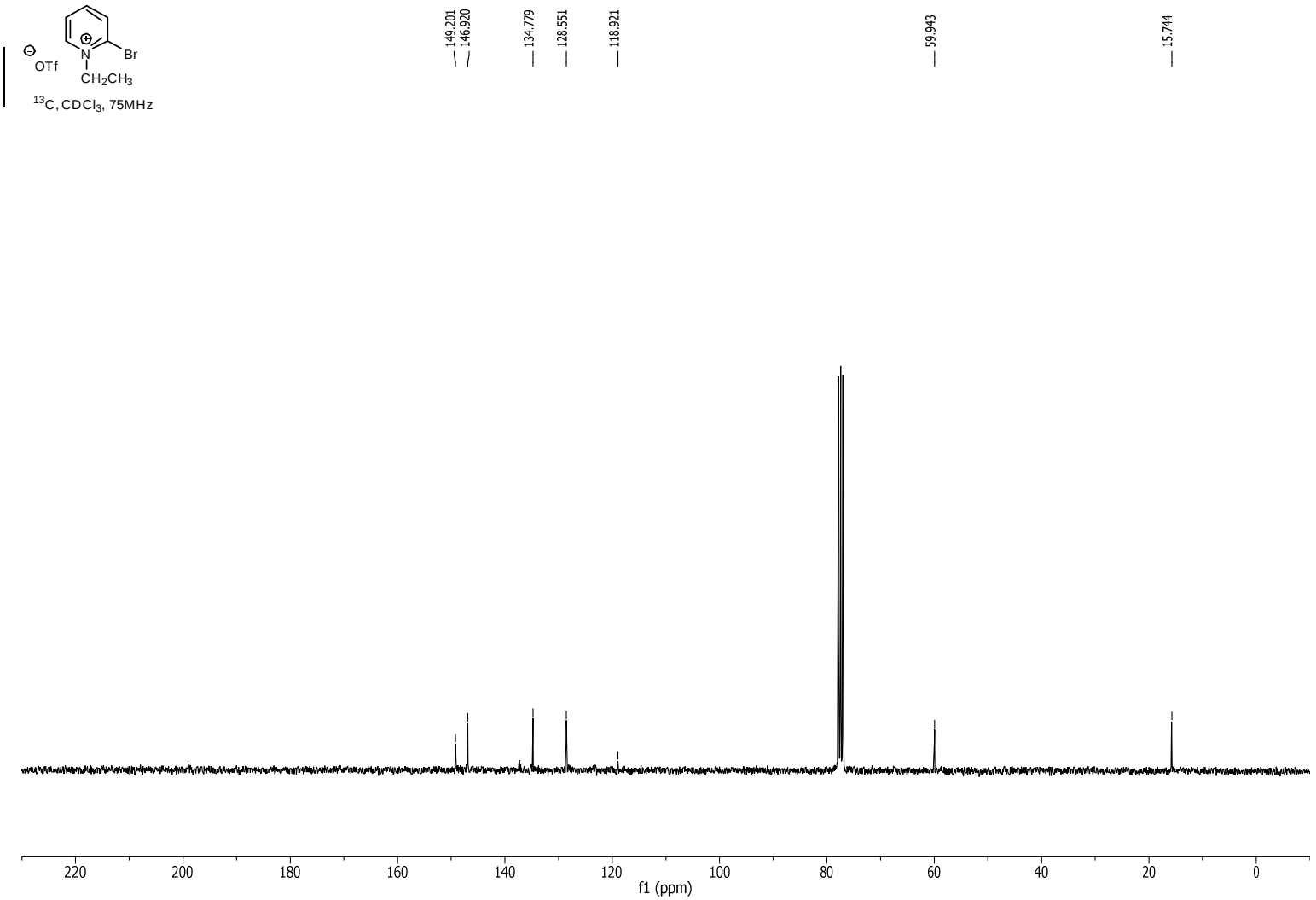
III) NMR ^{1}H and ^{13}C Spectrum



29

Mis en forme : Police :20 pt, Gras

Mis en forme : Police :20 pt, Gras, Français (France)



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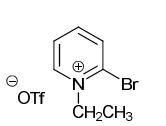
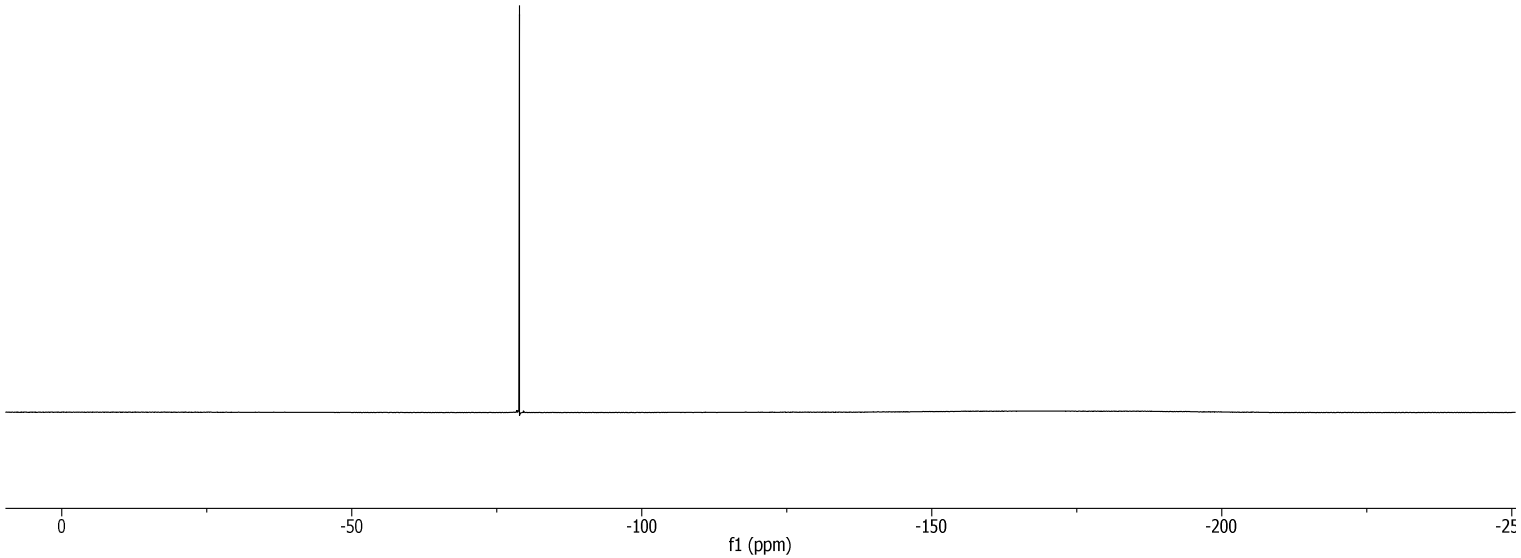


^{19}F, $CDCl_3$, 282MHz

-78.883



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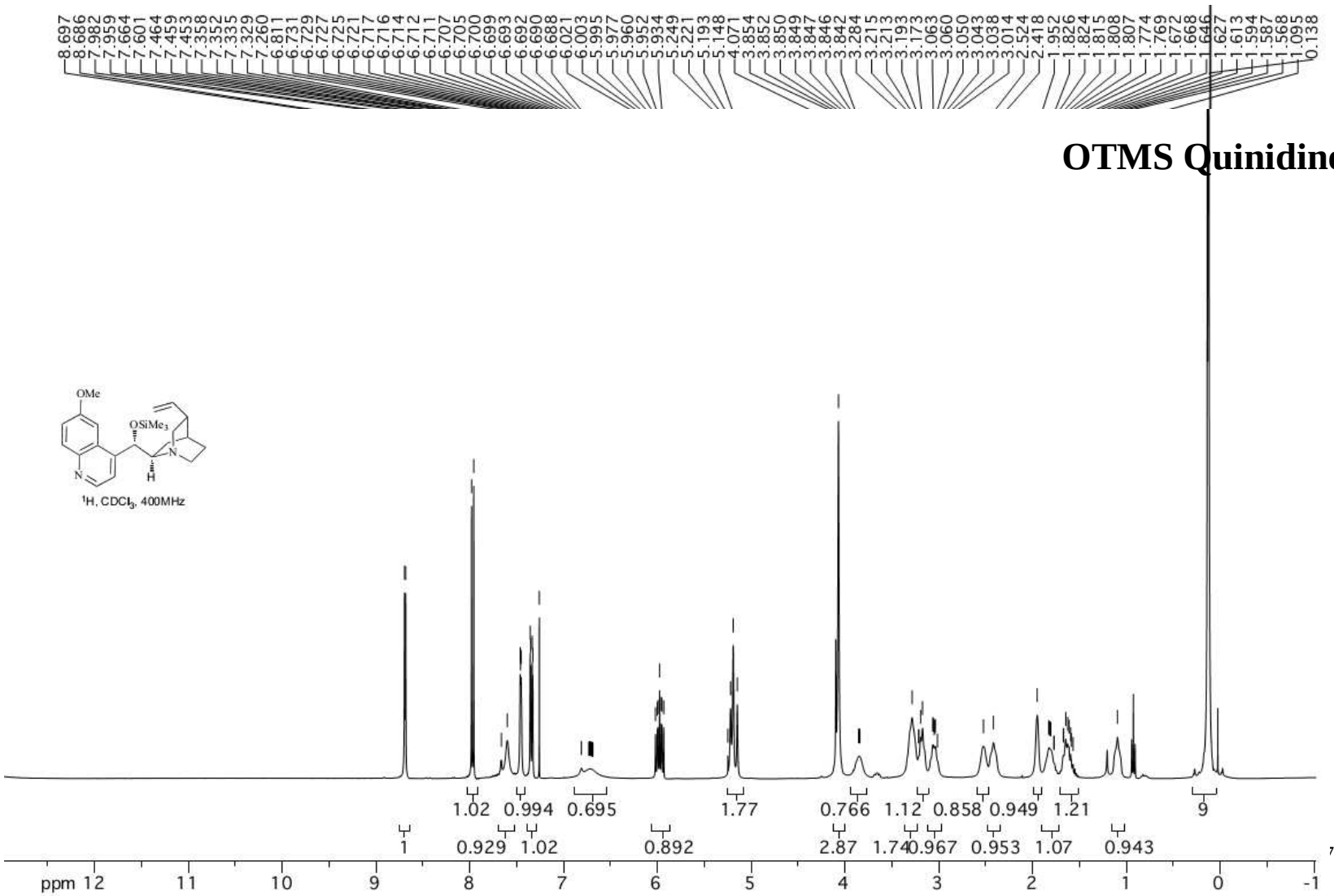

OTMS Quinidine

Mis en forme : Police :20 pt, Gras, Français (France)

OTMS Quinidine

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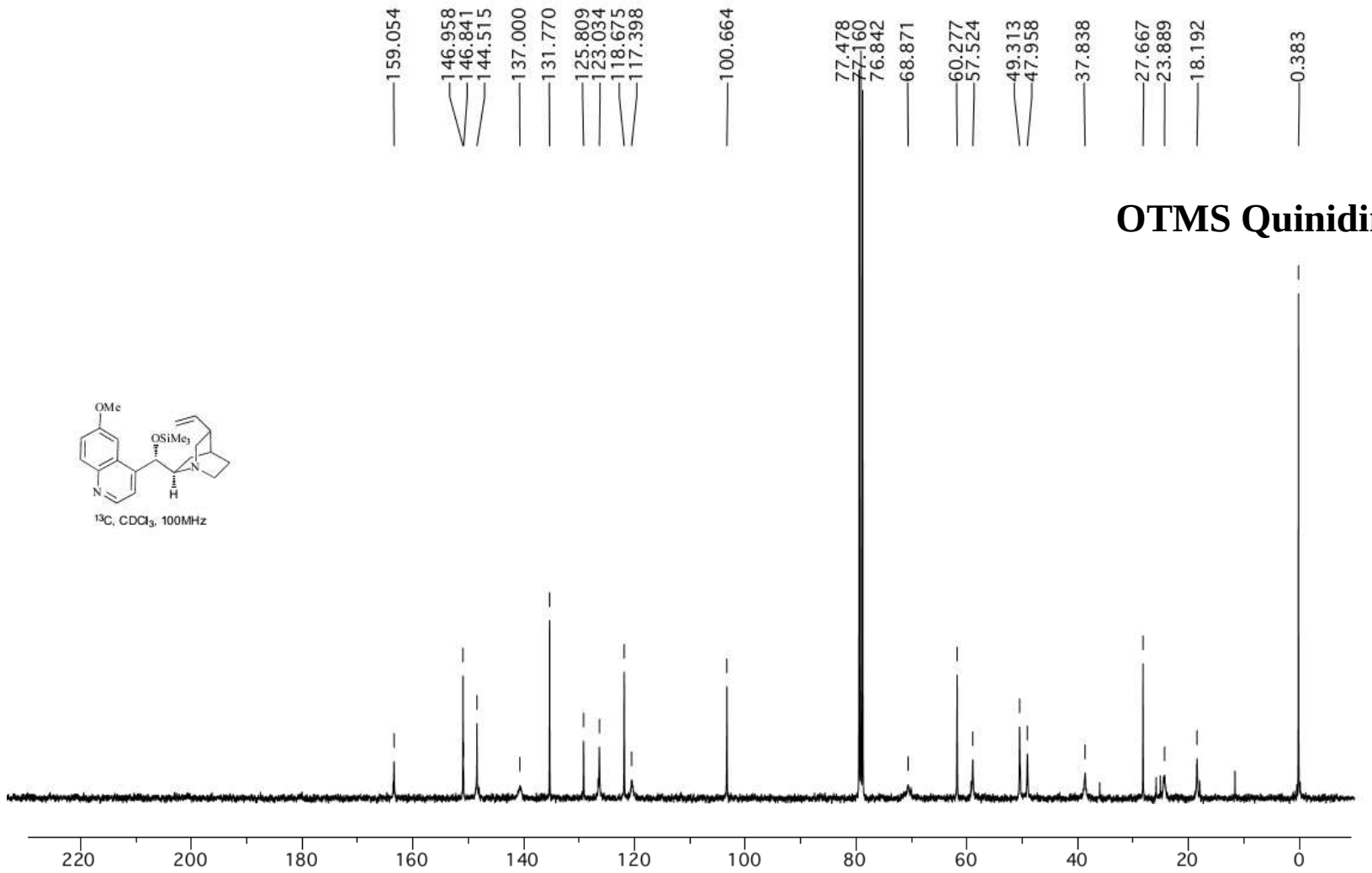
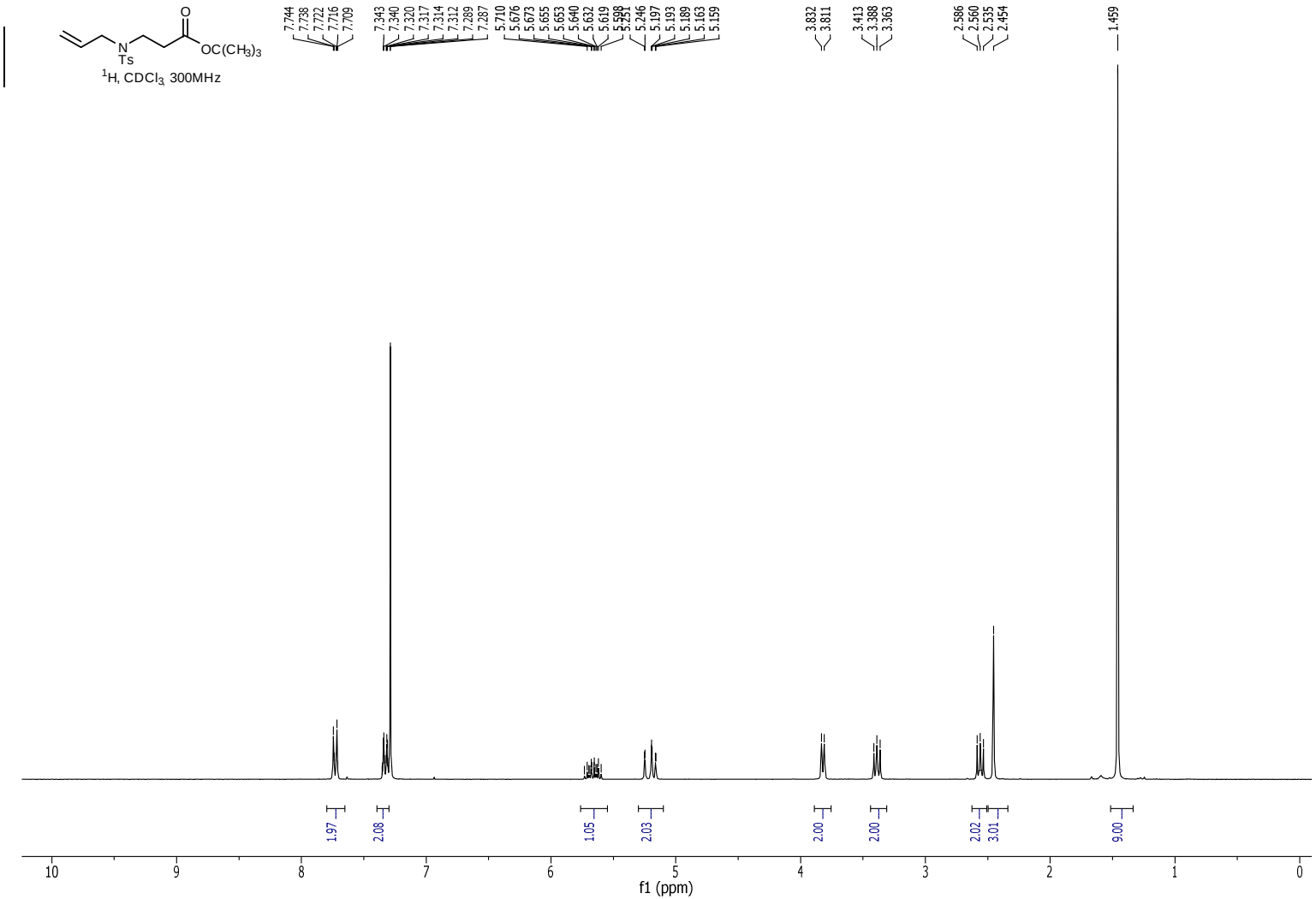
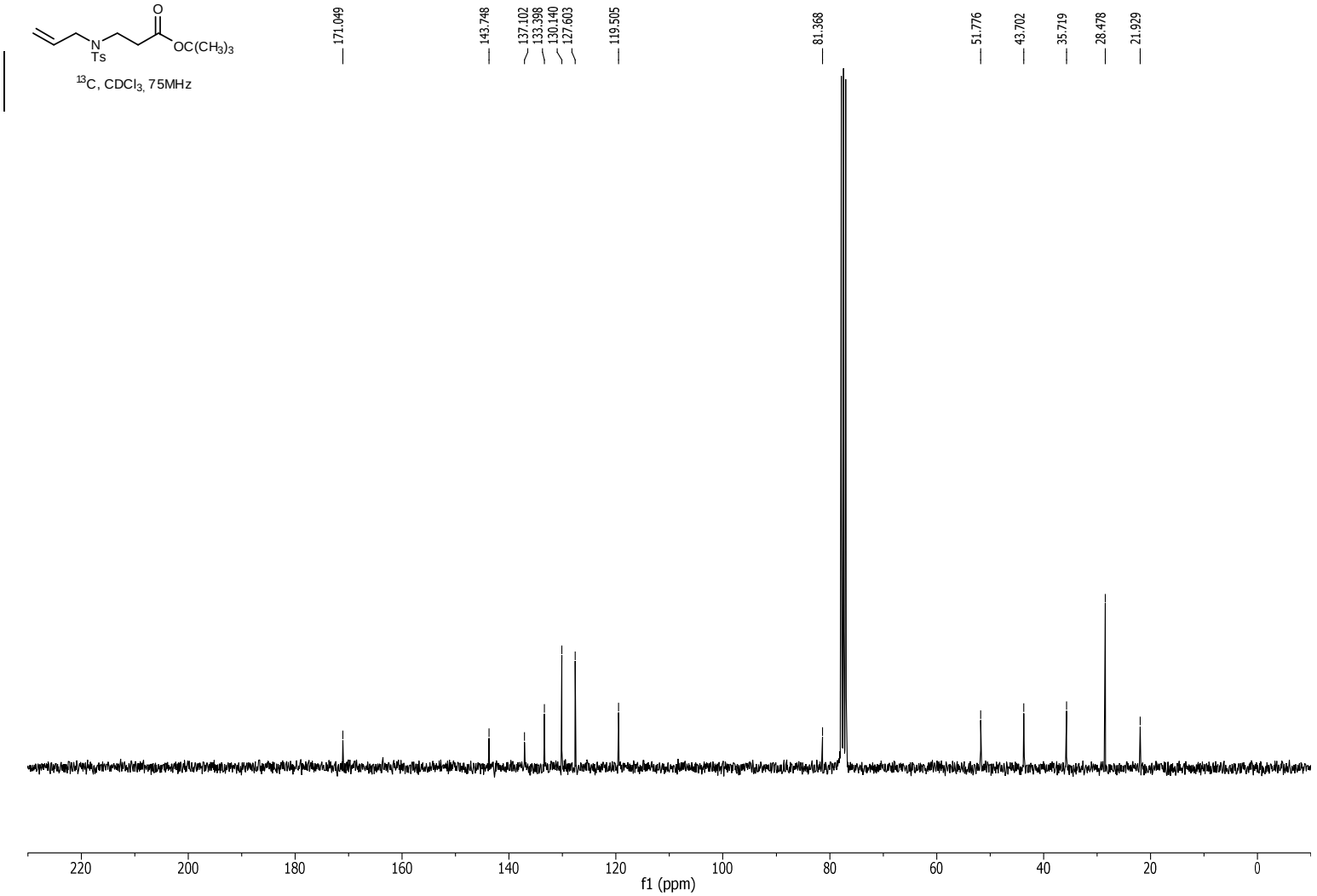




S4

Mis en forme : Police :20 pt, Gras, Français (France)



S4

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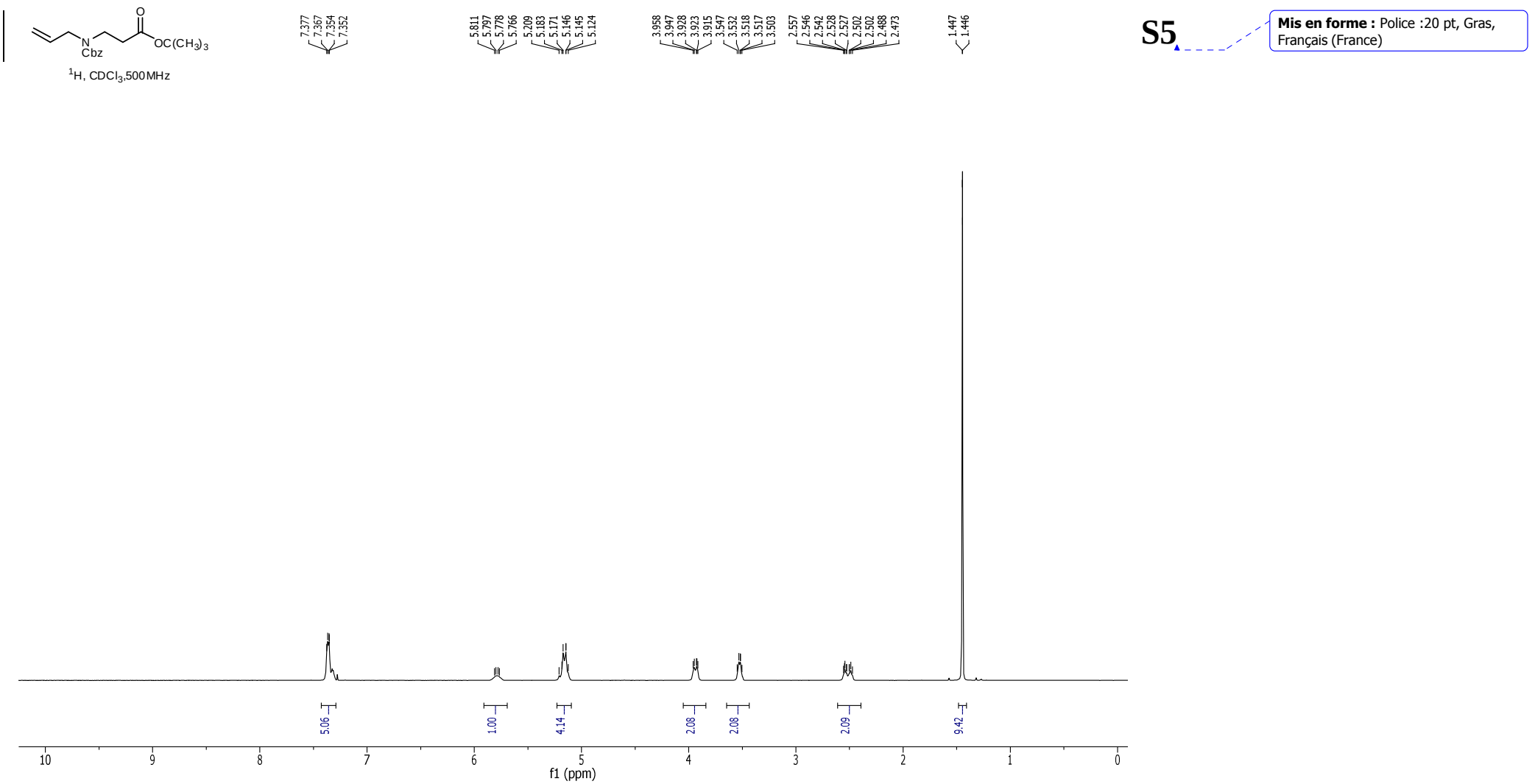

S5

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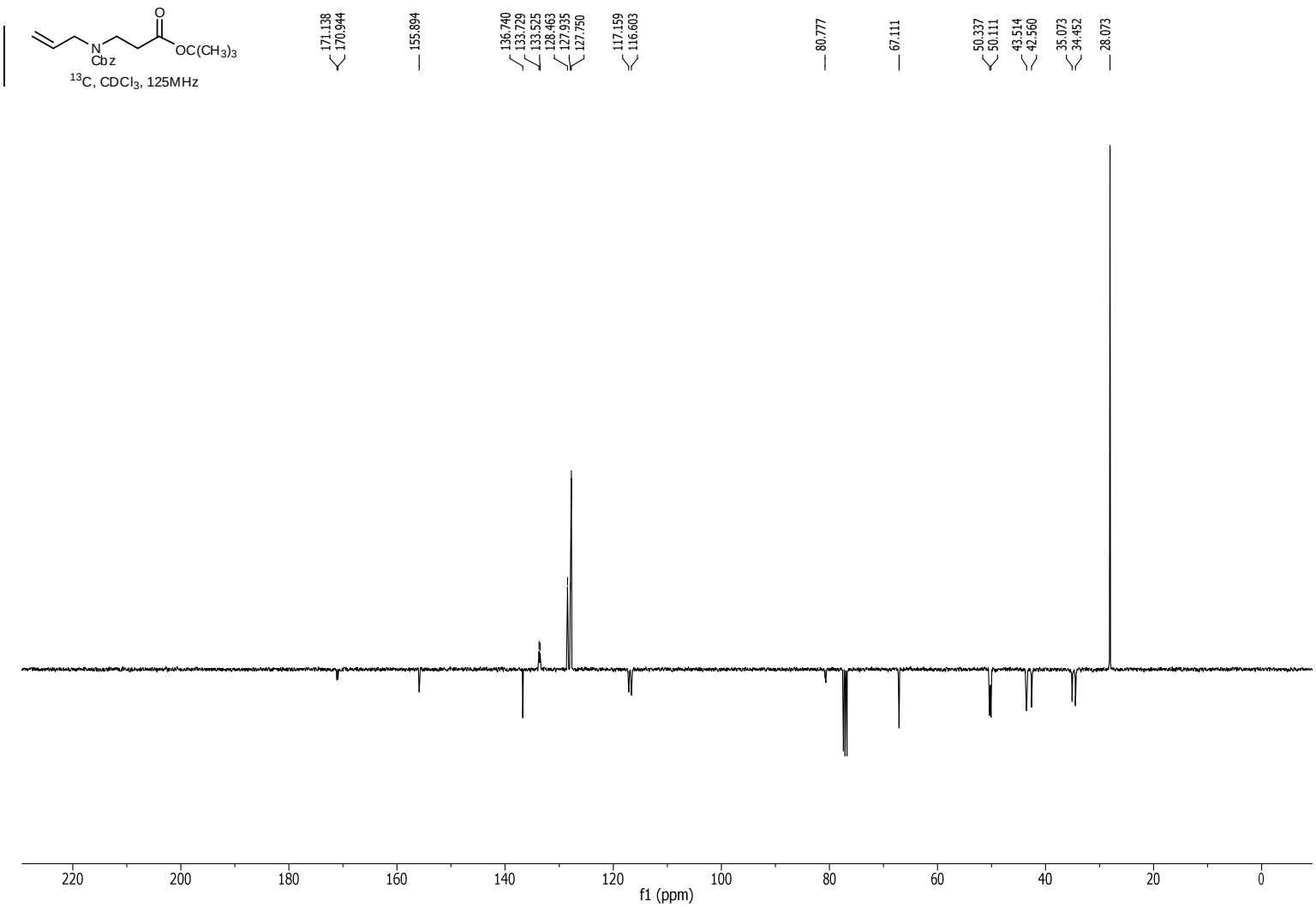
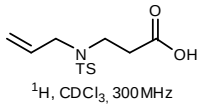


S5

Mis en forme : Police :20 pt, Gras, Français (France)

