Supplementary Material (ESI) for New Journal of Chemistry

Supporting Information

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

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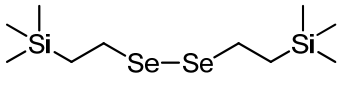
General

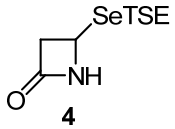
All reactions were performed in round-bottom flask fitted with balloon filled with argon, otherwise specified. Transfer of air- and moisture-sensitive liquids were performed via cannula under a positive pressure of argon. TLC analysis was performed on Merck TLC (silica gel $60F_{254}$ on glass plate). 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 ^{1}H NMR spectra were measured on JEOL:JNM ECX-400 P, JEOL:JNM ECA-500, JEOL:JNM ECA-600 spectrometers in $CDCl_3$. 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 ^{13}C NMR spectra or ^{77}Se NMR spectra were obtained from the JEOL:JNM ECX-400 P, JEOL:JNM ECA-500 or JEOL:JNM ECA-600 spectrometers in $CDCl_3$. The ^{77}Se chemical shifts were expressed in δ values deshielded with respect to neat Me_2Se. $^{1}J(^{77}Se\text{-}^{1}H)$ values are observed as ^{77}Se satellites of the ^{1}H NMR spectra. HRMS was measured on a JEOL JMS-700.



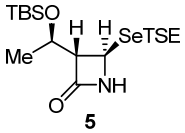
1

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 (SiO_2: 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 ($CDCl_3$): δ 0.00 (s, 9H), 0.96-1.03 (m, 2H), 2.87-2.94 (m, 2H). ^{13}C NMR ($CDCl_3$): δ -1.82 ($^1J_{13C\text{-}29Si}$ = 50.3 Hz), 19.5 ($^1J_{13C\text{-}29Si}$ = 46.8 Hz), 25.0 ($^1J_{13C\text{-}77Se}$ = 69.6 Hz). ^{77}Se NMR ($CDCl_3$): δ 354.6. MS (EI): *m/z* = 262 [M^+].



4

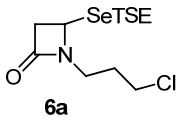
Preparation of 4-[2-(Trimethylsilyl)ethylseleno]-2-azetidinone **(4)**: Sodium borohydride was added, in portions, to a stirred suspension of bis[2-(Trimethylsilyl)ethyl]-diselenide **1** (0.952 g, 2.64 mmol) in absolute ethanol (15 mL), under argon until the characteristic yellow color of the diselenide 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 (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 23.5 Hz, 1H), 6.60 (drs, 1H). ^{13}C NMR ($CDCl_3$): δ -1.94, 18.4, 18.7, 44.0, 47.1, 166.5. ^{77}Se NMR ($CDCl_3$): δ 338.6. MS (EI): *m/z* = 251 [M^+]. HRMS (EI): *m/z* = 251.0245 calcd. for $C_8H_{17}NOSeSi$, found 251.0228.



5

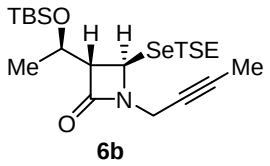
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylselen o]-2-azetidinone **(5):** Sodium borohydride was added, in portions, to a stirred

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 was cooled to 0 °C 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 (SiO_2: 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, $CHCl_3$). IR (KBr): 3152, 3097, 1761, 1712 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 27.3 Hz, 1H), 6.30 (brs, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 325.6. MS (EI): *m/z* = 352 [M^+-57]. HRMS: *m/z* = 409.1372, calcd. for $C_{16}H_{35}NO_2SeSi_2$, found 409.1397 [M^+]. Anal. Calcd for $C_{16}H_{35}NO_2SeSi_2$: C, 47.03; H, 8.63; N, 3.43. Found: C, 46.60; H, 8.46; N, 3.40.



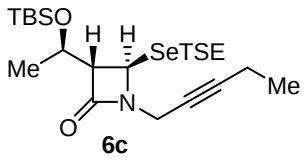
6a

Preparation of 1-(3-chloropropyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (**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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 23.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ -1.92, 17.9, 18.7, 30.5, 38.7, 42.2, 45.8, 50.1, 165.7. ^{77}Se NMR ($CDCl_3$): δ 275.2. MS (EI): *m/z* = 327 [M^+]. HRMS (EI): *m/z* = 327.0324 calcd. for $C_{11}H_{22}ClNOSeSi$, found 327.0310.



