Supporting Information

Synthetic Approaches to Selenacephams and Selenacephems via a Clevage of Diselenide and Selenium Anion

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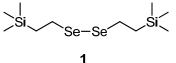
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General

All reactions were performed in round-bottom flask fitted with balloon filled with argon, otherwise specified. Transfer of air- and moisture-sensitive liquids were performed via cannula under a positive pressure of argon. TLC analysis was performed on Merck TLC (silica gel 60F₂₅₄ on glass plate). Evaporation and condensation were carried out *in vacuo*. Silica gel 60N (spherical, neutral) manufactured by Kanto Chemical Co. Inc. was used for flash column chromatography. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl prior to use. (2-bromoethyl)-trimethylsilane, and tetramethylammonium fluoride were purchased from Tokyo Chemical Industry Ltd. 1-Bromo-3-chloropropane, 1-bromo-2-octyne, acetic anhydride, and acetic acid were purchased from Wako Pure Chemical Industries Ltd. NaH was purchased from Nacalai Tesque Inc. 1-bromo-butyne, 1-bromo-2-pentyne, ethyl 2-(bromomethyl)acrylate, and LHMDS (1.0 M THF solution) were purchased from Aldrich Chemical Company.

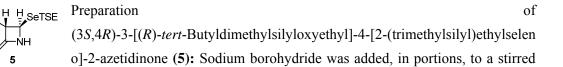
Melting points were measured by a Yanagimoto micromelting point apparatus (uncorrected). Optical rotation was recorded by Union PM-201 Automatic Digital Polarimeter (Horiba) at 28°C. IR spectra were measured on JASCO FT/IR-410 Fourier Transform Infrared Spectrometer. The ¹H NMR spectra were measured on JEOL:JNM ECX-400 P, JEOL:JNM ECA-500, JEOL:JNM ECA-600 spectrometers in CDCl₃. Chemical shifts of protons are reported in δ values referred to TMS as an internal standard, and the following abbreviation were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. The ¹³C NMR spectra or ⁷⁷Se NMR spectra were obtained from the JEOL:JNM ECX-400 P, JEOL:JNM ECA-500 or JEOL:JNM ECA-600 spectrometers in CDCl₃. The ⁷⁷Se chemical shifts were expressed in δ values deshielded with respect to neat Me₂Se. ¹J(⁷⁷Se-¹H) values are observed as ⁷⁷Se satellites of the ¹H NMR spectra. HRMS was measured on a JEOL JMS-700.



Preparation of bis[2-(Trimethylsilyl)ethyl]-diselenide (1): Selenium (0.150 g, 1.90 mmol) was added to a stirred solution of sodium borohydride (0.144 g, 3.80 mmol) in DMF (10 mL)

followed by the addition of absolute ethanol (0.673 mL, 11.4 mmol) at 0 °C. Stirring was continued for 30 min at this temp. and additional Se (0.150 g, 1.90 mmol) was added to reaction mixture and stirred for 30 min at 0 °C. Finally the 2-bromoethyltrimethylsilyl (0.699 mL, 4.34 mmol) was added over a period of 5 min. After stirring for a further hour at room temp., the reaction mixture was extracted with diethyl ether and washed with water, dried over sodium sulphate and concentrated *in vacuo*. The crude product was purified over silica gel column chromatography (SiO₂: hexane / toluene = 20/1) to afford the diselenide **1** as yellow oil (1.260 g, 92%). IR (neat): 2951, 1412, 1247, 1229, 1142, 1072, 1015, 859, 839 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.96-1.03 (m, 2H), 2.87-2.94 (m, 2H). ¹³C NMR (CDCl₃): δ -1.82 (¹*J*_{13C-29Si} = 50.3 Hz), 19.5 (¹*J*_{13C-29Si} = 46.8 Hz), 25.0 (¹*J*_{13C-77Se} = 69.6 Hz). ⁷⁷Se NMR (CDCl₃): δ 354.6. MS (EI): m/z = 262 [M⁺].

SeTSE Preparation of 4-[2-(Trimethylsilyl)ethylseleno]-2-azetidinone (4): Sodium borohydride was added, in portions, to a stirred suspension of NΗ bis[2-(Trimethylsilyl)ethyl]-diselenide 1 (0.952 g, 2.64 mmol) in absolute ethanol (15 mL), under argon until the characteristic yellow color of the diselenide had disappeared. The mixture was cooled to 0 °C and 4-acetoxy-2-azetidinone 2 (0.620 g, 4.80 mmol) in absolute ethanol (10 mL) was added over a period of 1 h. After stirring for a further hr, 10% sodium bicarbonate (30 mL) was added. The mixture was extracted with ethyl acetate (3 x 50 mL), the combined organic extracts were washed with brine (50 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 5/1) to afford the key intermediate product 4 as pale yellow oil (1.022 g, 85%). IR (neat): 2952, 1756, 1667, 1409, 1247, 1154, 860 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.90-1.00 (m, 2H), 2.66-2.74 (m, 2H), 3.02 (dt, J = 1.7 & 15.4 Hz, 1H), 3.44 (ddd, J = 1.7, 5.1 & 15.4, 1H), 4.90 (dd, J = 2.3 & 5.1 Hz, ${}^{2}J({}^{77}Se^{-1}H) = 23.5 Hz$, 1H), 6.60 (drs, 1H). ¹³C NMR (CDCl₃): δ -1.94, 18.4, 18.7, 44.0, 47.1, 166.5. ⁷⁷Se NMR (CDCl₃): δ 338.6. MS (EI): m/z = 251 [M⁺]. HRMS (EI): m/z = 251.0245 calcd. for C₈H₁₇NOSeSi, found 251.0228.

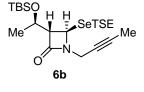


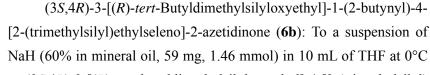
suspension of bis[2-(Trimethylsilyl)ethyl]-diselenide 1 (2.100 g, 5.87 mmol) in absolute ethanol (25 mL), under argon until the characteristic yellow color of the diselenide had disappeared. The mixture cooled 0 °C was to and (3R,4R)-4-acetoxy-3-[(R)-(tert-butyldimethylsilyloxy)ethyl]-azetidinone 3 (3.045 g, 10.6 mmol) in absolute ethanol (30 mL) was added over a period of 1 h at 0 °C. After stirring for a further hr at room temp., 10% sodium bicarbonate (100 mL) was added. The mixture was extracted with ethyl acetate (3 x 75 mL), the combined organic extracts were washed with brine (100 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 5/1) to afford the title compound **5** as white solid (4.294 g, 99%). Melting point: 67.1-68.1°C. $[\alpha]_{D} = +54.4$ (c = 0.34, CHCl₃). IR (KBr): 3152, 3097, 1761, 1712 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.04 (s, 3H), 0.05 (s, 3H), 0.85 (s, 9H), 0.93-0.97 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H), 2.64-2.75 (m, 2H), 3.00.3.20 (m, 1H), 4.18-4.25 (m, 1H), 4.95 (d, J = 2.3 Hz, ${}^{2}J({}^{77}\text{Se}^{-1}\text{H}) = 27.3 \text{ Hz}$, 1H), 6.30 (brs, 1H). ¹³C NMR (CDCl₃): δ -5.08, -4.36, -1.89, 17.9, 18.3, 18.7, 22.2, 25.7, 46.5, 64.9, 67.2, 167.5. ⁷⁷Se NMR (CDCl₃): δ 325.6. MS (EI): m/z = 352 [M⁺-57]. HRMS: m/z = 409.1372, calcd. for C₁₆H₃₅NO₂SeSi₂, found 409.1397 [M⁺]. Anal. Calcd for C₁₆H₃₅NO₂SeSi₂: C, 47.03; H, 8.63; N, 3.43. Found: C, 46.60; H, 8.46; N, 3.40.

SeTSE Preparation of 1-(3-chloropropyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (**6a**): 6a Lithium bis(trimethylsilyl)-amide (LHMDS) (499 µL of 1.0 M solution in THF) was added dropwise to a stirred solution of 4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone 4 (100 mg, 0.40 mmol) in THF (10 mL) at -78 °C under argon. The resultant solution was stirred at -78 °C for 10 minutes. 1-Bromo-3-chloropropane (396 µL, 4.00 mmol) was added over 5 minutes and the resulting mixture allowed to warm to ambient temperature for 2 hr. The resulting mixture was quenched with 10% HCl and extracted with ethyl acetate. The combined organic extracts were dried (Na₂SO₄) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the title compound **6a** as pale yellow oil (33 mg, 25%). IR (neat): 2953, 1756, 1633, 1390, 1248, 842 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.95 (t, J = 9.2 Hz, 3H), 2.00-2.12 (m, 2H), 2.57-2.76 (m, 2H), 3.00 (d, J = 15.2 Hz, 1H), 3.10-3.25 (m, 1H), 3.30-3.65 (m, 4H), 4.21 (dq, J = 2.0 & 17.1 Hz, 1H), 4.92 (dd, J = 2.1 & 4.8 Hz, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 23.3$ Hz, 1H). ${}^{13}\text{C}$ NMR (CDCl₃): δ -1.92, 17.9, 18.7, 30.5, 38.7, 42.2, 45.8, 50.1, 165.7. ⁷⁷Se NMR (CDCl₃): δ 275.2. MS (EI): m/z = 327 [M⁺]. HRMS (EI): m/z = 327.0324 calcd. for C₁₁H₂₂ClNOSeSi, found 327.0310.

Preparation

of

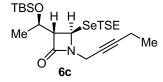




added (3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl) was ethylseleno]-2-azetidinone 5 (500 mg, 1.22 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0°C for an additional 30 minutes and 1-bromo-2-butyne (166 µL, 1.84 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 4 hours and then taken in 50 mL of ammonium chloride solution. The organic layer was washed with 50 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 50 mL of diethyl ether each. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to give 434 mg (77% yield) of a clear oil identified as **6b**. IR (neat): 2952, 2232, 1764, 1464, 1385, 1250, 837 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.04 (s, 6H), 0.85 (s, 9H), 0.95-1.02 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H), 1.74 (t, J = 2.7 Hz, 3H), 2.60-2.78 (m, 2H), 3.11 (t, J = 2.3 Hz, 1H), 3.56 (dd, J = 2.3 & 8.8, 1H), 4.16-4.30 (m, 2H), 5.02 (d, J = 2.3 Hz, ${}^{2}J({}^{77}Se^{-1}H) = 24.7 Hz$, 1H). ¹³C NMR (CDCl₃): δ -5.11, -4.45, -1.95, 3.42, 17.9, 18.8, 19.0, 22.2, 25.6, 29.6, 51.2, 64.6, 65.4, 71.9, 79.8, 165.5. ⁷⁷Se NMR (CDCl₃): δ 269.4. MS (EI): m/z = 404 [M⁺-^tBu]. HRMS (EI): m/z= 404.0980 calcd. for C₁₆H₃₀NO₂SeSi₂, found 3404.0975.





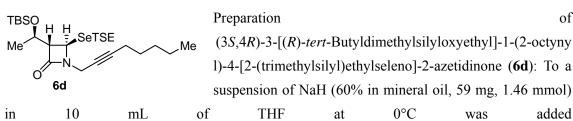


(3S,4R)-3-[(R)-tert-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6c): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at

0°C added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl) was ethylseleno]-2-azetidinone 5 (500 mg, 1.22 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0°C for an additional 30 minutes and 1-bromo-2-pentyne (188 µL, 1.84 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 4 hours and then taken in 50 mL of ammonium chloride solution. The organic layer was washed with 50 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 50 mL of diethyl ether each. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to give 418 mg (72% yield) of a clear oil identified as 6c. IR (neat): 2952, 2234, 1764, 1630, 1385, 1250, 837 cm⁻¹. ¹H NMR (CDCl₃): δ 0.04 (s, 9H), 0.08 (s, 6H), 0.89 (s, 9H), 0.99-1.07 (m, 2H), 1.12 (t, J = 7.3 Hz, 3H), 1.25 (d, J = 6.4 Hz, 3H), 2.12-2.20 (m, 2H), 2.68-2.80 (m, 2H), 3.12-3.16 (m, 1H), 3.60-3.68 (m, 1H), 4.22-4.30 (m, 2H), 5.05 (d, J = 2.3 Hz, ${}^{2}J({}^{77}\text{Se}^{-1}\text{H}) = 22.0$

Hz, 1H). ¹³C NMR (CDCl₃): δ -5.06, -4.43, -1.91, 12.3, 13.7, 17.9, 18.9, 22.3, 25.7, 29.7, 51.3, 64.7, 65.5, 72.0, 85.7, 165.5. ⁷⁷Se NMR (CDCl₃): δ 268.9. MS (EI): m/z = 418 [M⁺-¹Bu]. HRMS (EI): m/z = 418.1137 calcd. for C₁₇H₃₂NO₂SeSi₂, found 418.1100.

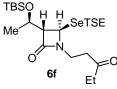
of



(3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone 5 (500 mg, 1.22 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0°C for an additional 30 minutes and 1-bromo-2-octyne (294 µL, 1.84 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 6 hours and then taken in 50 mL of ammonium chloride solution. The organic layer was washed with 50 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 50 mL of diethyl ether each. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to give 468 mg (74%) yield) of a clear oil identified as 6d. IR (neat): 2954, 2229, 1935, 1766, 1690, 1466, 1250, 1069, 837 cm⁻¹. ¹H NMR (CDCl₃): δ 0.04 (s, 9H), 0.08 (s, 6H), 0.87-0.3 (m, 12H), 0.99-1.06 (m, 2H), 1.25 (d, J = 6.3 Hz, 3H), 1.26-1.38 (m, 4H), 1.45-1.53 (m, 2H), 2.12-2.23 (m, 2H), 2.67-2.83 (m, 2H), 2.672H), 3.15 (m, 1H), 3.64 (d, J = 16.7 Hz, 1H), 4.20-4.32 (m, 2H), 5.04 (d, J = 2.3 Hz, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H})$ = 20.0 Hz, 1H). ¹³C NMR (CDCl₃): δ -5.04, -4.44, -1.91, 13.9, 17.9, 18.6, 18.9, 22.2, 22.3, 25.7, 28.3, 29.7, 31.1, 51.3, 51.4, 64.7, 65.5, 72.5, 84.5, 165.5. ⁷⁷Se NMR (CDCl₃): δ 268.2. MS (EI): $m/z = 460 \text{ [M^+}^{+}\text{Bu]}$. HRMS (EI): $m/z = 460.1606 \text{ calcd. for } C_{20}H_{38}NO_2SeSi_2$, found 460.1605.

Preparation of Ethyl 2-[methyl-3-[(3S,4R)-3-[(R)-tert-Butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl]]acrylate (6e): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at 0°C was added (3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone 5 (500 mg, 1.22 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0°C for an

additional 30 minutes and ethyl 2-(bromomethyl)acrylate (253 µL, 1.84 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 2 hours and then taken in 50 mL of ammonium chloride solution. The organic layer was washed with 50 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 50 mL of diethyl ether each. The combined organic layers were dried (Na₂SO₄) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to give 580 mg (91% yield) of a clear oil identified as **6e**. IR (neat): 2954, 1764, 1716, 1635, 1470, 1250, 838 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.03 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 0.90-1.00 (m, 2H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 2.58-2.68 (m, 2H), 3.22 (dd, *J* = 1.1 & 2.3 Hz, 1H), 3.84 (d, *J* = 16.6 Hz, 1H), 4.16-4.29 (m, 4H), 4.92 (d, *J* = 2.3 Hz, ²*J*(⁷⁷Se⁻¹H) = 40.6 Hz, 1H), 5.85 (d, *J* = 1.1 Hz, 1H), 6.30 (d, *J* = 1.1 Hz, 1H). ¹³C NMR (CDCl₃): δ -4.72, -4.64, -1.95, 14.2, 18.0, 18.3, 18.7, 22.3, 25.8, 40.8, 52.7, 61.0, 65.0, 66.0, 127.0, 135.0, 165.6, 166.6. ⁷⁷Se NMR (CDCl₃): δ 264.6. MS (EI): *m/z* = 464 [M⁺-^{*t*}Bu]. HRMS (EI): *m/z* = 464.1192 calcd. for C₁₈H₃₄NO₄SeSi₂, found 464.1180.

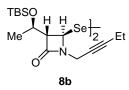


Preparation of (3S,4R)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-1 -(3-oxopentyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6f): To a suspension of NaH (60% in mineral oil, 73 mg, 1.84 mmol) in 5 mL of THF at 0 °C was added (3S,4R)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]

-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **5** (500 mg, 1.22 mmol) in 15 mL THF over 15 min. The mixture was stirred at 0 °C. After 30 min, ethyl vinyl ketone (190 μL, 1.84 mmol) was added dropwise. The reaction mixture was stirred at r.t. for 8 h and then taken in 50 mL of ammonium chloride solution. The aqueous layer was extracted 3 times with 50 mL of diethyl ether each. The combined organic layers were dried (Na₂SO₄) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to give 404 mg (67% yield) of a clear oil identified as **6f**. IR (neat): 2954, 1757, 1716, 1666, 1461, 1374, 1249, 837 cm⁻¹. ¹H NMR (CDCl₃): δ 0.04 (s, 9H), 0.06 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 0.94-1.03 (m, 2H), 1.06 (t, *J* = 7.3 Hz, 3H), 1.23 (d, *J* = 6.4 Hz, 3H), 2.38-2.48 (m, 2H), 2.64-2.75 (m, 2H), 2.79 (t, *J* = 6.9 Hz, 2H), 3.17 (t, *J* = 1.8 Hz, ¹*H*, 3.24-3.34 (m, 1H), 3.47-3.55 (m, 1H), 4.18-4.27 (m, 1H), 4.85 (d, *J* = 1.8 Hz, ²*J*(⁷⁷Se-¹H) = 27.5 Hz, 1H). ¹³C NMR (CDCl₃): δ -4.93, -4.47, -1.89, 7.59, 17.8, 17.9, 18.6, 22.3, 25.7, 35.6, 35.9, 40.1, 52.6, 64.8, 65.7, 166.7, 208.6. ⁷⁷Se NMR (CDCl₃): δ 265.5. MS (EI): *m/z* = 436 [M⁺ - ¹Bu]. HRMS: *m/z* = 436.1242, calcd. for C₁₇H₃₄NO₃SeSi₂, found 436.1258.

Preparation of 1-aza-5-selenabicyclo[4.2.0]oct-8-one (7): To a stirred solution of 1-(3-chloropropyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **6a** (15 **Selenacepham 7** mg, 0.05 mmol) in 1 mL THF was added tetrabutylammonium fluoride (92 μ L of 1.0 M solution in THF) at r.t. After stirring at this temperature for 1 h, AcOH (6 μ L, 0.09 mmol) was added and stirring continued for additional 15 min. The reaction mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 1/1) to afford the selenacepham **7** (8.3 mg, 91%). IR (neat): 2923, 1745, 1645, 1296, 1205, 1097, 909 cm⁻¹. ¹H NMR (CDCl₃): δ 1.80-1.90 (m, 1H), 1.92-1.98 (m, 1H), 2.75-2.88 (m, 2H), 2.98 (dt, J = 2.3 & 12.6 Hz, 1H), 3.02 (dd, J = 1.7 & 14.9 Hz, 1H), 3.47 (ddd, J = 1.7, 5.6 & 14.9 Hz, 1H), 4.02 (d, J = 13.7 Hz, 1H), 4.84 (dd, J = 1.7 & 4.6 Hz, ²J(⁷⁷Se-¹H) = 18.9 Hz, 1H). ¹³C NMR (CDCl₃): δ 18.3, 24.0, 40.1, 40.4, 47.1, 163.8. ⁷⁷Se NMR (CDCl₃): δ 283.1. MS (EI): $m/z = 191 [M^+]$. HRMS (EI): m/z = 190.9849 calcd. for C₆H₉NOSe, found 190.9823.

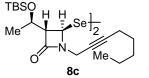
TBSC Preparation of bis[(3S,4R)-3-[(R)-tert-Butyldimethylsilyloxyethyl]-1-(2-butynyl)-2-azetidin one]-4-diselenide (8a): Tetrabutylammonium fluoride (239 µL of 1.0 M 8a solution in THF) was added dropwise to а stirred solution of (3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-1-(2-butynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone 6b (100 mg, 0.22 mmol) in THF (1 mL) at -20 °C under argon. The resultant solution was stirred for 24 hr, during this time it was allowed to warm to ambient temperature. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the title compound 8a as an oil (47 mg, 60%). IR (neat): 2928, 2359, 2233, 1767, 1631, 1471, 1384, 1254, 835 cm⁻¹. ¹H NMR (CDCl₃): δ 0.08 (s, 6H), 0.88 (s, 9H), 1.23 (d, J = 6.3 Hz, 3H), 1.80 (t, J = 2.3 Hz, 3H), 3.29 (s, 1H), 3.58-3.64 (m, 1H), 4.18-4.32 (m, 2H), 5.15 (d, J = 2.3 Hz, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 39.0 \text{ Hz}, 1\text{H}). {}^{13}\text{C} \text{ NMR} (\text{CDCl}_3): \delta -5.10, -4.51, 3.49, 17.9, 22.3, 25.7, 29.9, 52.7, 29.9, 52.7, 29.9, 52.7, 29.9, 52.7, 29.9, 52.7, 5$ 64.4, 66.6, 71.6, 80.6, 165.2. ⁷⁷Se NMR (CDCl₃): δ 323.4. MS (EI): m/z = 664 [M⁺-^tBu]. HRMS: m/z = 664.1170, calcd. for C₂₆H₄₄N₂O₄Se₂Si₂, found 664.1175.