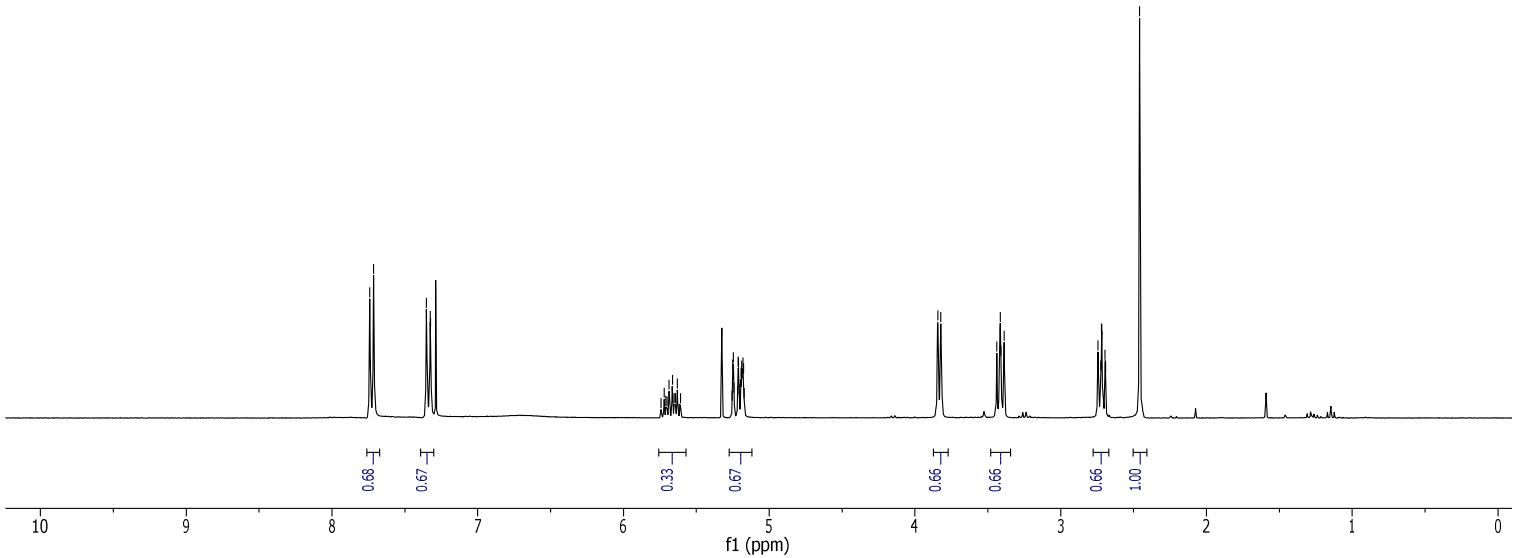


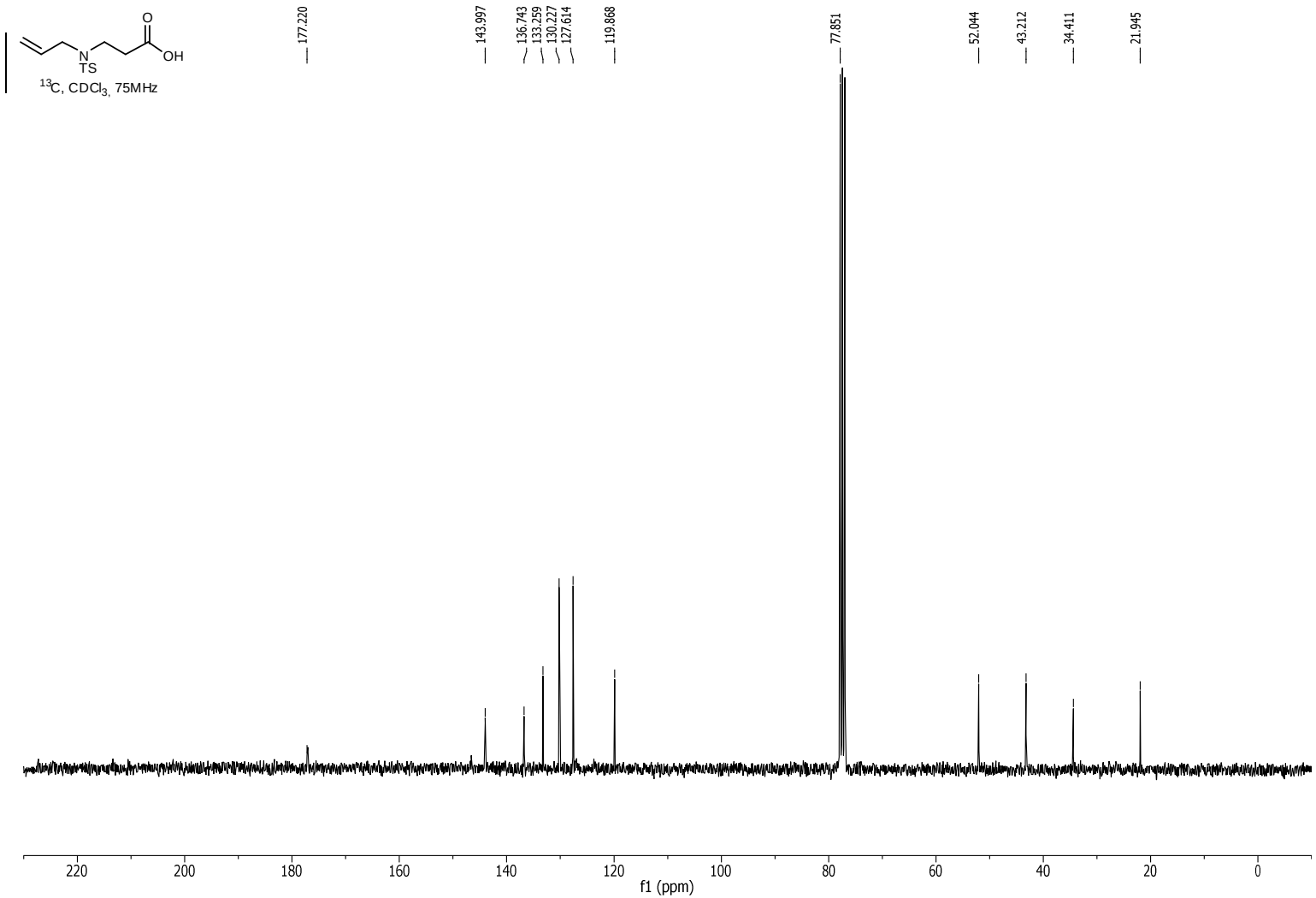
^{1}H, $CDCl_3$, 300MHz

7.741
7.736
7.714
7.352
7.326
7.323
5.742
5.721
5.709
5.700
5.687
5.664
5.652
5.643
5.631
5.618
5.609
5.250
5.246
5.241
5.218
5.214
5.210
5.206
5.193
5.189
5.184
5.181
3.822
3.439
3.415
3.411
3.389
2.745
2.742
2.724
2.720
2.717
2.695
2.692
2.458

4

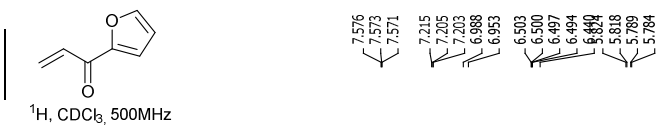
Mis en forme : Police :20 pt, Gras, Français (France)





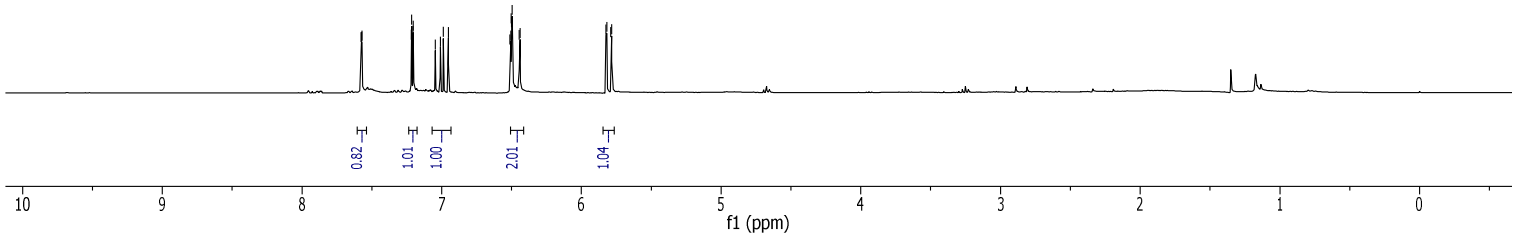
4

Mis en forme : Police :20 pt, Gras, Français (France)



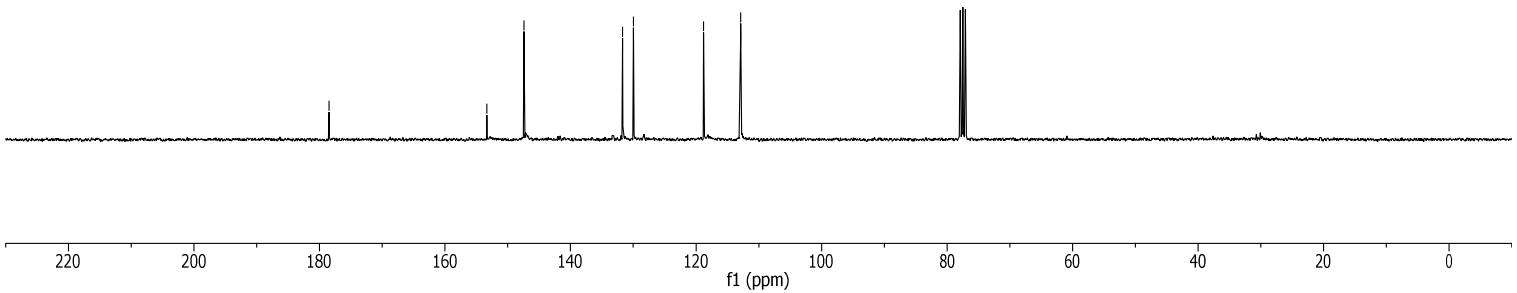
S6

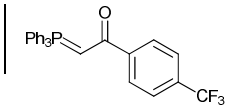
Mis en forme : Police :20 pt, Gras, Français (France)



S6

Mis en forme : Police :20 pt, Gras, Français (France)

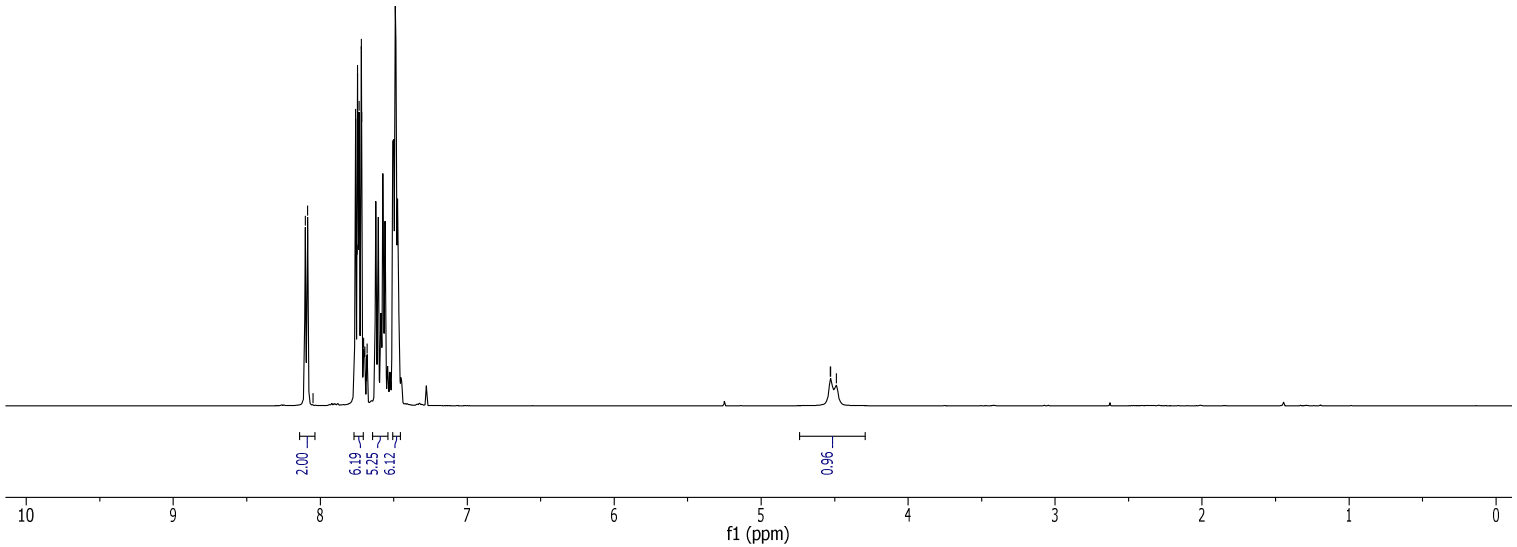


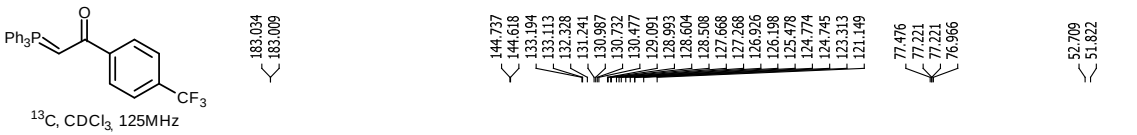


^{1}H, $CDCl_3$, 400MHz

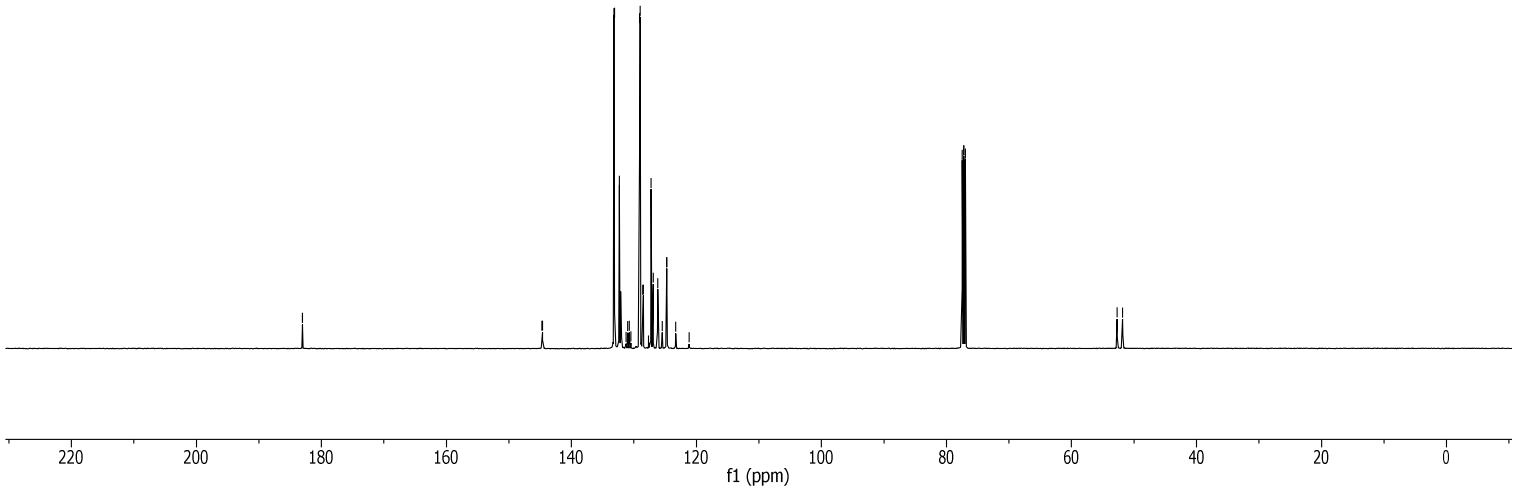
S12

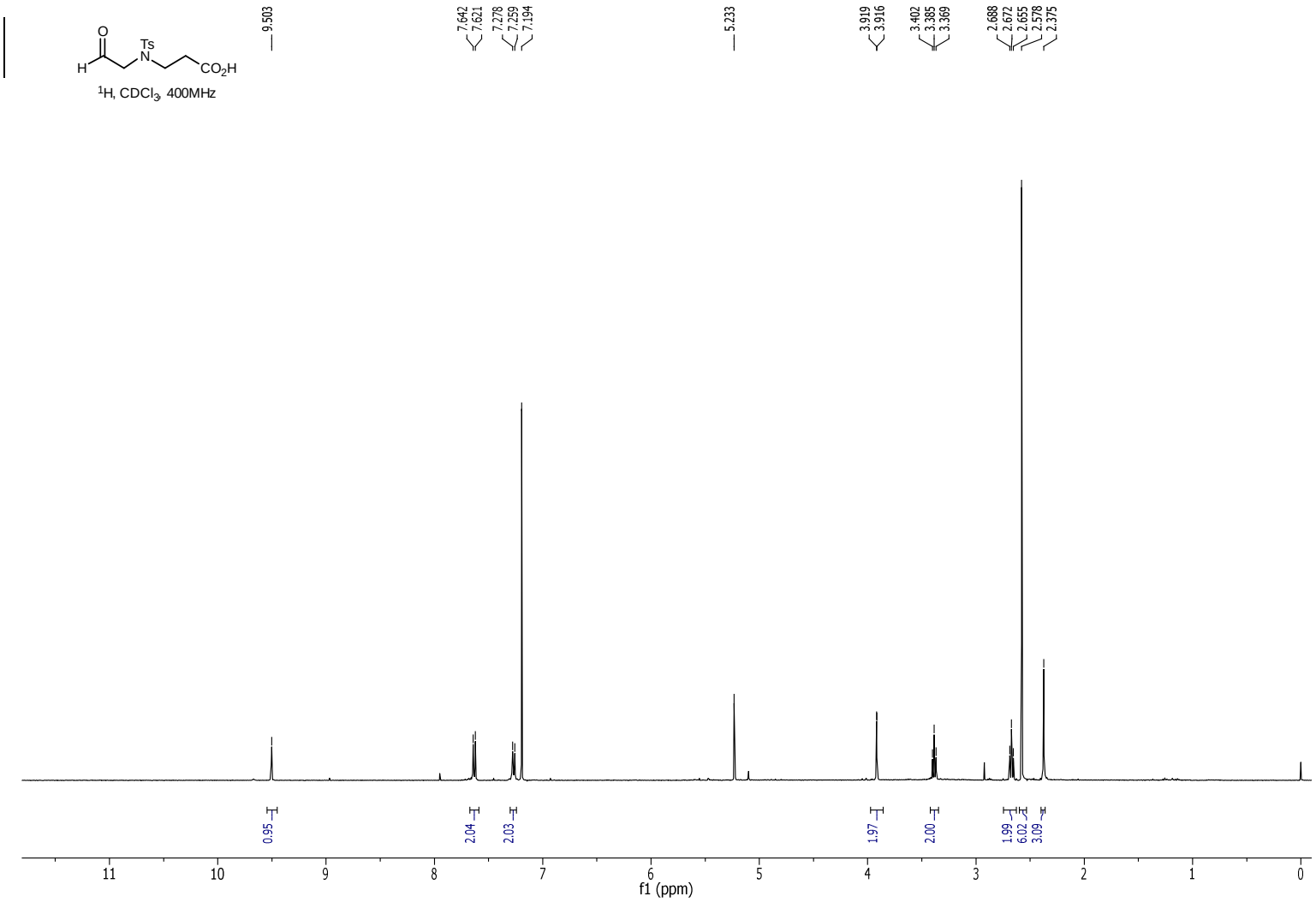
Mis en forme : Police :20 pt, Gras, Français (France)





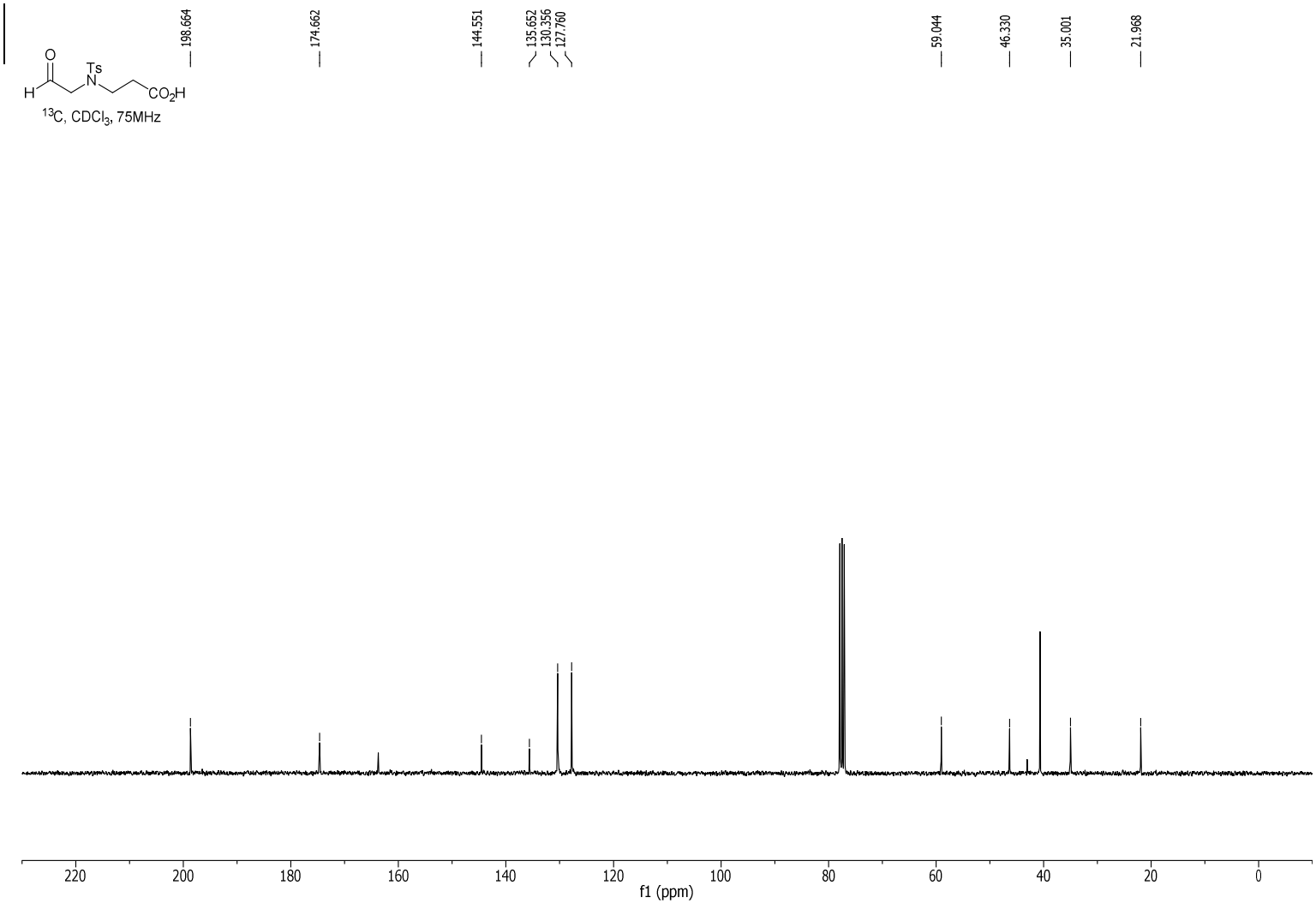
Mis en forme : Police :20 pt, Gras, Français (France)





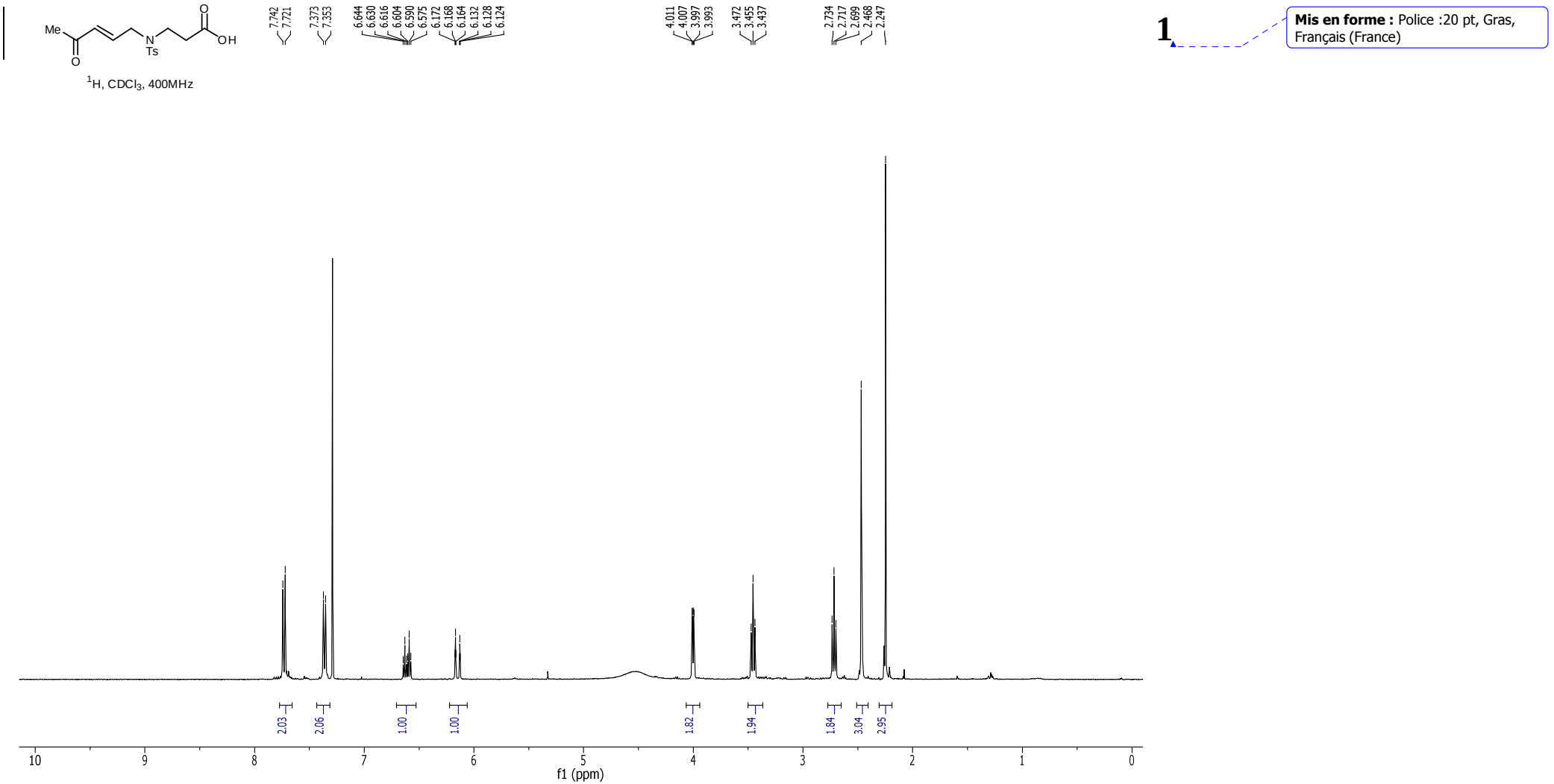
S1a

Mis en forme : Police :20 pt, Gras, Français (France)



S1a

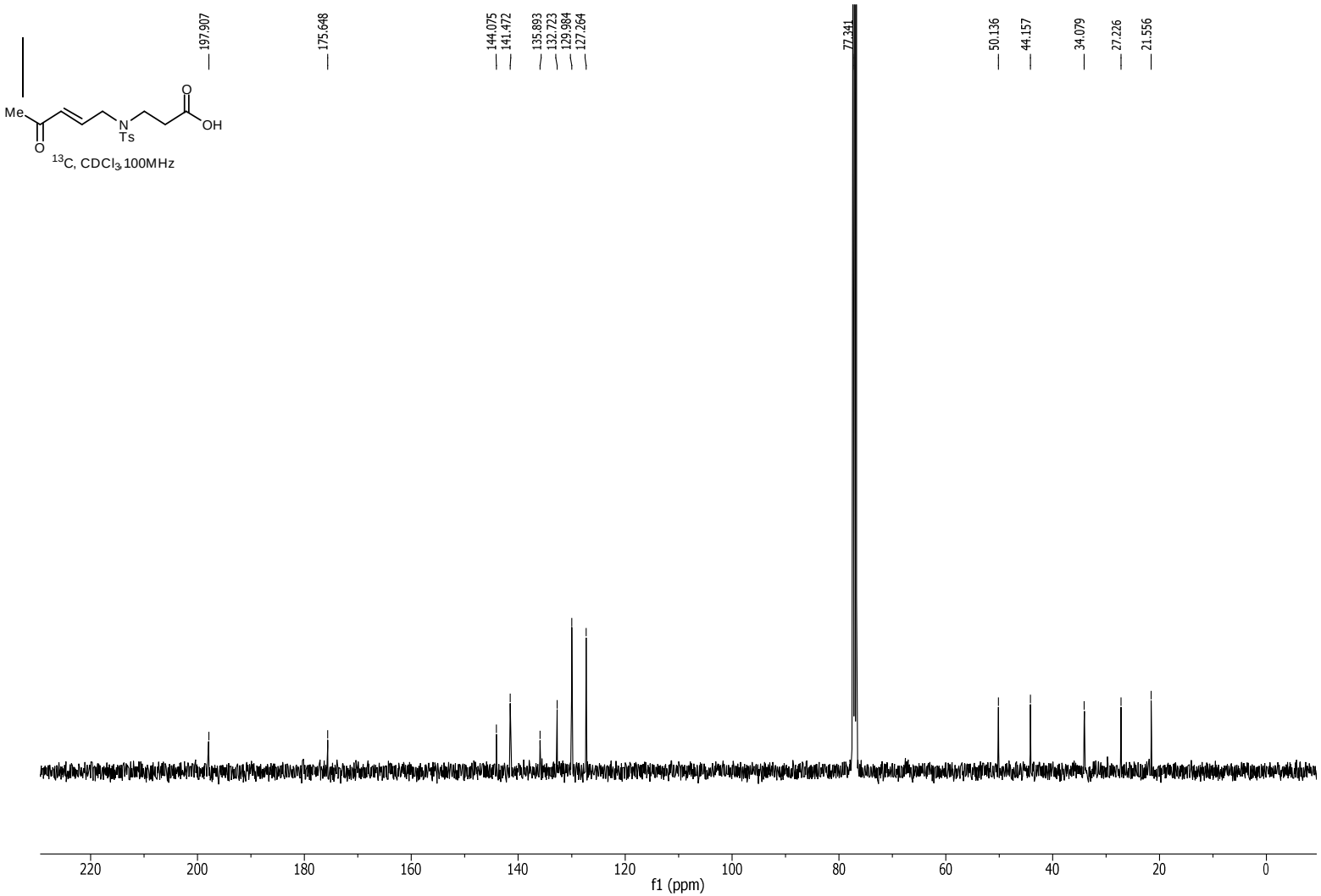
Mis en forme : Police :20 pt, Gras, Français (France)



^{1}H, $CDCl_3$, 400MHz

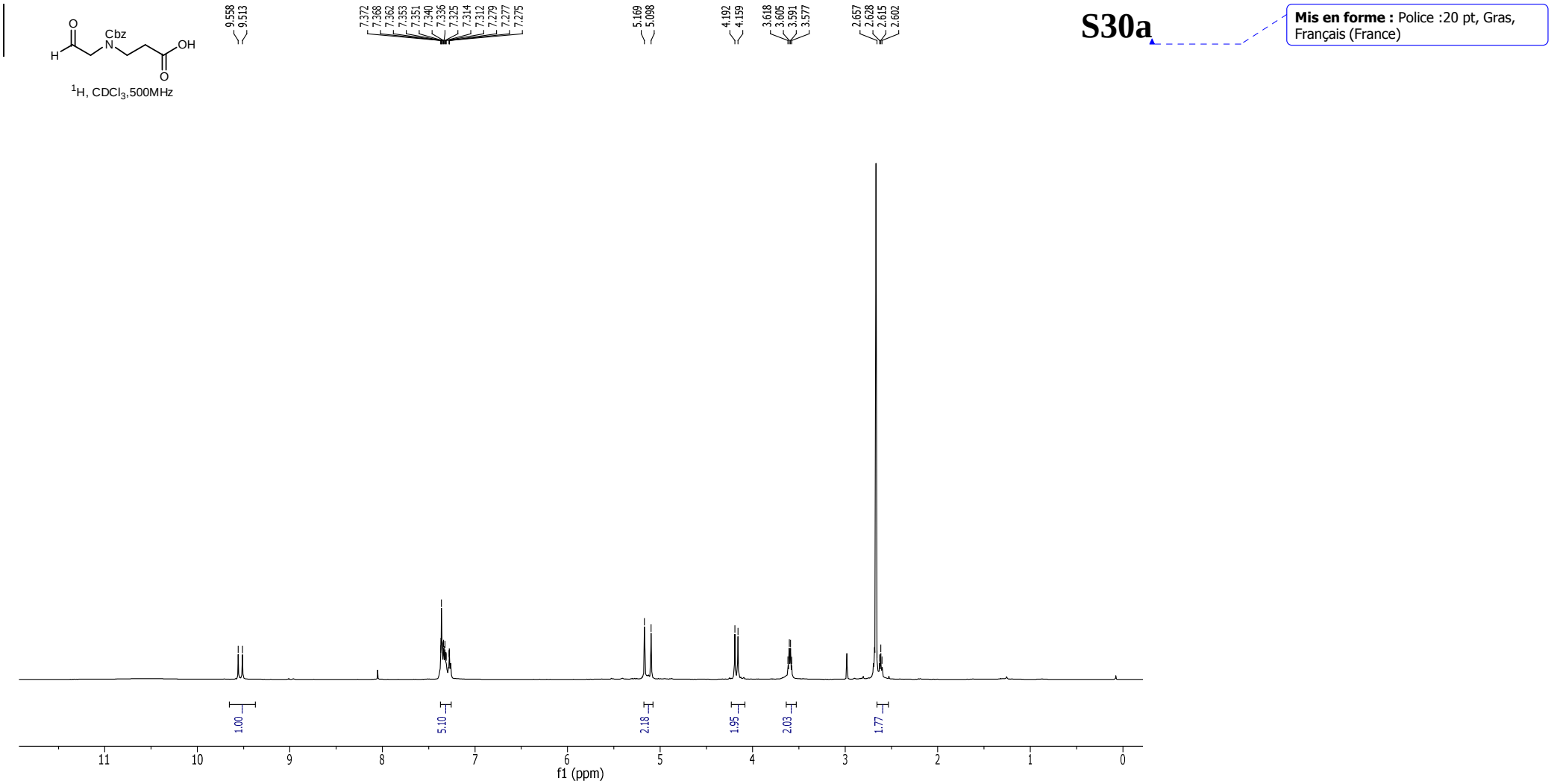
1

Mis en forme : Police :20 pt, Gras, Français (France)