6b

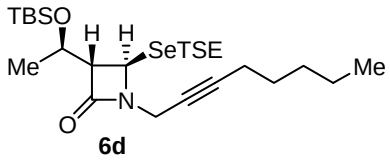
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-butynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (**6b**): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at 0°C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl) 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-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 (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 24.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 269.4. MS (EI): *m/z* = 404 [M^+-^{t}Bu]. HRMS (EI): *m/z* = 404.0980 calcd. for $C_{16}H_{30}NO_2SeSi_2$, found 3404.0975.



6c

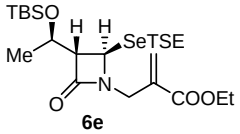
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (**6c**): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at 0°C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl) 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-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 (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 22.0

Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 268.9. MS (EI): *m/z* = 418 [M^+-^{t}Bu]. HRMS (EI): *m/z* = 418.1137 calcd. for $C_{17}H_{32}NO_2SeSi_2$, found 418.1100.



6d

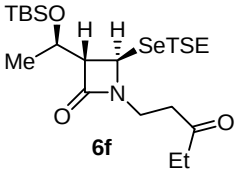
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (**6d**): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at 0°C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (SiO_2: 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}. ^{1}H NMR ($CDCl_3$): 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), 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, ^2J(^{77}Se-^{1}H) = 20.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 268.2. MS (EI): *m/z* = 460 [M^+-^{t}Bu]. HRMS (EI): *m/z* = 460.1606 calcd. for $C_{20}H_{38}NO_2SeSi_2$, found 460.1605.



6e

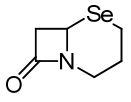
Preparation of Ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl]]acrylate (**6e**): To a suspension of NaH (60% in mineral oil, 59 mg, 1.46 mmol) in 10 mL of THF at 0°C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (Na_2SO_4) and concentrated. The residue

was purified by column chromatography (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 40.6 Hz, 1H), 5.85 (d, *J* = 1.1 Hz, 1H), 6.30 (d, *J* = 1.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 264.6. MS (EI): *m/z* = 464 [M^+-^{t}Bu]. HRMS (EI): *m/z* = 464.1192 calcd. for $C_{18}H_{34}NO_4SeSi_2$, found 464.1180.



6f

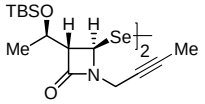
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-1-(3-oxopentyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6f): To a suspension of NaH (60% in mineral oil, 73 mg, 1.84 mmol) in 5 mL of THF at 0 °C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: 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 ($CDCl_3$): 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, 1H), 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, $^2J(^{77}Se\text{-}^1H)$ = 27.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 265.5. MS (EI): *m/z* = 436 [M^+ - ^{t}Bu]. HRMS: *m/z* = 436.1242, calcd. for $C_{17}H_{34}NO_3SeSi_2$, found 436.1258.



Selenacepham 7

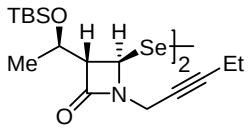
Preparation of 1-aza-5-selenabicyclo[4.2.0]oct-8-one (**7**): To a stirred solution of 1-(3-chloropropyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **6a** (15 mg, 0.05 mmol) in 1 mL THF was added tetrabutylammonium fluoride (92 µL of 1.0 M solution in THF) at r.t. After stirring at this temperature for 1 h, AcOH (6 µL, 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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash

chromatography (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 18.9 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 18.3, 24.0, 40.1, 40.4, 47.1, 163.8. ^{77}Se NMR ($CDCl_3$): δ 283.1. MS (EI): *m/z* = 191 [M^+]. HRMS (EI): *m/z* = 190.9849 calcd. for C_6H_9NOSe, found 190.9823.



8a

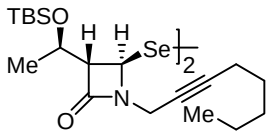
Preparation of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-butynyl)-2-azetidinone]-4-diselenide (**8a**): Tetrabutylammonium fluoride (239 μL of 1.0 M solution in THF) was added dropwise to a stirred solution of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-1-(2-butynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 39.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ -5.10, -4.51, 3.49, 17.9, 22.3, 25.7, 29.9, 52.7, 64.4, 66.6, 71.6, 80.6, 165.2. ^{77}Se NMR ($CDCl_3$): δ 323.4. MS (EI): *m/z* = 664 [M^+-^{t}Bu]. HRMS: *m/z* = 664.1170, calcd. for $C_{26}H_{44}N_2O_4Se_2Si_2$, found 664.1175.