Preparation of bis[(3S,4R)-3-[(R)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-2-azetidinone]-4-diselenide (**8b**): Tetrabutylammonium fluoride (232 µL of 1.0 M solution in THF) was added dropwise to a stirred solution of

(3S,4R)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-4-[2-(trimethylsilyl)ethylseleno] -2-azetidinone **6c** (100 mg, 0.21 mmol) in THF (1 mL) at -20 °C under argon. The resultant solution was stirred for 24 hr, during this time it was allowed to warm to ambient temperature. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the title compound **8b** as an oil (43 mg, 56%). IR (neat): 2933, 2234, 2038, 1766, 1632, 1463, 1254, 1065, 834 cm⁻¹. ¹H NMR (CDCl₃): δ 0.07 (s, 6H), 0.88 (s, 9H), 1.13 (t, *J* = 7.6 Hz, 3H), 1.24 (d, *J* = 6.2 Hz, 3H), 2.14-2.21 (m, 2H), 3.29 (s, 1H), 3.63 (dd, *J* = 2.4 & 17.9 Hz, 1H), 4.20-4.31 (m, 2H), 5.14 (d, *J* = 1.3 Hz, ²*J*(⁷⁷Se⁻¹H) = 42.6 Hz, 1H). ¹³C NMR (CDCl₃): δ -5.06, -4.50, 12.4, 13.7, 17.9, 22.3, 25.7, 29.9, 52.9, 64.4, 66.5, 71.6, 86.5, 165.2. ⁷⁷Se NMR (CDCl₃): δ 324.5. MS (EI): *m*/*z* = 691 [M⁺-^{*t*}Bu]. HRMS: *m*/*z* = 662.1483, calcd. for C₂₈H₄₈N₂O₄Se₂Si₂, found 662.1474.

Preparation



bis[(3S,4R)-3-[(R)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-2-az etidinone]-4-diselenide (**8c**): Tetrabutylammonium fluoride (212 µL of 1.0 M solution in THF) was added dropwise to a stirred solution of

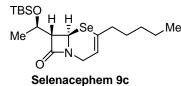
of

(3S,4R)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **6d** (100 mg, 0.19 mmol) in THF (1 mL) at -20 °C under argon. The resultant solution was stirred for 24 hr, during this time it was allowed to warm to ambient temperature. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the title compound **8c** as an oil (37 mg, 46%). IR (CHCl₃): 2929, 2230, 1769, 1635, 1470, 1382, 1256, 1067, 837 cm⁻¹. ¹H NMR (CDCl₃): δ 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.91 (t, *J* = 6.8 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.28-1.37 (m, 4H), 1.46-1.53 (m, 2H), 2.12-2.18 (m, 2H), 3.30 (s, 1H), 3.64 (d, *J* = 16.2 Hz, 1H), 4.20-4.32 (m, 2H), 5.12 (d, *J* = 2.3 Hz, ²*J*(⁷⁷Se-¹H) = 41.8 Hz, 1H). ¹³C NMR (CDCl₃): δ -5.05, -4.50, 14.0, 17.9, 18.7, 22.2, 22.3, 25.7, 28.3, 30.3, 31.1, 52.8, 64.4, 66.4, 72.1, 85.3, 165.2. ⁷⁷Se NMR (CDCl₃): δ 323.4. MS (EI): *m/z* = 775 [M⁺-^tBu]. HRMS: *m/z* = 776.9422, calcd. for C₃₄H₆₀N₂O₄Se₂Si₂, found 774.9417.

Preparation of (6R,7S)-7-[(R)-1-tert-butyldimethylsilyloxyethyl]-4-methyl-1-aza-5selenabicyclo[4.2.0]oct-3-en-8 -one (9a): Sodium borohydride (3 mg, 0.03 Selenacephem 9a added stirred suspension mmol) was to а of bis[(3S,4R)-3-[(R)-tert-Butyldimethylsilyloxyethyl]-1-(2-butynyl)-2-azetidinone]-4-diselenide **8a** (25 mg, 0.03 mmol) in absolute ethanol (2 mL), under argon until the characteristic yellow color of the diselenide had disappeared. After stirring for a further hr at room temp., 10% sodium bicarbonate (10 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), the combined organic extracts were washed with brine (10 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the selenacephem **9a** as an oil

(16 mg, 65%). IR (CHCl₃): 2928, 1765, 1649, 1597, 1375, 1256, 835 cm⁻¹. ¹H NMR (CDCl₃): δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.24 (d, *J* = 5.7 Hz, 3H), 2.06 (d, *J* = 1.8 Hz, 3H), 3.27 (dd, *J* = 1.1 & 4.6 Hz, 1H), 3.53 (dt, *J* = 2.3 & 18.3 Hz, 1H), 4.20-4.34 (m, 2H), 4.88 (s, ²*J*(⁷⁷Se⁻¹H) = 19.4 Hz, 1H), 5.63-5.67 (m, 1H). ¹³C NMR (CDCl₃): δ -5.12, -4.23, 17.9, 22.8, 25.6, 25.9, 38.9, 43.7, 65.1, 69.6, 112.8, 124.6, 165.1. ⁷⁷Se NMR (CDCl₃): δ 313.3. MS (EI): *m*/*z* = 304 [M⁺-^{*i*}Bu]. HRMS: *m*/*z* = 304.0272, calcd. for C₁₁H₁₈NO₂SeSi, found 304.0274.

TBSC of Preparation (6R,7S)-7-[(R)-1-tert-Butyldimethylsilyloxyethyl]-4-ethyl-1-aza-5-selenabicyc lo[4.2.0]oct-3-en-8 -one (9b): Sodium borohydride (4 mg, 0.07 mmol) was Selenacephem 9b added to а stirred suspension of bis[(3S,4R)-3-[(R)-tert-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-2-azetidinone]-4-diselenide 8b (25 mg, 0.03 mmol) in absolute ethanol (2 mL), under argon until the characteristic yellow color of the diselenide had disappeared. After stirring for a further hr at room temp., 10% sodium bicarbonate (10 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), the combined organic extracts were washed with brine (10 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the title selenacephem **9b** as an oil (13.7 mg, 55%). IR (CHCl₃): 2928, 1766, 1636, 1597, 1375, 1256, 835 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta 0.07$ (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.11 (t, J = 7.5 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H), 2.30-2.36 (m, 2H), 3.27 (d, J = 3.4 Hz, 1H), 3.55 (dt, J = 1.1 & 18.3 Hz, 1H), 4.21-4.33 (m, 2H), 4.87 (s, ${}^{2}J({}^{77}\text{Se}^{-1}\text{H}) = 18.3 \text{ Hz}$, 1H), 5.68 (t, J = 3.4 Hz, 1H). ${}^{13}\text{C}$ NMR (CDCl₃): δ -5.12, -4.24, 13.6, 17.9, 22.7, 25.7, 33.1, 38.9, 43.5, 65.1, 69.6, 111.6, 131.8, 165.1. MS (EI): m/z = 318 [M⁺-^tBu]. HRMS: m/z = 318.0429, calcd. for C₁₂H₂₀NO₂SeSi, found 318.0411.



(6R,7S)-7-[(R)-1-*tert*-Butyldimethylsilyloxyethyl]-4-pentyl-1-az a-5-selenabicyclo[4.2.0]oct-3-en-8-one (**9c**): Sodium borohydride (3 mg, 0.07 mmol) was added to a stirred

of

suspension of bis[(3S,4R)-3-[(R)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-2-azetidinone] -4-diselenide **8c** (18 mg, 0.02 mmol) in absolute ethanol (2 mL), under argon until the characteristic yellow color of the diselenide had disappeared. After stirring for a further hr at room temp., 10% sodium bicarbonate (10 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), the combined organic extracts were washed with brine (10 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the selenacephem **9c** as

Preparation

an oil (2 mg, 22%). IR (CHCl₃): 2928, 1767, 1662, 1638, 1465, 1392, 1254, 835 cm⁻¹. ¹H NMR (CDCl₃): δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 0.89 (t, *J* = 6.3 Hz, 3H), 1.22-1.34 (m, 7H), 1.46-1.52 (m, 2H), 2.30 (t, *J* = 7.4 Hz, 3H), 3.26 (d, *J* = 3.4 Hz, 1H), 3.55 (dt, *J* = 1.1 & 17.2 Hz, 1H), 4.21-4.31 (m, 2H), 4.85 (s, ²*J*(⁷⁷Se-¹H) = 18.3 Hz, 1H), 5.67 (t, *J* = 3.4 Hz, 1H). ¹³C NMR (CDCl₃): δ -5.11, -4.23, 14.0, 17.9, 22.4, 22.7, 25.7, 28.4, 31.0, 38.9, 40.0, 43.5, 65.1, 69.5, 112.4, 130.5, 165.1. ⁷⁷Se NMR (CDCl₃): δ 235.1. MS (EI): *m*/*z* = 360 [M⁺-^{*t*}Bu]. HRMS (EI): *m*/*z* = 360.0898 calcd. for C₁₅H₂₆NO₂SeSi, found 360.0894.

Preparation of (6R,7S)-7-[(R)-1-Hydroxyethyl]-4-methyl-1-aza-5-selenabicyclo[4.2.0] oct-3-en-8-one **(I)**: То а stirred solution of Selenacephem I (3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-1-(2-butynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **6b** (40 mg, 0.09 mmol) in 1 mL THF was added tetrabutylammonium fluoride (434 μ L of 1.0 M solution in THF) at rt. After stirring at this temperature for 1 h, AcOH (11 μ L, 0.20 mmol) was added and stirring continued for additional 15 min. The reaction mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 1/1) to afford the selenacephem I as white solid (1.4 mg, 6%). Melting point: 123-124°C. IR (neat): 2966, 1752, 1725, 1638, 1628, 1417, 1276, 825 cm⁻¹. ¹H NMR (CDCl₃): δ 1.35 (d, J = 6.9 Hz, 3H), 2.05-2.07 (m, 3H), 3.35 (dd, J = 1.4 & 6.2 Hz, 1H), 3.60 (dt, J = 2.8 & 18.6 Hz, 1H), 4.23-4.34 (m, 2H), 4.90 (s, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 18.0 Hz$, 1H), 5.65-5.69 (m, 1H). ¹³C NMR (CDCl₃): δ 21.8, 25.8, 39.1, 43.8, 65.1, 69.1, 112.8, 124.6, 165.0. ⁷⁷Se NMR (CDCl₃): δ 317.6. MS (EI): m/z = 247 [M⁺]. HRMS (EI): m/z = 247.0112calcd. for C₉H₁₃NO₂Se, found 247.0137.

TBSC Preparation of Ethyl (5R,6S)-7-[(R)-1-tert-Butyldimethylsilyloxyethyl]-1-aza-5-COOEt selenabicyclo[4.2.0]oct-3-(*S*)-carboxylate (**II**): Tetrabutylammonium Selenacepham II fluoride (211 µL of 1.0 M solution in THF) was added dropwise to a stirred solution of ethyl 2-[methyl-3-[(3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylsel eno]-1-azetidinyl]]acrylate 6e (100 mg, 0.19 mmol) in THF (1 mL) at -20 °C under argon. The resultant solution was stirred for 24 hr, during this time it was allowed to warm to ambient temperature. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the selenacepham II (4 mg, 5%) and diselenide III (15 mg, 18%) as an oil.

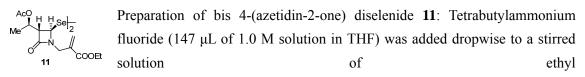
Selenacepheam II: IR (neat): 2954, 1764, 1731, 1538, 1373, 1256, 836 cm⁻¹. ¹H NMR (CDCl₃): δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 2.74-2.89 (m, 2H), 2.98-3.06 (m, 2H), 3.22 (dd, *J* = 1.4 & 4.3 Hz, 1H), 4.14-4.27 (m, 4H), 4.85 (d, *J* = 1.7 Hz, ²*J*(⁷⁷Se-¹H) = 14.3 Hz, 1H). ¹³C NMR (CDCl₃): δ -5.16, -4.25, 14.1, 17.9, 19.8, 22.6, 25.6, 40.2, 40.9, 42.9, 61.3, 64.8, 68.3, 171.6, 180.9. ⁷⁷Se NMR (CDCl₃): δ 393.9. MS (EI): *m*/*z* = 364 [M⁺-^{*t*}Bu]. HRMS (EI): *m*/*z* = 364.0483 calcd. for C₁₃H₂₂NO₄SeSi, found 364.0467.

Diselenide III: IR (neat): 2929, 2360, 1768, 1714, 1635, 1373, 1258, 836 m^{-1} . ¹H NMR (CDCl₃): δ 0.02 (s, 3H), 0.07 (s, 3H), 0.84 (s, 9H), 1.23 (d, J = 6.2 Hz, 3H), 1.32 (t, J = 6.9 Hz, 3H), 3.38 (dd, J = 2.1 & 3.4 Hz, 1H), 3.79 (d, J = 16.5 Hz, 1H), 4.17-4.30 (m, 4H), 5.04 (d, J = 2.0 Hz, ²J(⁷⁷Se-¹H) = 42.0 Hz, 1H), 5.90 (s, 1H), 6.33 (s, 1H). ¹³C NMR (CDCl₃): δ -4.76, -4.74, 14.2, 17.9, 22.4, 25.8, 41.2, 54.4, 61.1, 64.7, 66.7, 128.3, 134.6, 165.7, 165.9. ⁷⁷Se NMR (CDCl₃): δ 316.1. MS (EI): m/z = 783 [M⁺-¹Bu].

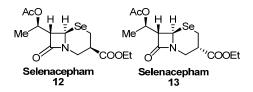
Preparation of Ethyl 2-[methyl-3-[(3S,4R)-3-[(R)-hydroxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethyl seleno]-1-azetidinyl]]acrylate (10a): Trifluoroacetic acid (excess) was 10a of added dropwise to а stirred solution ethyl 2-[methyl-3-[(3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylsel eno]-1-azetidinyl]]acrylate 6e (100 mg, 0.19 mmol) in DCM (2 mL) at r.t. The resultant solution was stirred for 3 days until the TLC shows the complete conversion of the starting material. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the hydroxy compound 10a (61 mg, 78%) and compound 10b (5 mg, 5%) as an oil. Compound 10a: IR (neat): 3424, 2954, 1745, 1714, 1635, 1402, 1248, 859 cm⁻¹. ¹H NMR (CDCl₃): δ 0.00 (s, 9H), 0.89-1.01 (m, 2H), 1.27-1.33 (m, 6H), 2.58-2.69 (m, 2H), 3.28 (dd, J = 2.3 & 4.0 Hz, 1H), 3.78 (d, J = 16.6 Hz, 1H), 4.21 (q, J = 7.45 Hz, 2H), 4.25-4.35 (m, 2H), 4.89 (d, J = 2.3 Hz, ${}^{2}J({}^{77}\text{Se-}{}^{1}\text{H}) = 32.9 \text{ Hz}, 1\text{H}), 5.87 \text{ (s, 1H)}, 6.32 \text{ (s, 1H)}. {}^{13}\text{C NMR (CDCl_3)}: \delta -1.95, 14.2, 18.5,$ 18.8, 21.1, 41.0, 51.9, 61.1, 64.4, 65.6, 127.2, 134.4, 165.5, 166.6. ⁷⁷Se NMR (CDCl₃): δ 276.6. MS (EI): $m/z = 407 [M^+]$.

Compound 10b: IR (neat): 2954, 1764, 1753, 1713, 1640, 1537, 1248, 860 f_{3C} Me f_{3C} Ne 18.9, 41.3, 53.3, 61.2, 63.0, 72.8, 127.8, 134.4, 163.5, 165.5, 169.9. ⁷⁷Se NMR (CDCl₃): δ 271.2. MS (EI): $m/z = 503 [M^+]$.

Preparation of Ethyl SeTSF 2-[methyl-3-[(3S,4R)-3-[(R)-acetoxyethyl]-2-oxo-4-[2-(trimethylsilyl)eth ylseleno]-1-azetidinyl]]acrylate (10): Acetic anhydride (70 µL, 0.74 10 dropwise stirred solution of mmol) was added to а ethyl 2-[methyl-3-[(3S,4R)-3-[(R)-hydroxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl] acrylate 10a (100 mg, 0.25 mmol) and catalytic amount of 4-dimethylaminopyridine in DCM (2 mL) at r.t. The resultant solution was stirred for 30 min at r.t. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the acetoxy compound **10** (109) mg, 99%) as an oil. IR (neat): 2953, 1766, 1743, 1715, 1635, 1373, 1237, 860 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta 0.00$ (s, 9H), 0.91-1.01 (m, 2H), 1.30 (t, J = 6.9 Hz, 3H), 1.36 (d, J = 6.3 Hz, 3H), 2.01 (s, 3H), 2.56-2.69 (m, 2H), 3.35 (d, J = 6.3 Hz, 1H), 3.78 (d, J = 16.6 Hz, 1H), 4.17-4.30 (m, 3H), 4.80 (s, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 22.9 \text{ Hz}$, 1H), 5.19-5.27 (m, 1H), 5.80 (s, 1H), 6.33 (s, 1H). ${}^{13}\text{C}$ NMR (CDCl₃): δ -1.99, 14.1, 18.2, 18.3, 18.6, 21.0, 40.9, 53.4, 61.1, 63.6, 67.7, 127.1, 134.7, 164.8, 165.4, 169.9. ⁷⁷Se NMR (CDCl₃): δ 268.3. MS (EI): m/z = 449 [M⁺]. HRMS (EI): m/z =449.1137 calcd. for C₁₈H₃₁NO₅SeSi, found 449.1137.

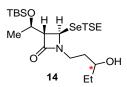


2-[methyl-3-[(3S,4R)-3-[(R)-*tert*-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylsel eno]-1-azetidinyl]]acrylate **10** (60 mg, 0.13 mmol) in THF (1 mL) at -20 °C under argon. The resultant solution was stirred for 24 hr, during this time it was allowed to warm to ambient temperature. The resulting mixture was extracted with chloroform and washed with water. The combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO₂: hexane / diethyl ether = 12/1) to afford the diselenide **11** (32 mg, 68%) as an oil. ¹H NMR (CDCl₃): δ 1.33 (t, J = 6.9 Hz, 3H), 1.39 (d, J = 6.3 Hz, 3H), 2.04 (s, 3H), 3.45-3.51 (m, 1H), 3.71 (d, J = 16.0 Hz, 1H), 4.22-4.30 (m, 3H), 4.92 (d, J = 2.3 Hz, ²J(⁷⁷Se-¹H) = 46.39 Hz, 1H), 5.24-5.32 (m, 1H), 5.87 (s, 1H), 6.38 (s, 1H). ⁷⁷Se NMR (CDCl₃): δ 304.4.



Preparationofethyl(5R,6S)-7-[(R)-1-acetoxyethyl]-1-aza-5-selenabicyclo[4.2.0]octane-3-(R)-carboxylate(12)andethyl(5R,6S)-7-[(R)-1-tert-Butyldimethylsilyloxyethyl]-1-

aza-5-selenabicyclo[4.2.0]octane-3-(S)-carboxylate (13): Sodium borohydride (4 mg, 0.11 mmol) was added to a stirred suspension of diselenide 11 (26 mg, 0.04 mmol) in absolute ethanol (2 mL), under argon until the characteristic yellow color of the diselenide had disappeared. After stirring for a further hr at room temp., 10% sodium bicarbonate (10 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), the combined organic extracts were washed with brine (10 mL), dried over sodium sulphate and concentrated in vacuo. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the selenacepham 12 (12.2 mg, 47%) and selenacepham 13 (11.7 mg, 45%) as an oil. Selenacepham 12: IR (CHCl₃): 2930, 1762, 1730, 1447, 1373, 1240, 1028, 755 cm⁻¹. ¹H NMR (CDCl₃): δ 1.27 (t, J = 6.9 Hz, 3H), 1.37 (d, J = 6.3 Hz, 3H), 2.04 (s, 3H), 2.74-2.82 (m, 1H), 2.90 (dd, J = 12.0 & 13.7 Hz, 1H), 3.01 (d, J = 8.1 Hz, 1H), 3.38 (dd, J = 1.2 & 7.5 Hz, 1H), 4.14-4.20 (m, 2H), 4.26 (dd, J = 4.1 & 13.8 Hz, 1H), 4.79 (d, J = 1.1 Hz, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 10.9$ Hz, 1H), 5.19-5.26 (m, 1H). ¹³C NMR (CDCl₃): δ 14.1, 18.6, 19.8, 21.1, 40.2, 41.1, 44.0, 61.4, 65.5, 68.0, 162.8, 170.2, 171.1. ⁷⁷Se NMR (CDCl₃): δ 277.2. MS (EI): m/z = 349 [M⁺]. HRMS (EI): m/z = 349.0428 calcd. for C₁₃H₁₉NO₅Se, found 349.0418. Selenacepham 13: IR (CHCl₃): 2929, 1767, 1735, 1648, 1442, 1374, 1239, 1026 cm⁻¹. ¹H NMR (CDCl₃): δ 1.28 (t, J = 6.9 Hz, 3H), 1.36 (d, J = 6.3 Hz, 3H), 2.03 (s, 3H), 2.80-2.86 (m, 1H), 2.98 (dd, J = 4.6 & 14.3 Hz, 1H), 3.10-3.23 (m, 2H), 3.33 (dd, J = 1.7 & 8.0 Hz, 1H), 4.14-4.29 (m, 2H), 4.47 (dt, J = 1.7 & 13.8 Hz, 1H), 4.78 (d, J = 1.7 Hz, ${}^{2}J({}^{77}\text{Se}{}^{-1}\text{H}) = 10.9$ Hz, 1H), 5.15-5.22 (m, 1H). ${}^{13}\text{C}$ NMR (CDCl₃): δ 14.2, 18.6, 20.1, 21.2, 36.0, 40.3, 44.1, 61.5, 65.9, 68.2, 162.6, 170.2, 170.3. ⁷⁷Se NMR (CDCl₃): δ 223.4. MS (EI): m/z = 349 [M⁺]. HRMS (EI): m/z = 349.0428 calcd. for C₁₃H₁₉NO₅Se, found 349.0382.