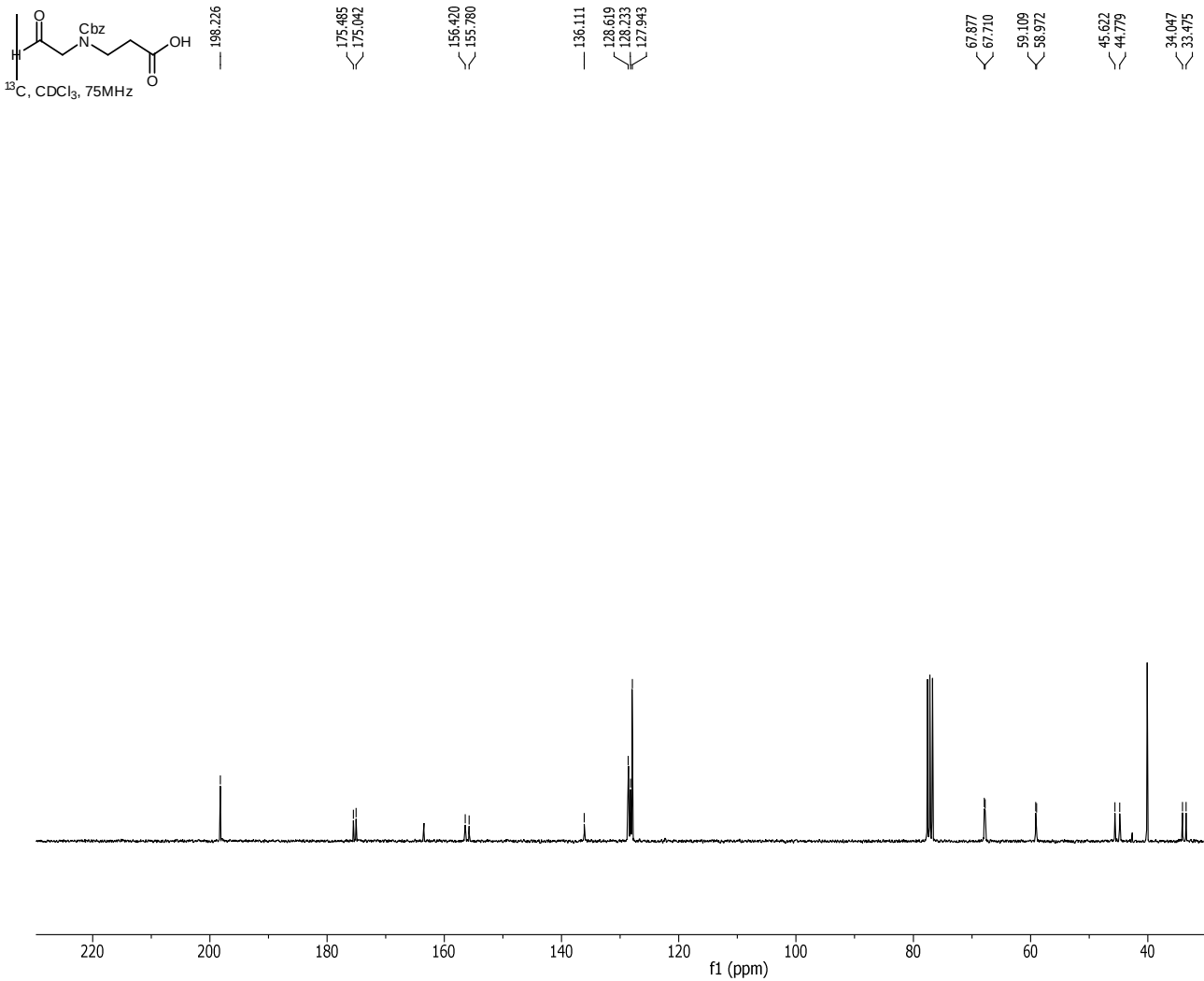
1

Mis en forme : Police :20 pt, Gras, Français (France)



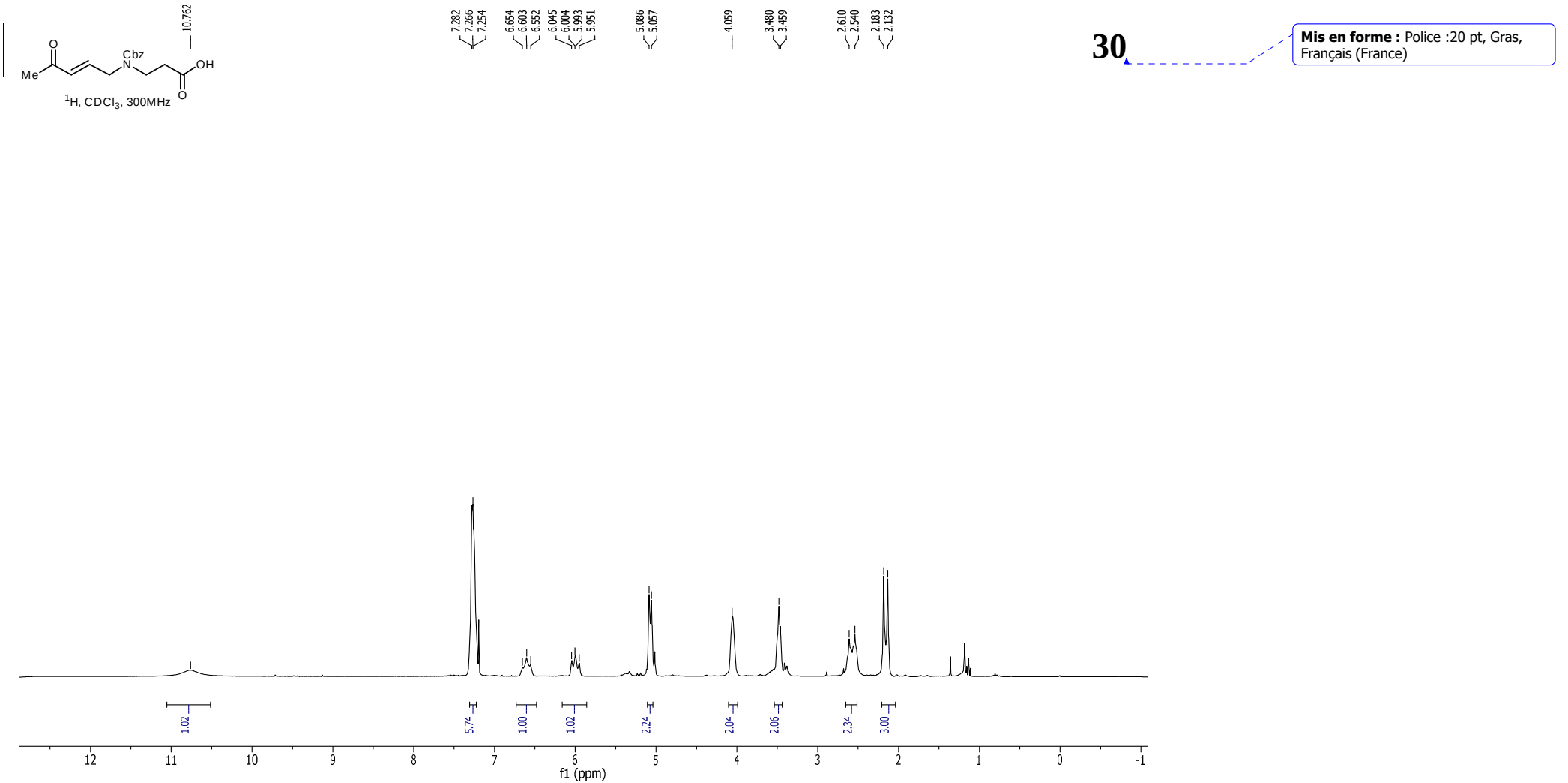
S30a

Mis en forme : Police :20 pt, Gras, Français (France)



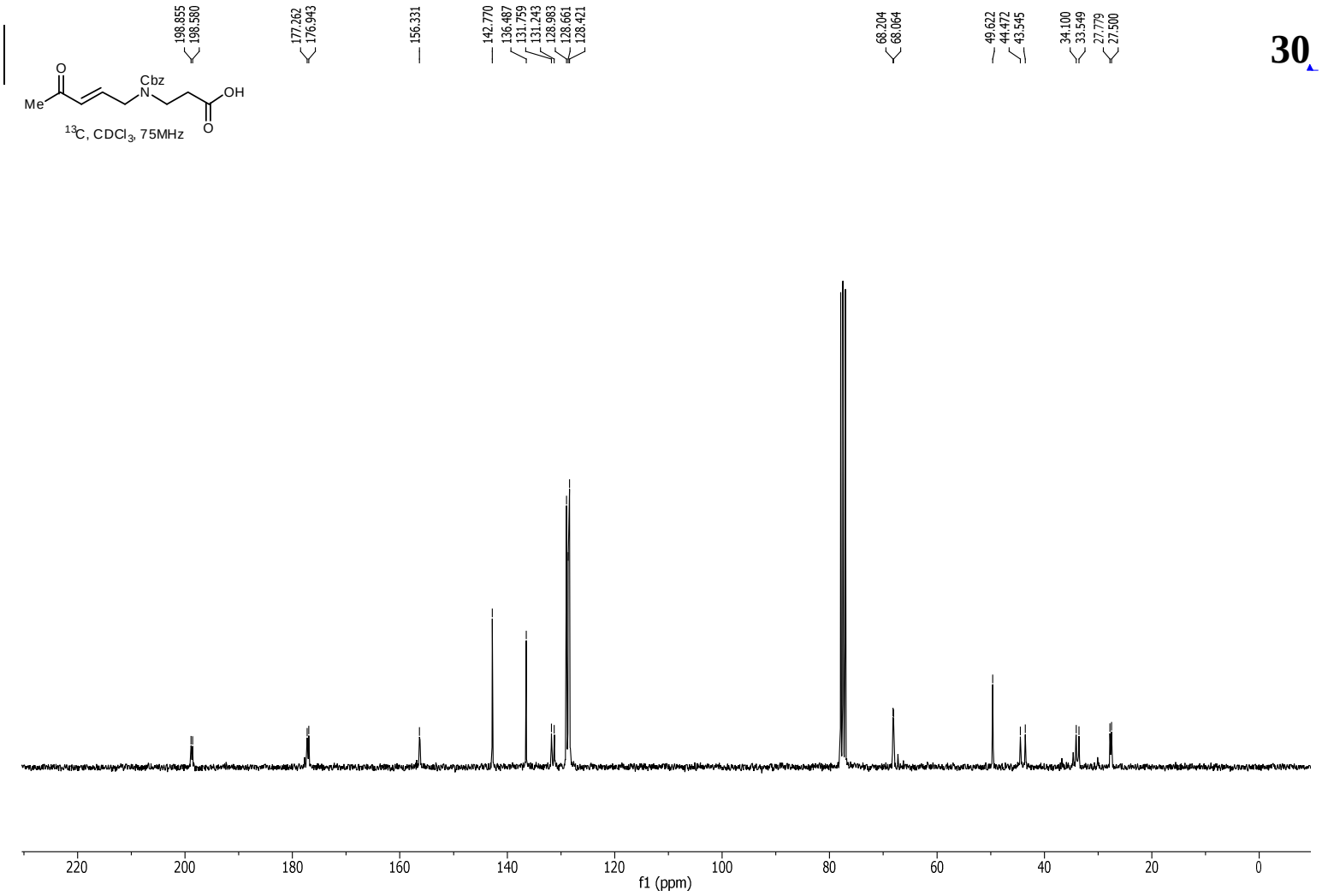
S30a

Mis en forme : Police :20 pt, Gras, Français (France)



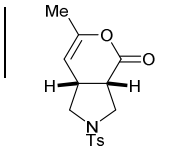
30

Mis en forme : Police :20 pt, Gras, Français (France)



30

Mis en forme : Police :20 pt, Gras, Français (France)

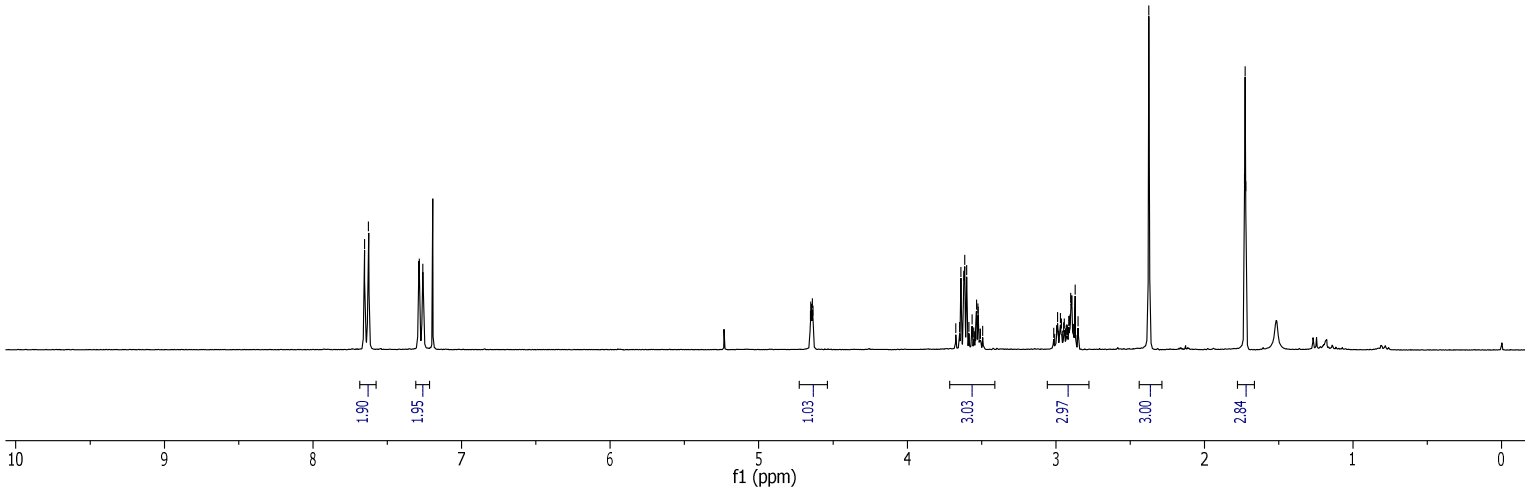


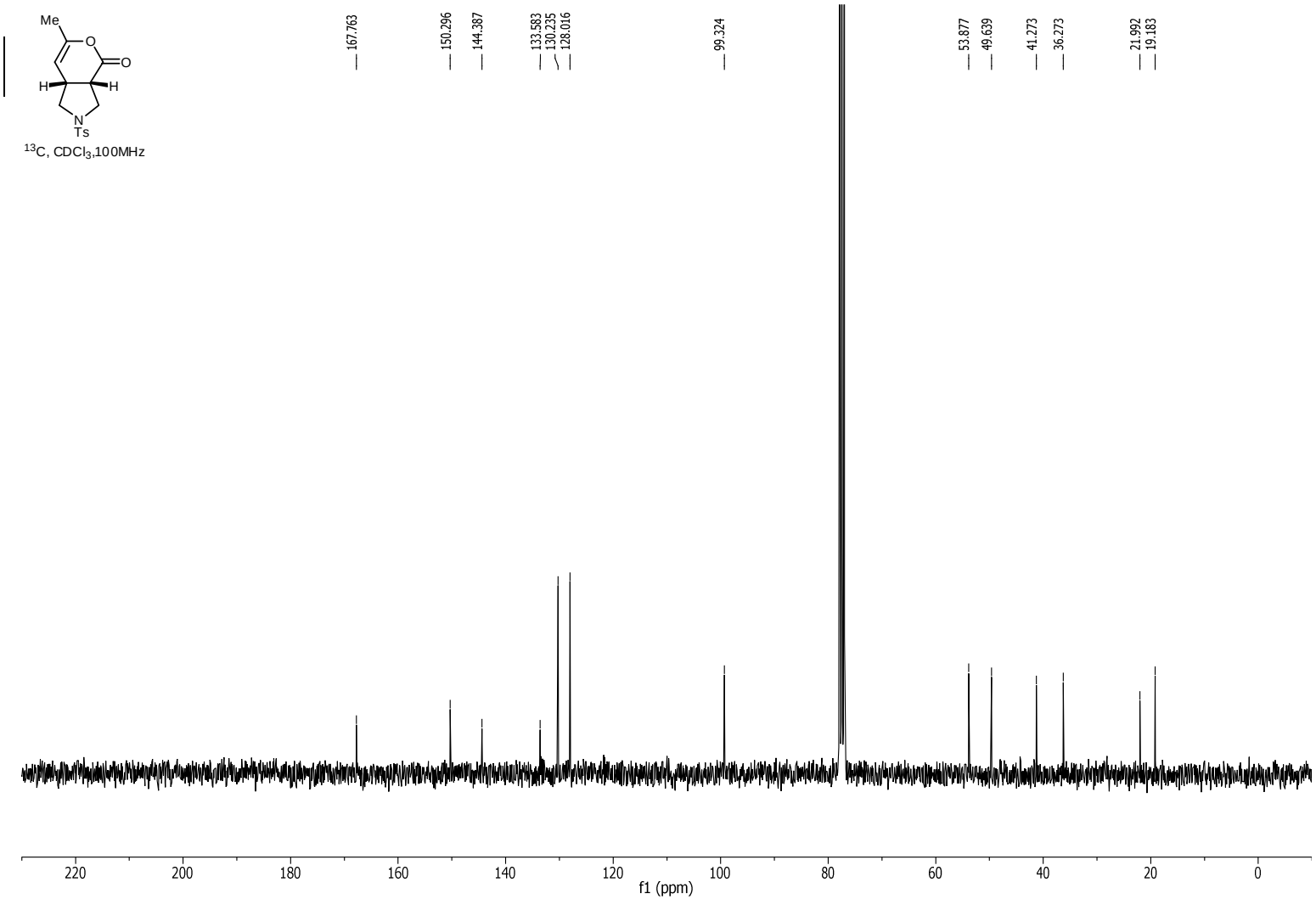
^{1}H, $CDCl_3$, 400MHz

7.654 7.626 7.289 7.285 7.260 4.652 4.649 4.645 4.639 4.635 3.640 3.620 3.613 3.601 3.585 3.565 3.535 3.524 3.522 2.989 2.970 2.900 2.896 2.891 2.871 2.374 1.730 1.726 1.722

2

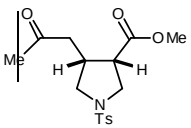
Mis en forme : Police :20 pt, Gras, Français (France)





2

Mis en forme : Police :20 pt, Gras, Français (France)



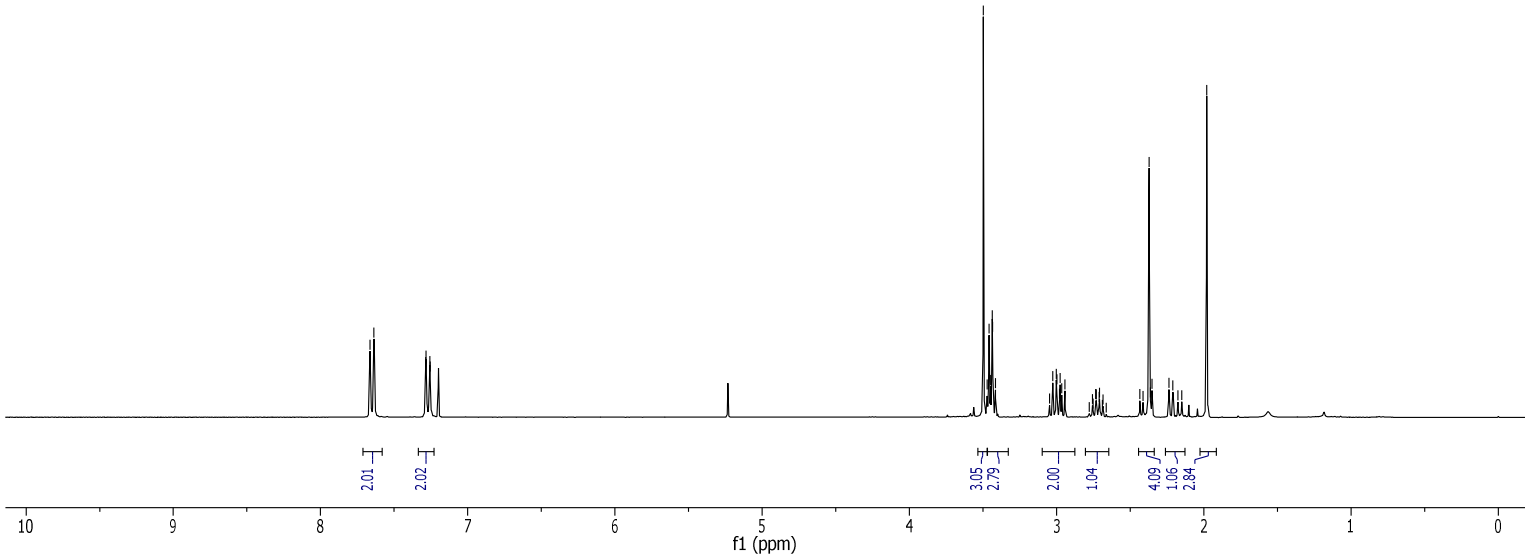
^{1}H, $CDCl_3$, 300MHz

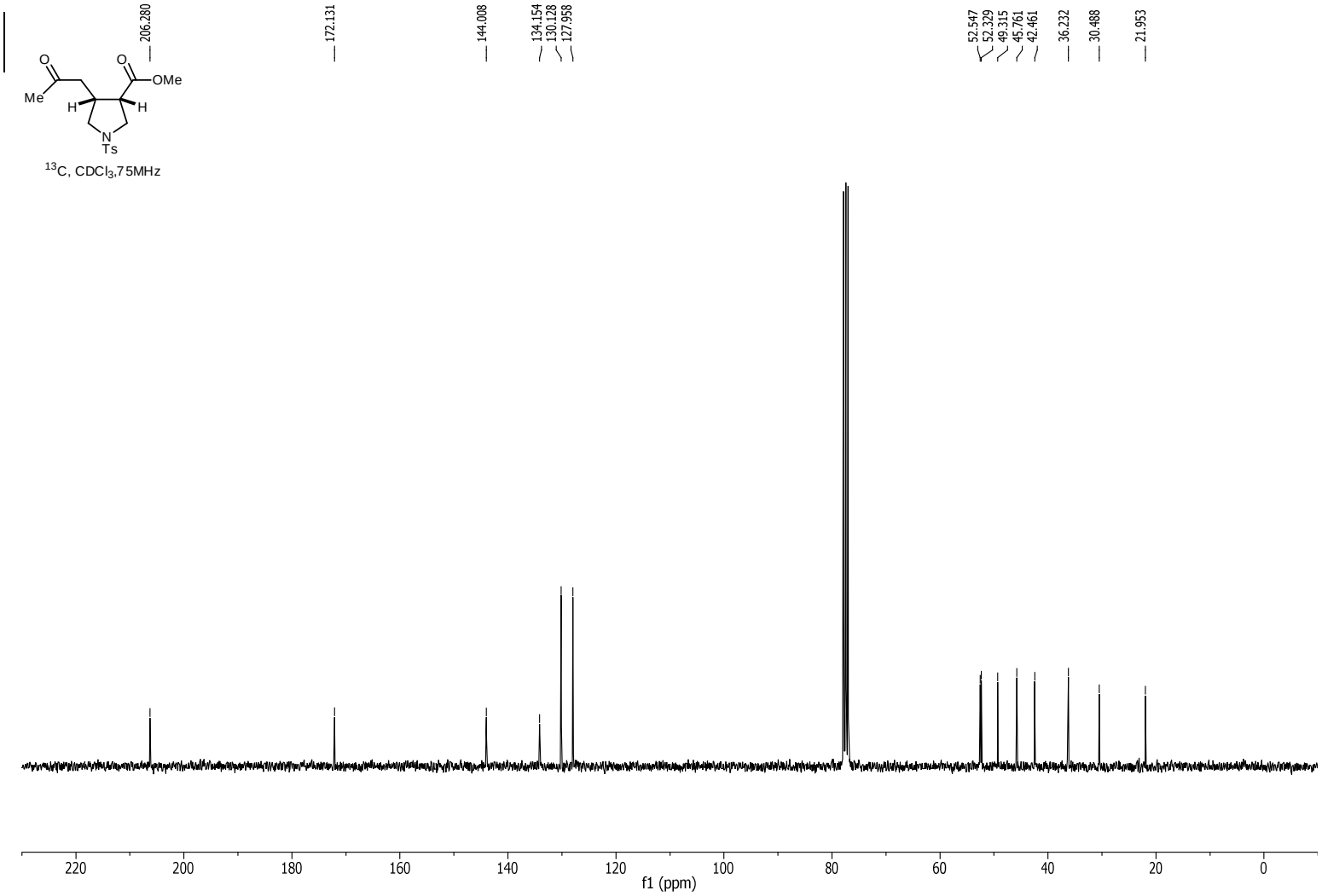
7.664
7.637
7.287
7.284
7.258
7.256

3.498
3.471
3.460
3.449
3.438
3.436
3.416
3.049
3.026
3.003
2.999
2.980
2.977
2.966
2.944
2.779
2.757
2.753
2.734
2.730
2.712
2.708
2.689
2.685
2.663
2.434
2.413
2.373
2.363
2.352
2.237
2.211
2.176
2.149
1.981

3

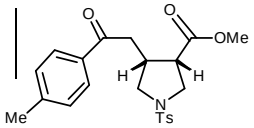
Mis en forme : Police :20 pt, Gras, Français (France)





3

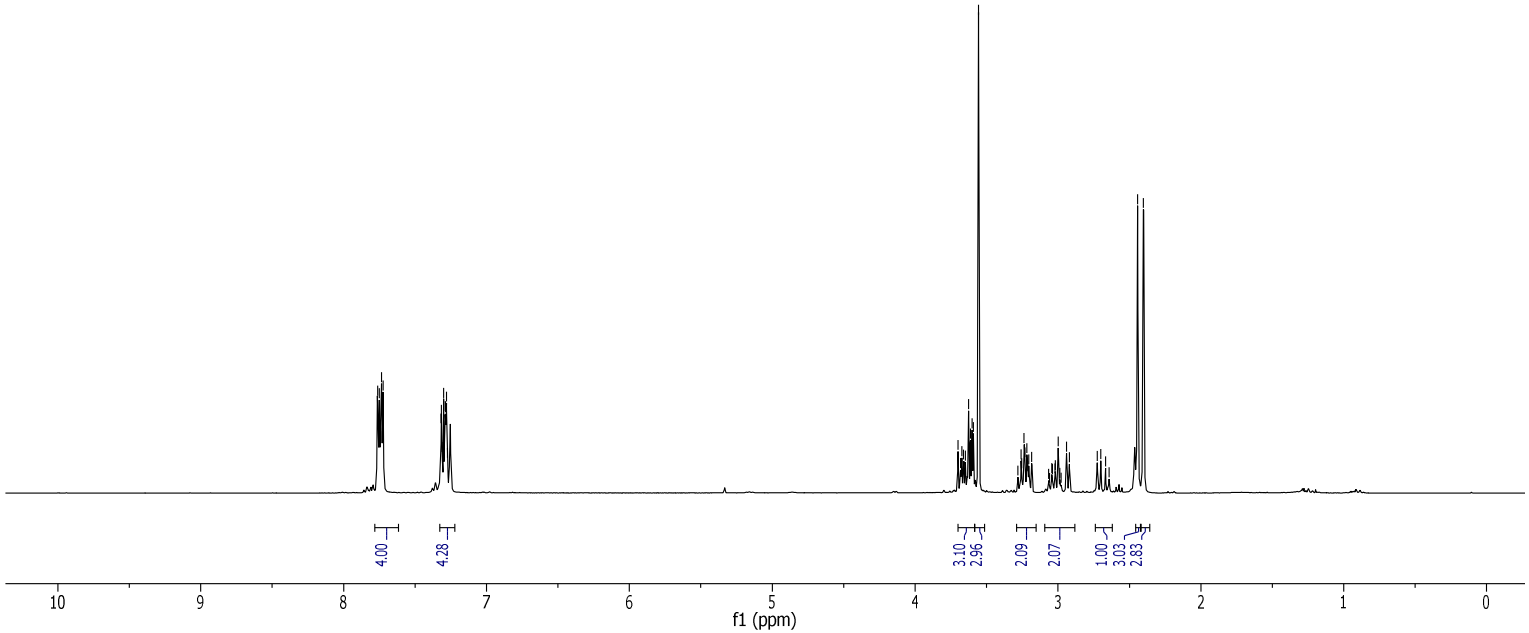
Mis en forme : Police :20 pt, Gras, Français (France)

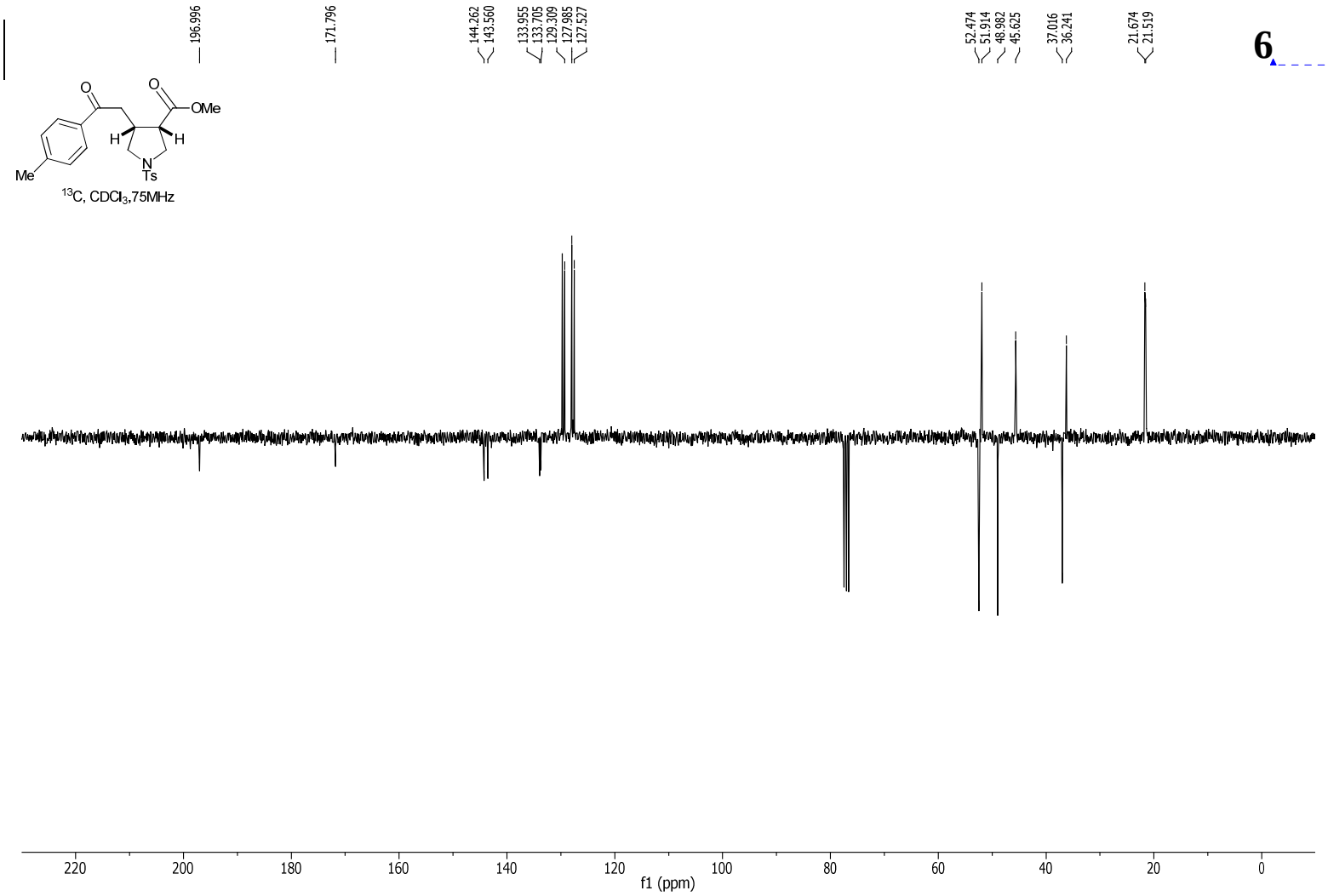


^{1}H, $CDCl_3$, 300MHz

6

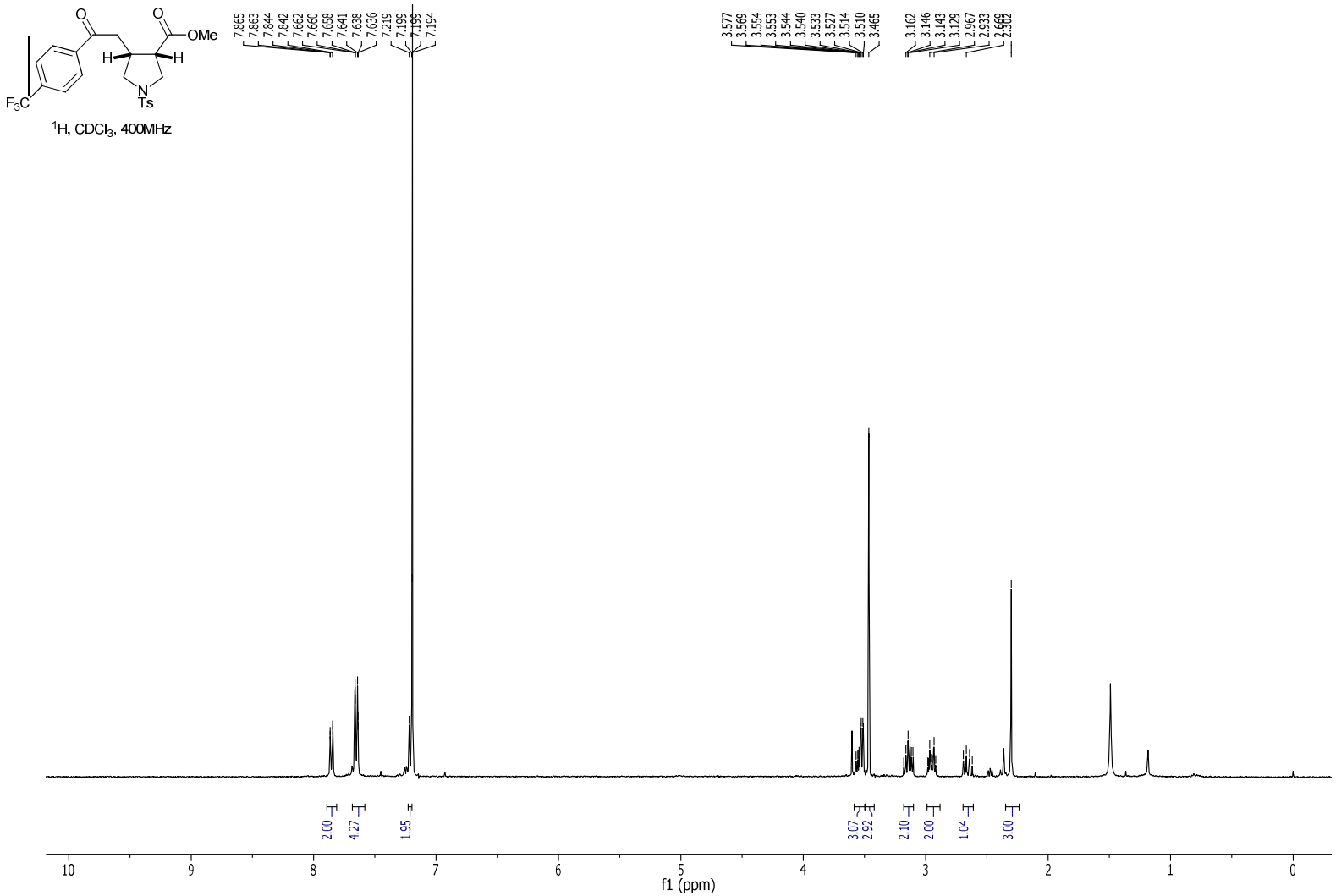
Mis en forme : Police :20 pt, Gras, Français (France)