8b

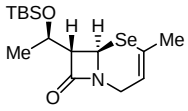
Preparation of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-2-azetidinone]-4-diselenide (**8b**): Tetrabutylammonium fluoride (232 μL of 1.0 M solution in THF) was added dropwise to a stirred solution of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 42.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 324.5. MS (EI): *m/z* = 691 [M^+-^{t}Bu]. HRMS: *m/z* = 662.1483, calcd. for $C_{28}H_{48}N_2O_4Se_2Si_2$, found 662.1474.



8c

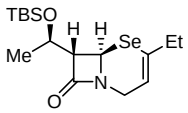
Preparation of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-2-azetidinone]-4-diselenide (**8c**): Tetrabutylammonium fluoride (212 µL of 1.0 M solution in THF) was added dropwise to a stirred solution of (3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: hexane / diethyl ether = 12/1) to afford the title compound **8c** as an oil (37 mg, 46%). IR ($CHCl_3$): 2929, 2230, 1769, 1635, 1470, 1382, 1256, 1067, 837 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 41.8 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 323.4. MS (EI): *m/z* = 775 [M^+-^{t}Bu]. HRMS: *m/z* = 776.9422, calcd. for $C_{34}H_{60}N_2O_4Se_2Si_2$, found 774.9417.



Selenacephem 9a

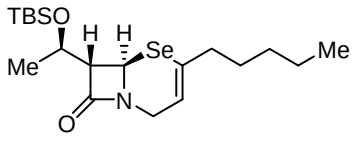
Preparation of (6*R*,7*S*)-7-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-4-methyl-1-aza-5-selenabicyclo[4.2.0]oct-3-en-8 -one (**9a**): Sodium borohydride (3 mg, 0.03 mmol) was added to a stirred suspension of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-butynyl)-2-azetidinone]-4-diselenide **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 (SiO_2: hexane / diethyl ether = 15/1) to afford the selenacephem **9a** as an oil

(16 mg, 65%). IR ($CHCl_3$): 2928, 1765, 1649, 1597, 1375, 1256, 835 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 19.4 Hz, 1H), 5.63-5.67 (m, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 313.3. MS (EI): *m/z* = 304 [M^+-^{t}Bu]. HRMS: *m/z* = 304.0272, calcd. for $C_{11}H_{18}NO_2SeSi$, found 304.0274.



Selenacephem 9b

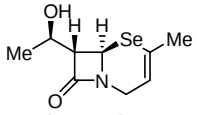
Preparation of (6*R*,7*S*)-7-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-4-ethyl-1-aza-5-selenabicyclo[4.2.0]oct-3-en-8 -one (**9b**): Sodium borohydride (4 mg, 0.07 mmol) was added to a stirred suspension of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-pentynyl)-2-azetidinone]-4-diselenide **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 (SiO_2: hexane / diethyl ether = 15/1) to afford the title selenacephem **9b** as an oil (13.7 mg, 55%). IR ($CHCl_3$): 2928, 1766, 1636, 1597, 1375, 1256, 835 cm^{-1}. ^1H NMR ($CDCl_3$): δ 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, $^2J(^{77}Se\text{-}^1H)$ = 18.3 Hz, 1H), 5.68 (t, *J* = 3.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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^+-^{t}Bu]. HRMS: *m/z* = 318.0429, calcd. for $C_{12}H_{20}NO_2SeSi$, found 318.0411.



Selenacephem 9c

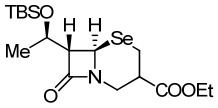
Preparation of (6*R*,7*S*)-7-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-4-pentyl-1-aza-5-selenabicyclo[4.2.0]oct-3-en-8-one (**9c**): Sodium borohydride (3 mg, 0.07 mmol) was added to a stirred suspension of bis[(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-octynyl)-2-azetidinone]-4-diselenide **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 (SiO_2: hexane / diethyl ether = 15/1) to afford the selenacephem **9c** as

an oil (2 mg, 22%). IR ($CHCl_3$): 2928, 1767, 1662, 1638, 1465, 1392, 1254, 835 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 18.3 Hz, 1H), 5.67 (t, *J* = 3.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 235.1. MS (EI): *m/z* = 360 [M^+-^{t}Bu]. HRMS (EI): *m/z* = 360.0898 calcd. for $C_{15}H_{26}NO_2SeSi$, found 360.0894.