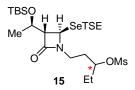


Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl] -1-(3-hydroxypentyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone

(14): Sodium borohydride (38 mg, 1.01 mmol) was added to a stirred suspension of ketone **6f** (200 mg, 0.41 mmol) in absolute ethanol (5

mL), under argon atmosphere. After stirring for a further 1 h at r.t., 10% sodium bicarbonate (10 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), the combined organic extracts were washed with brine (10 mL), dried over sodium sulphate and concentrated *in vacuo*. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the title compound **14** (183 mg, 91%) as an oil, as an inseparable

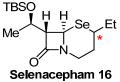
mixture of two diastereomers confirmed by ¹H NMR and ¹³C NMR. IR (CHCl₃): 3412, 2955, 1741, 1405, 1250, 1137, 837 cm⁻¹. MS (EI): m/z = 438 [M⁺ - ^{*t*}Bu]. HRMS (EI): m/z = 438.1399 calcd. for C₁₇H₃₆NO₃SeSi₂, found 438.1373.



Preparation of 4-[(3S,4R)-3-[(R)-tert-butyldimethylsilyloxyethyl] -2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl]-3-pentanyl

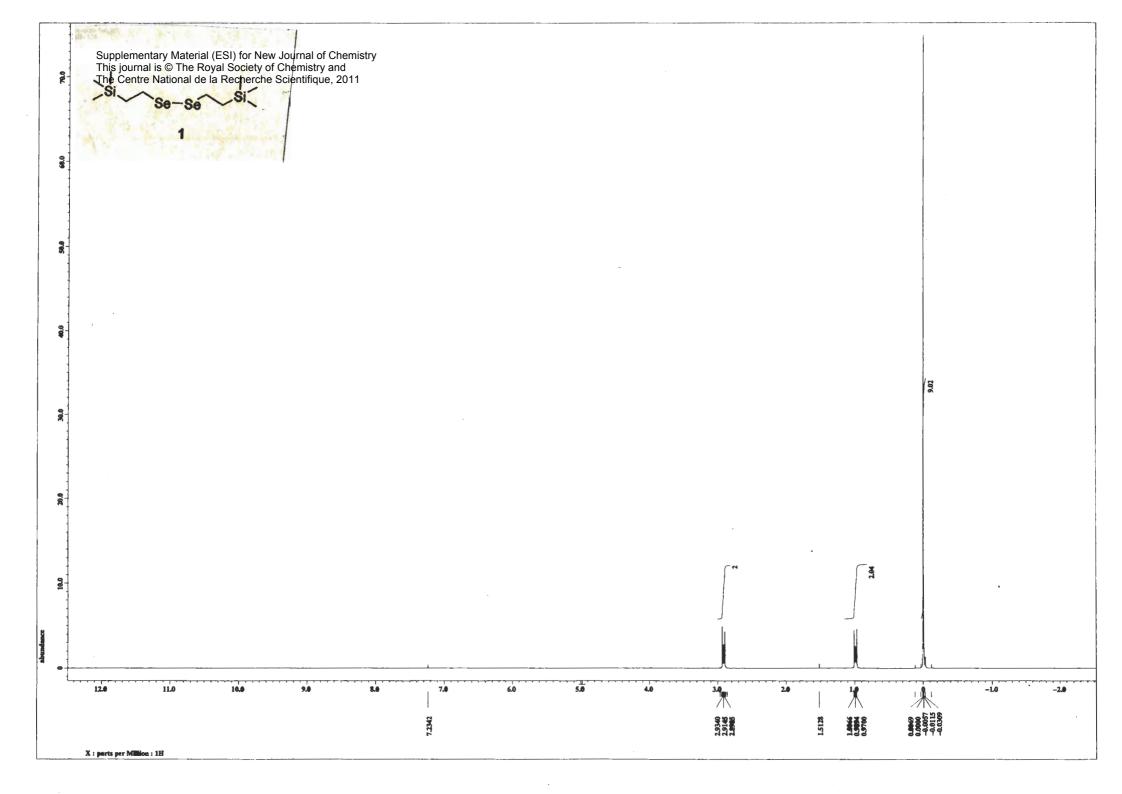
methanesulfonate (15): To a stirred solution of compound **14** (100 mg, 0.20 mmol) in DCM (2 mL) was added triethylamine (84 μ L, 0.60

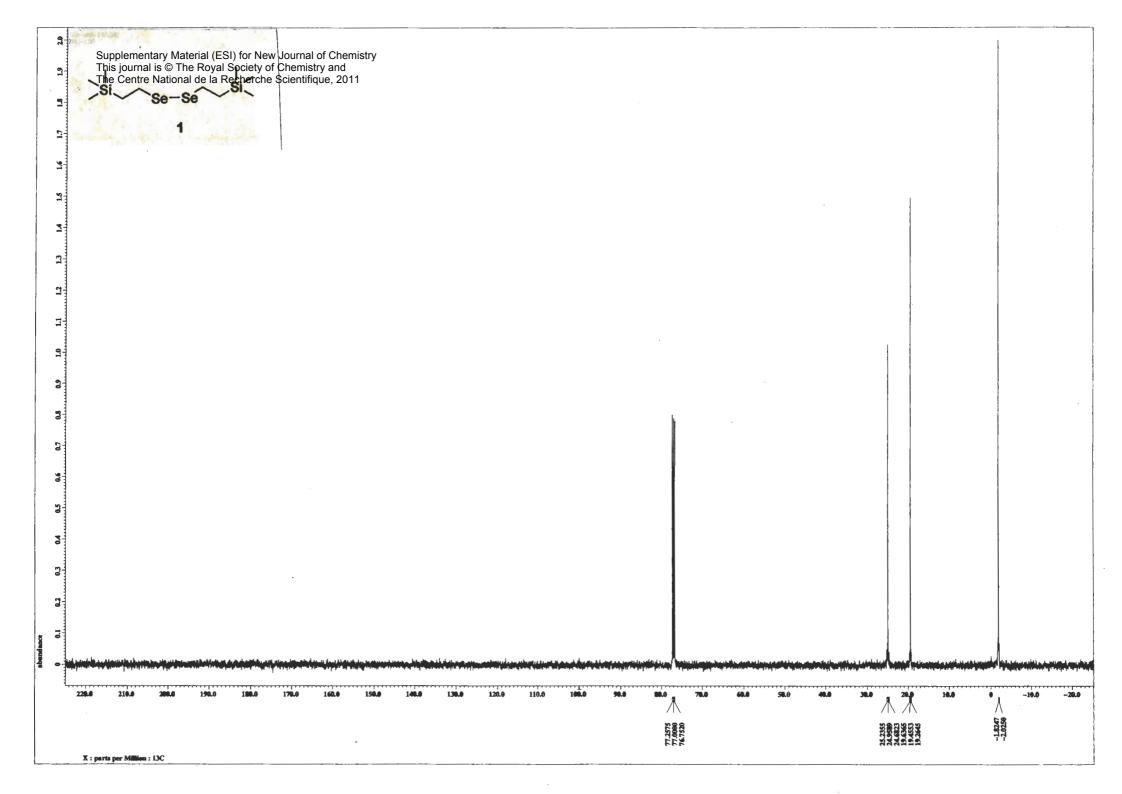
mmol) and mesyl chloride (24 μ L, 0.30 mmol) at 0 °C under argon atmosphere. The stirring was continued for 30 min at r.t. and the reaction mixture was extracted with ethyl acetate washed with water, dried over sodium sulphate and concentrated *in vacuo*. The crude product was purified over silica gel column chromatography (SiO₂: hexane / diethyl ether = 10/1) to afford the title compound **15** (103 mg, 89%) as an oil, as an inseparable mixture of two diastereomers confirmed by ¹H NMR and ¹³C NMR. IR (CHCl₃): 2955, 2359, 1753, 1642, 1463, 1359, 1249, 837 cm⁻¹. MS (EI): m/z = 516 [M⁺ - ^{*t*}Bu]. HRMS (EI): m/z = 516.1174 calcd. for C₁₈H₃₈NO₅SSeSi₂, found 516.1124.

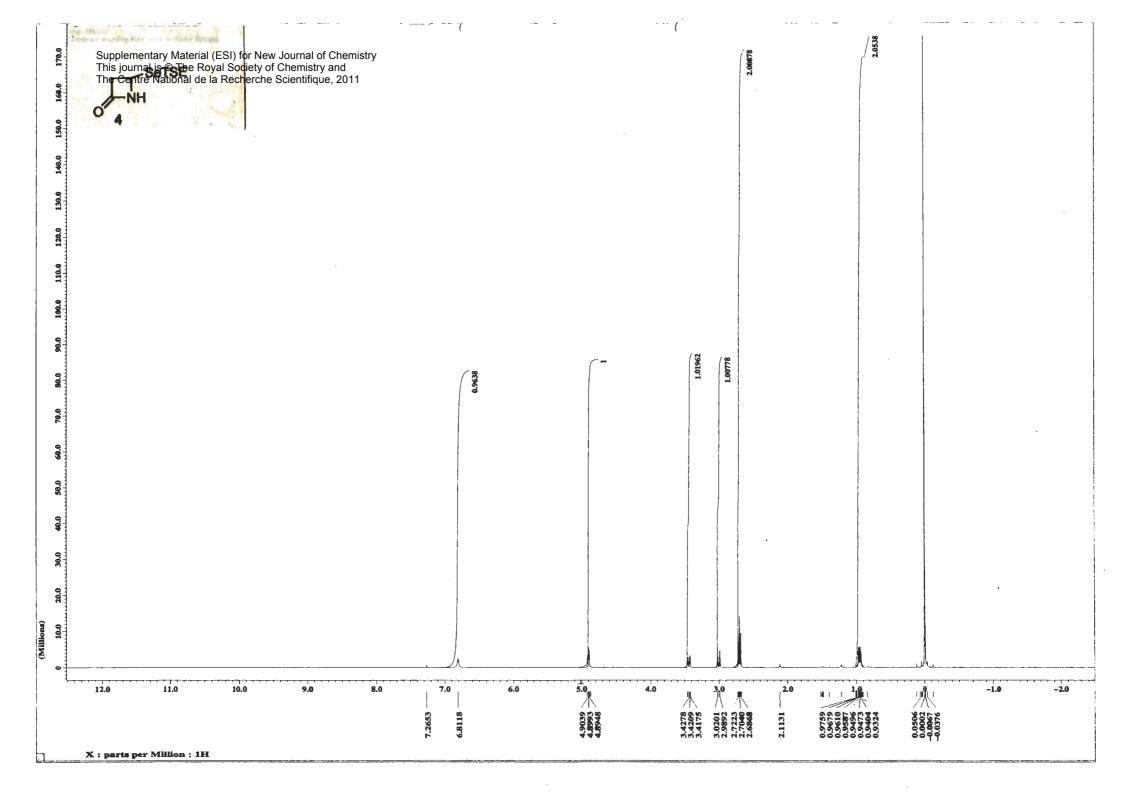


Preparation of (6R,7S)-7-[(*R*)-1-(*tert*-butyldimethylsilyloxy)ethyl] -4-ethyl-1-aza-5-selenabicyclo[4.2.0]oct-8-one (16): To a stirred solution of 15 (50 mg, 0.09 mmol) in degassed dry DMF (1.5 mL) was

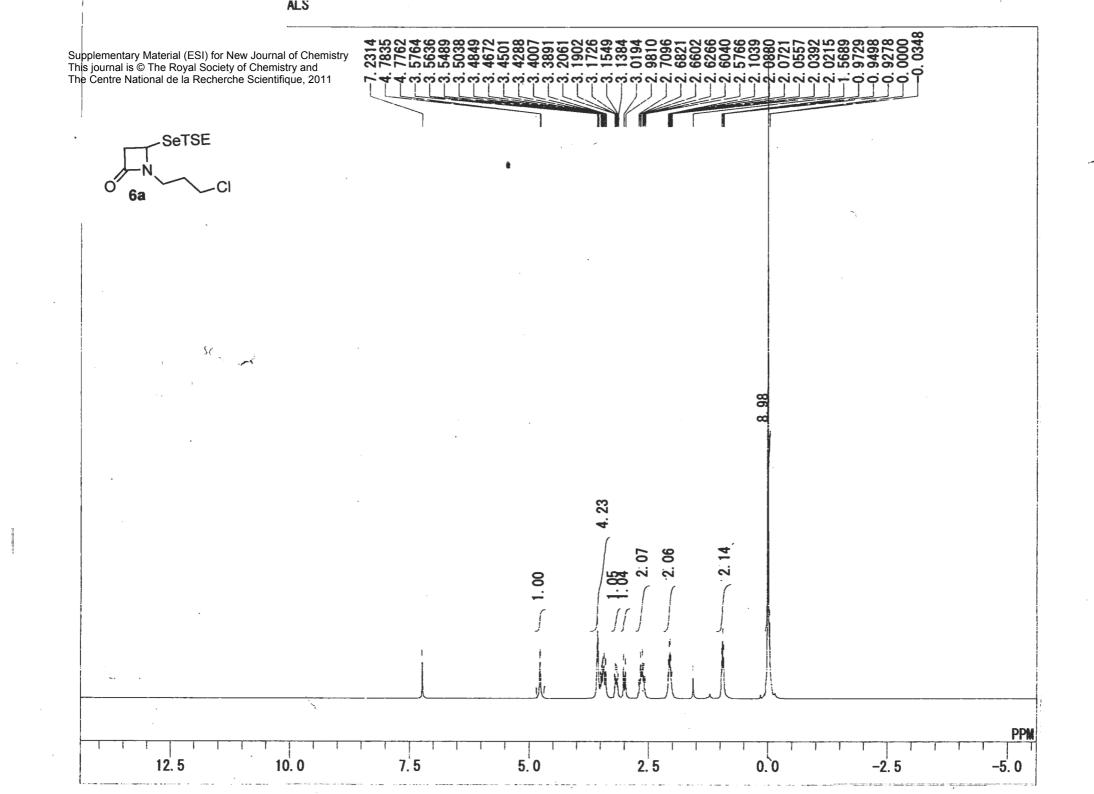
Selenacepham 16 added TBAF (0.22 mmol, 1 molar THF solution) at r.t. with argon bubbling to reaction mixture. The stirring was continued for additional 30 min and then extracted with chloroform and washed with water. The combined organic layers were dried (Na₂SO₄) and concentrated. The residue was purified by column chromatography (SiO₂: hexane / diethyl ether = 15/1) to afford the title compound **16** (25 mg, 76%) as an oil, as an inseparable mixture of two diastereomers confirmed by ¹H NMR and ¹³C NMR. IR (CHCl₃): 2957, 1759, 1640, 1471, 1394, 1256, 835 cm⁻¹. MS (EI): m/z = 320 [M⁺ - ^{*t*}Bu]. HRMS (EI): m/z = 320.0585calcd. for C₁₂H₂₂NO₂SeSi, found 320.0562.