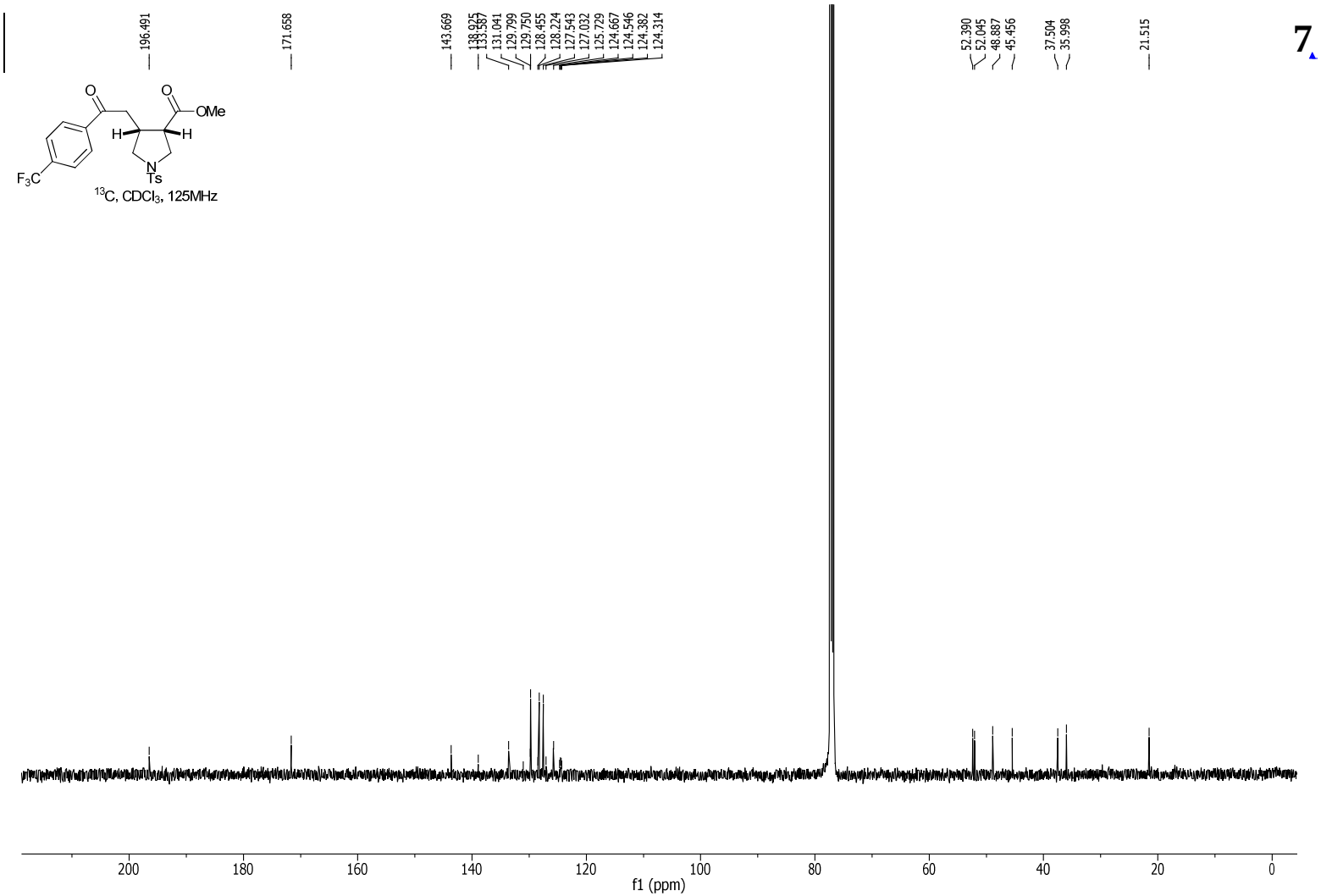
6

Mis en forme : Police :20 pt, Gras, Français (France)



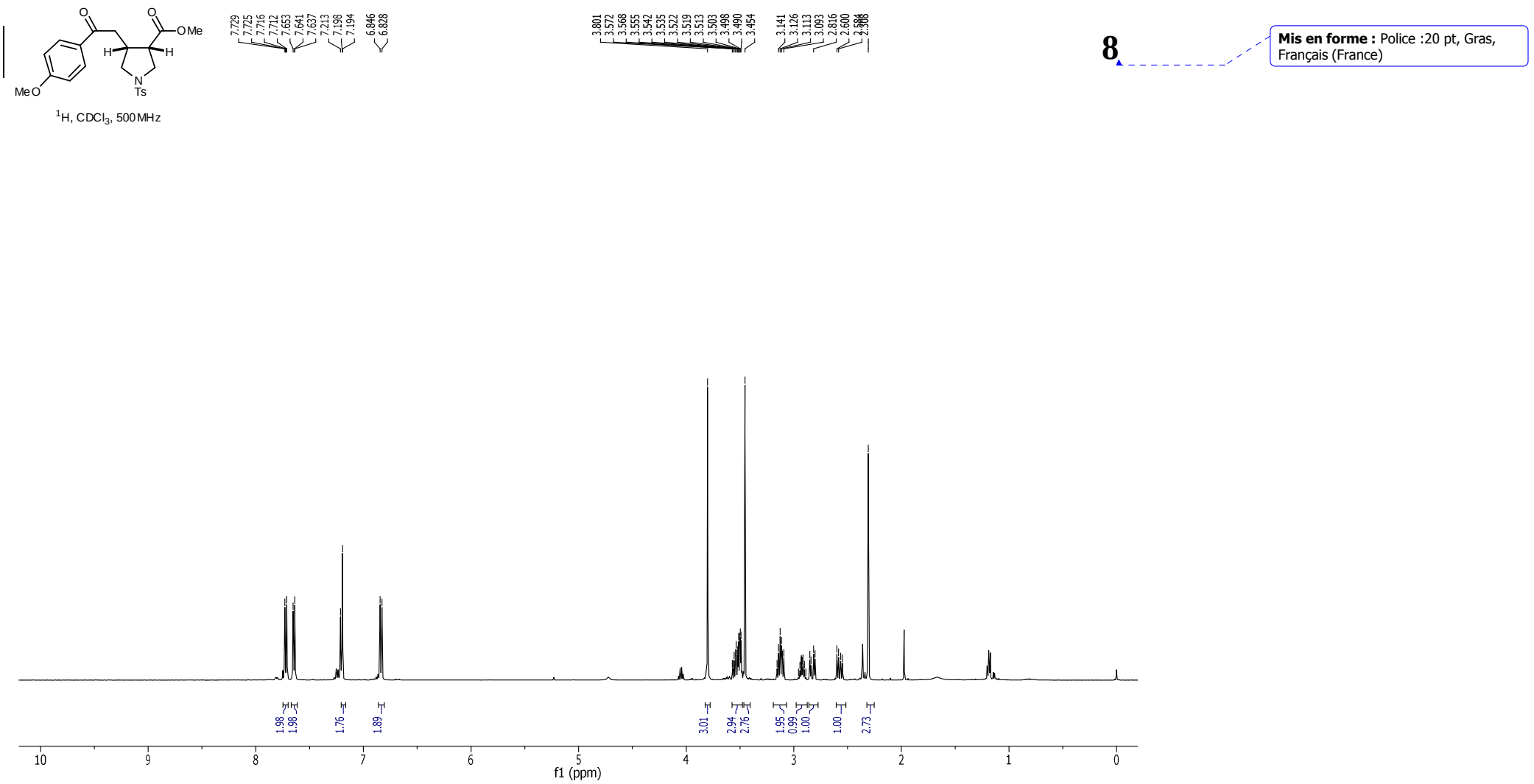
7

Mis en forme : Police :20 pt, Gras, Français (France)



7

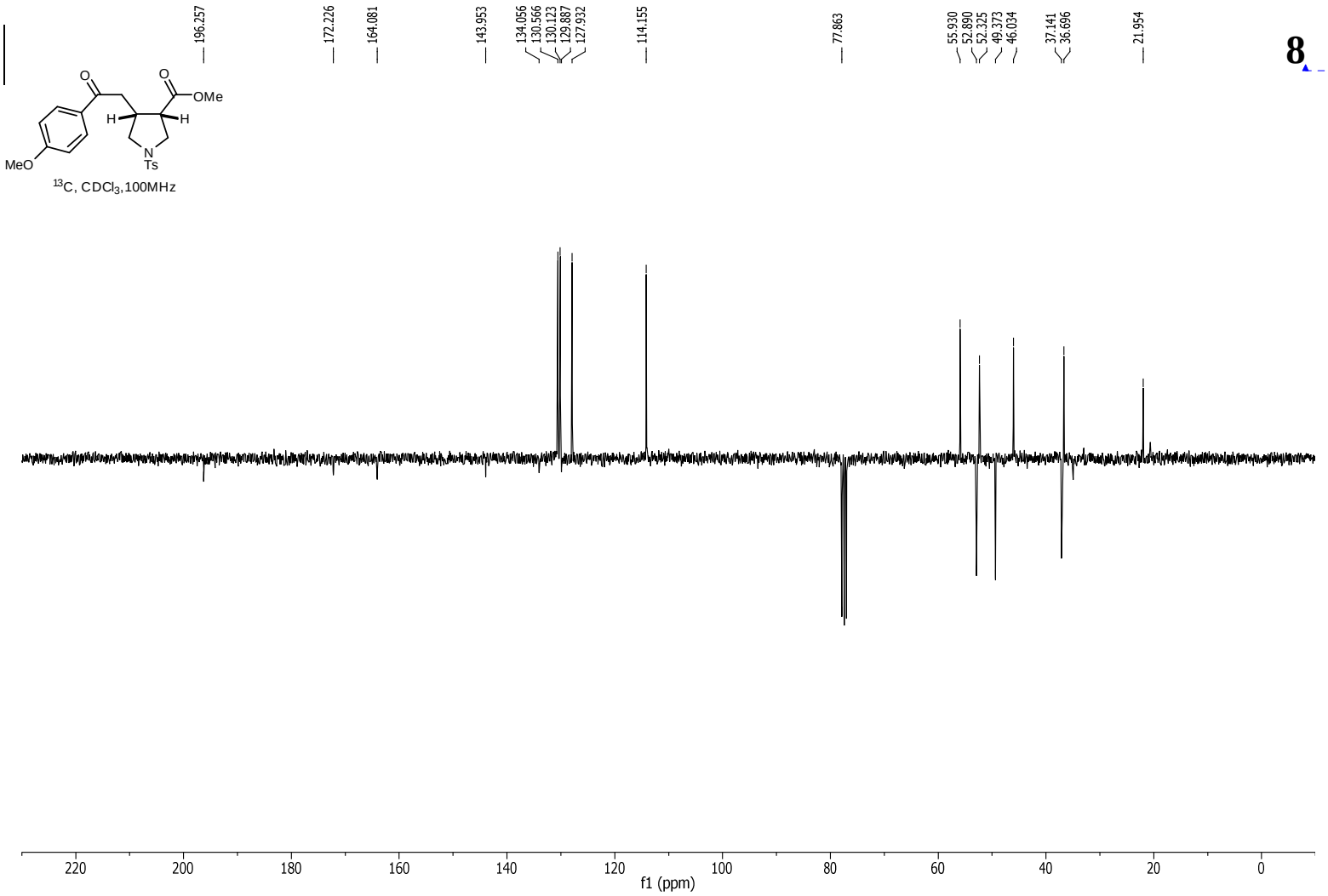
Mis en forme : Police :20 pt, Gras, Français (France)



^{1}H, $CDCl_3$, 500 MHz

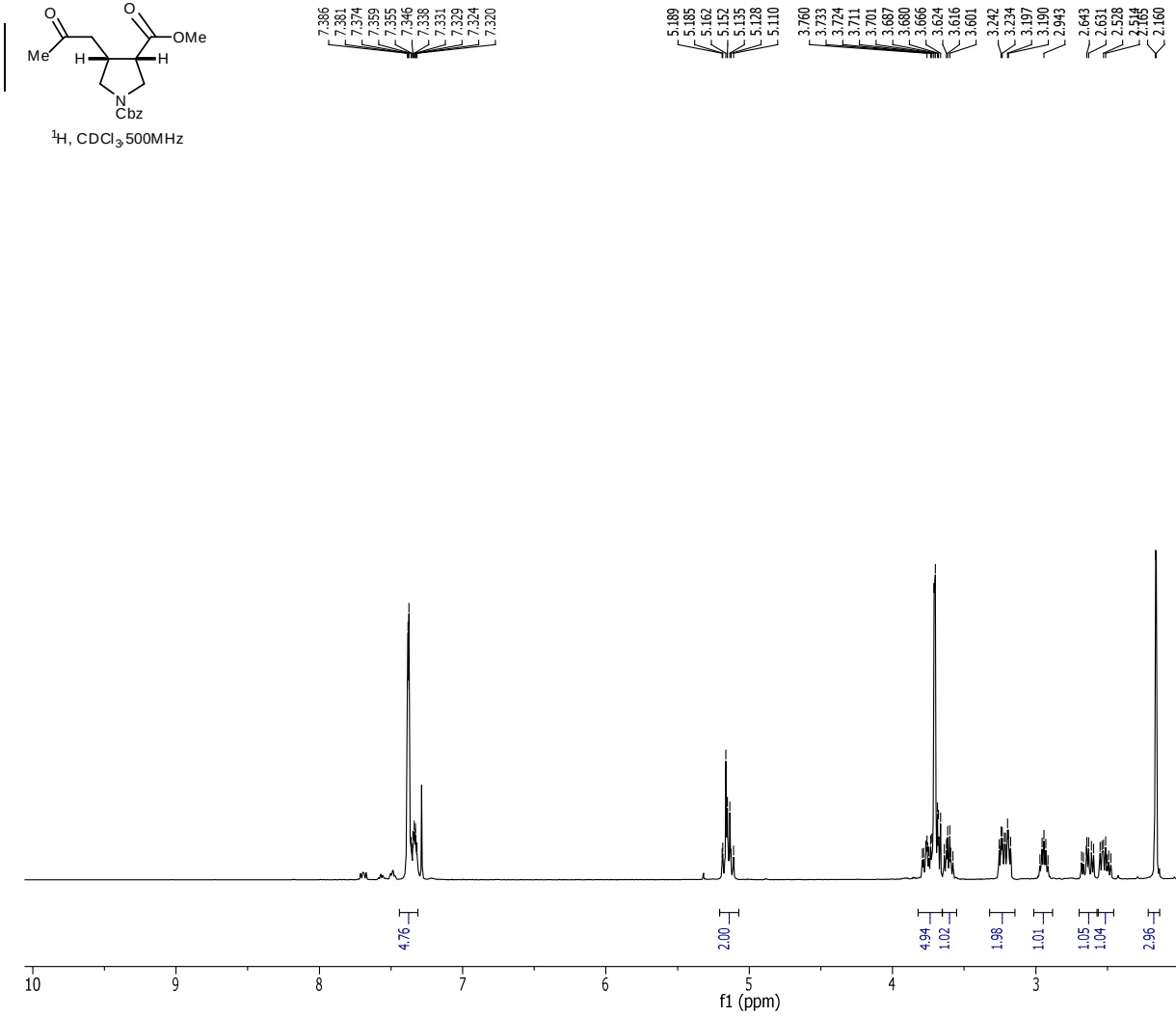
8

Mis en forme : Police :20 pt, Gras, Français (France)



8

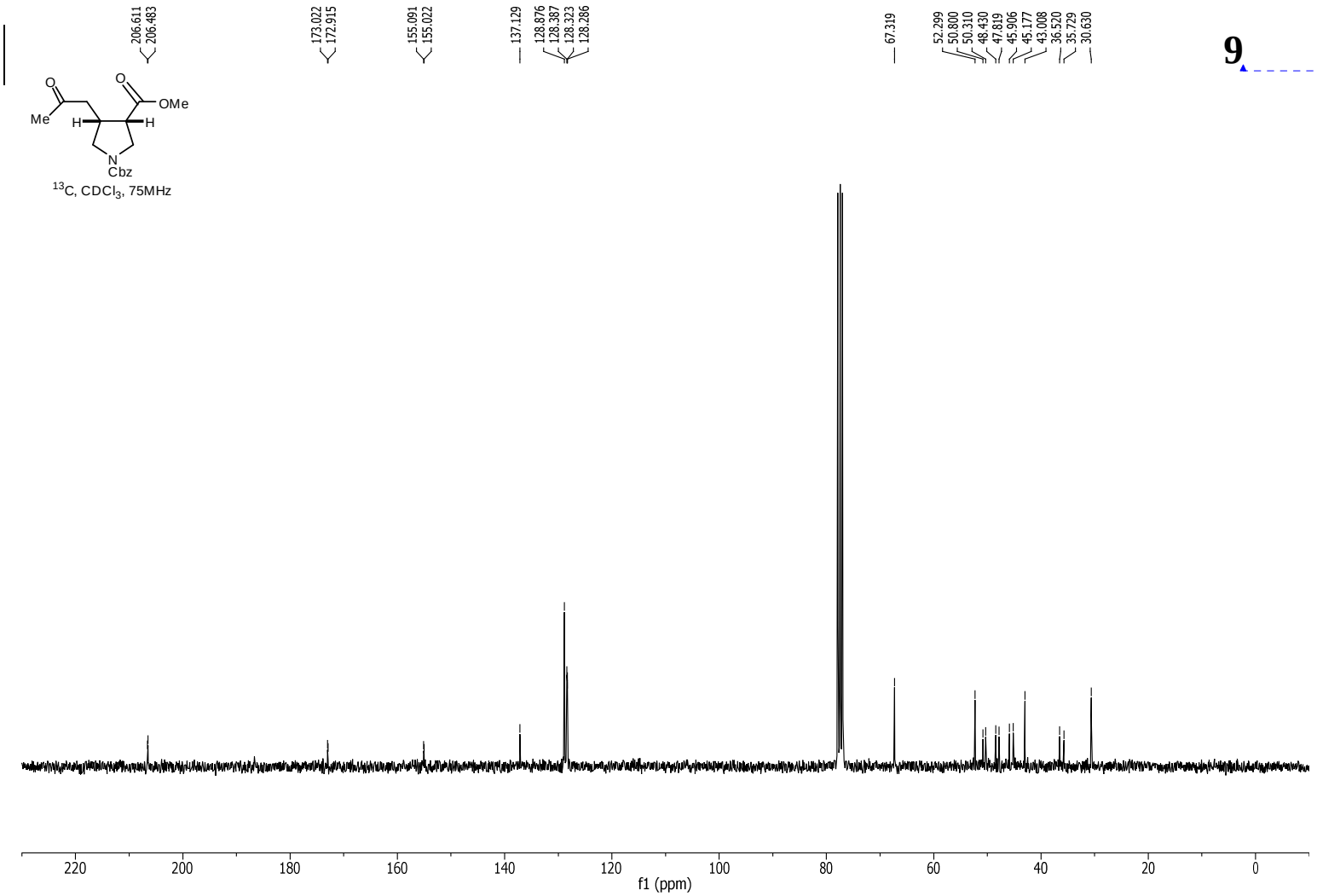
Mis en forme : Police :20 pt, Gras, Français (France)



^{1}H, $CDCl_3$ 500MHz

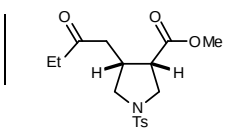
9

Mis en forme : Police :20 pt, Gras, Français (France)



9

Mis en forme : Police :20 pt, Gras, Français (France)

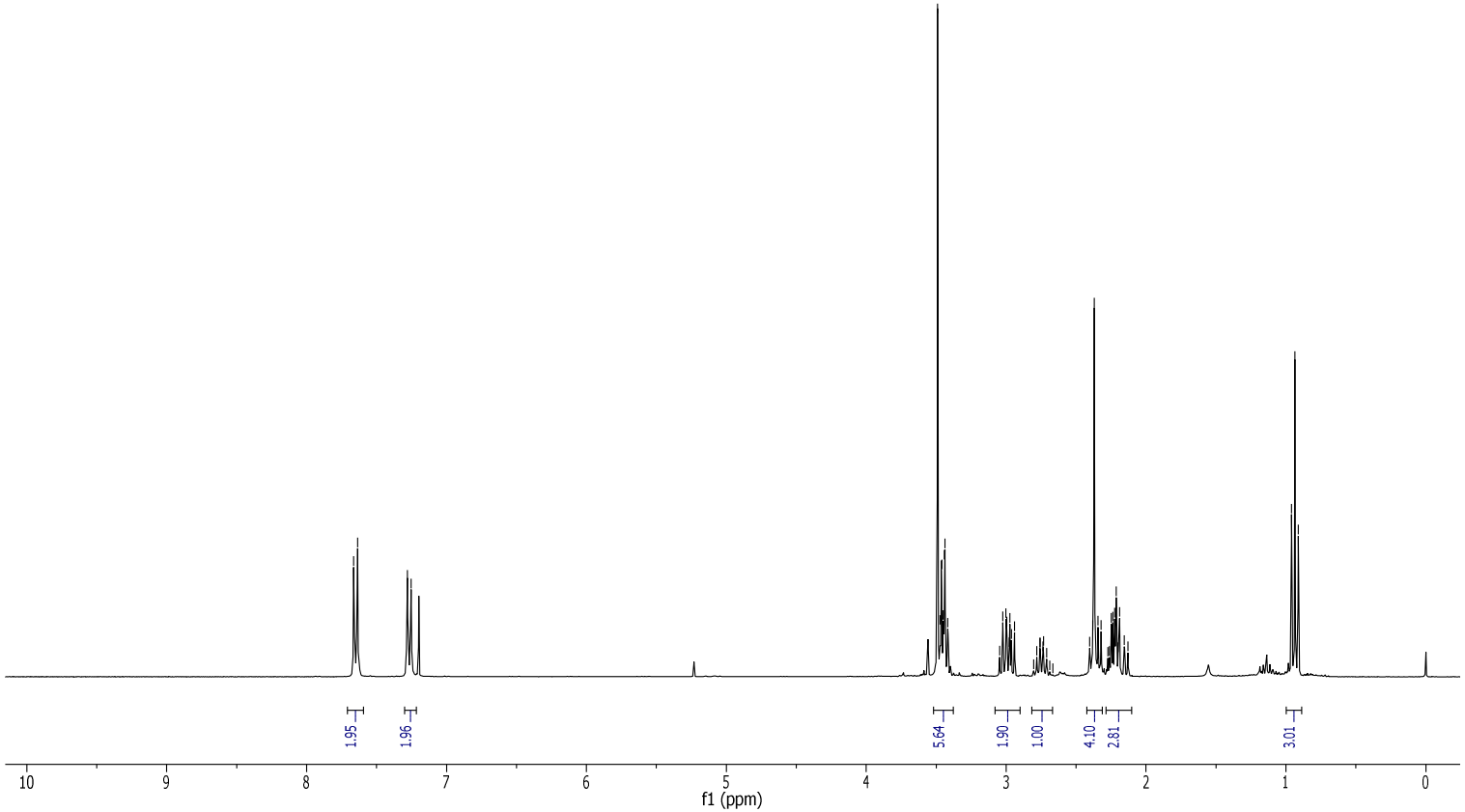


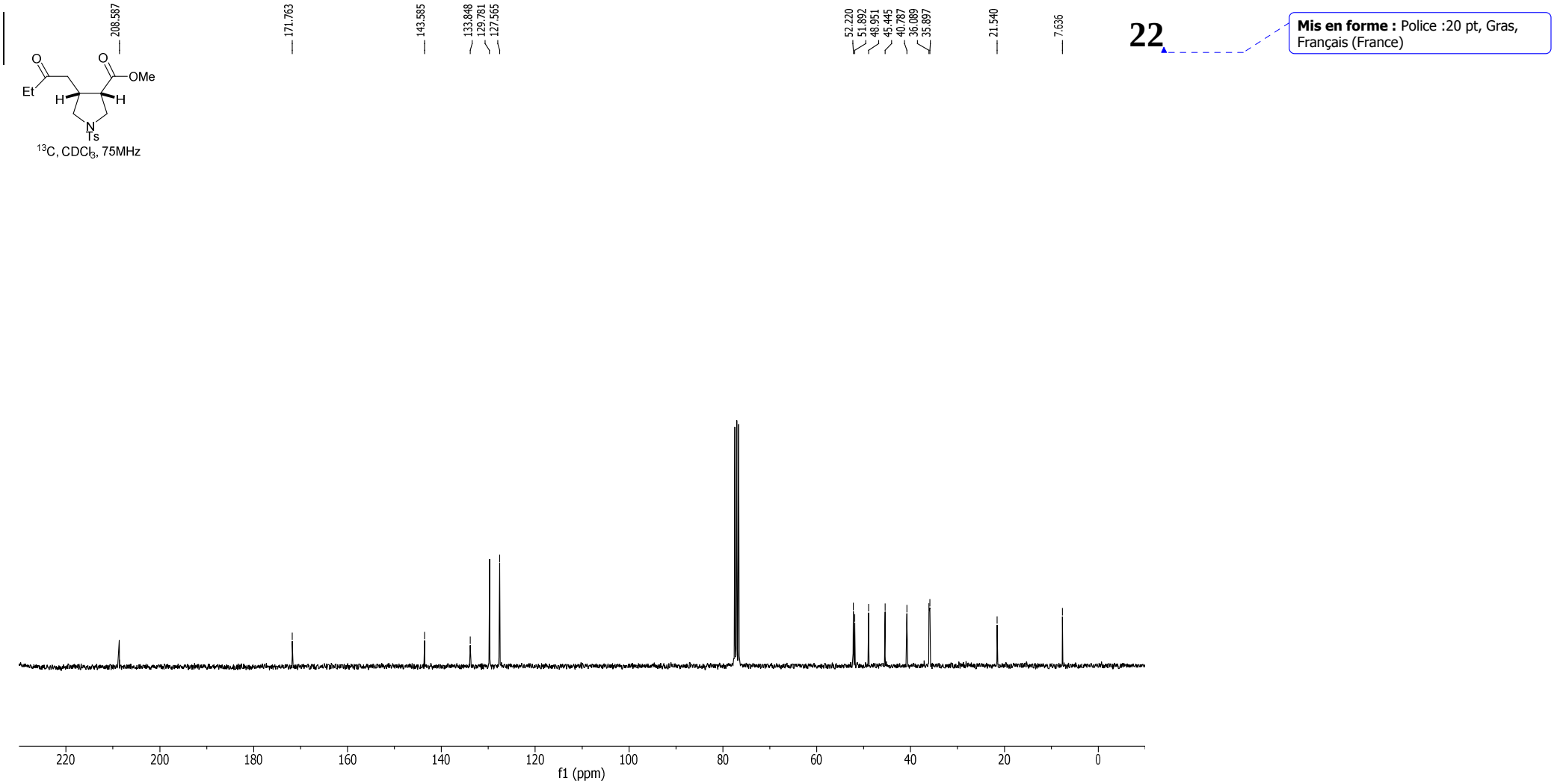
^{1}H, $CDCl_3$, 300MHz

7.663
7.636
7.279
7.254
3.490
3.471
3.463
3.460
3.450
3.441
3.437
3.417
3.024
3.001
2.996
2.973
2.941
2.403
2.381
2.370
2.342
2.321
2.248
2.237
2.223
2.214
2.189
2.155
0.966
0.936
0.911

22

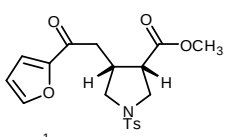
Mis en forme : Police :20 pt, Gras, Français (France)





22

Mis en forme : Police :20 pt, Gras, Français (France)