Selenacephem I

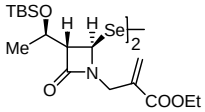
Preparation of (6*R*,7*S*)-7-[(*R*)-1-Hydroxyethyl]-4-methyl-1-aza-5-selenabicyclo[4.2.0] oct-3-en-8-one (**I**): To a stirred solution of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-1-(2-butynyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **6b** (40 mg, 0.09 mmol) in 1 mL THF was added tetrabutylammonium fluoride (434 μL of 1.0 M solution in THF) at rt. After stirring at this temperature for 1 h, AcOH (11 μL, 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 (SiO_2: 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 ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 18.0 Hz, 1H), 5.65-5.69 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 21.8, 25.8, 39.1, 43.8, 65.1, 69.1, 112.8, 124.6, 165.0. ^{77}Se NMR ($CDCl_3$): δ 317.6. MS (EI): *m/z* = 247 [M^+]. HRMS (EI): *m/z* = 247.0112 calcd. for $C_9H_{13}NO_2Se$, found 247.0137.



Selenacepham II

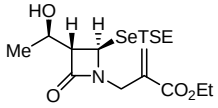
Preparation of Ethyl (5*R*,6*S*)-7-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-5-selenabicyclo[4.2.0]oct-3-(*S*)-carboxylate (**II**): Tetrabutylammonium fluoride (211 μL of 1.0 M solution in THF) was added dropwise to a stirred solution of ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: 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}. ^{1}H NMR ($CDCl_3$): 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, $^{2}J(^{77}Se\text{-}^{1}H)$ = 14.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 393.9. MS (EI): *m/z* = 364 [M^{+}-^{t}Bu]. HRMS (EI): *m/z* = 364.0483 calcd. for $C_{13}H_{22}NO_4SeSi$, found 364.0467.



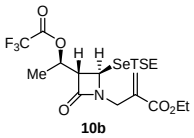
Diselenide III

Diselenide III: IR (neat): 2929, 2360, 1768, 1714, 1635, 1373, 1258, 836 cm^{-1}. ^{1}H NMR ($CDCl_3$): 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, $^{2}J(^{77}Se\text{-}^{1}H)$ = 42.0 Hz, 1H), 5.90 (s, 1H), 6.33 (s, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 316.1. MS (EI): *m/z* = 783 [M^{+}-^{t}Bu].



10a

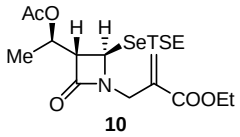
Preparation of Ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-hydroxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethyl seleno]-1-azetidinyl]]acrylate (**10a**): Trifluoroacetic acid (excess) was added dropwise to a stirred solution of ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl]]acrylate **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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: 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}. ^{1}H NMR ($CDCl_3$): 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, $^{2}J(^{77}Se\text{-}^{1}H)$ = 32.9 Hz, 1H), 5.87 (s, 1H), 6.32 (s, 1H). ^{13}C NMR ($CDCl_3$): δ -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. ^{77}Se NMR ($CDCl_3$): δ 276.6. MS (EI): *m/z* = 407 [M^{+}].



10b

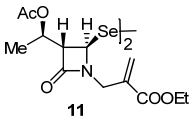
Compound 10b: IR (neat): 2954, 1764, 1753, 1713, 1640, 1537, 1248, 860 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.02 (s, 3H), 0.92-0.99 (m, 2H), 1.32 (t, *J* = 6.9 Hz, 3H), 1.52 (d, *J* = 6.3 Hz, 3H), 2.65-2.72 (m, 2H), 3.46 (dd, *J* = 6.3 & 1.7 Hz, 1H), 3.82 (d, *J* = 16.0 Hz, 1H), 4.20-4.30 (m, 3H), 4.86 (d, *J* = 1.7 Hz, $^{2}J(^{77}Se\text{-}^{1}H)$ = 18.9 Hz, 1H), 5.39-5.46 (m, 1H), 5.81 (s, 1H), 6.36 (s, 1H). ^{13}C NMR ($CDCl_3$): δ -1.98, 14.1, 17.95, 18.6,

18.9, 41.3, 53.3, 61.2, 63.0, 72.8, 127.8, 134.4, 163.5, 165.5, 169.9. ^{77}Se NMR ($CDCl_3$): δ 271.2. MS (EI): *m/z* = 503 [M^+].