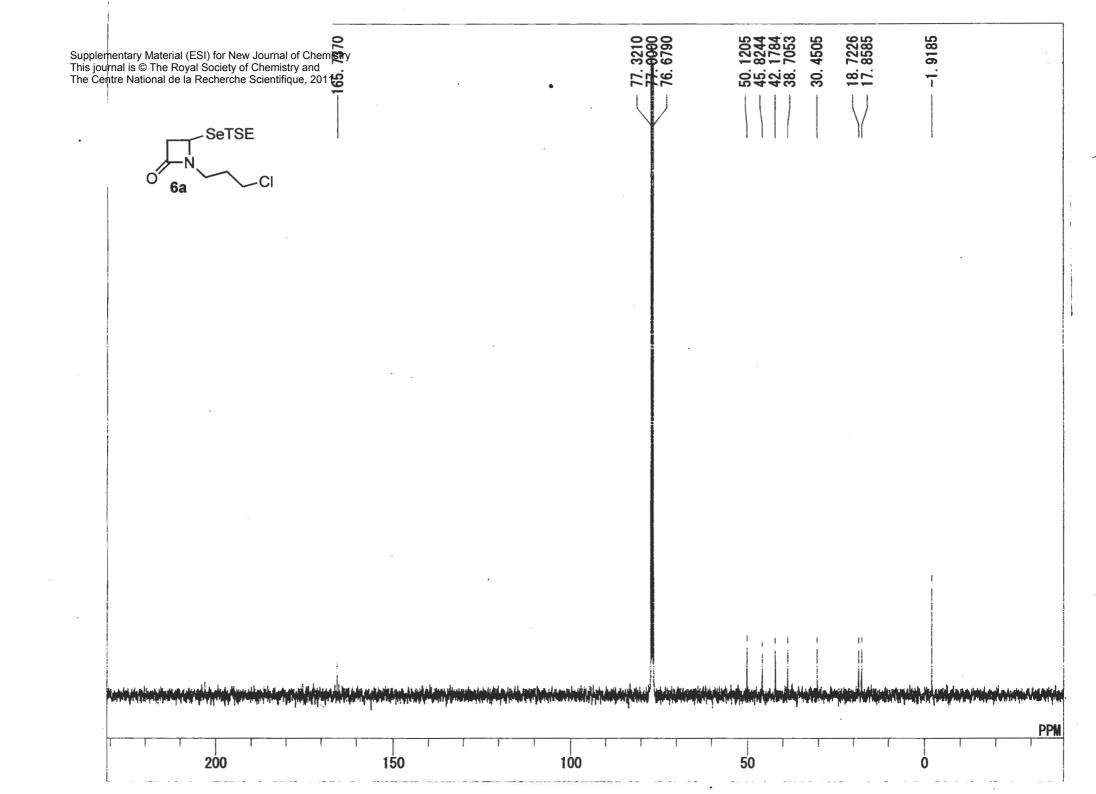


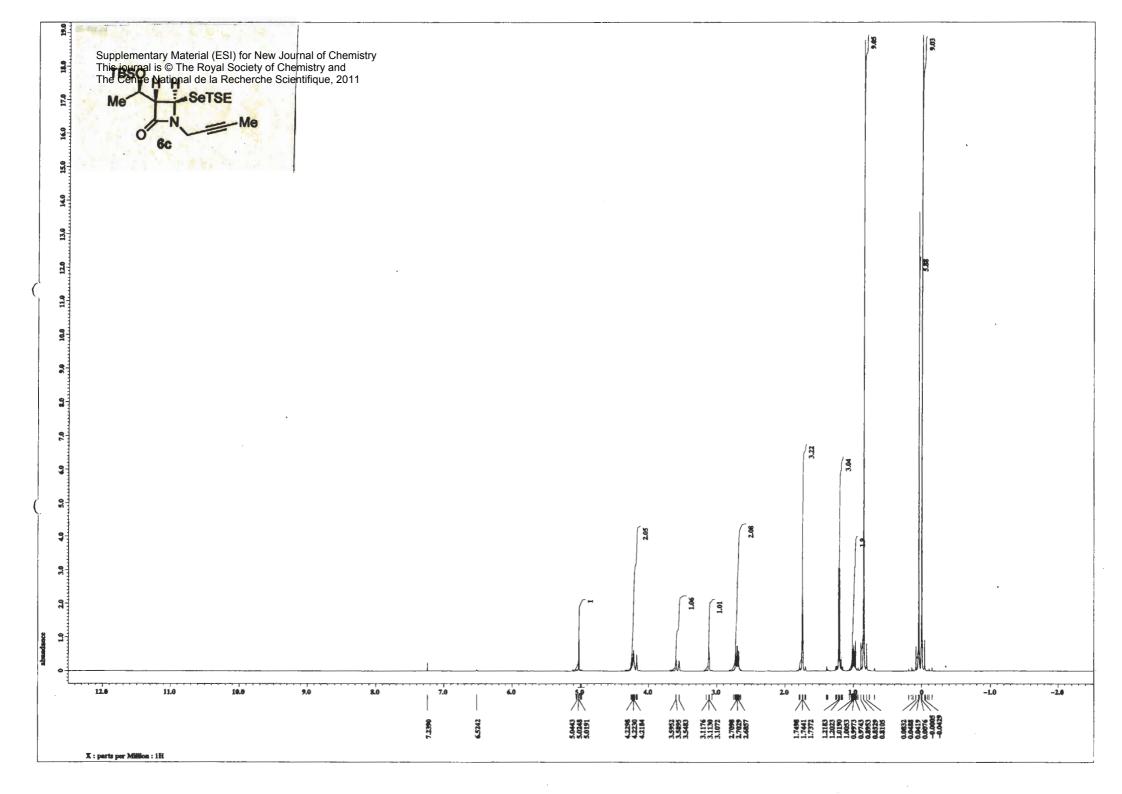


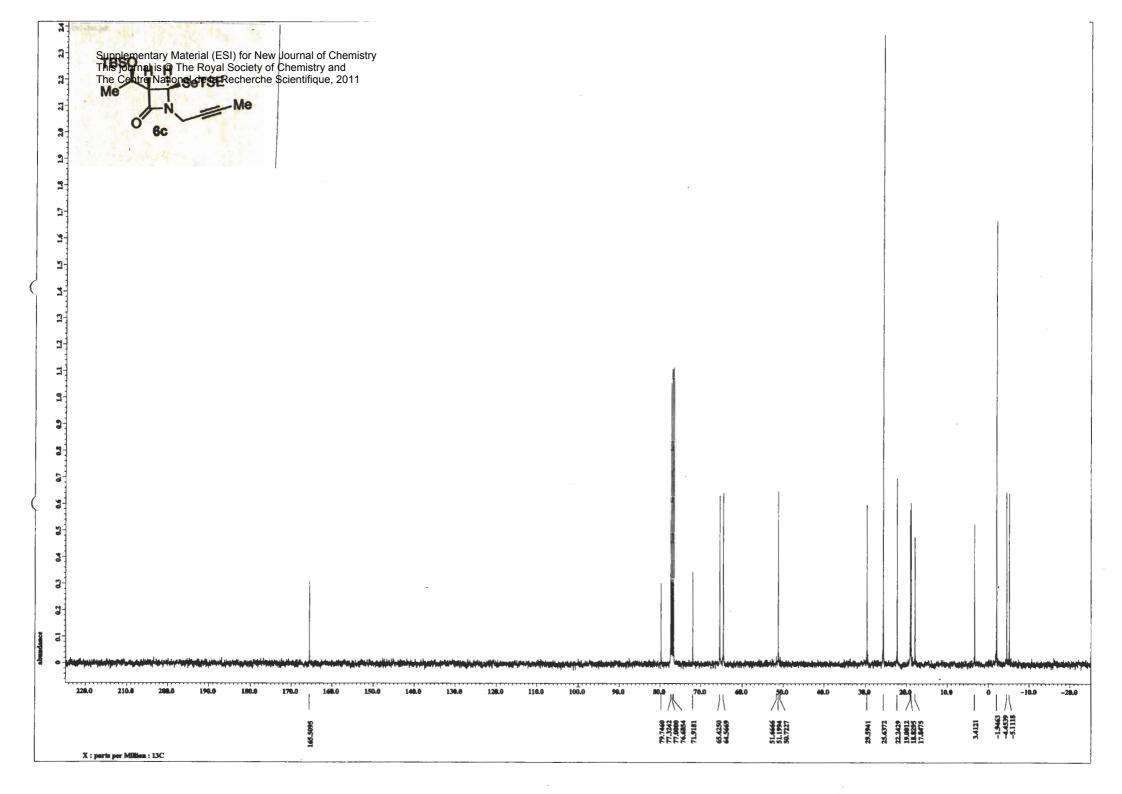


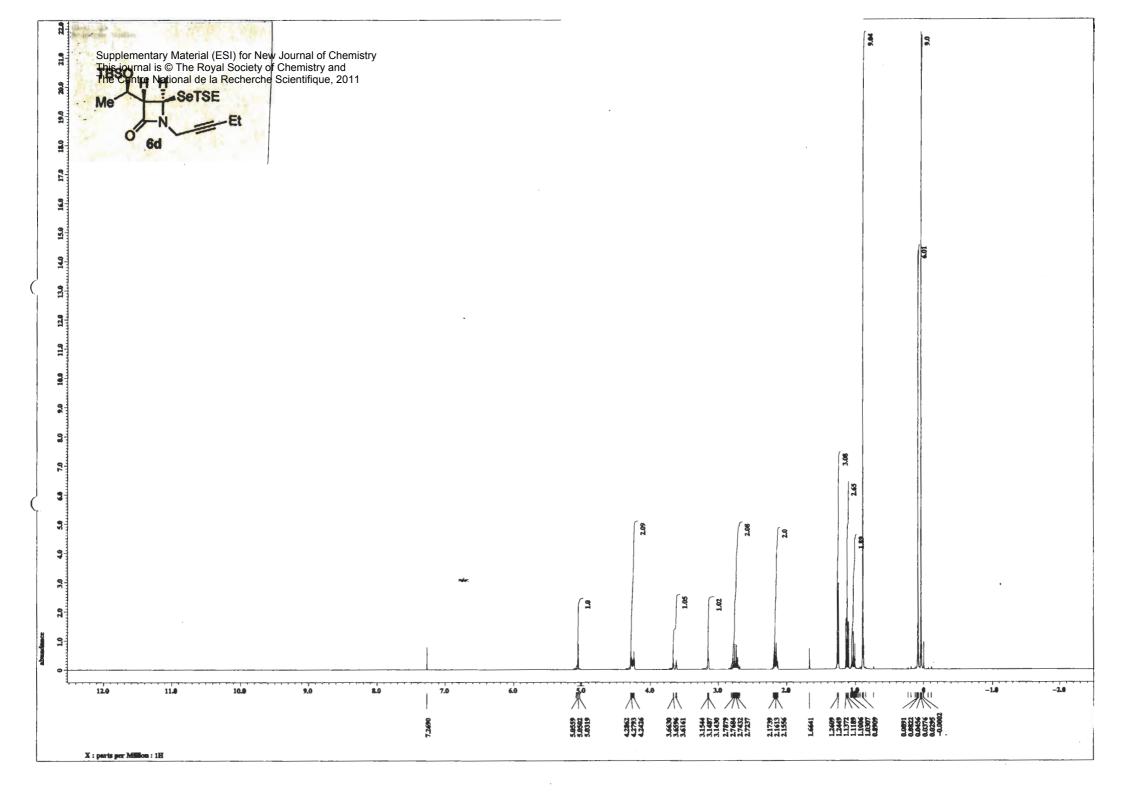
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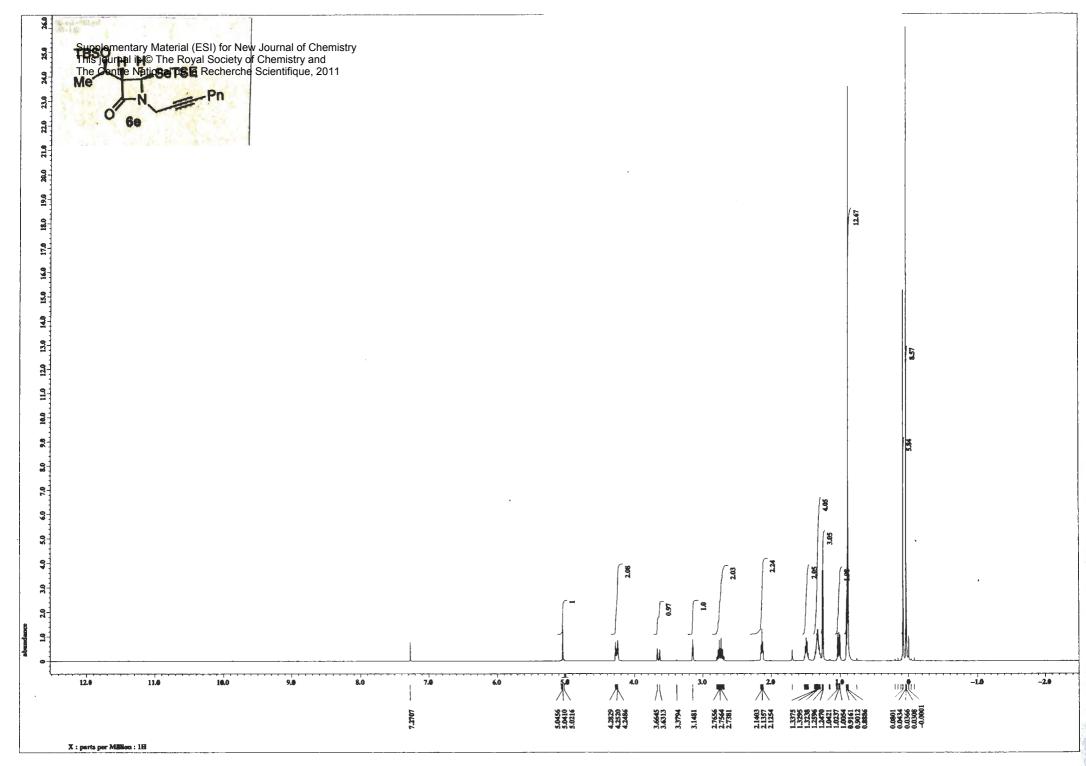






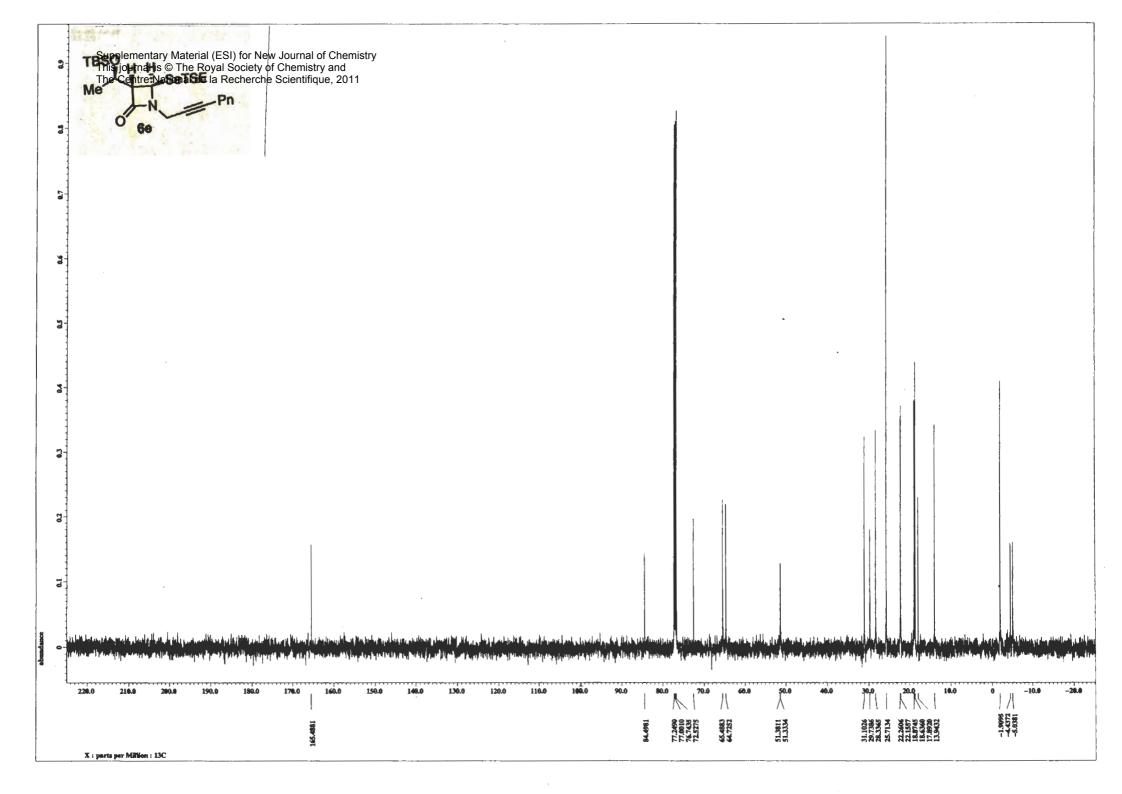


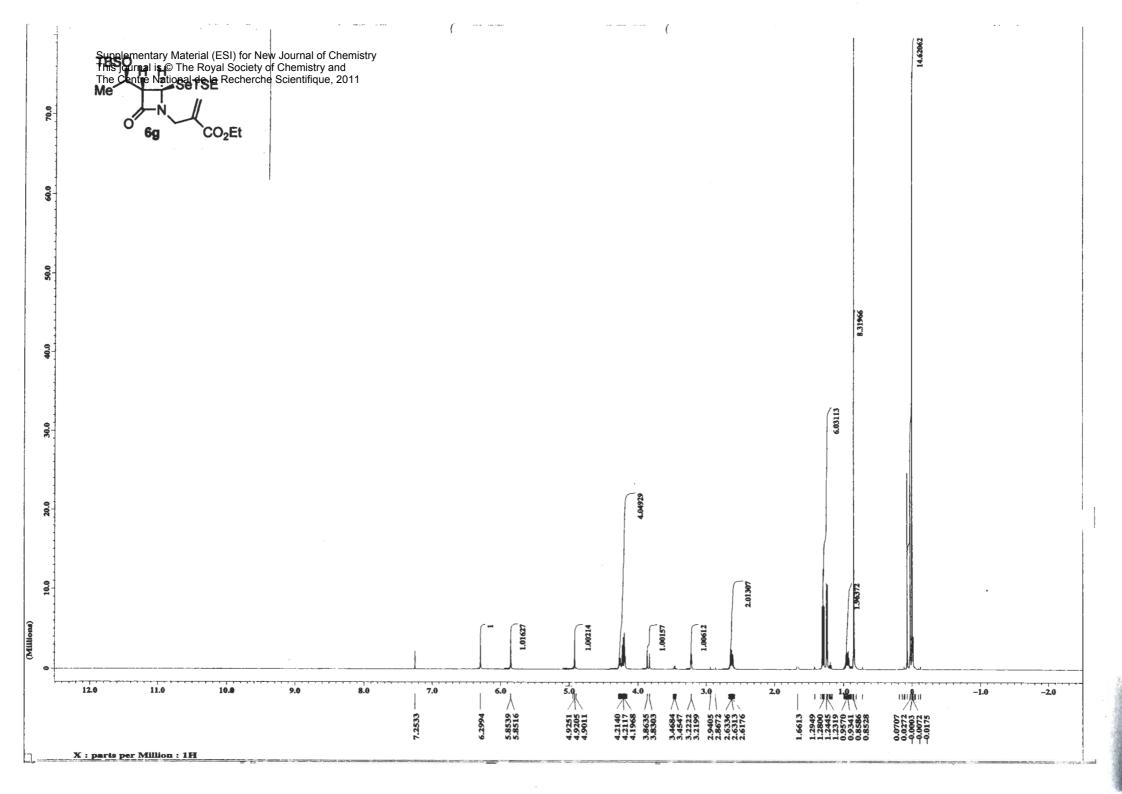
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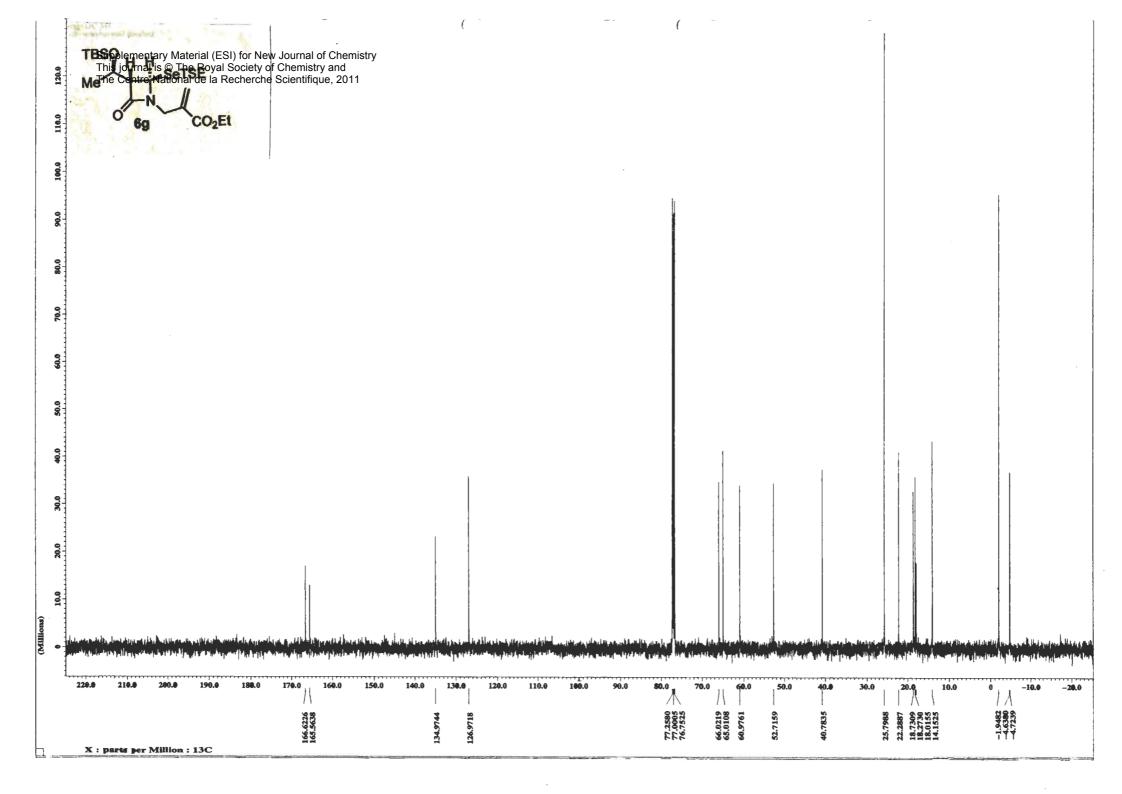


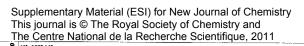
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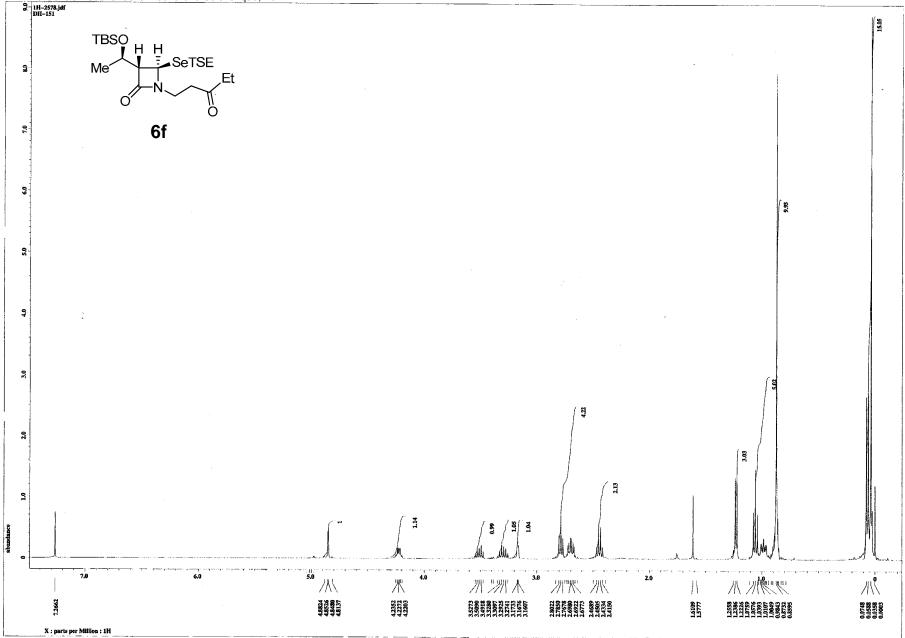
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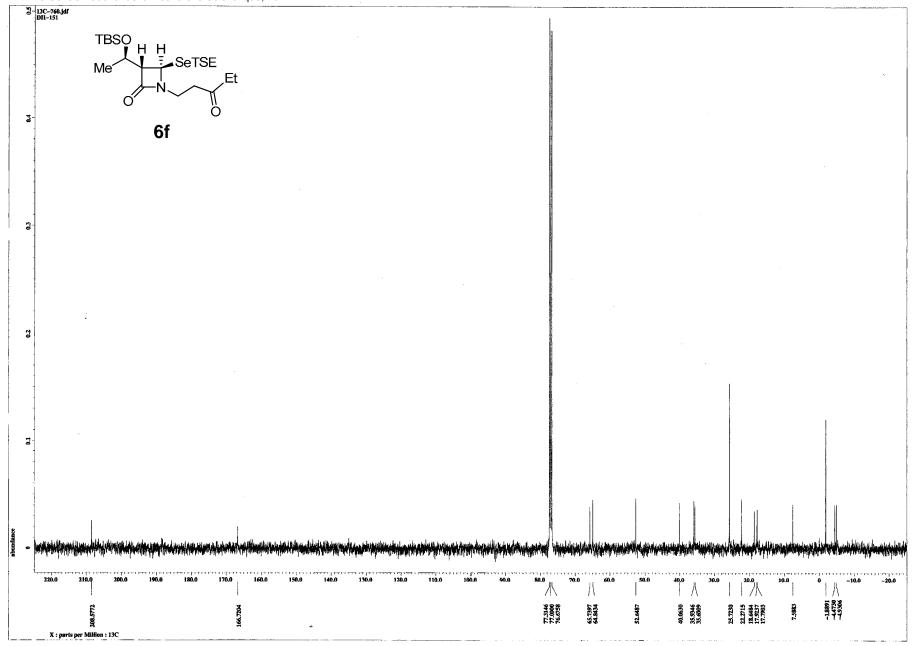