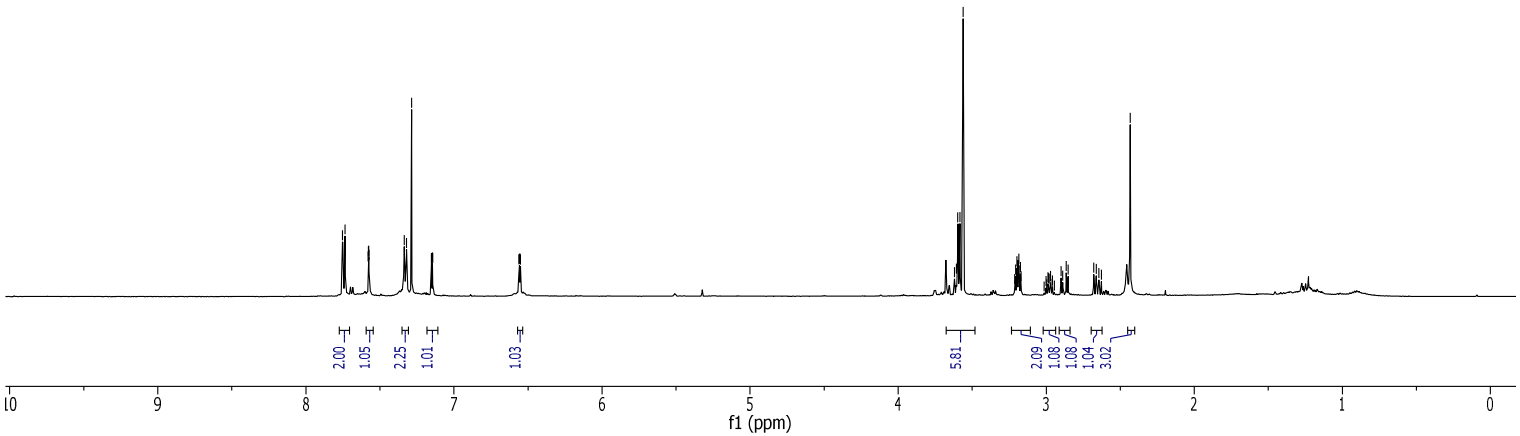
^{1}H, $CDCl_3$, 500MHz

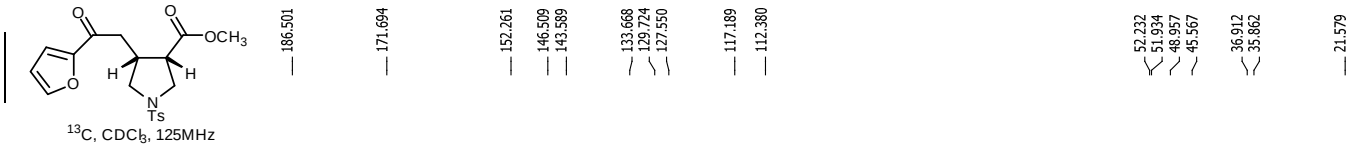
7.752
7.735
7.579
7.578
7.576
7.574
7.336
7.320
7.287
7.145
6.561
6.557
6.554
6.550

3.620
3.607
3.597
3.583
3.562
3.213
3.208
3.199
3.194
3.188
3.185
3.174
3.171
3.014
3.001
2.998
2.988
2.985
2.975
2.972
2.961
2.958
2.945
2.901
2.888
2.865
2.853
2.679
2.663
2.644
2.627
2.434

23

Mis en forme : Police :20 pt, Gras, Français (France)

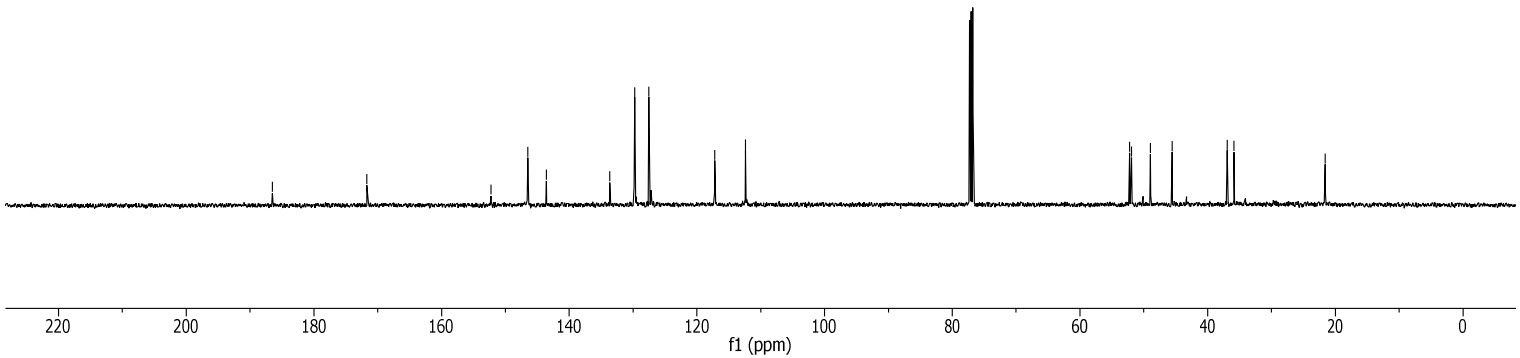


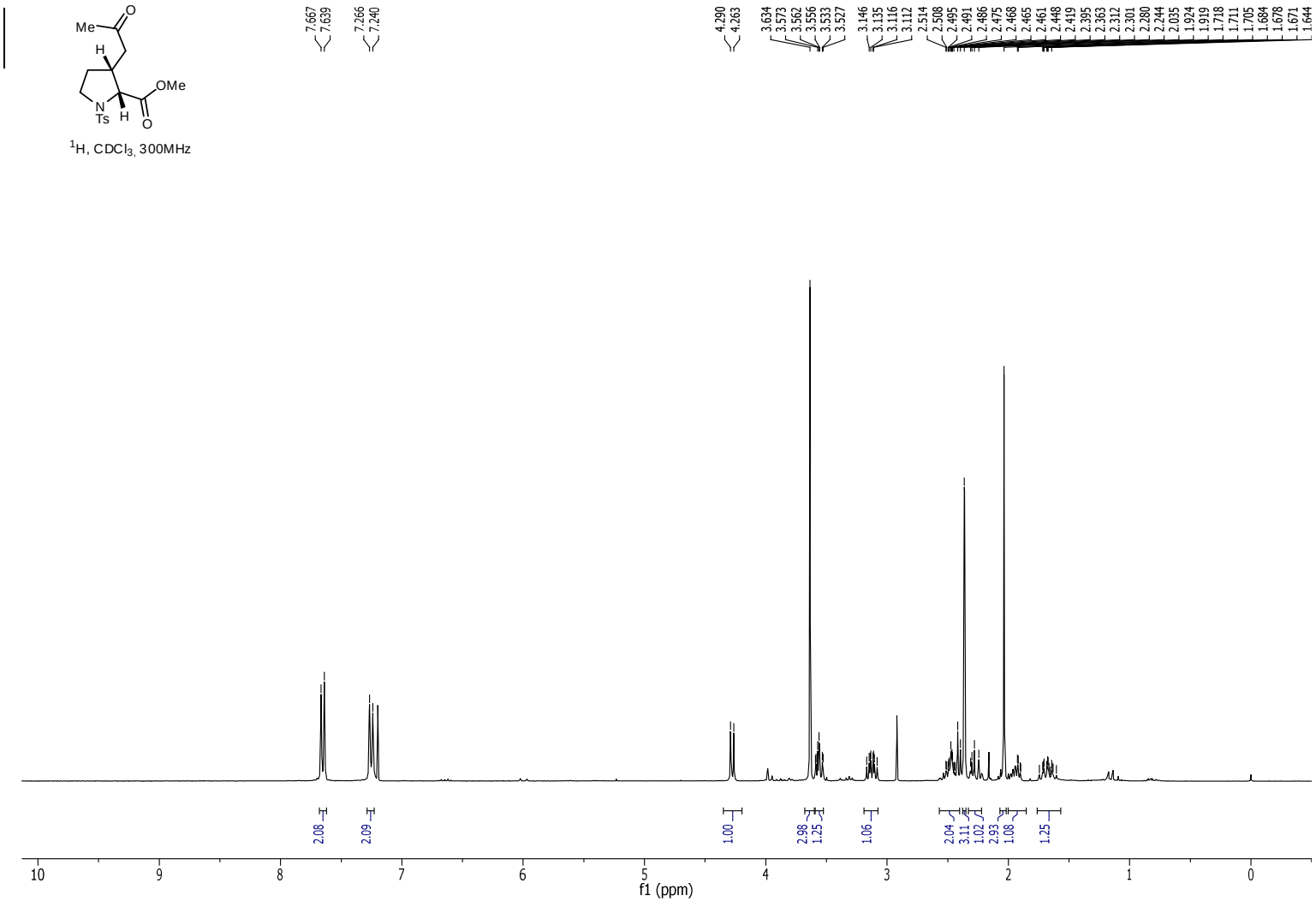


^{13}C, $CDCl_3$, 125MHz

23

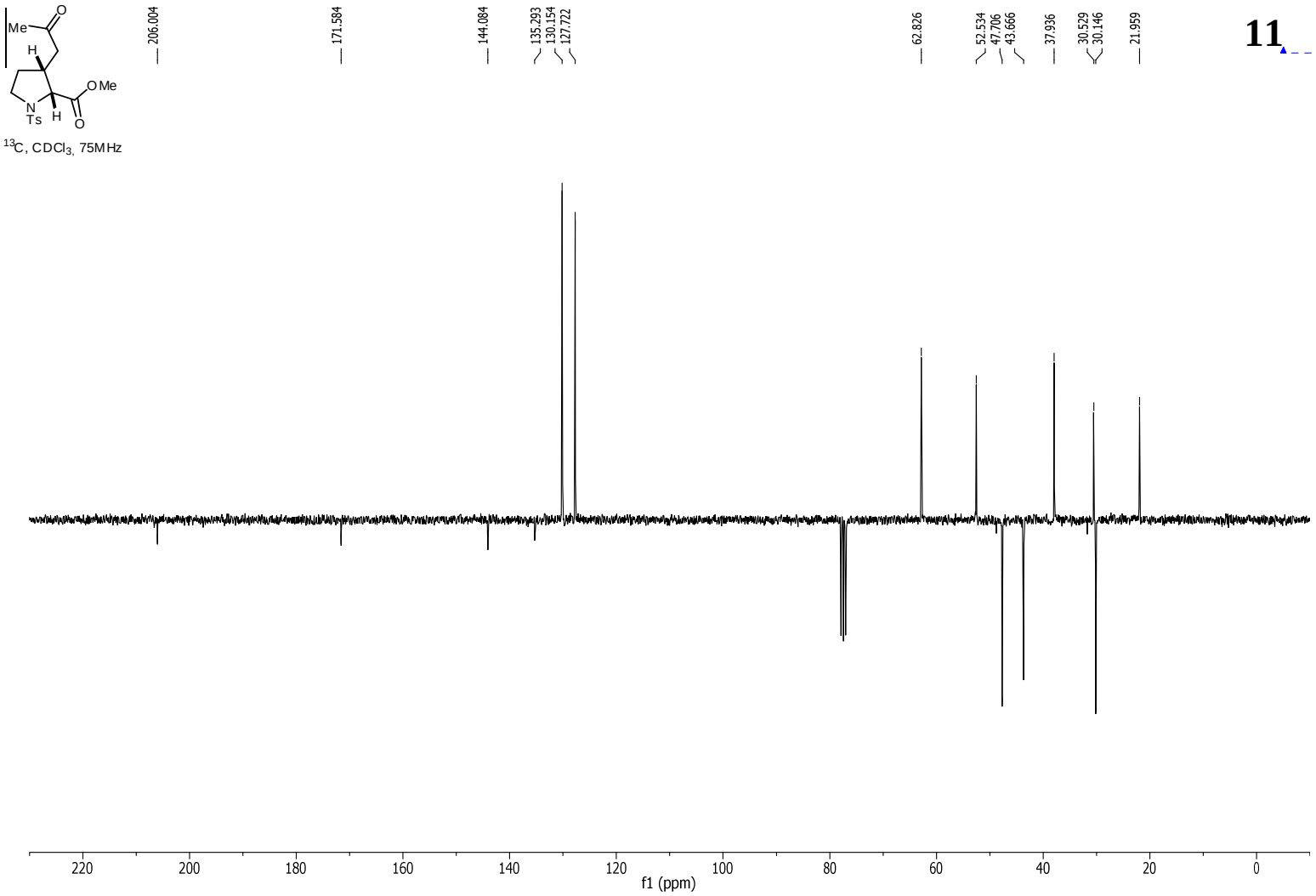
Mis en forme : Police :20 pt, Gras, Français (France)





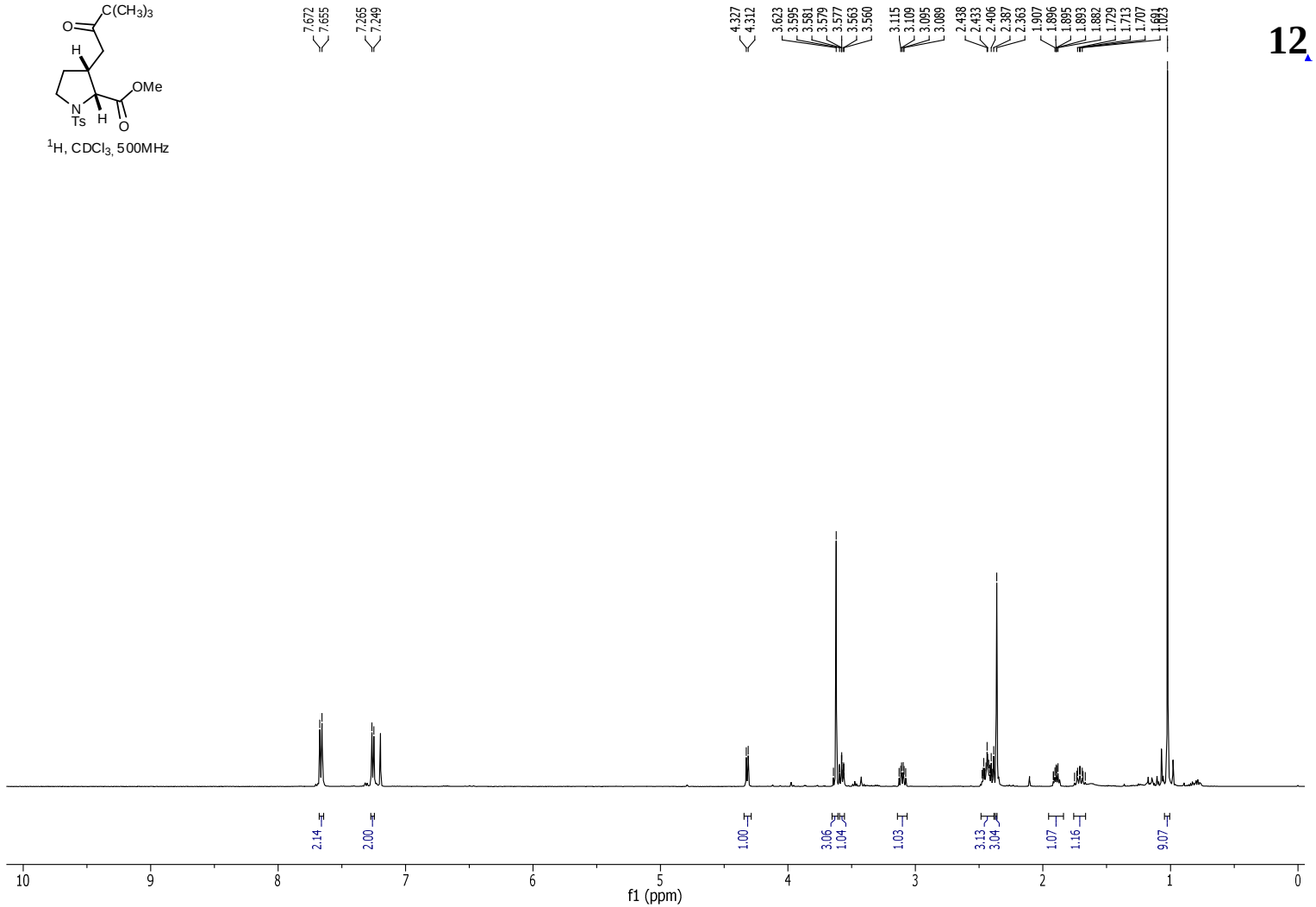
11

Mis en forme : Police :20 pt, Gras, Français (France)



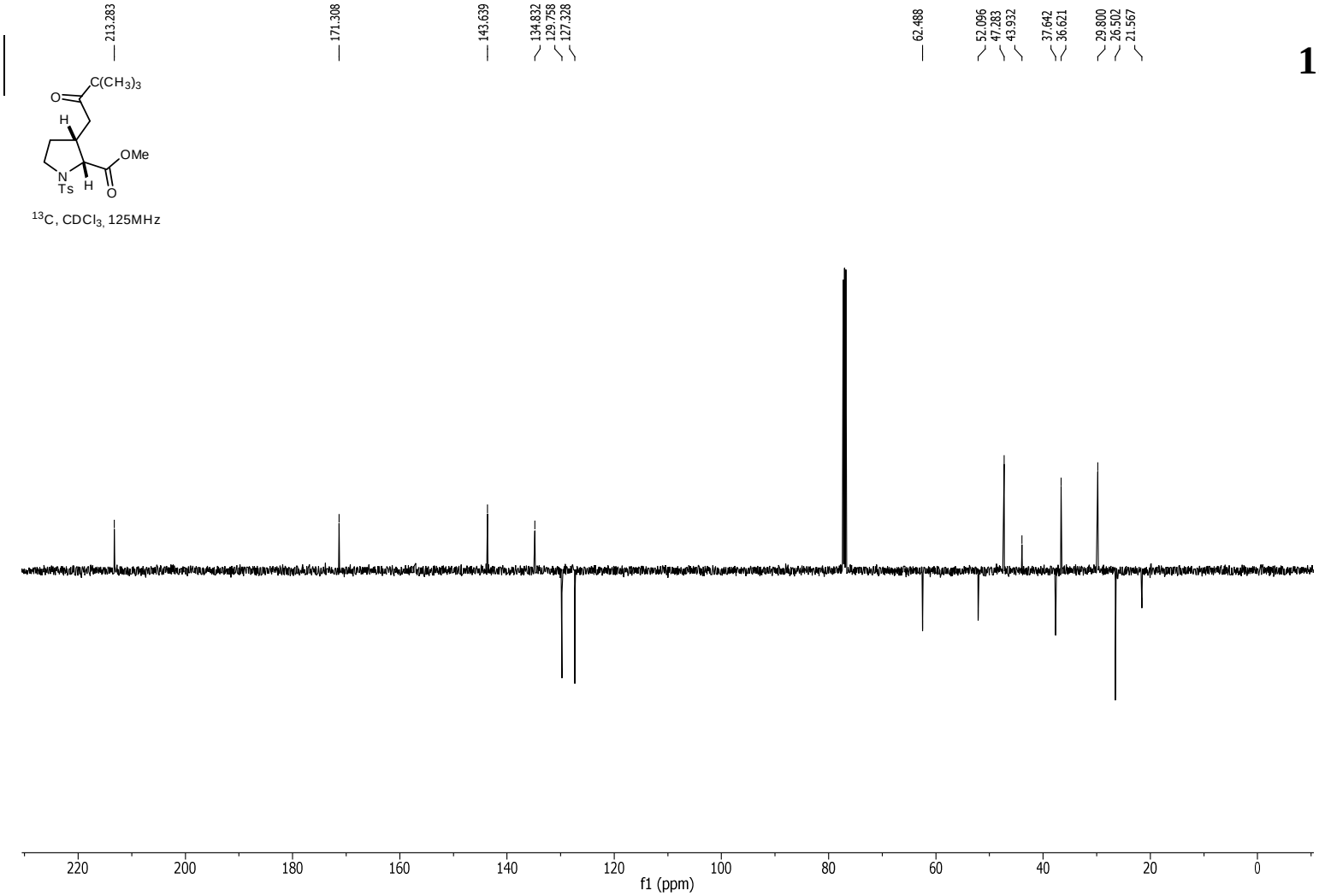
11

Mis en forme : Police :20 pt, Gras, Français (France)



12

Mis en forme : Police :20 pt, Gras, Français (France)

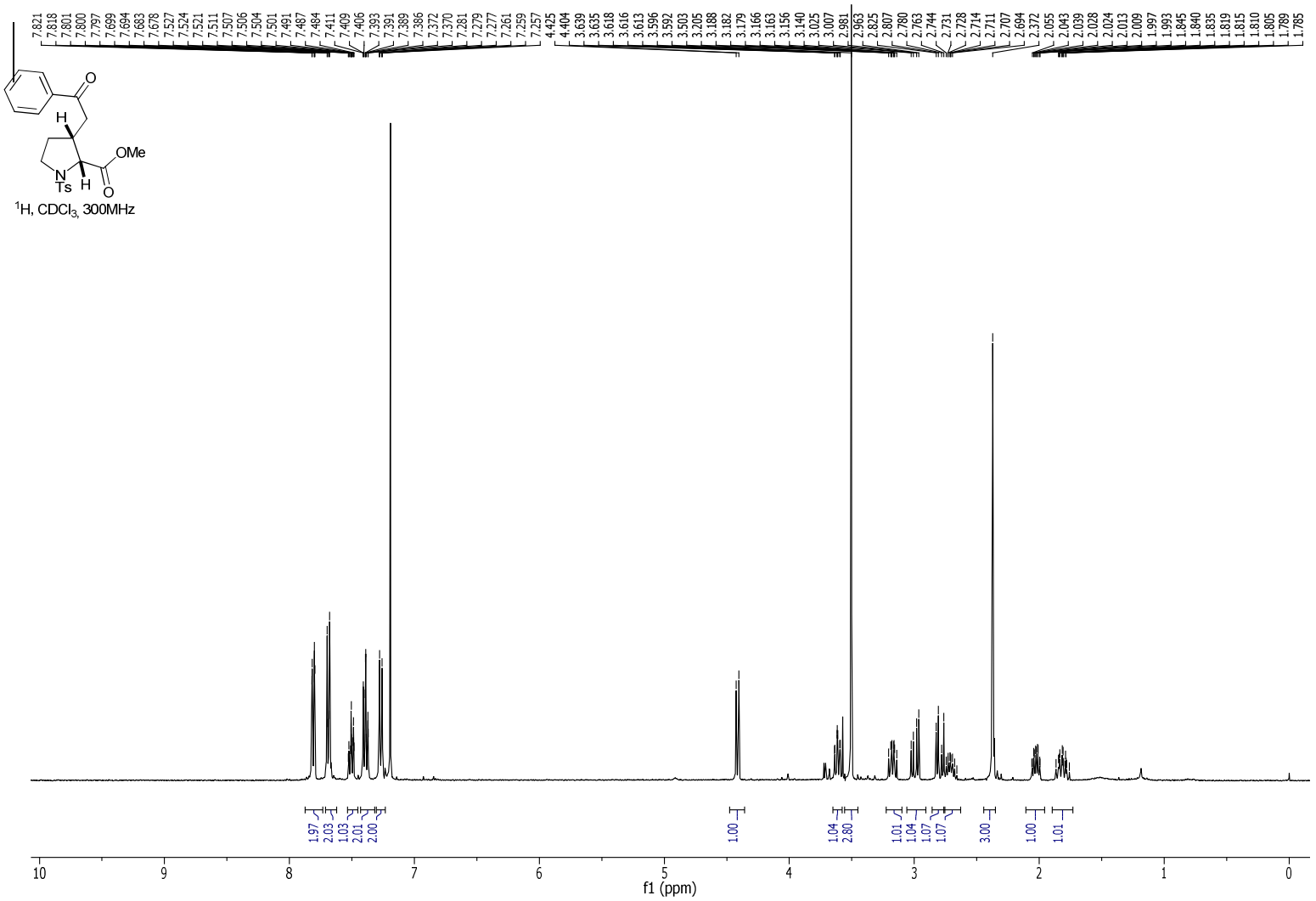


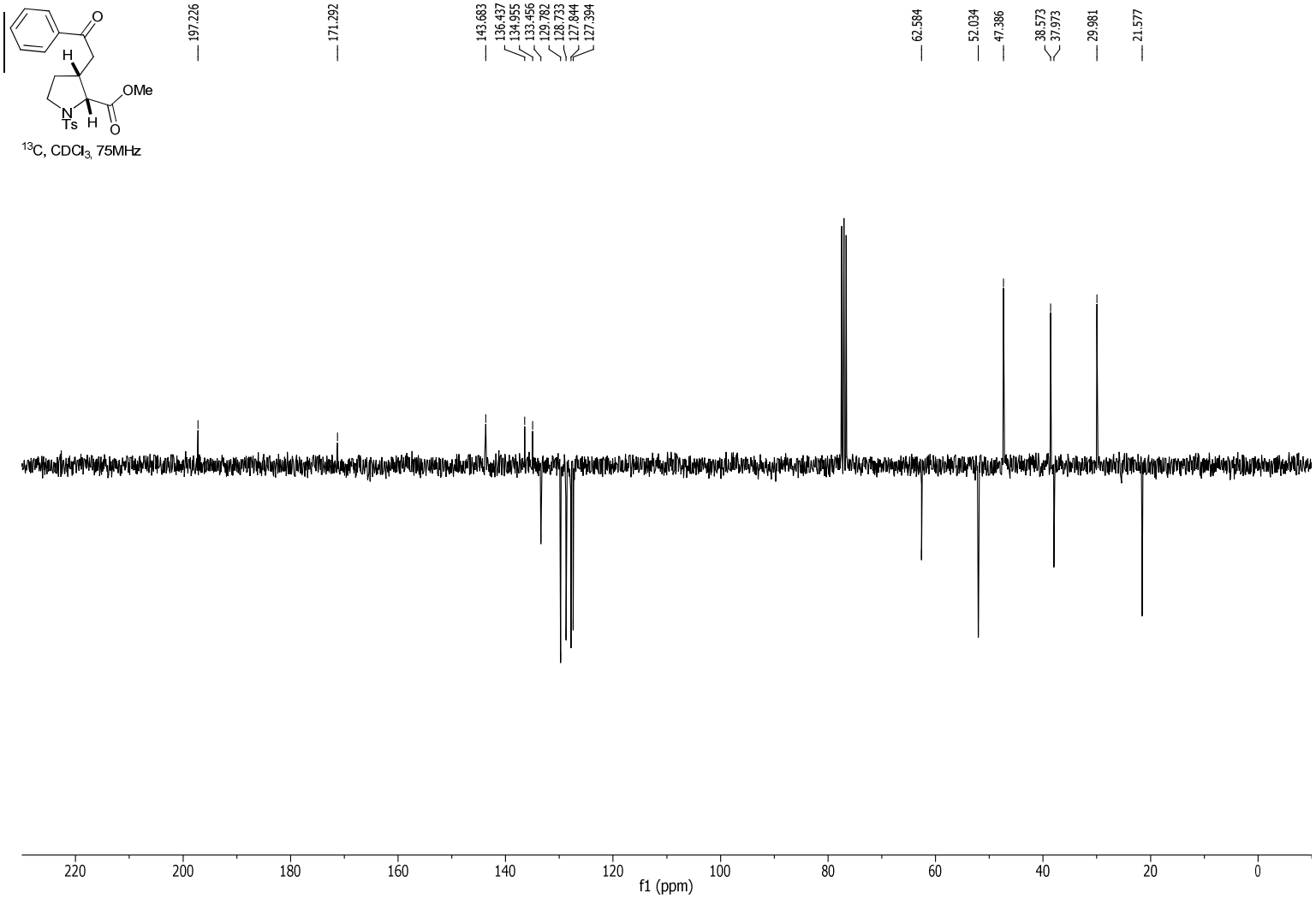
12

Mis en forme : Police :20 pt, Gras, Français (France)

13

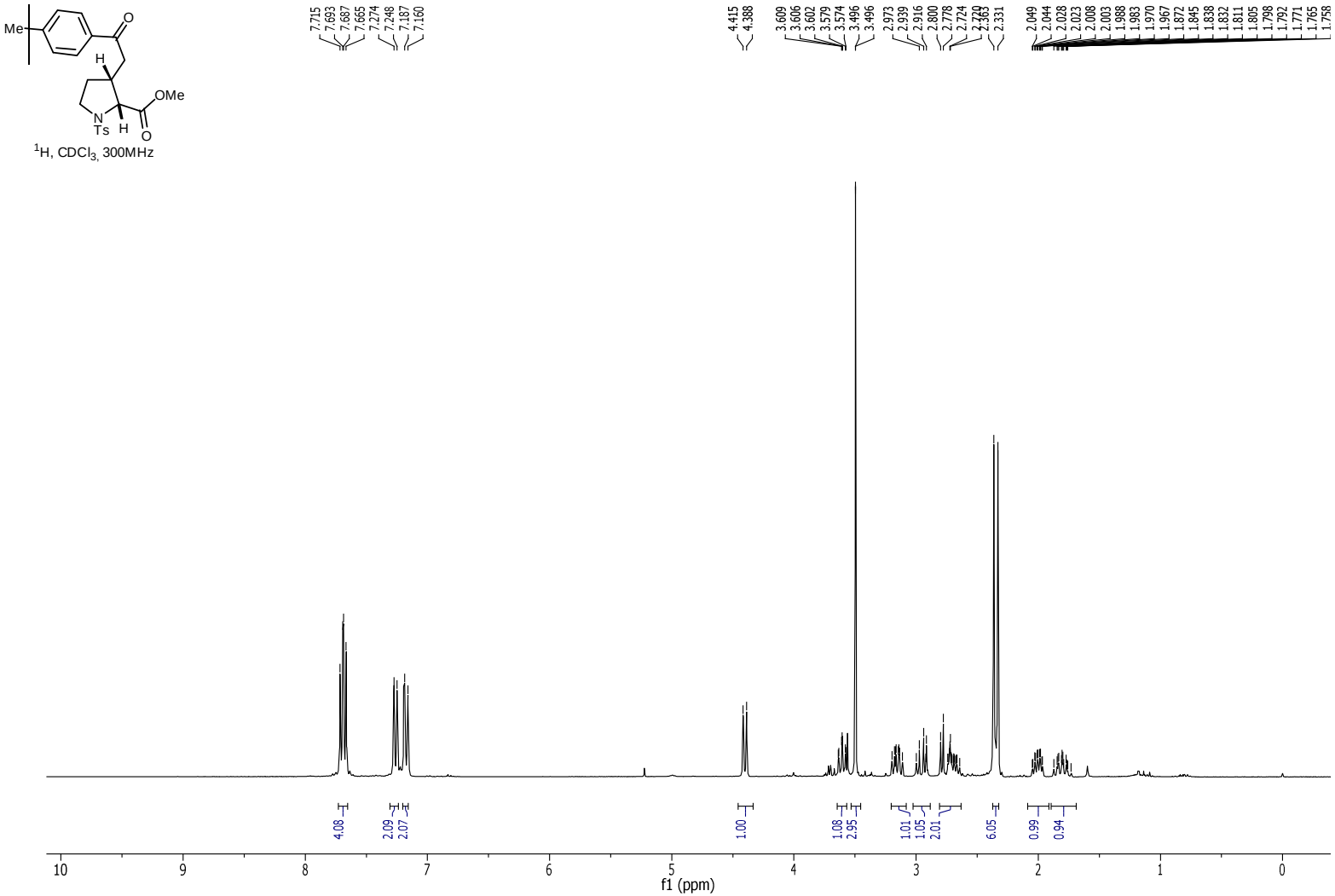
Mis en forme : Police :20 pt, Gras, Français (France)





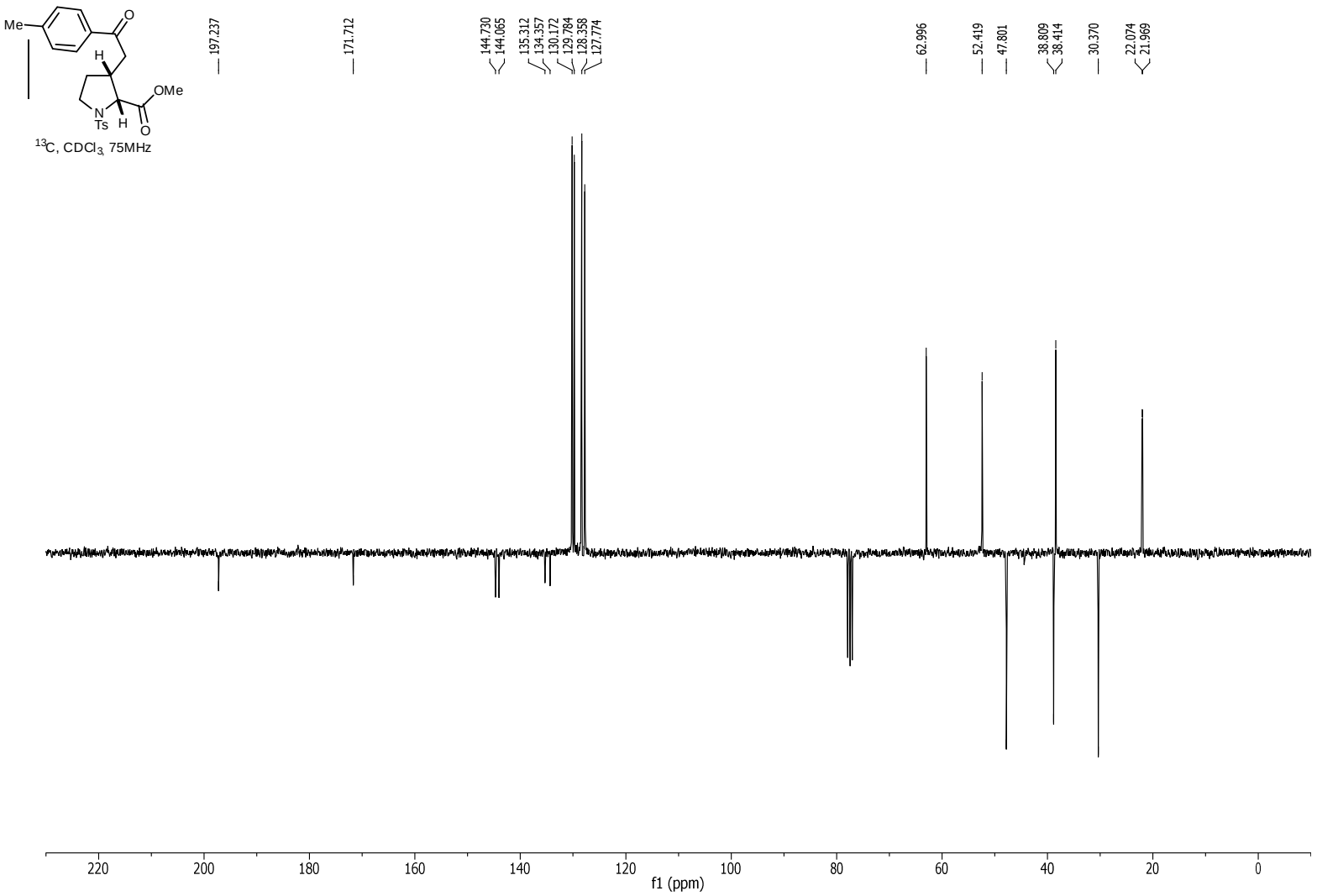
13

Mis en forme : Police :20 pt, Gras, Français (France)



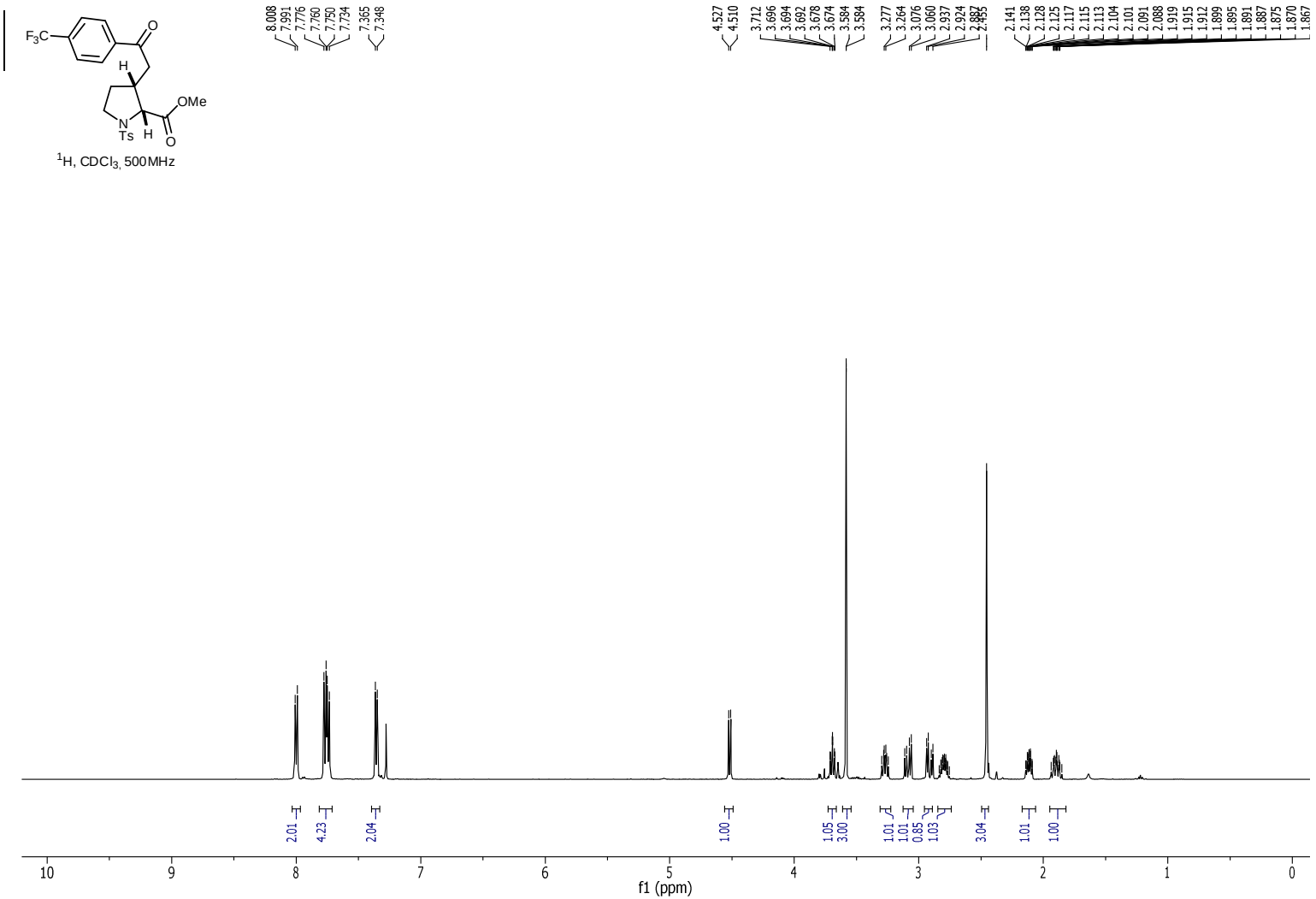
14

Mis en forme : Police :20 pt, Gras, Français (France)



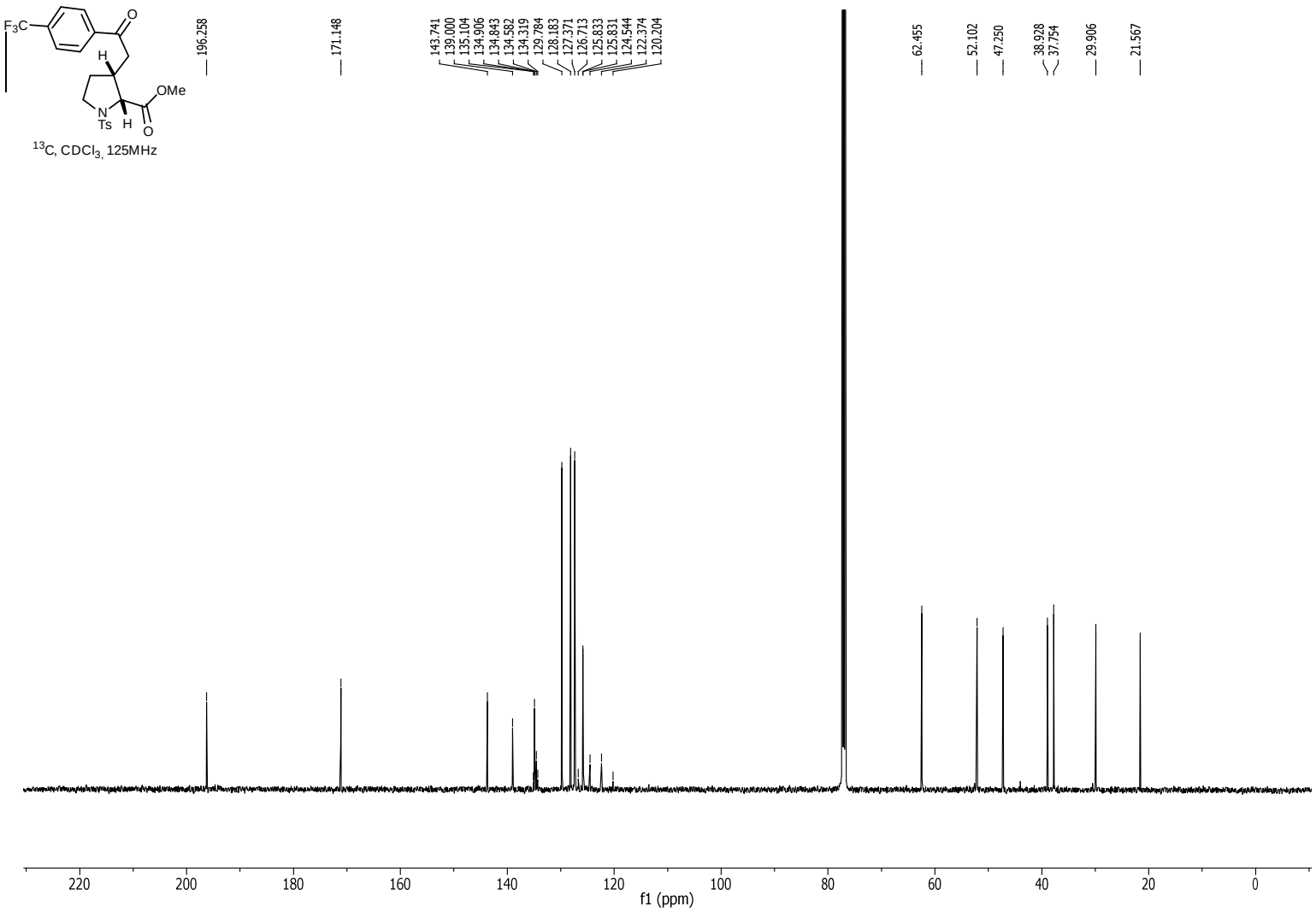
14

Mis en forme : Police :20 pt, Gras, Français (France)



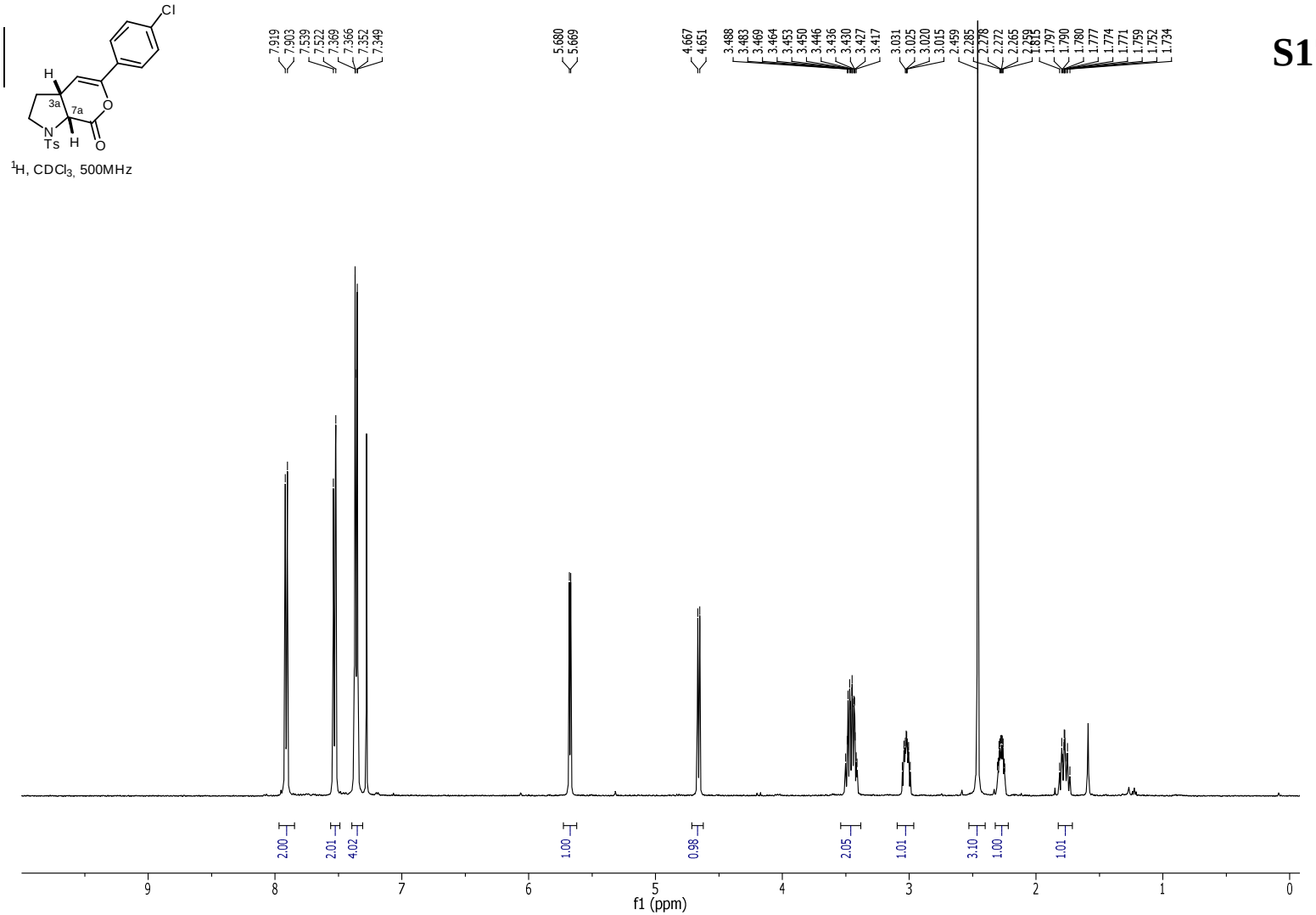
15

Mis en forme : Police :20 pt, Gras, Français (France)



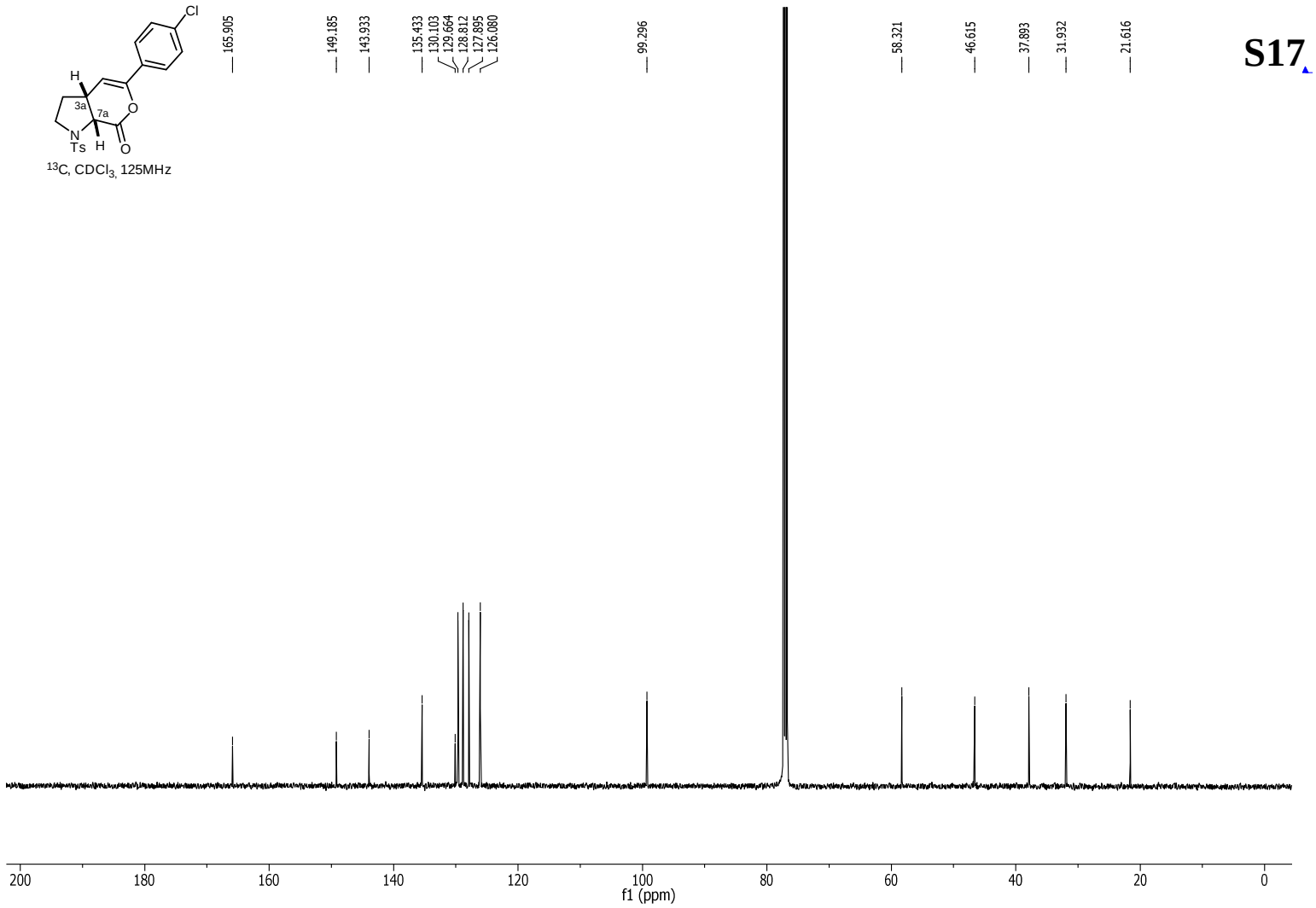
15

Mis en forme : Police :20 pt, Gras, Français (France)



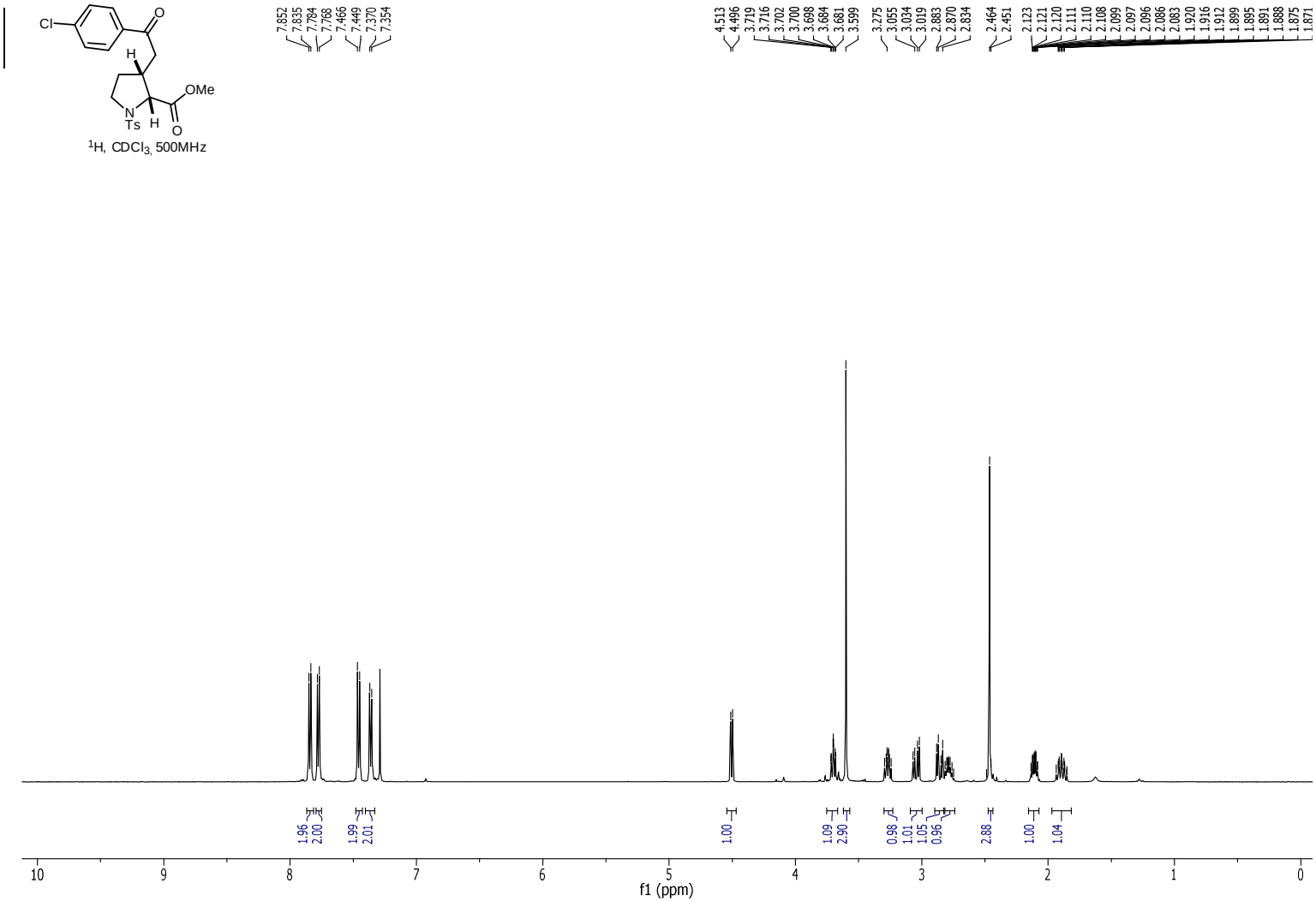
S17

Mis en forme : Police :20 pt, Gras, Français (France)



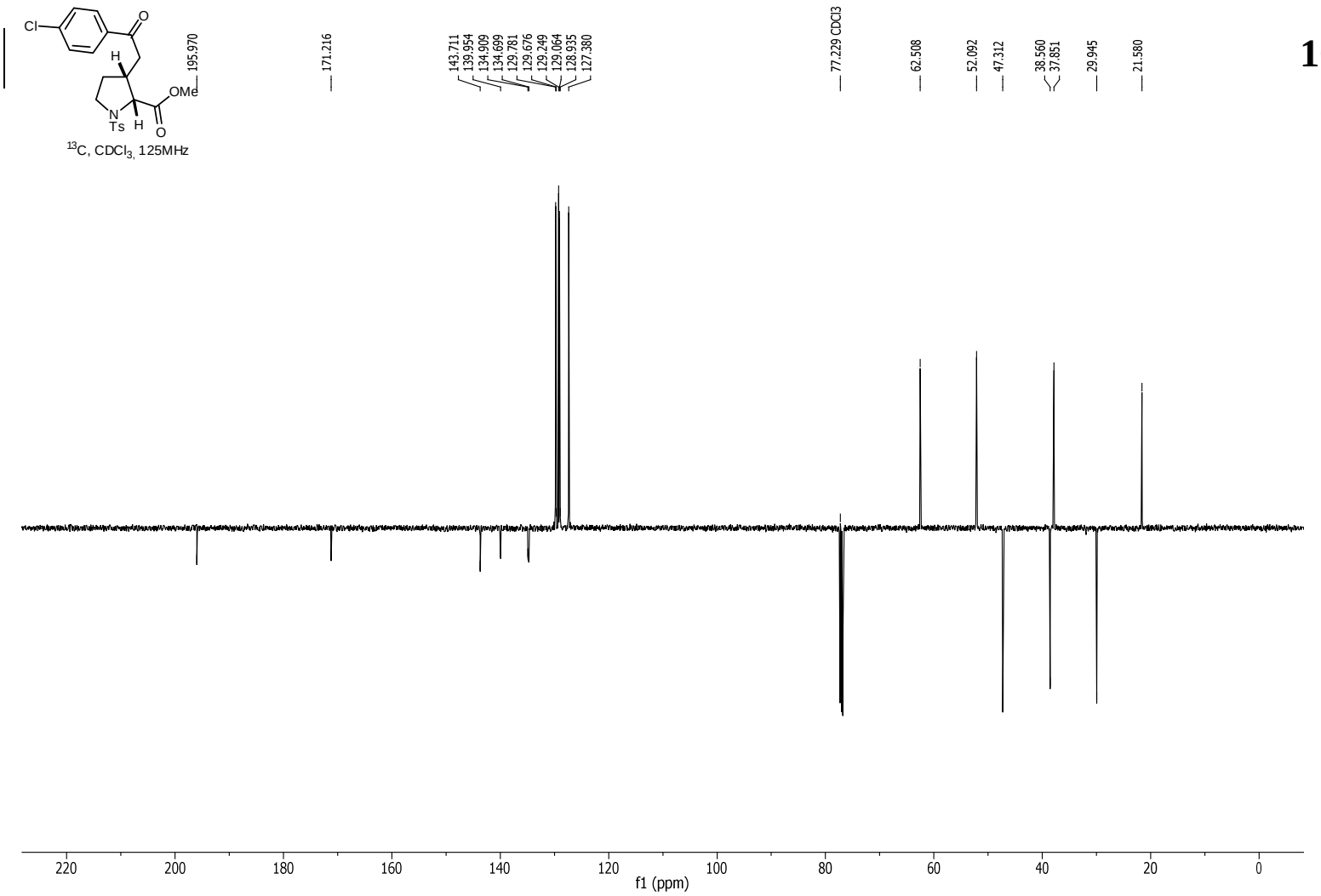
S17

Mis en forme : Police :20 pt, Gras, Français (France)



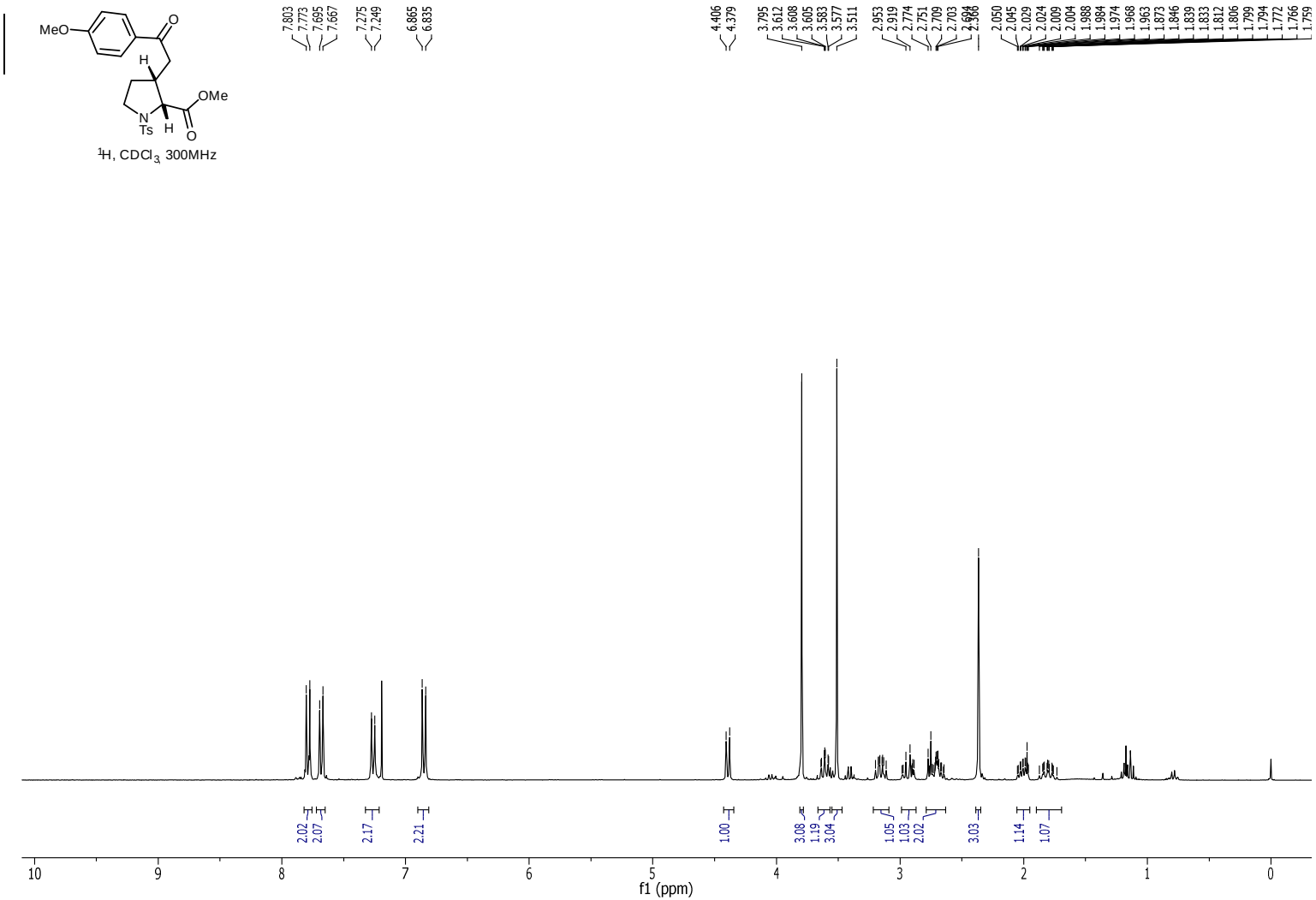
16

Mis en forme : Police :20 pt, Gras, Français (France)



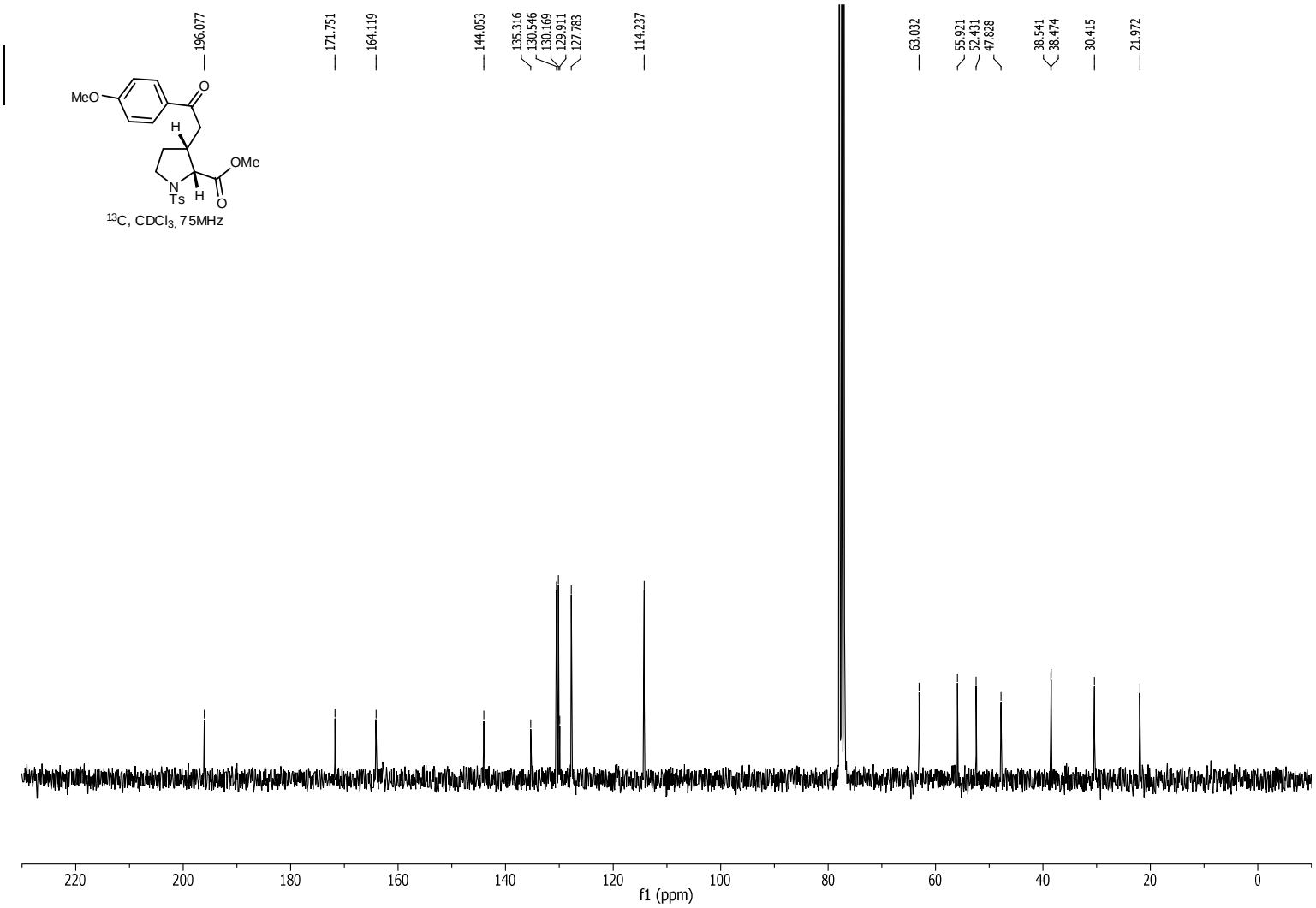
16

Mis en forme : Police :20 pt, Gras, Français (France)



17

Mis en forme : Police :20 pt, Gras, Français (France)