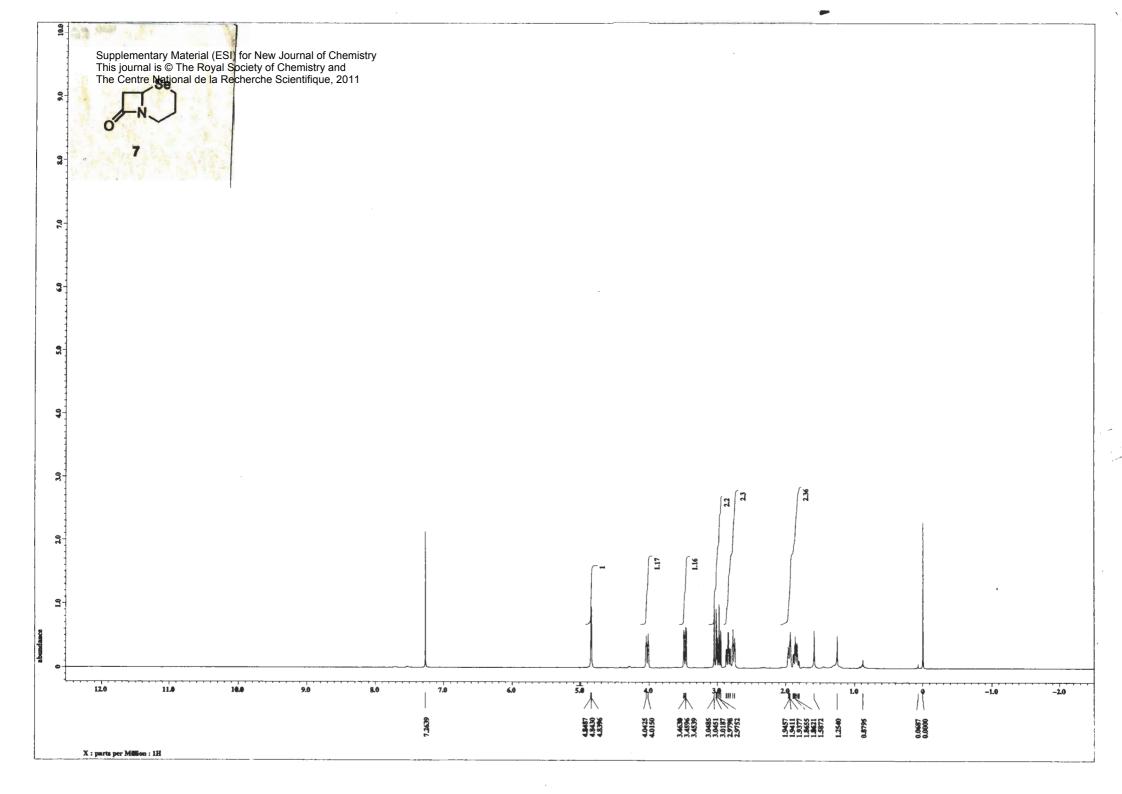




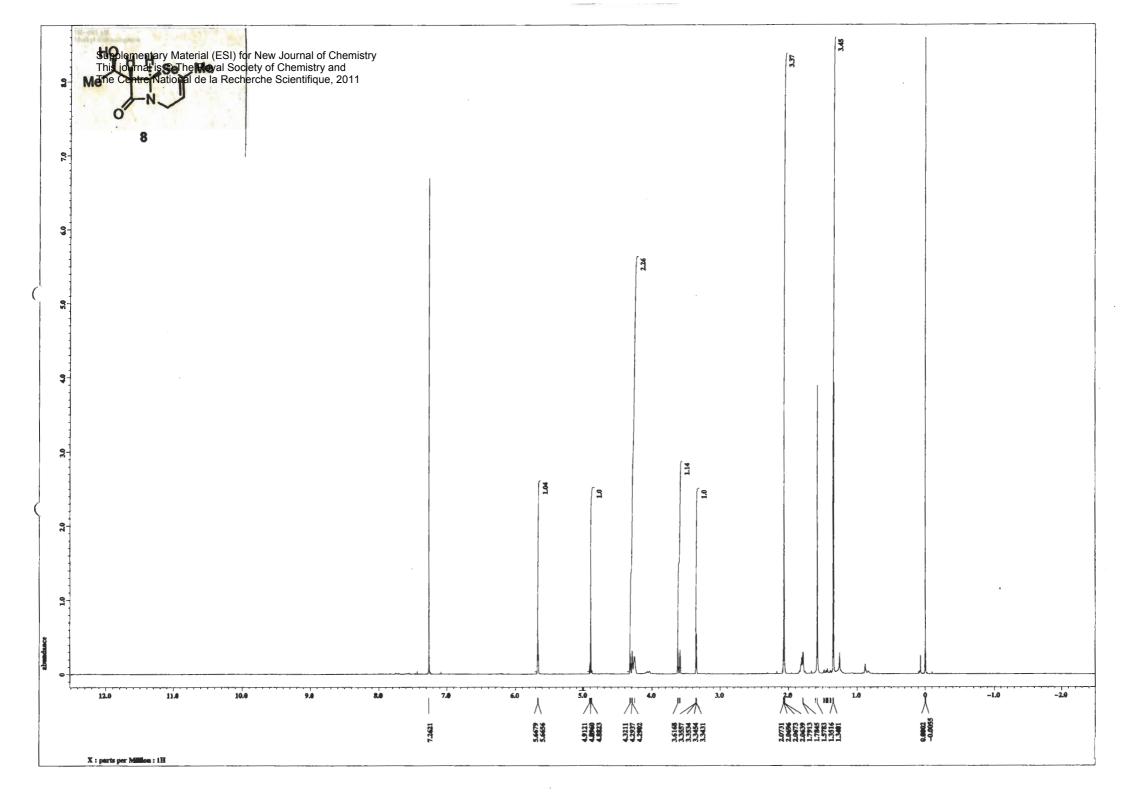


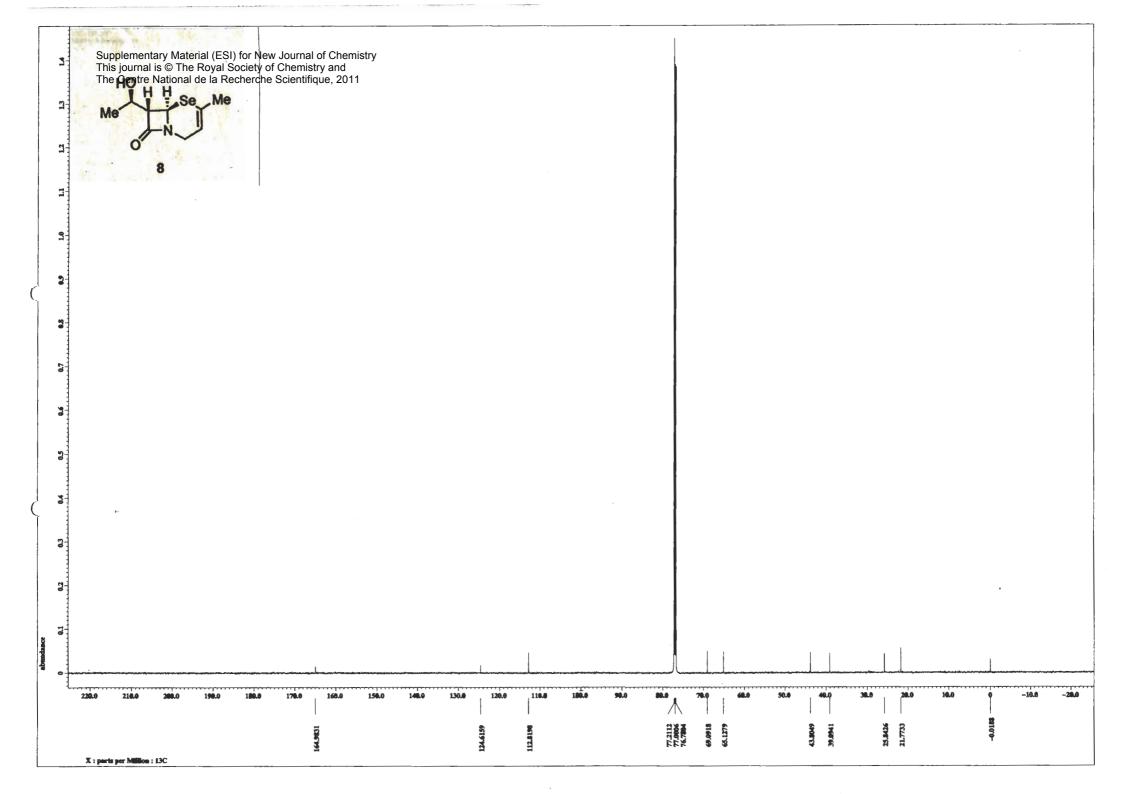
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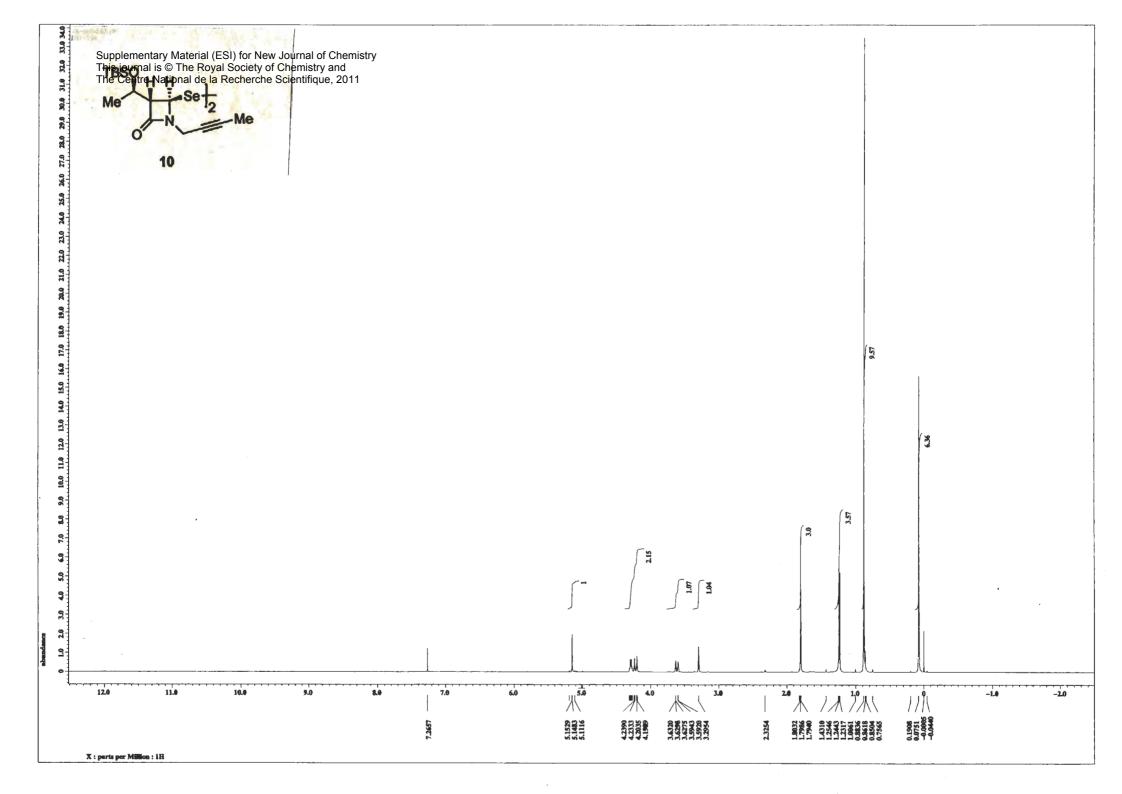




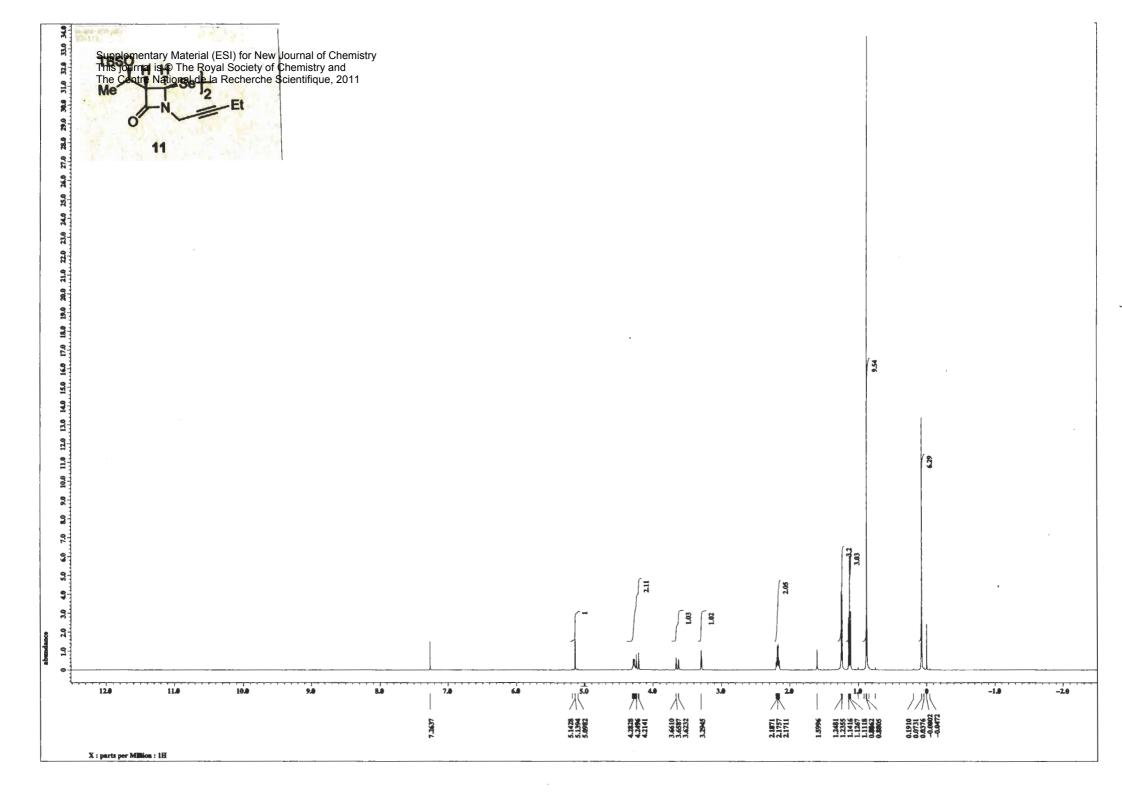
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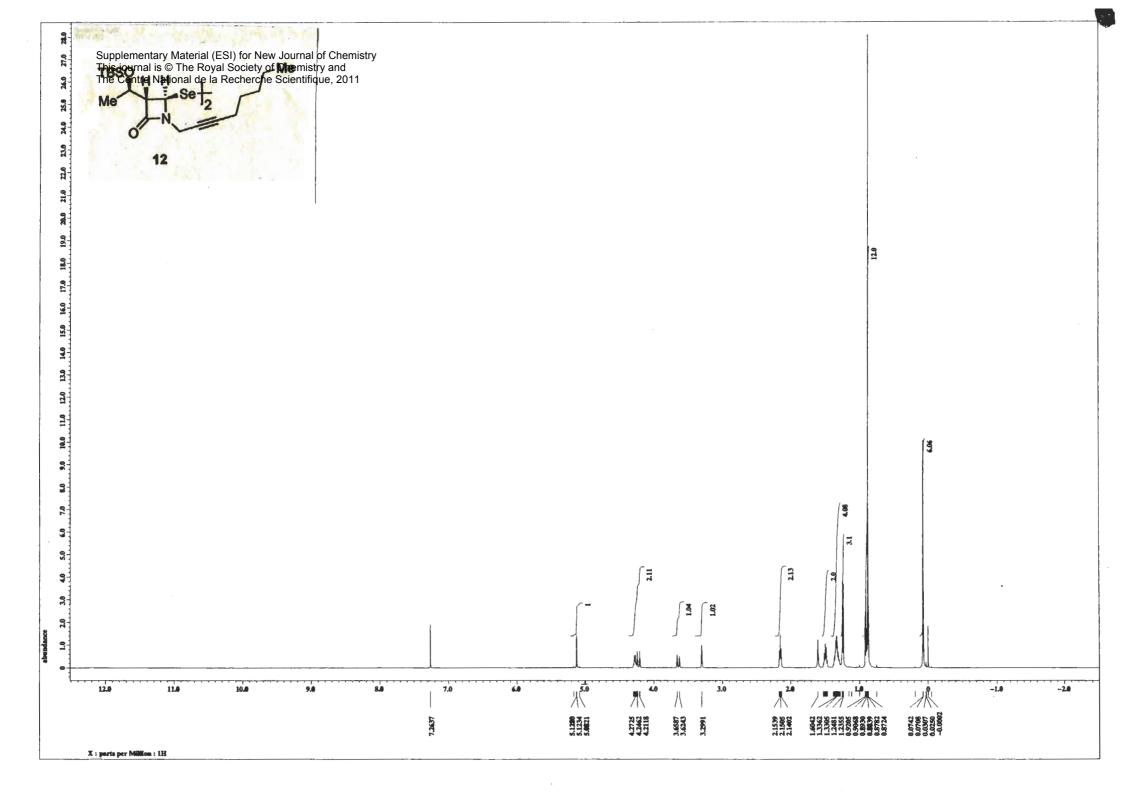


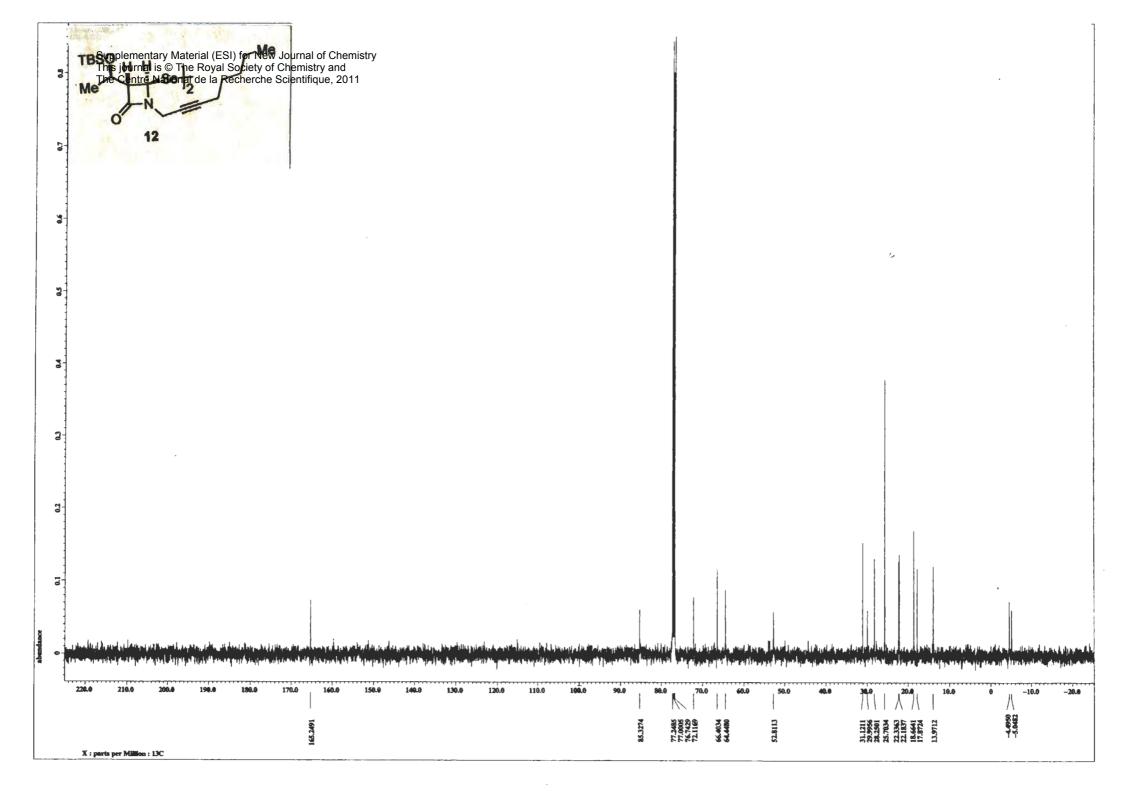


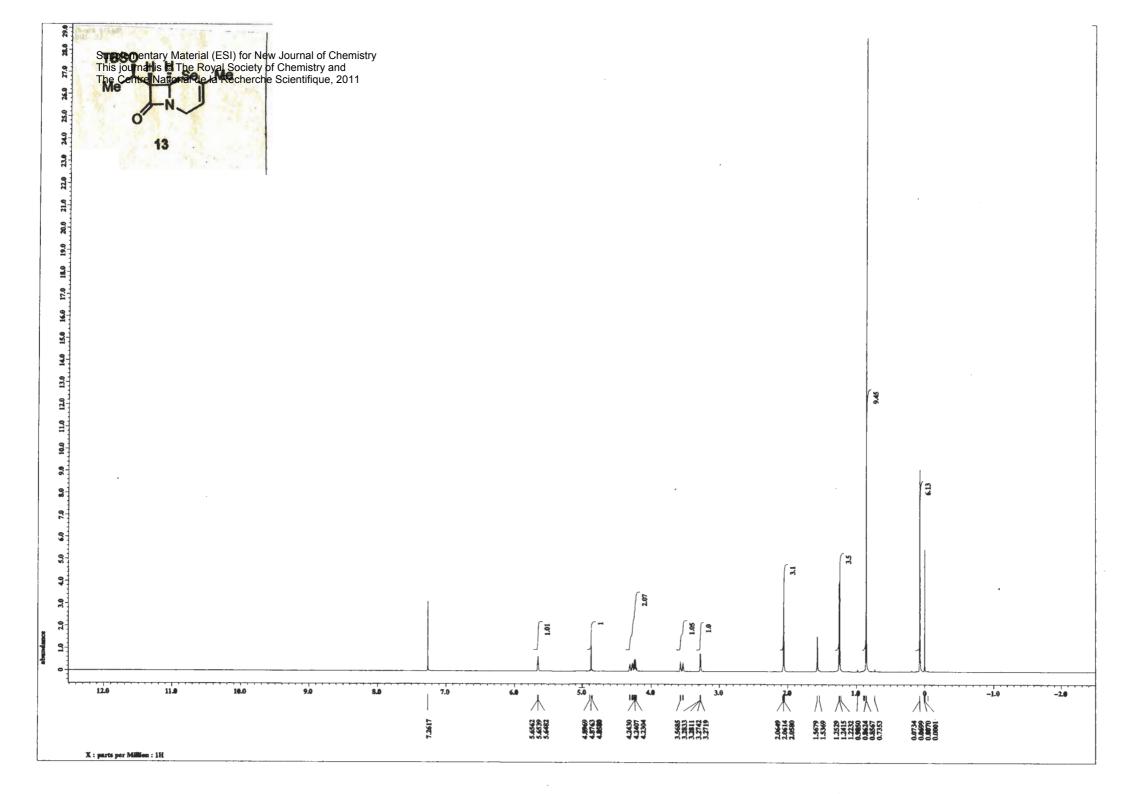
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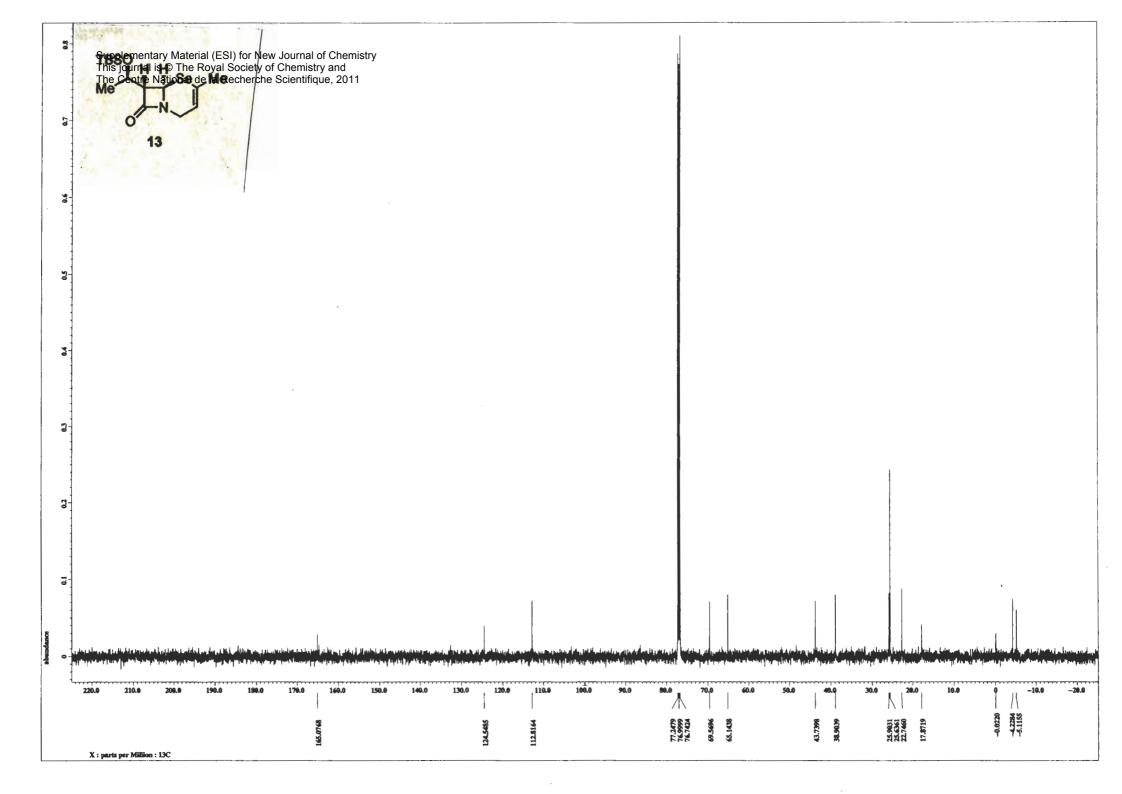