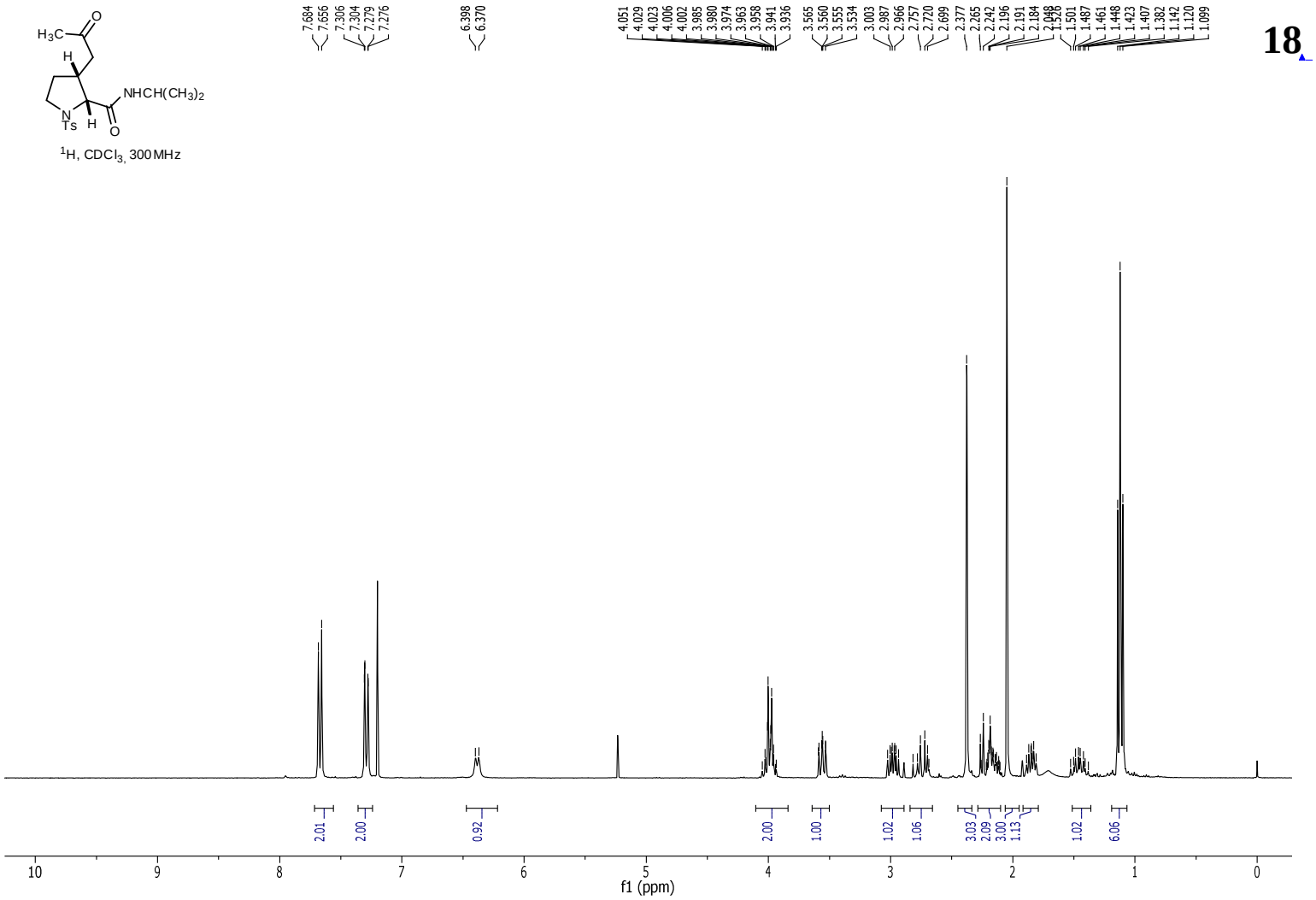


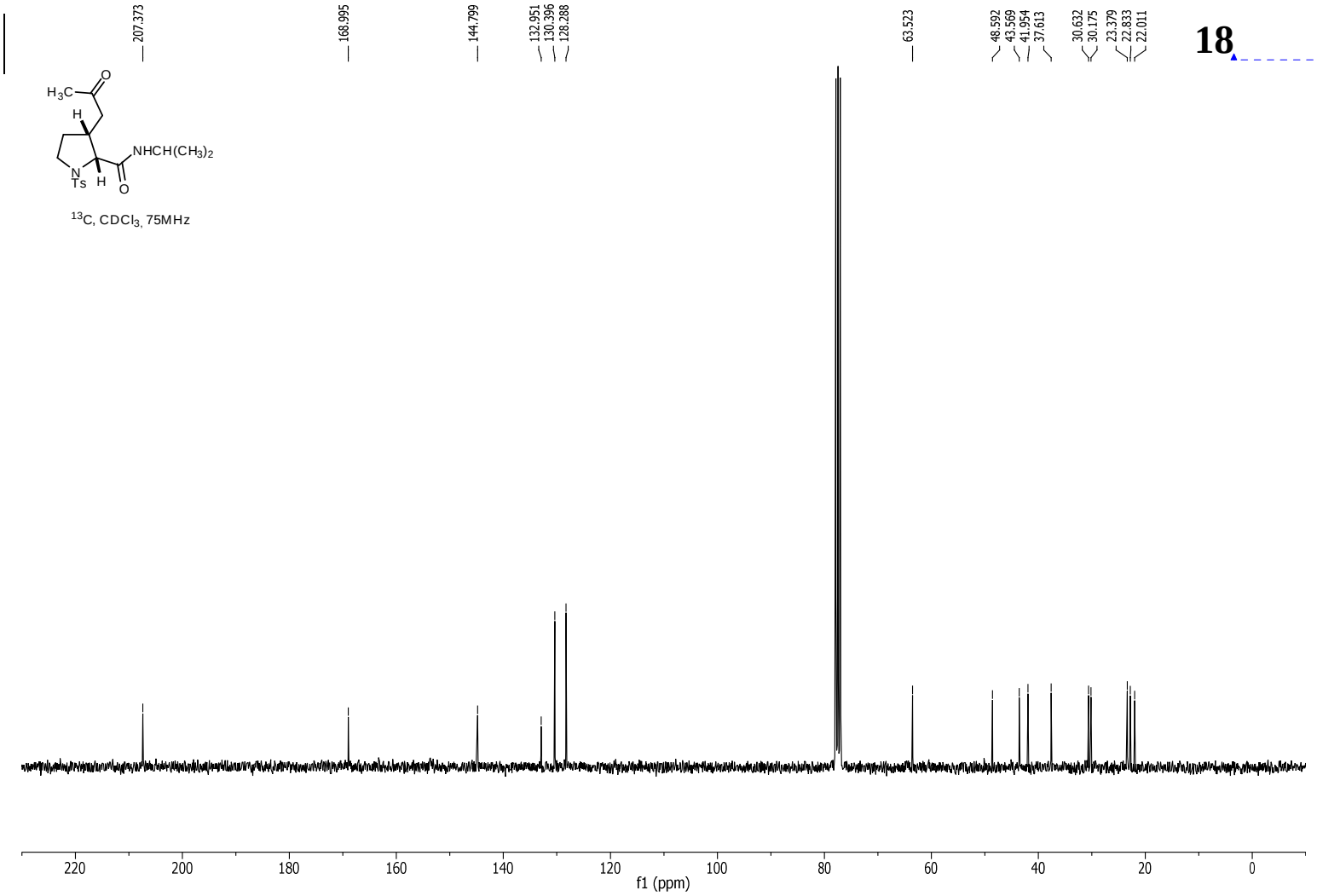
17

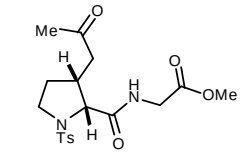
Mis en forme : Police :20 pt, Gras, Français (France)

18

Mis en forme : Police :20 pt, Gras, Français (France)




207.373
168.995
144.799
132.951
130.396
128.288
63.523
48.592
43.569
41.954
37.613
30.632
30.175
23.379
22.833
22.011
18
Mis en forme : Police :20 pt, Gras, Français (France)
H3C
O
H
NHCH(CH3)2
N
Ts
H
O
13C, CDCl3, 75MHz
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



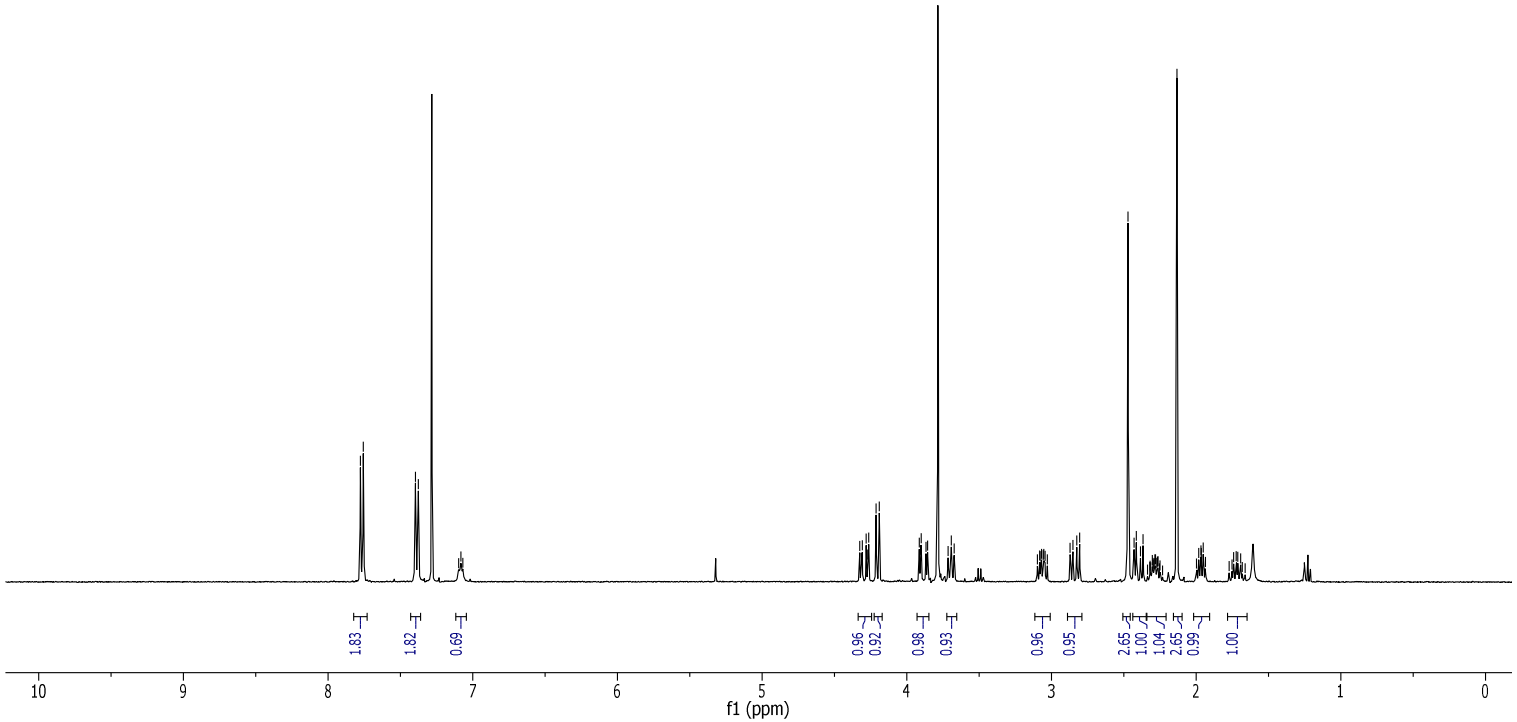
^{1}H, $CDCl_3$, 500MHz

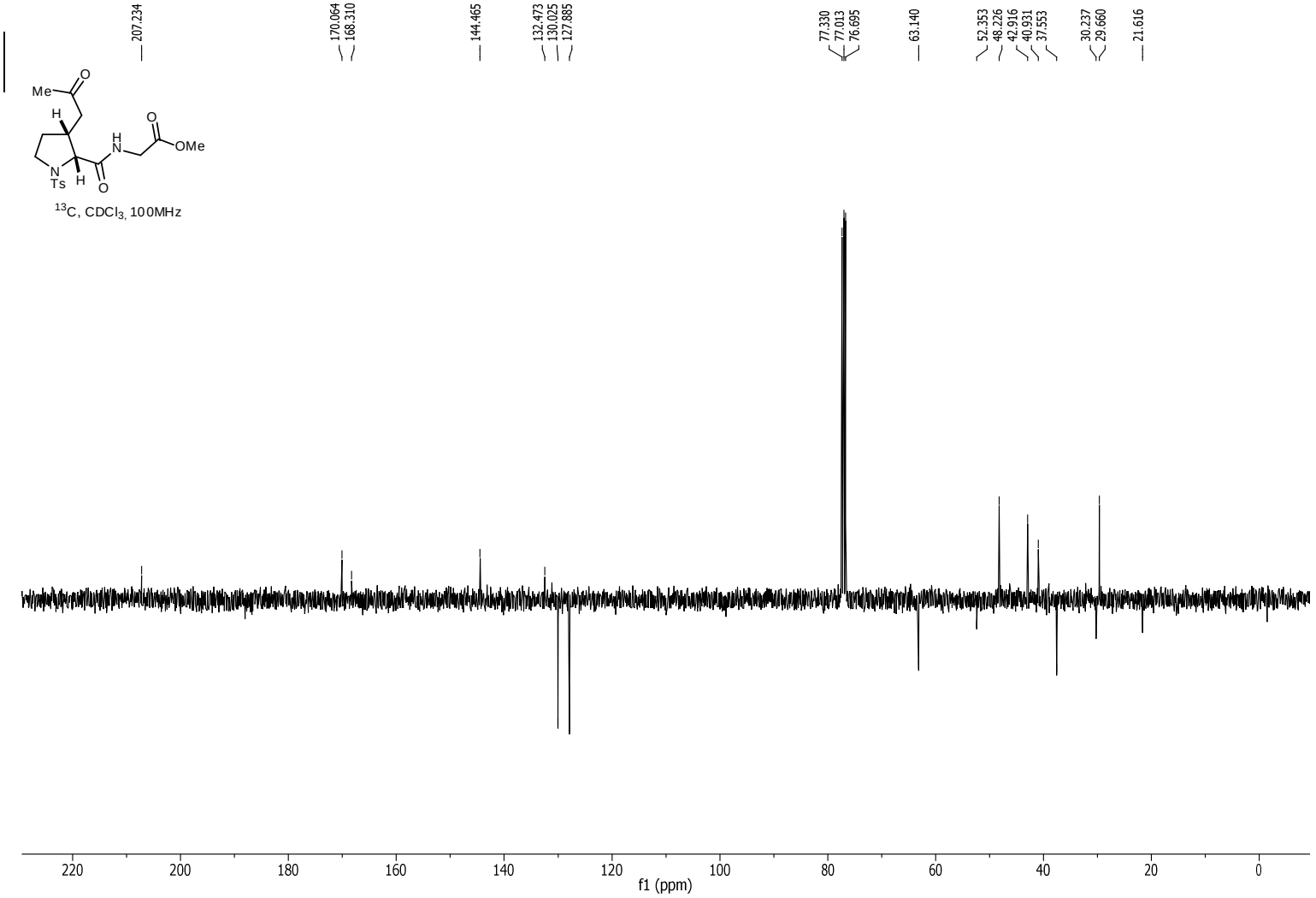
7.777 7.757 7.397 7.377 7.099 7.083 7.069

4.326 4.315 4.309 4.281 4.270 4.264 4.213 4.191 3.914 3.902 3.869 3.857 3.694 3.069 3.054 2.871 2.853 2.825 2.807 2.472 2.431 2.414 2.385 2.368 2.305 2.300 2.291 2.287 2.282 2.273 2.269 2.265 2.134 1.983 1.968 1.966 1.952 1.937 1.742 1.723 1.713 1.694

19

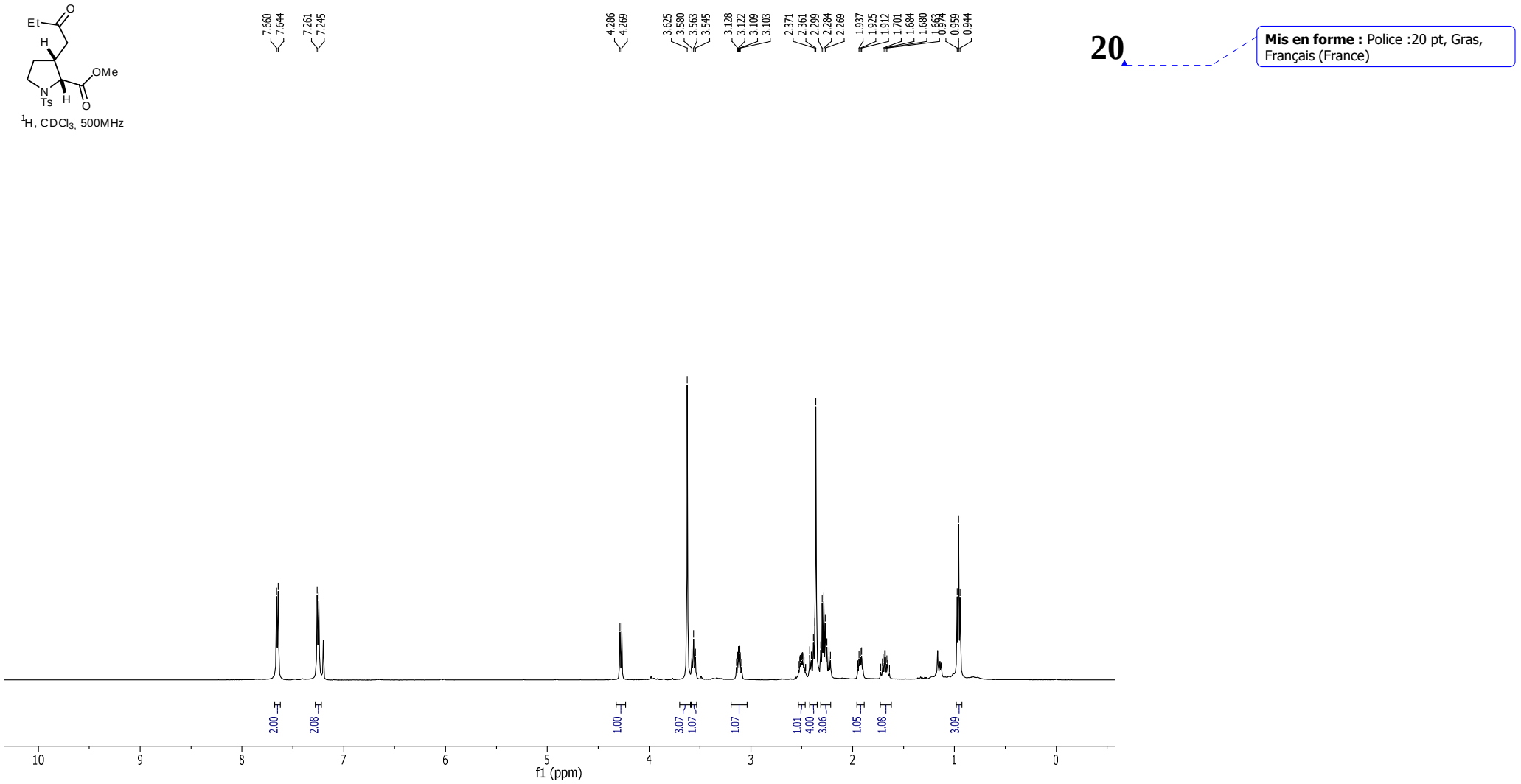
Mis en forme : Police :20 pt, Gras, Français (France)





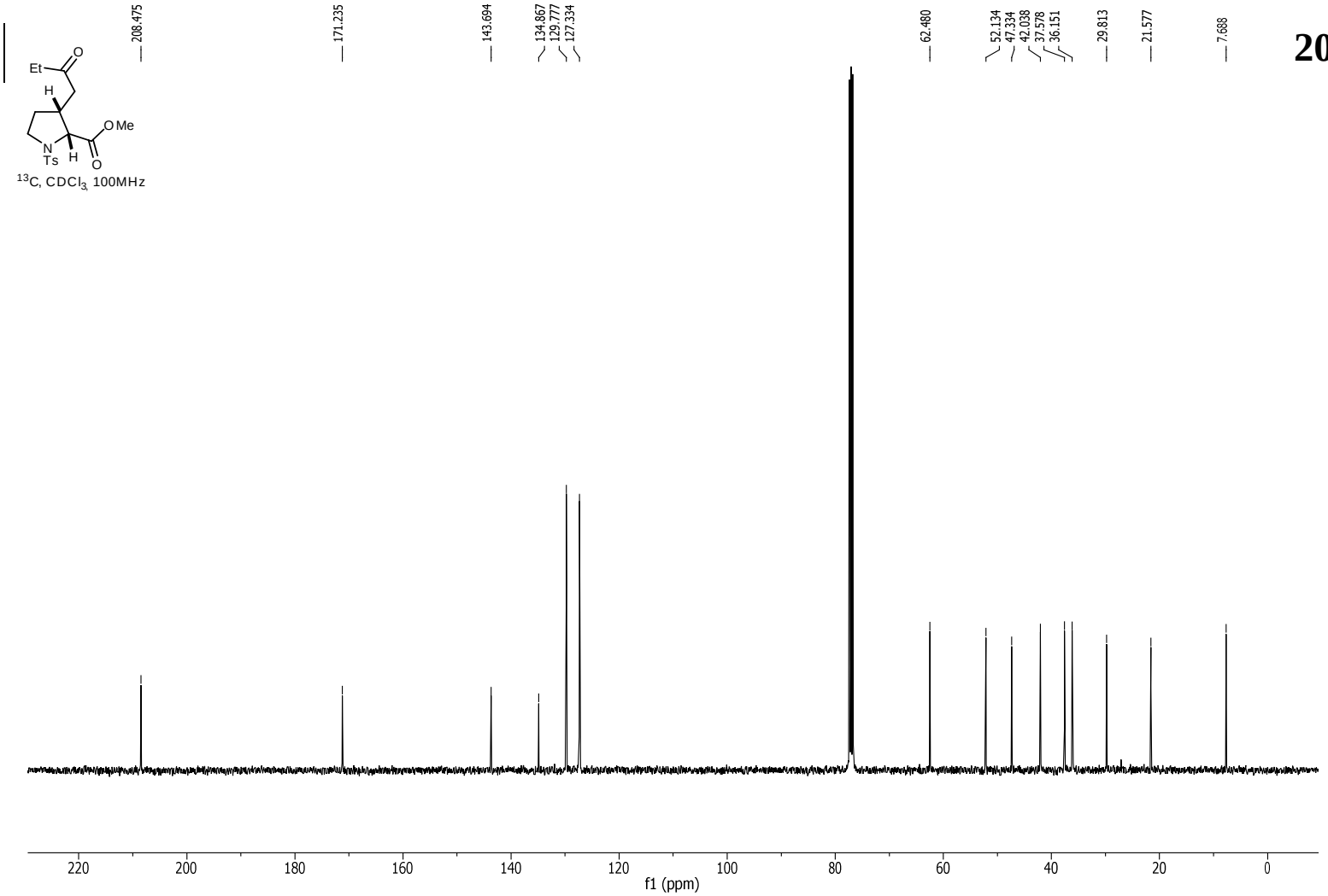
19

Mis en forme : Police :20 pt, Gras, Français (France)



20

Mis en forme : Police :20 pt, Gras, Français (France)

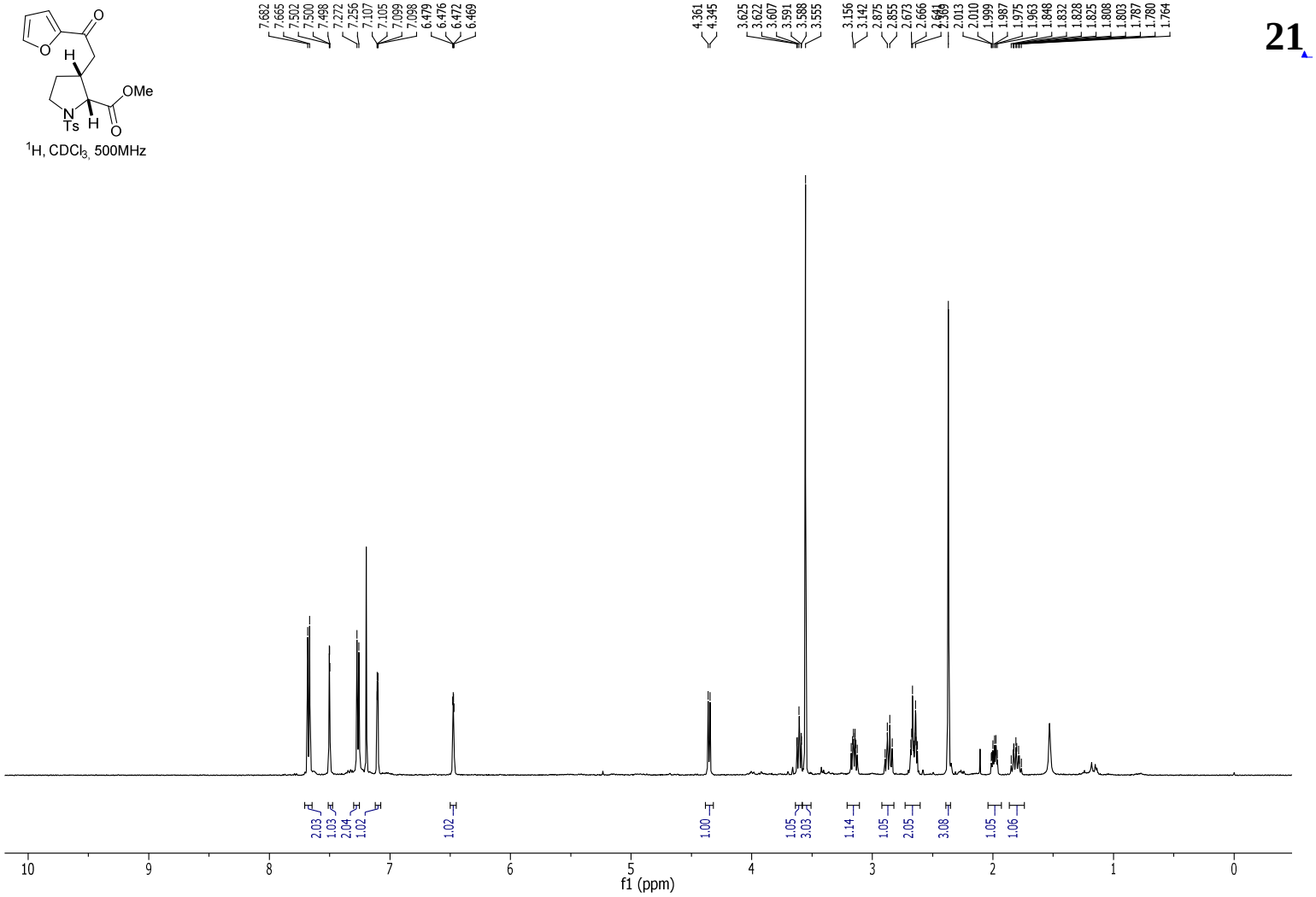


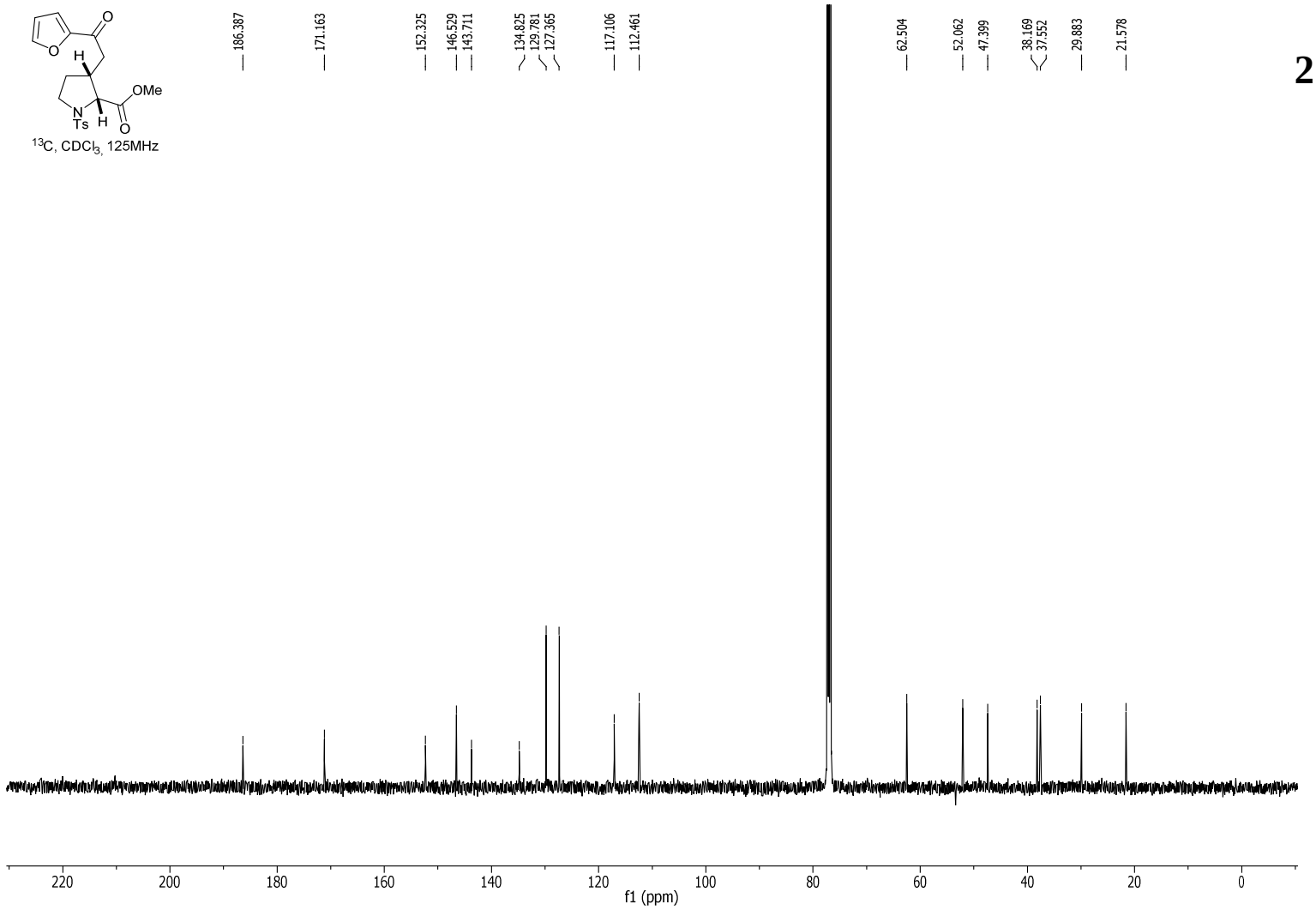
20

Mis en forme : Police :20 pt, Gras, Français (France)

21

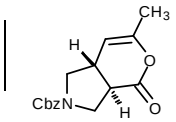
Mis en forme : Police :20 pt, Gras, Français (France)





21

Mis en forme : Police :20 pt, Gras, Français (France)