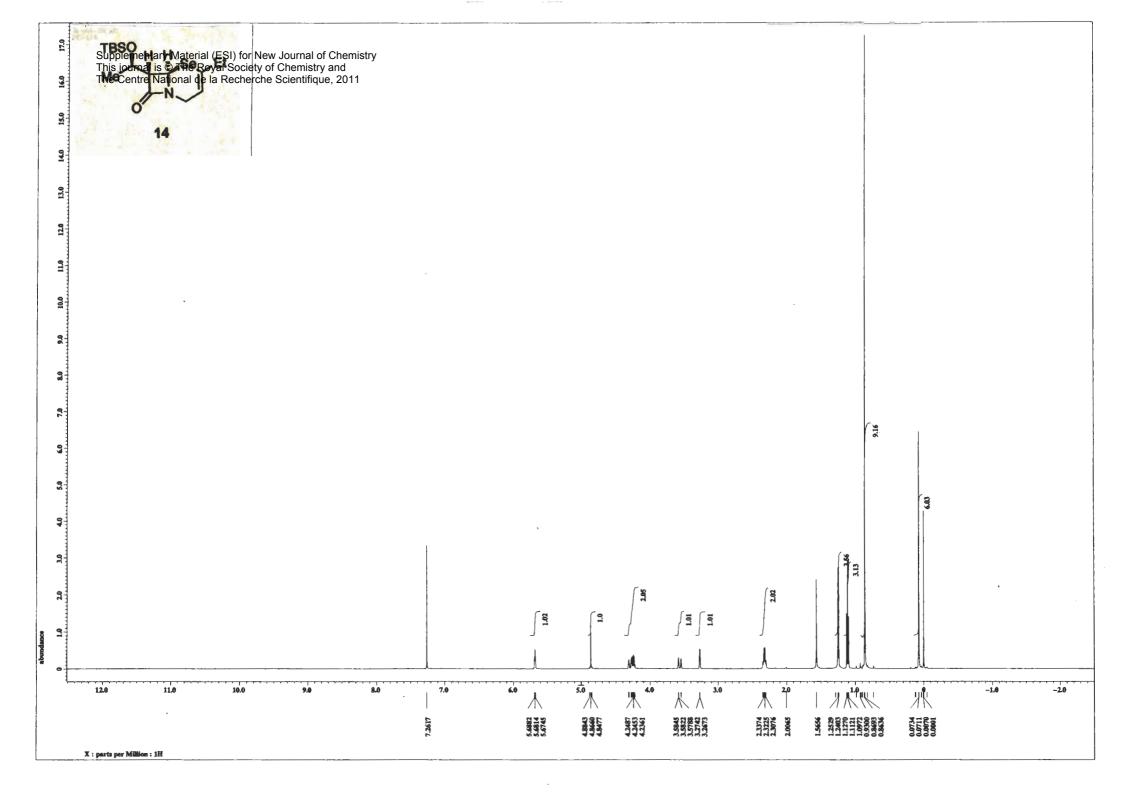
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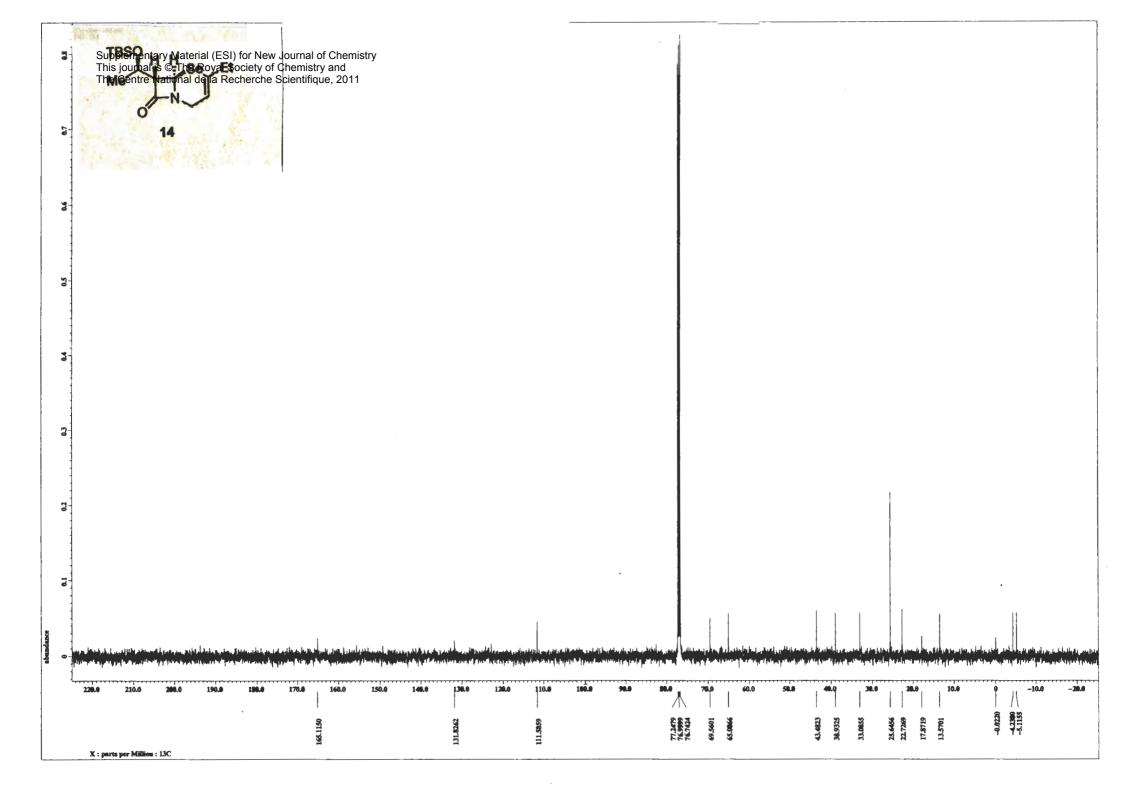


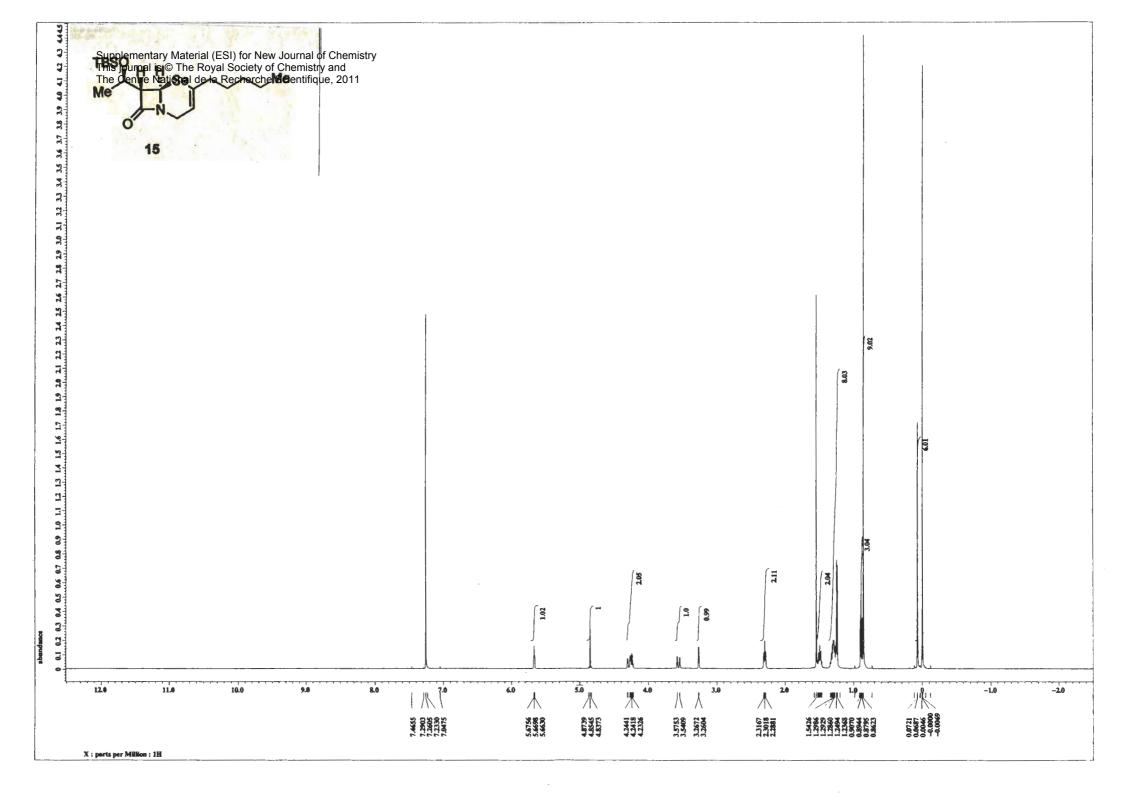


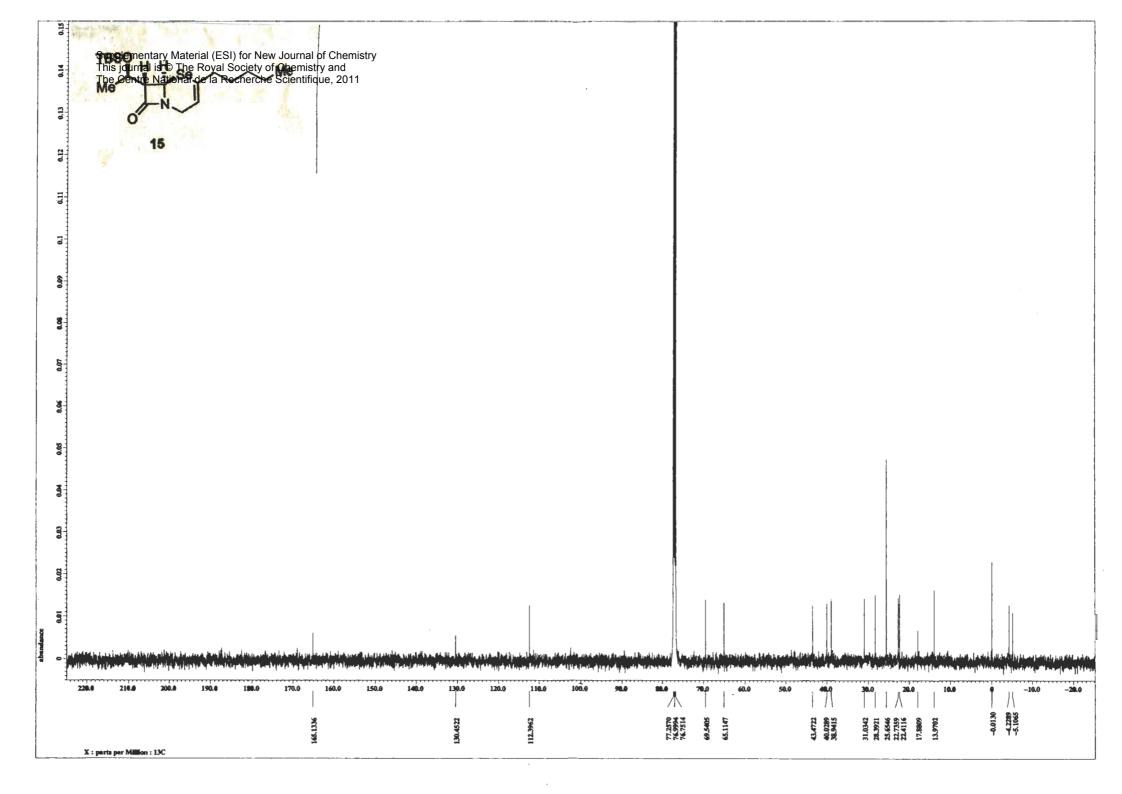


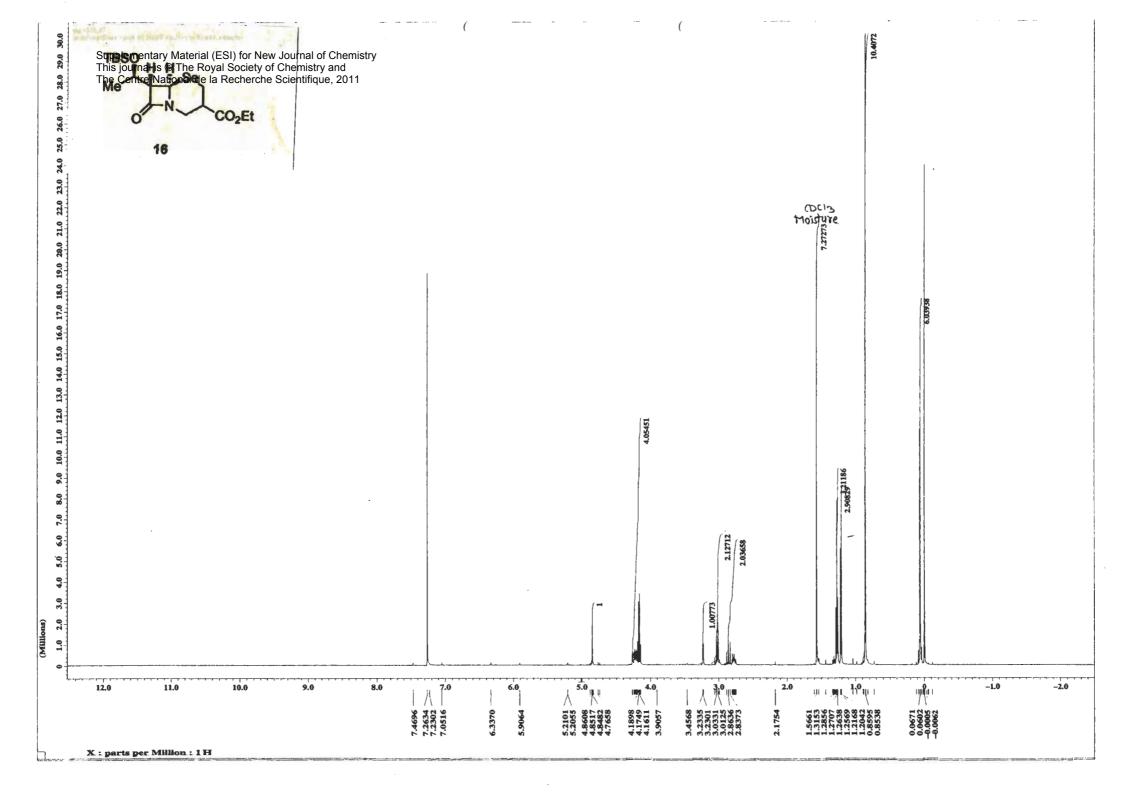


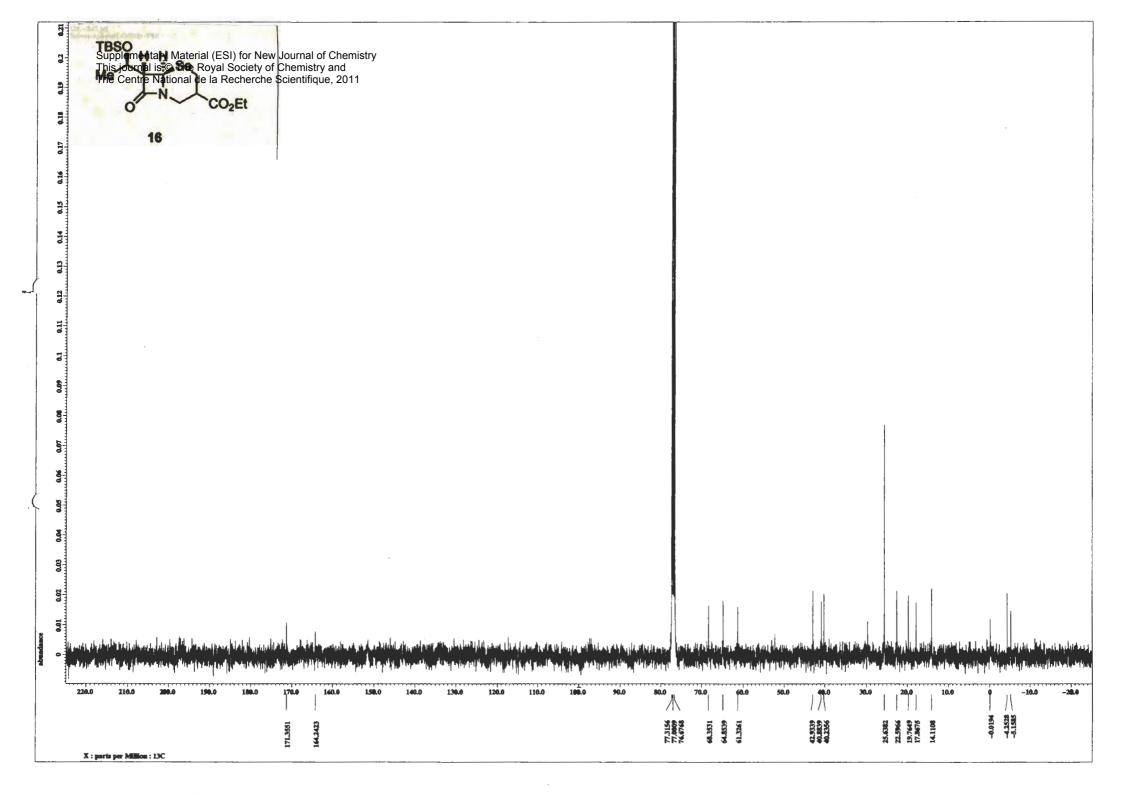


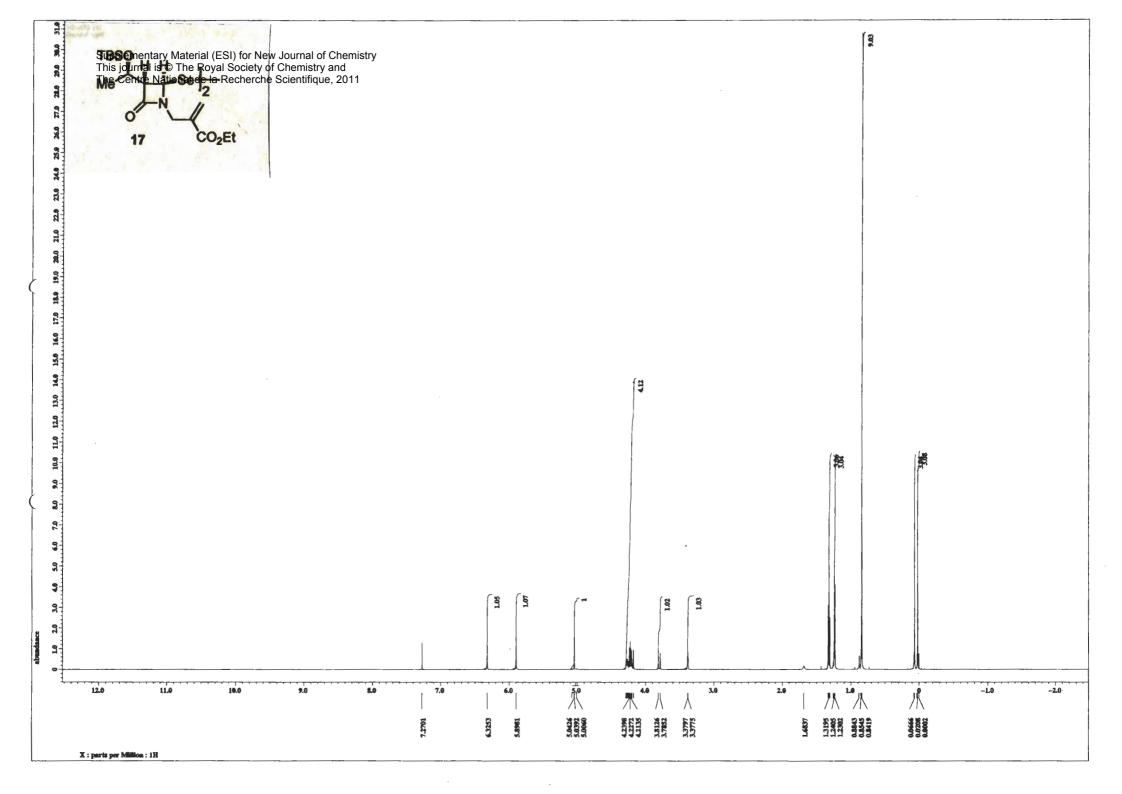


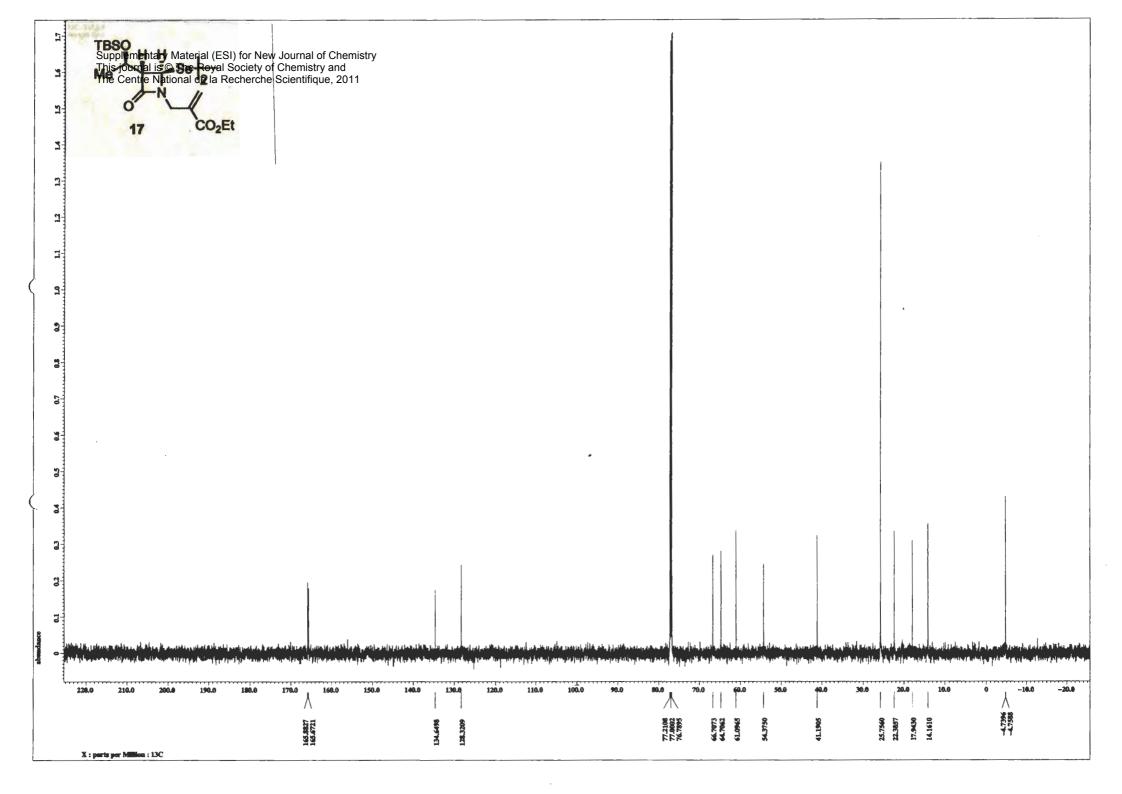


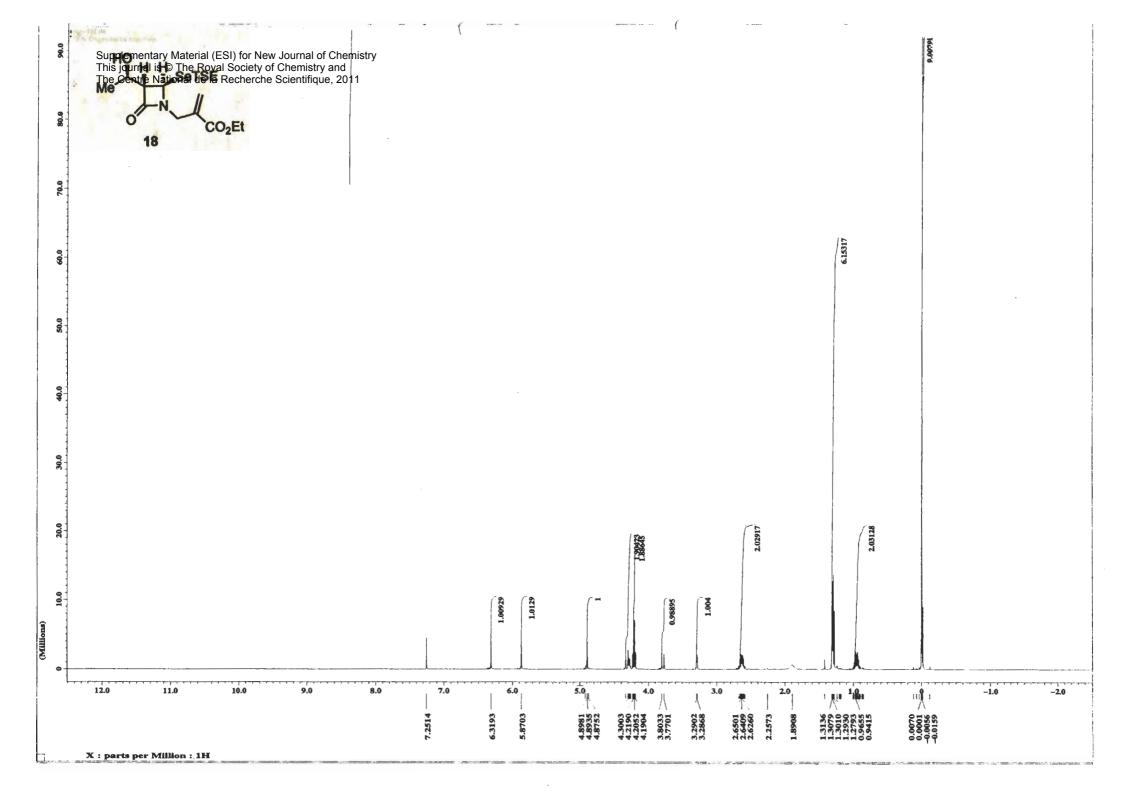




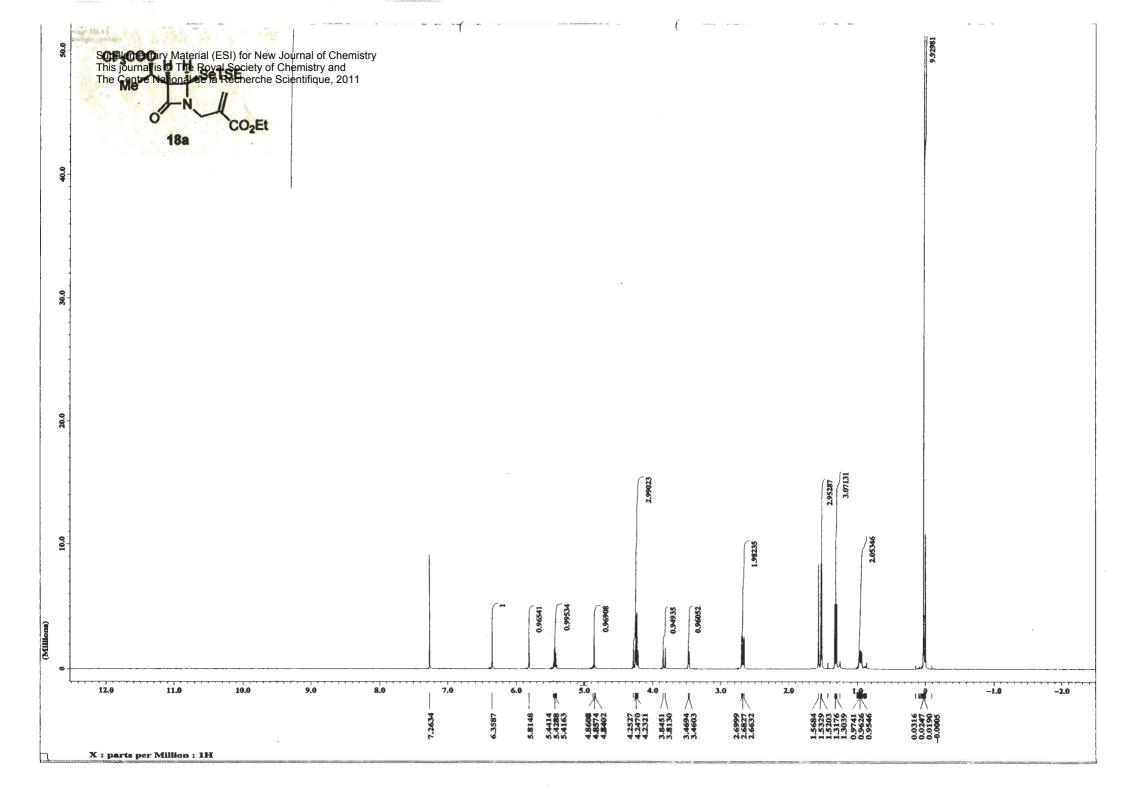


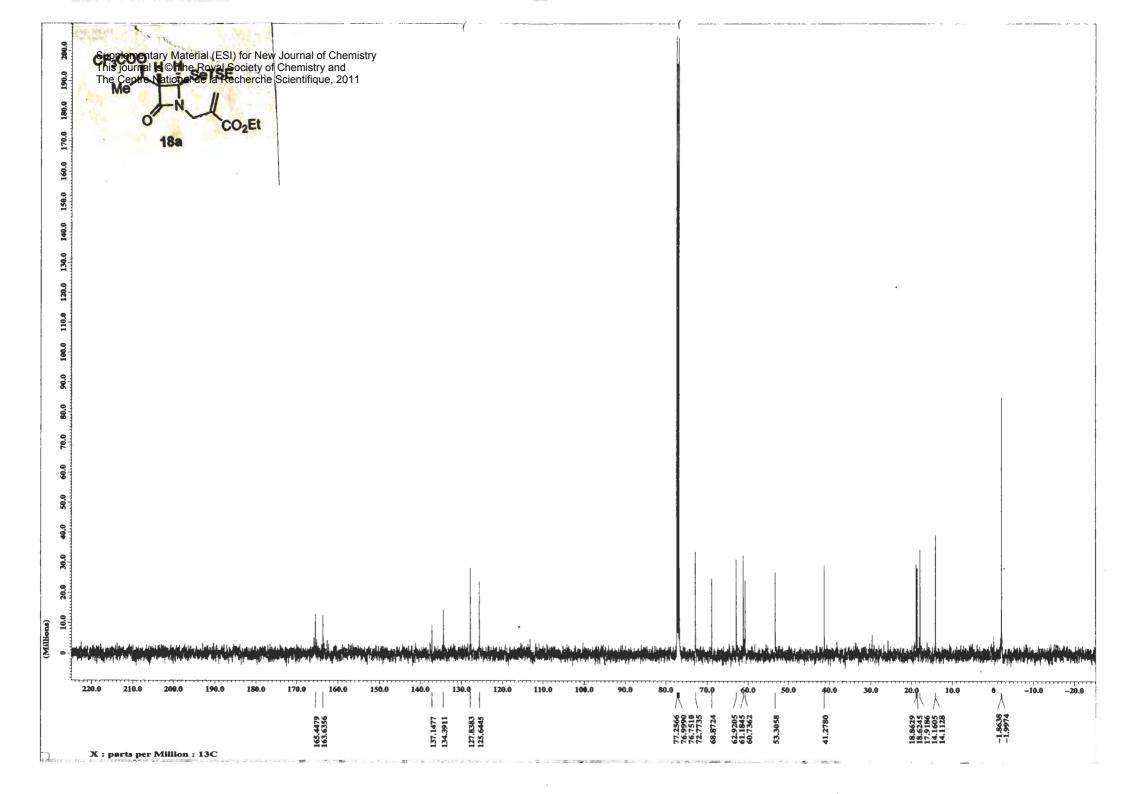


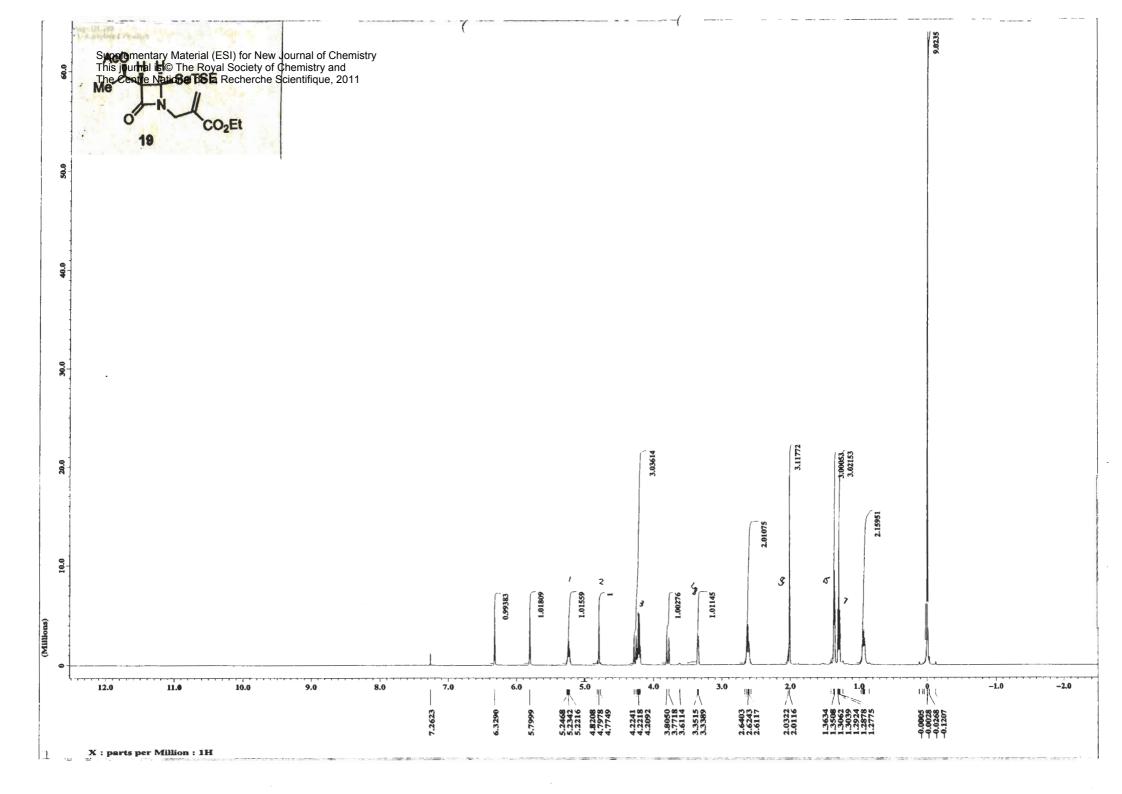


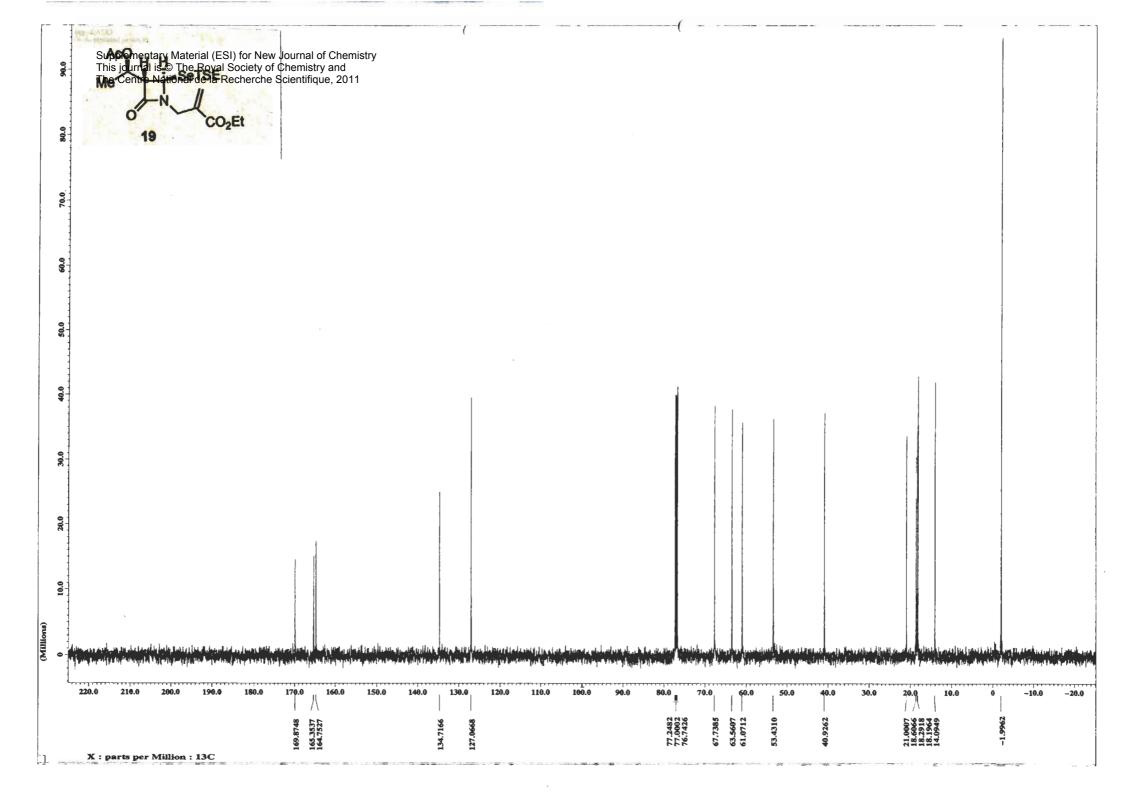


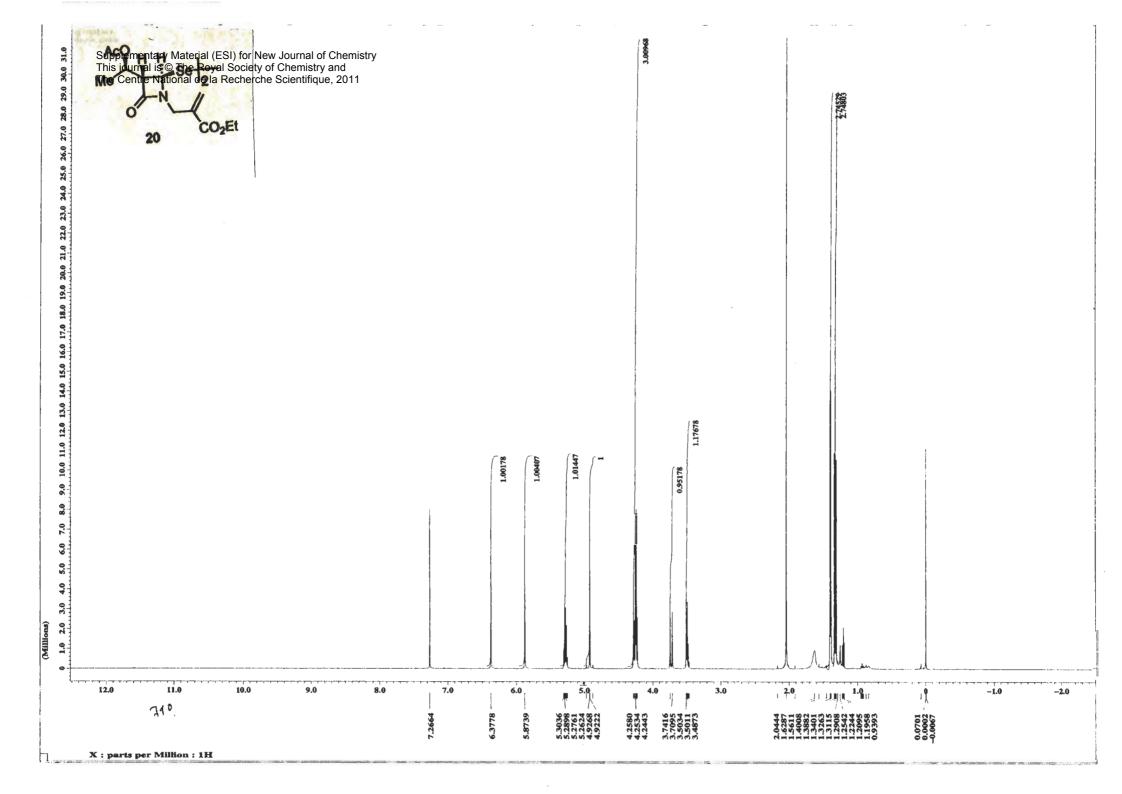
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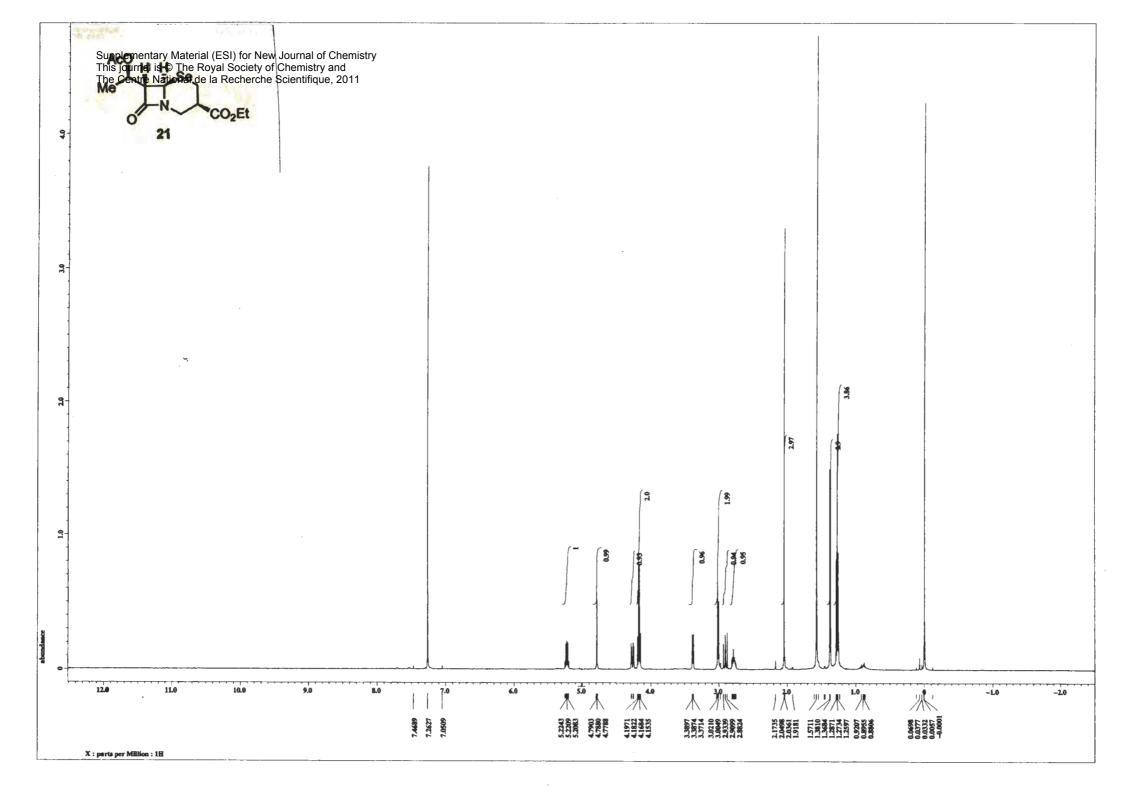