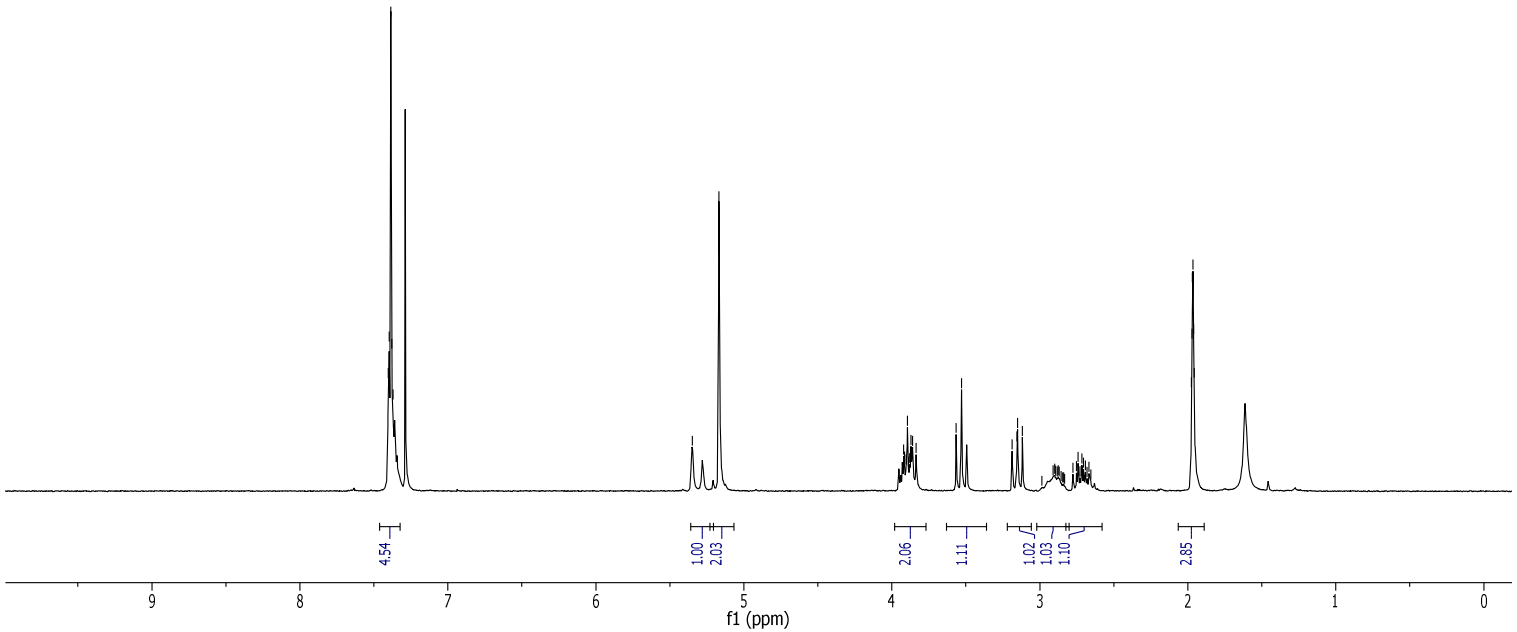


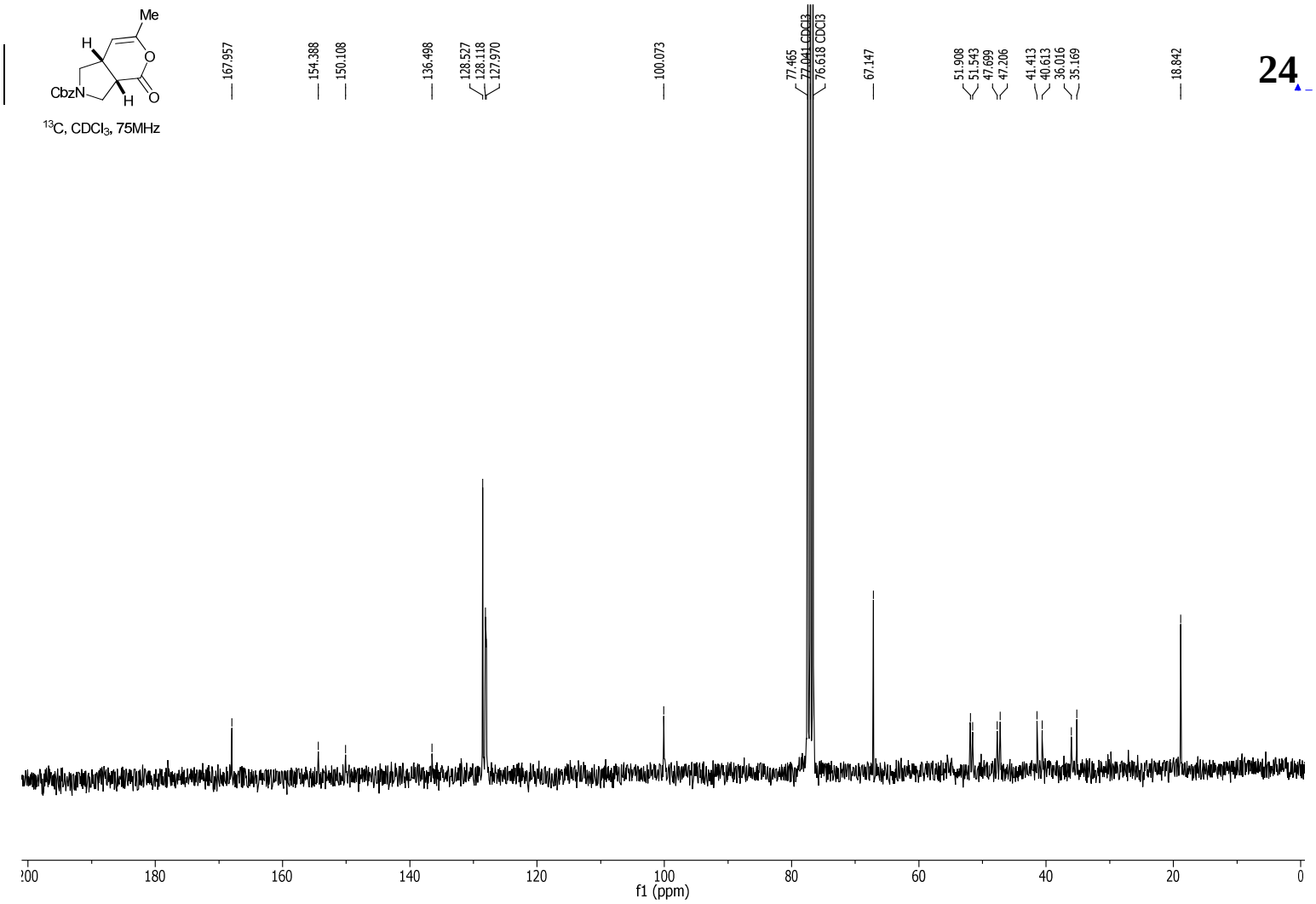
^{1}H, $CDCl_3$,300MHz

7.402
7.399
7.395
7.386
7.379
7.370
5.349
5.168
3.919
3.915
3.904
3.895
3.888
3.879
3.870
3.860
3.836
3.566
3.530
3.188
3.155
3.151
3.118
2.752
2.741
2.716
2.704
1.972
1.969
1.965
1.961
1.957

24

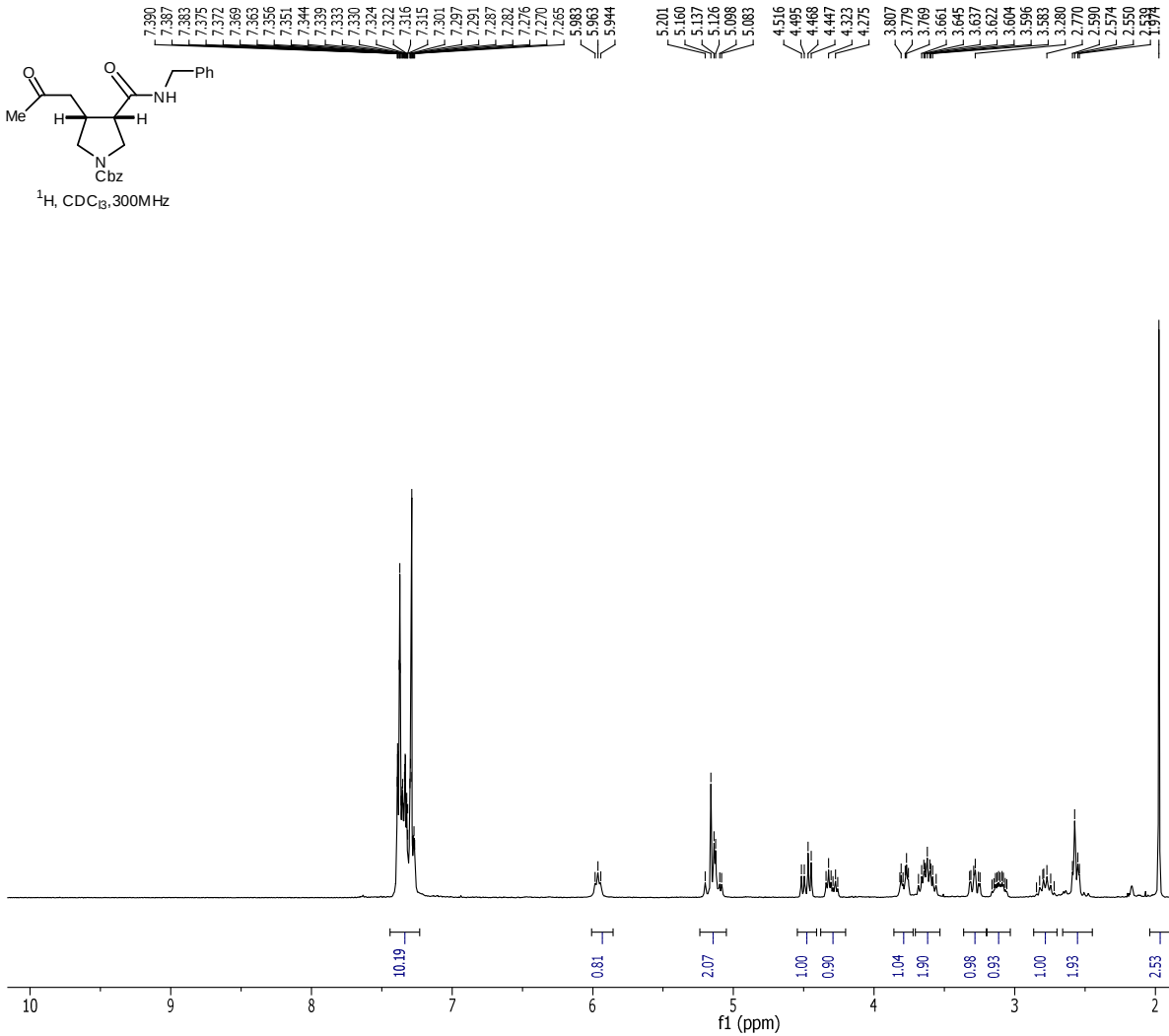
Mis en forme : Police :20 pt, Gras, Français (France)





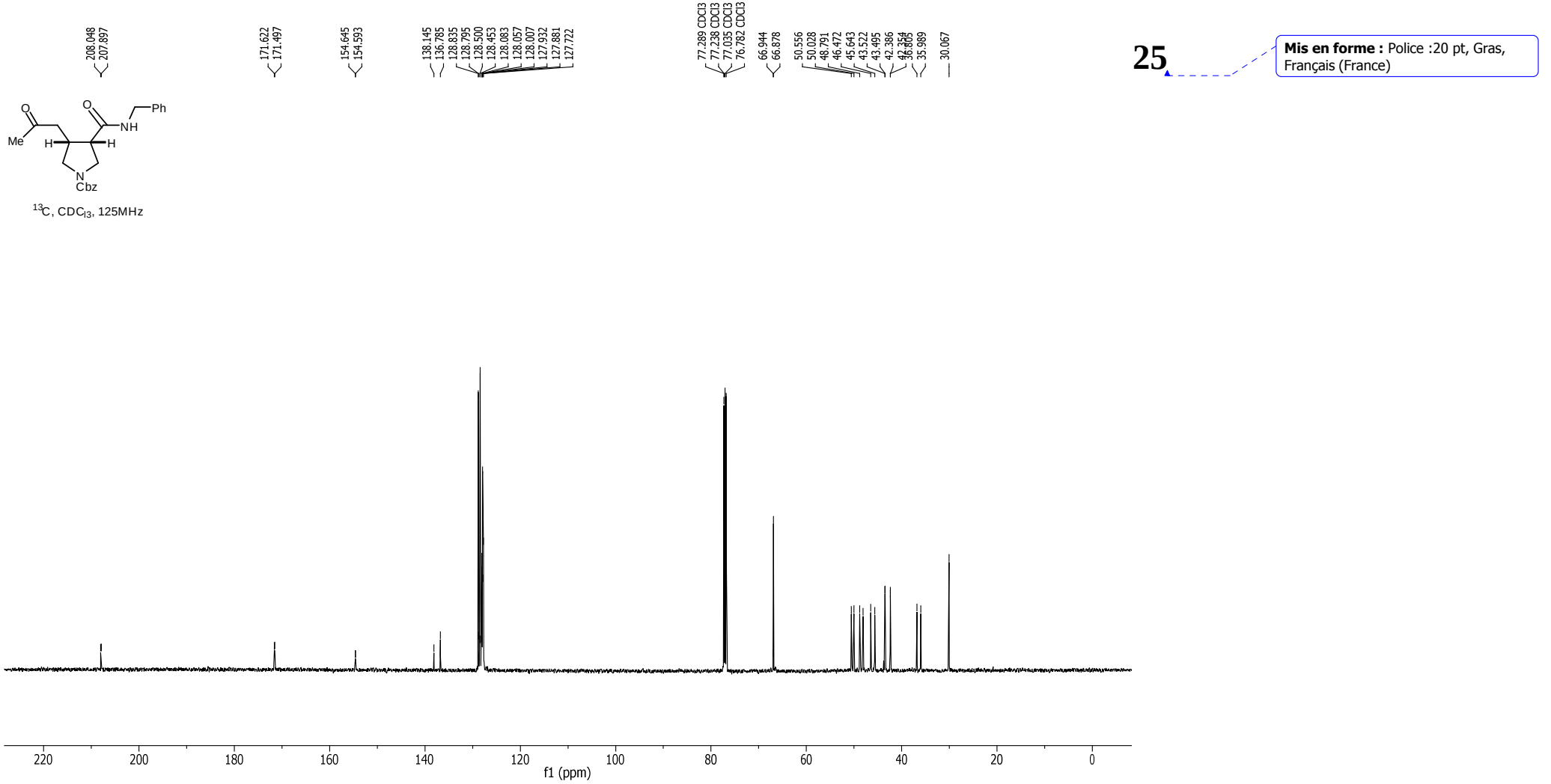
24

Mis en forme : Police :20 pt, Gras, Français (France)



25

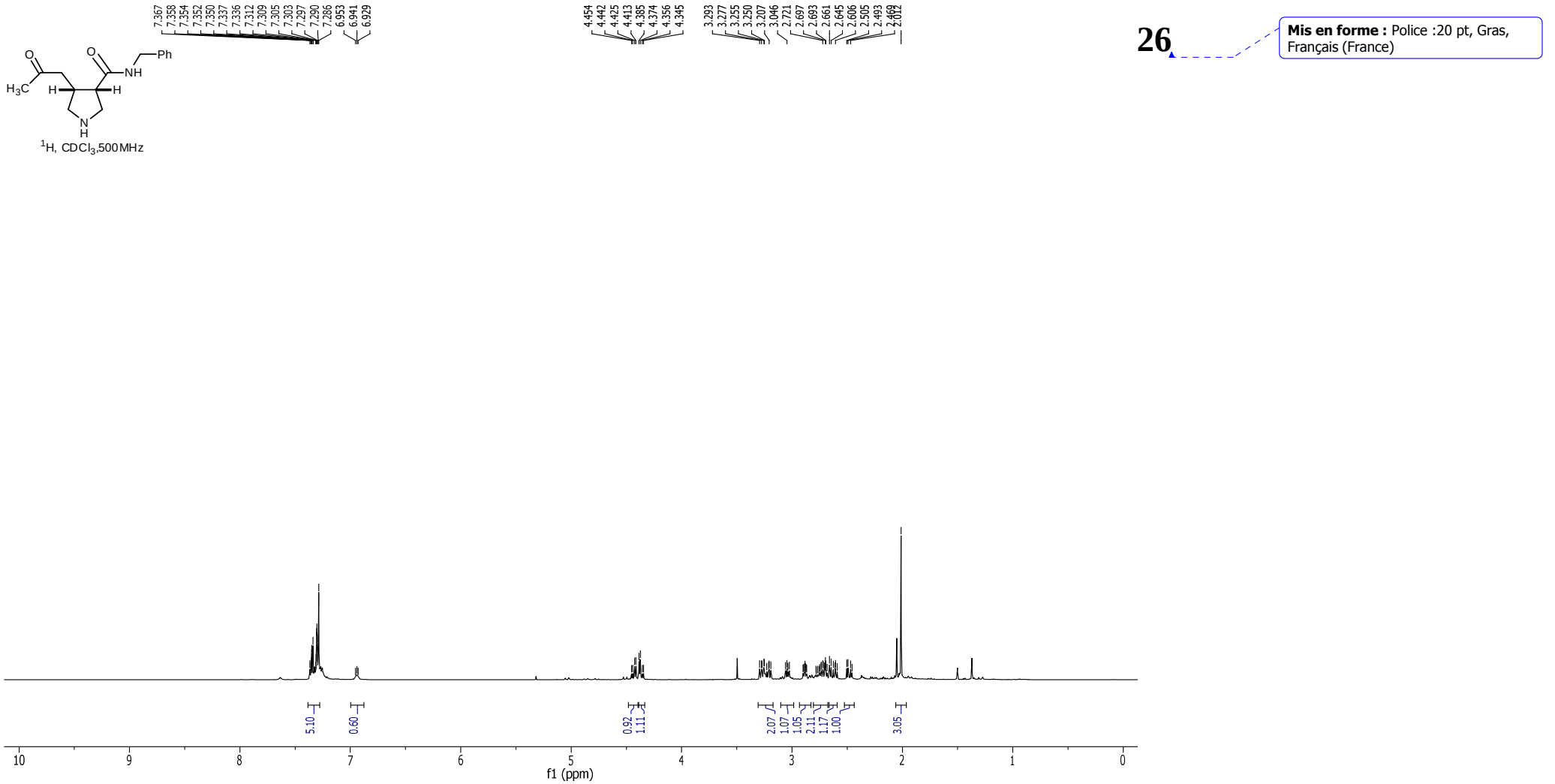
Mis en forme : Police :20 pt, Gras, Français (France)

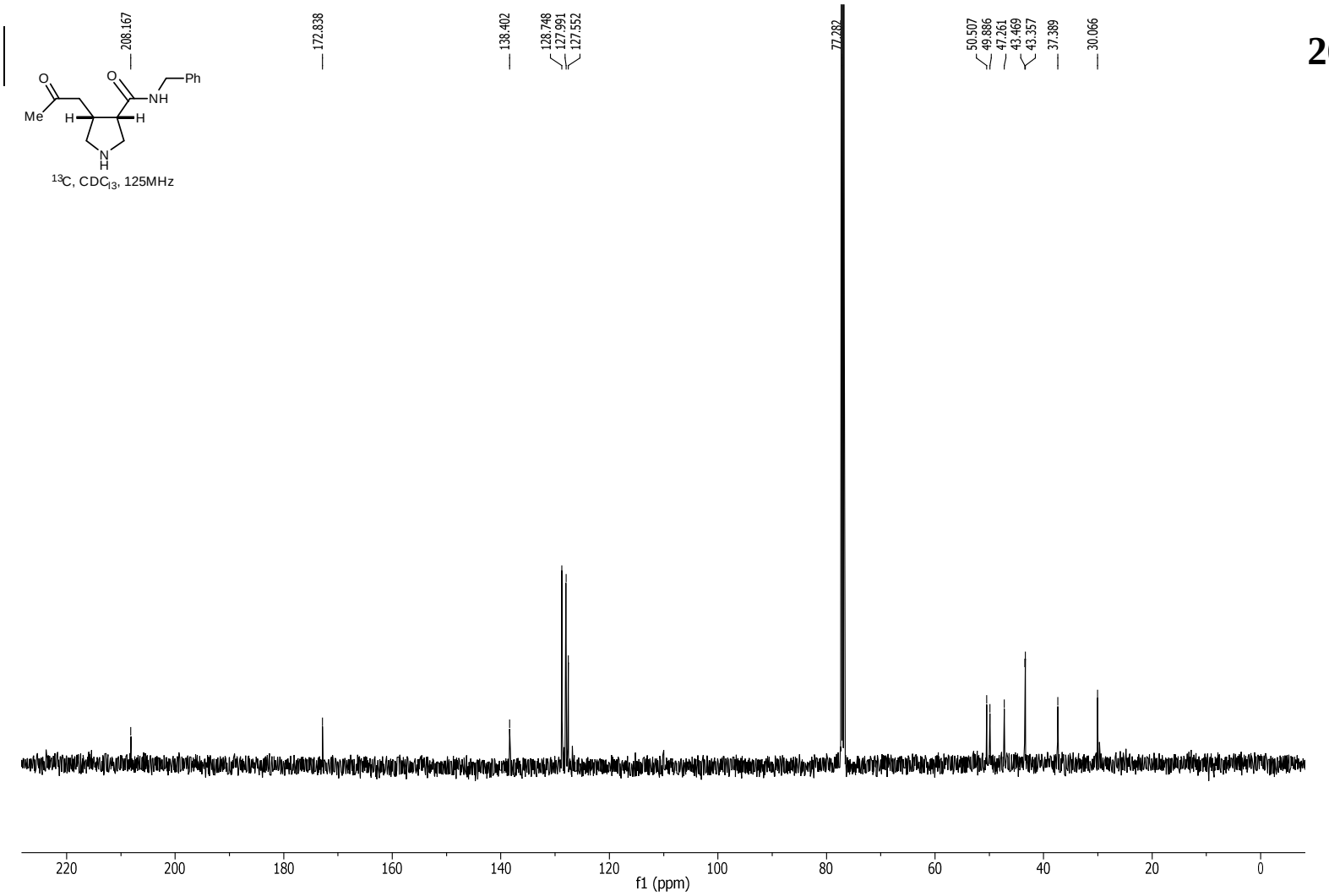


25

Mis en forme : Police :20 pt, Gras, Français (France)

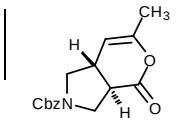
Mis en forme : Police :20 pt, Gras, Français (France)





26

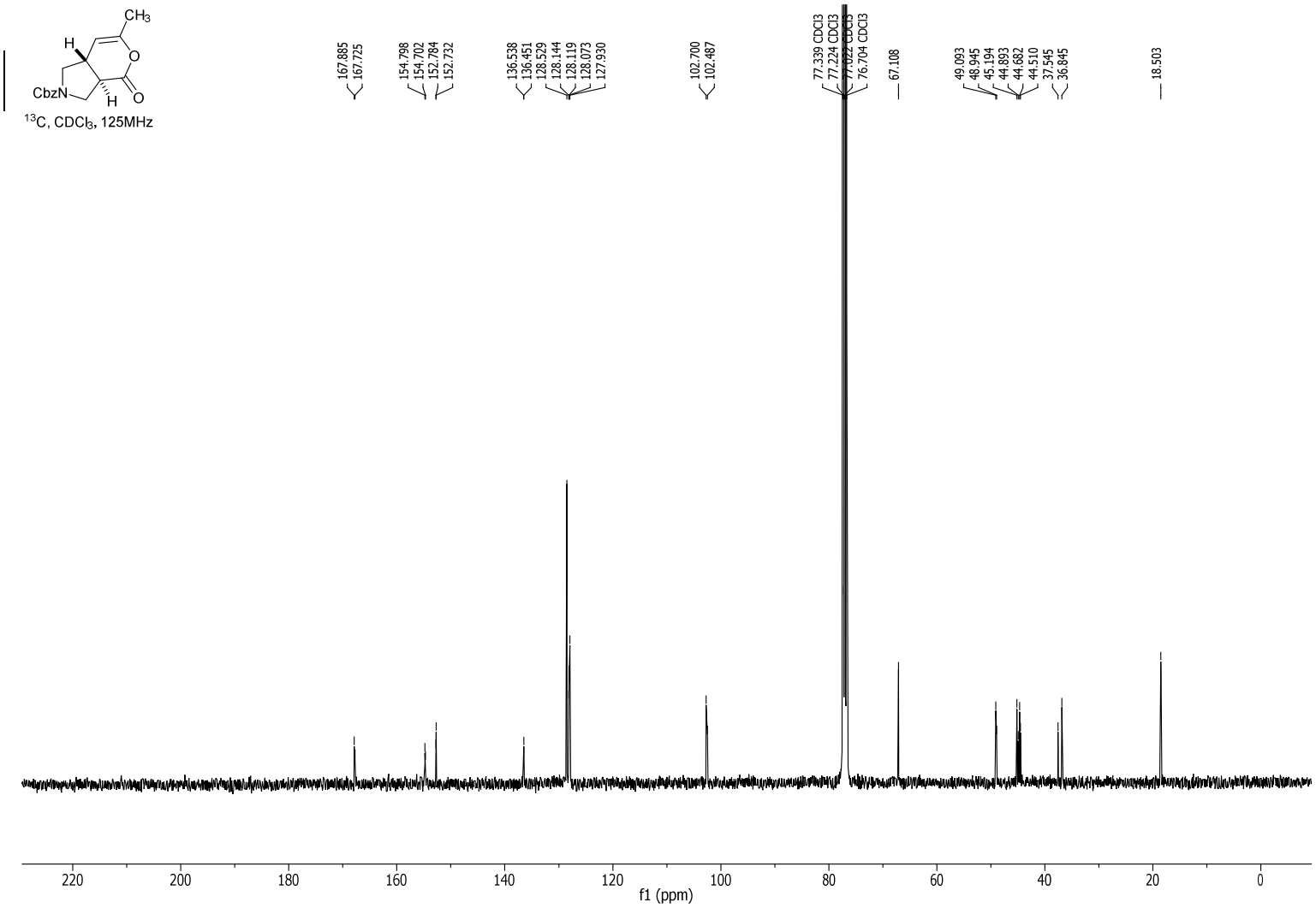
Mis en forme : Police :20 pt, Gras, Français (France)



^{1}H, $CDCl_3$,300MHz

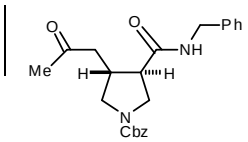
27

Mis en forme : Police :20 pt, Gras, Français (France)



27

Mis en forme : Police :20 pt, Gras, Français (France)

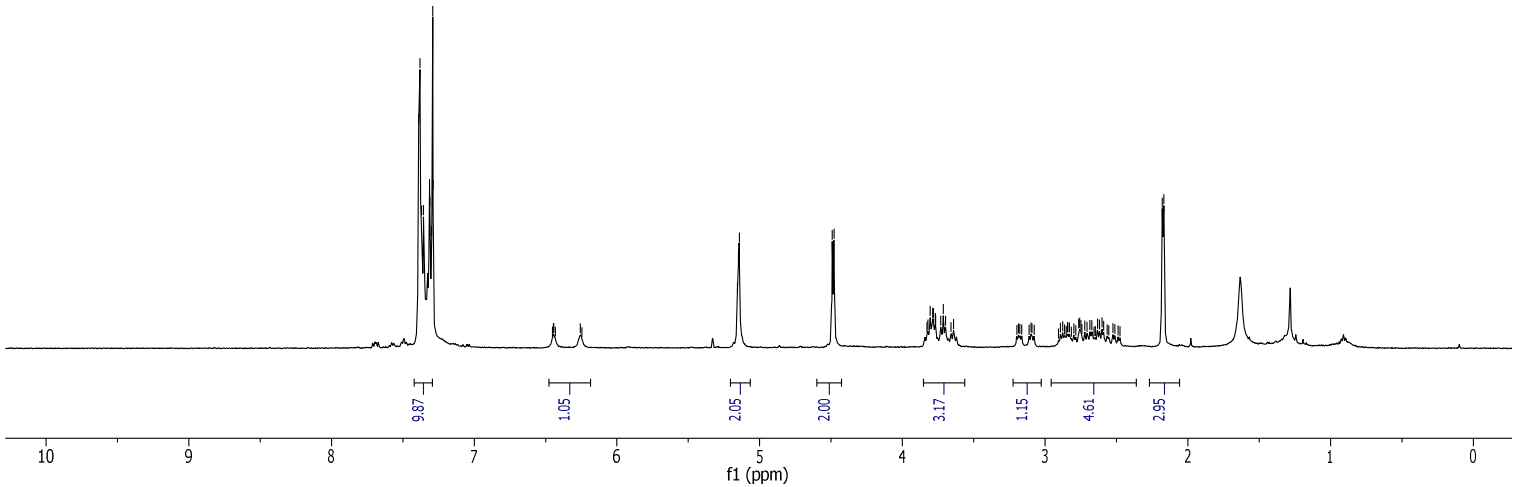


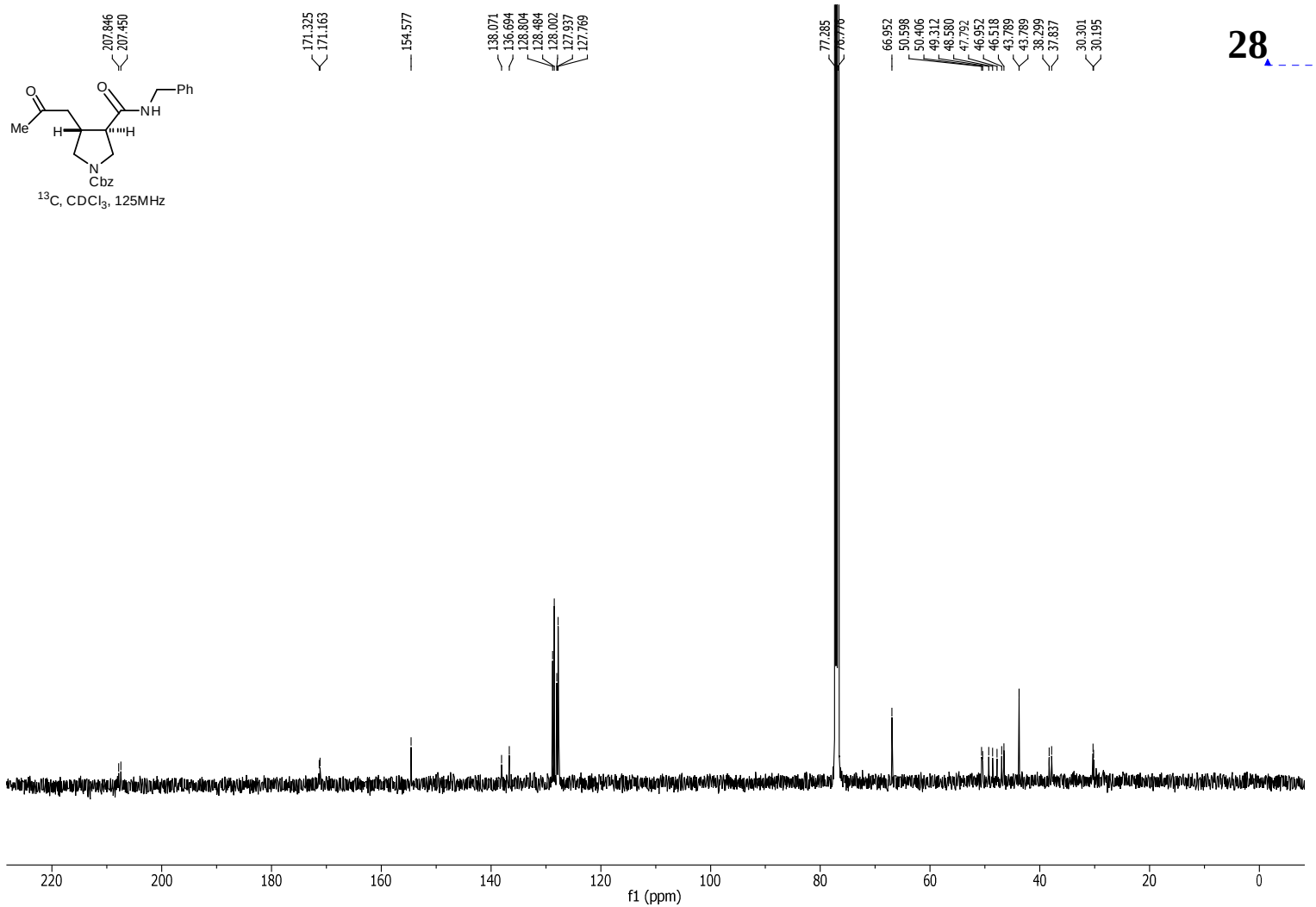
^{1}H, $CDCl_3$,500 MHz

7.389 7.380 7.369 7.355 7.314 7.310 7.298 7.291 7.289 6.453 6.444 6.443 6.432 6.257 6.245 5.156 5.149 5.143 4.491 4.479 3.806 3.787 3.783 3.771 3.767 3.732 3.714 2.764 2.759 2.750 2.723 2.686 2.672 2.634 2.619 2.602 2.181 2.169

28

Mis en forme : Police :20 pt, Gras, Français (France)





28

Mis en forme : Police :20 pt, Gras, Français (France)