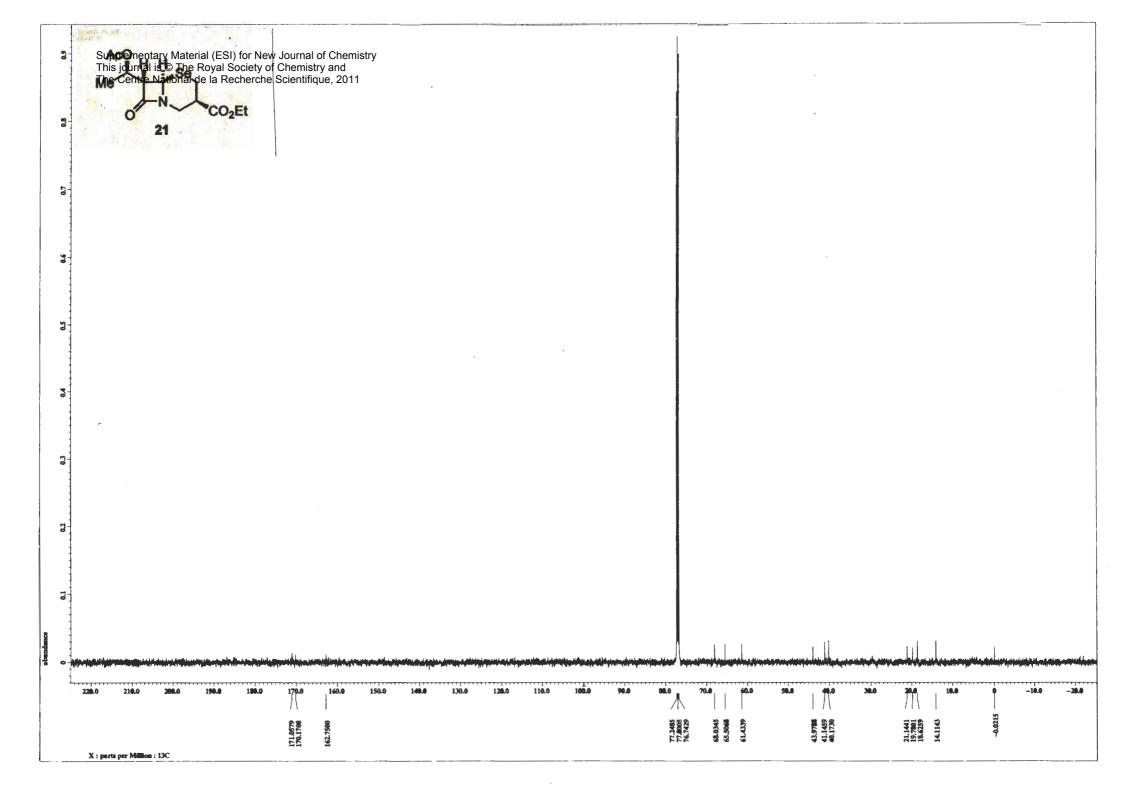


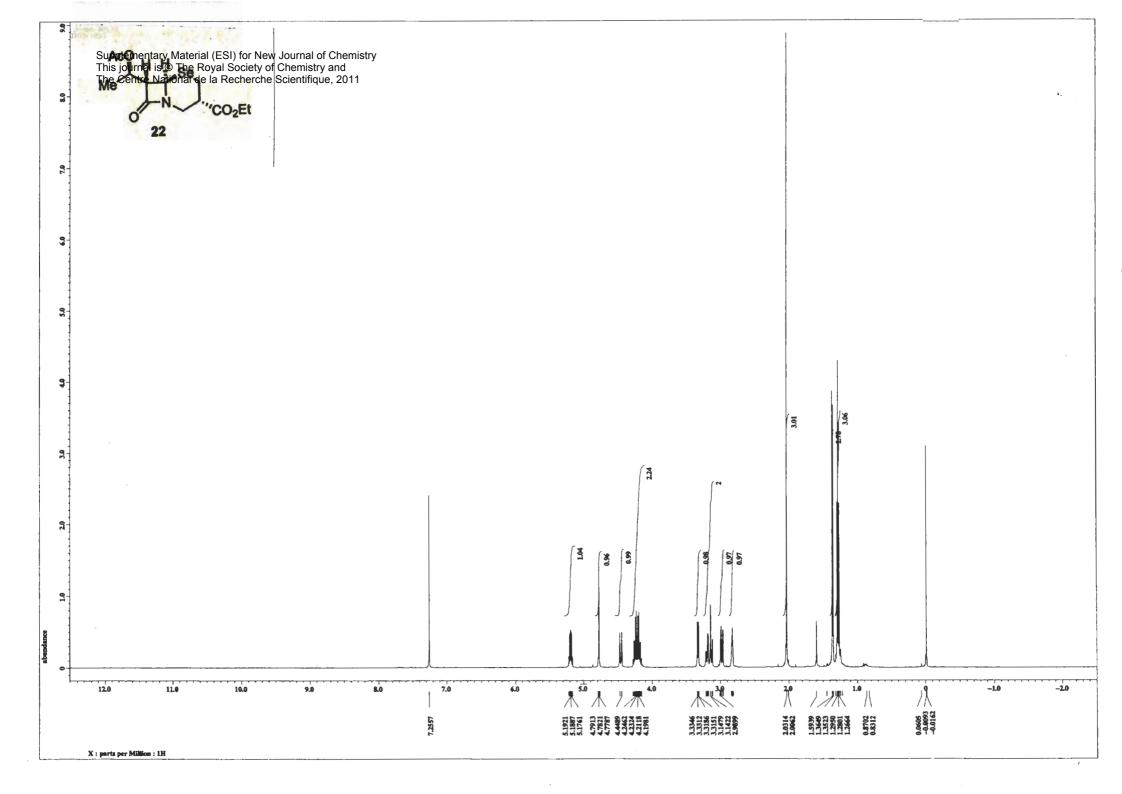


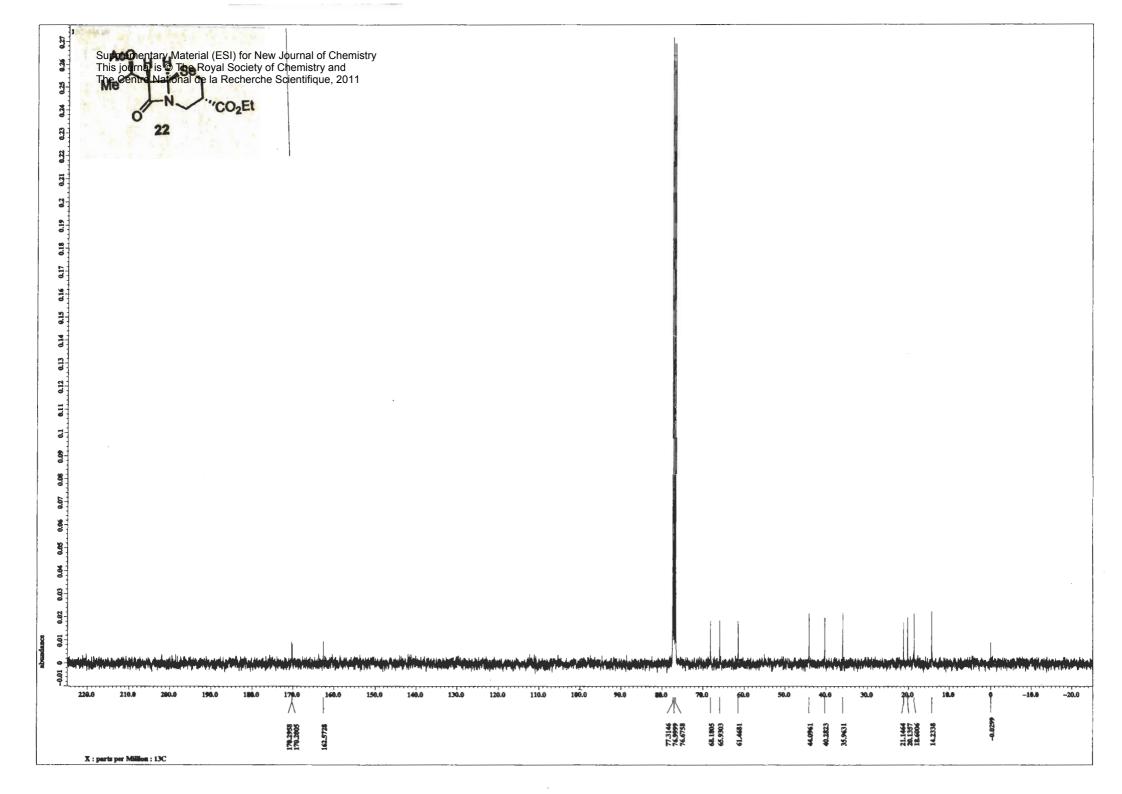


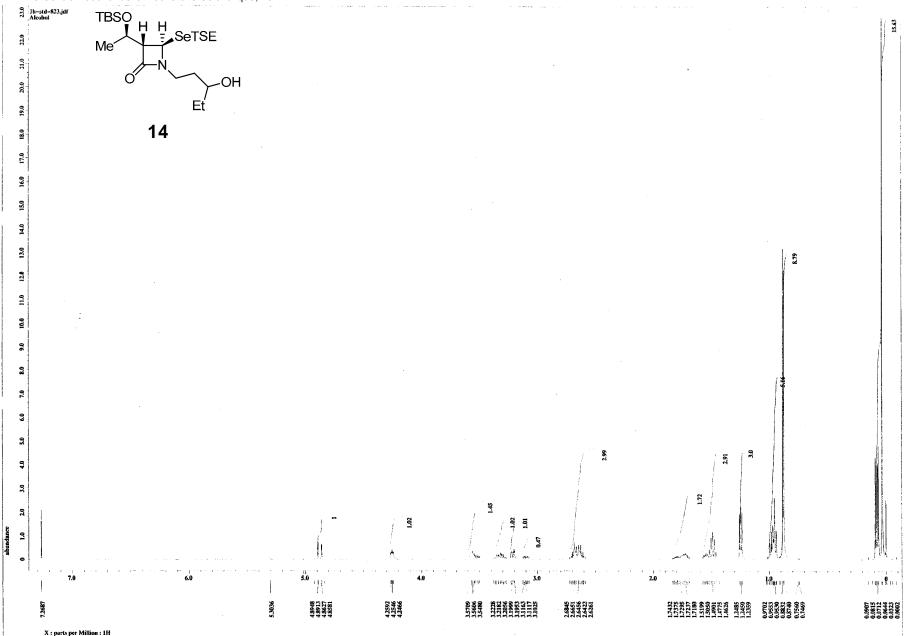




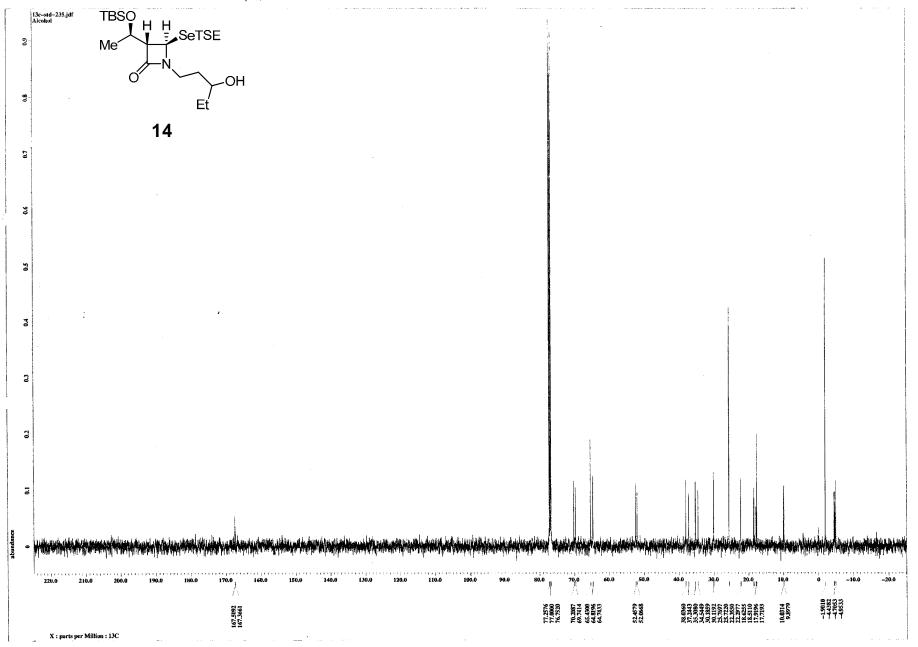


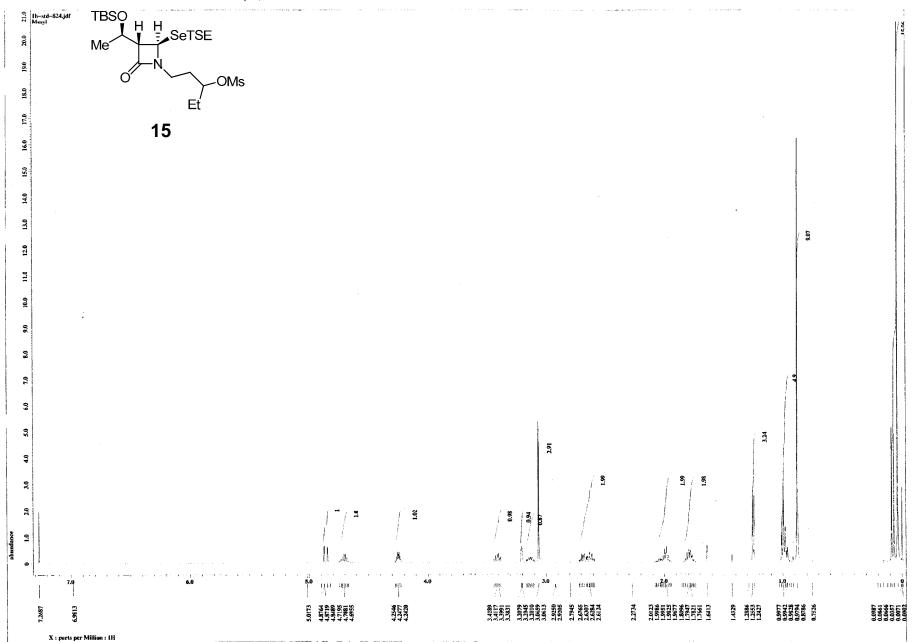


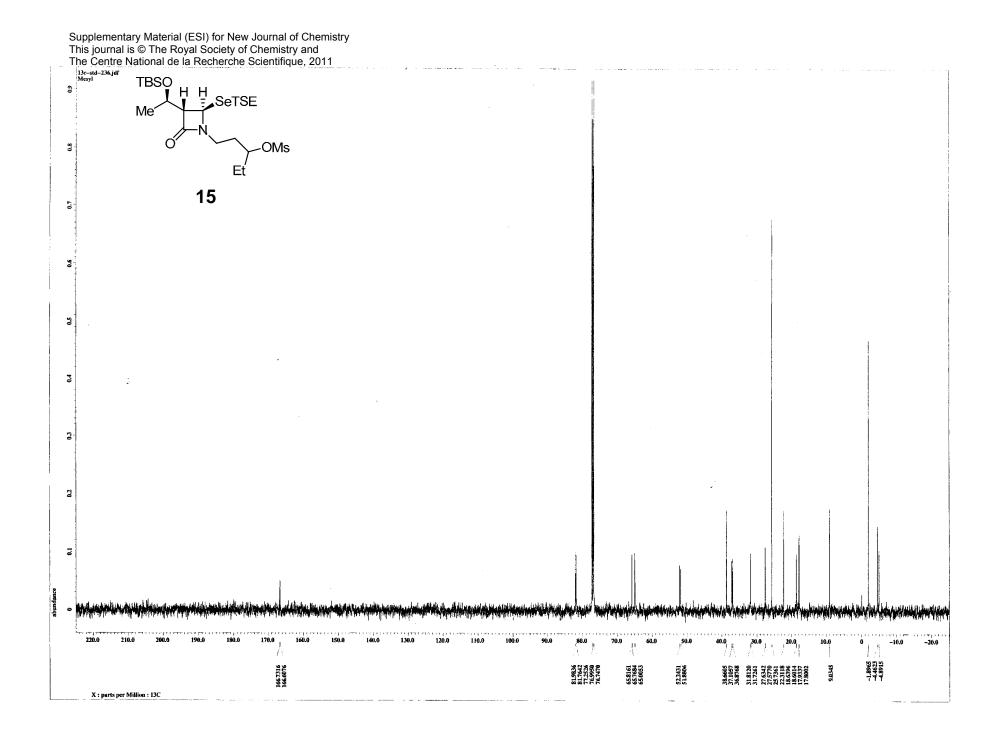


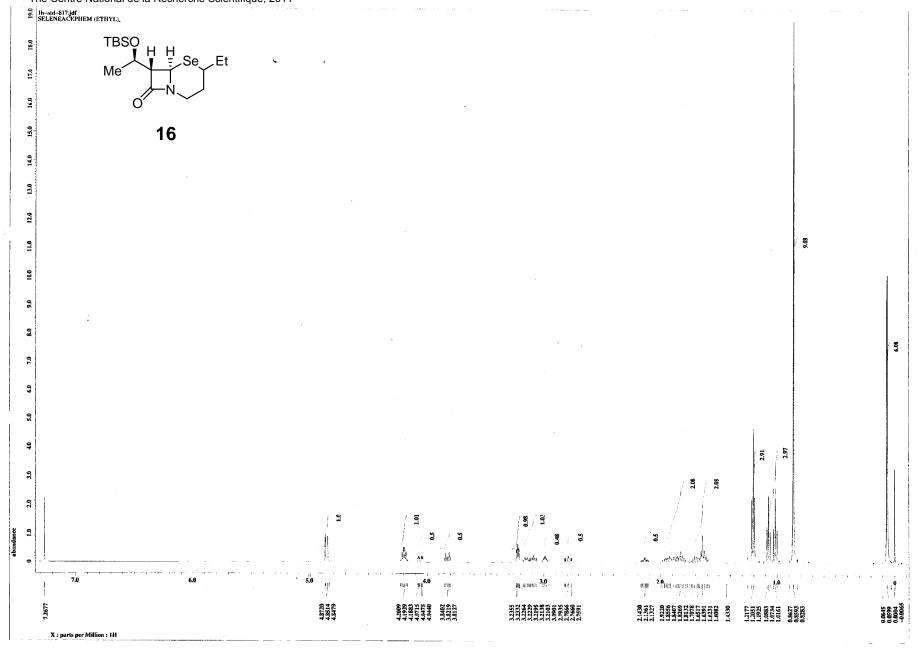


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