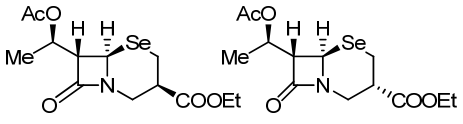
10

Preparation of Ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-acetoxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-1-azetidinyl]]acrylate (**10**): Acetic anhydride (70 μL, 0.74 mmol) was added dropwise to a stirred solution of ethyl 2-[methyl-3-[(3*S*,4*R*)-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 (SiO_2: 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}. ^{1}H NMR ($CDCl_3$): δ 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, $^2J(^{77}Se\text{-}^1H)$ = 22.9 Hz, 1H), 5.19-5.27 (m, 1H), 5.80 (s, 1H), 6.33 (s, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 268.3. MS (EI): *m/z* = 449 [M^+]. HRMS (EI): *m/z* = 449.1137 calcd. for $C_{18}H_{31}NO_5SeSi$, found 449.1137.

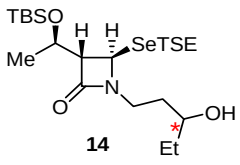


11

Preparation of bis 4-(azetidin-2-one) diselenide **11**: Tetrabutylammonium fluoride (147 μL of 1.0 M solution in THF) was added dropwise to a stirred solution of ethyl 2-[methyl-3-[(3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-2-oxo-4-[2-(trimethylsilyl)ethylseleno]-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 (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: hexane / diethyl ether = 12/1) to afford the diselenide **11** (32 mg, 68%) as an oil. ^{1}H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 46.39 Hz, 1H), 5.24-5.32 (m, 1H), 5.87 (s, 1H), 6.38 (s, 1H). ^{77}Se NMR ($CDCl_3$): δ 304.4.

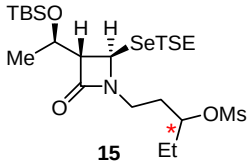


Preparation of ethyl (5*R*,6*S*)-7-[(*R*)-1-acetoxyethyl]-1-aza-5-selenabicyclo [4.2.0]octane-3-(*R*)-carboxylate (**12**) and ethyl (5*R*,6*S*)-7-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-5-selenabicyclo[4.2.0]octane-3-(*S*)-carboxylate (**13**): Sodium borohydride (4 mg, 0.11 mmol) was added 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 (SiO_2: 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 ($CHCl_3$): 2930, 1762, 1730, 1447, 1373, 1240, 1028, 755 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 10.9 Hz, 1H), 5.19-5.26 (m, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 277.2. MS (EI): *m/z* = 349 [M^+]. HRMS (EI): *m/z* = 349.0428 calcd. for $C_{13}H_{19}NO_5Se$, found 349.0418. **Selenacepham 13**: IR ($CHCl_3$): 2929, 1767, 1735, 1648, 1442, 1374, 1239, 1026 cm^{-1}. ^1H NMR ($CDCl_3$): 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, $^2J(^{77}Se\text{-}^1H)$ = 10.9 Hz, 1H), 5.15-5.22 (m, 1H). ^{13}C NMR ($CDCl_3$): 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. ^{77}Se NMR ($CDCl_3$): δ 223.4. MS (EI): *m/z* = 349 [M^+]. HRMS (EI): *m/z* = 349.0428 calcd. for $C_{13}H_{19}NO_5Se$, found 349.0382.



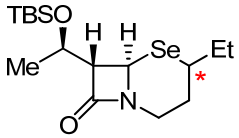
Preparation of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl] -1-(3-hydroxypentyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (14): Sodium borohydride (38 mg, 1.01 mmol) was added to a stirred suspension of ketone **6f** (200 mg, 0.41 mmol) in absolute ethanol (5 mL), under argon atmosphere. 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 (SiO_2: 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 ^{1}H NMR and ^{13}C NMR. IR ($CHCl_3$): 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 $C_{17}H_{36}NO_3SeSi_2$, found 438.1373.



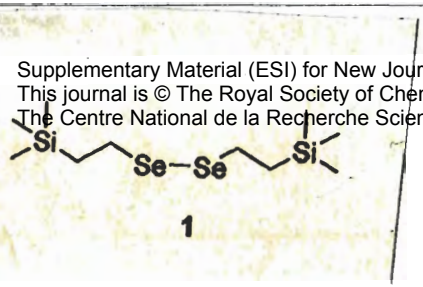
15

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 µL, 0.60 mmol) and mesyl chloride (24 µL, 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 (SiO_2: 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 ^{1}H NMR and ^{13}C NMR. IR ($CHCl_3$): 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 $C_{18}H_{38}NO_5SSeSi_2$, found 516.1124.



Selenacepham 16

Preparation of (6*R*,7*S*)-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 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 (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: 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 ^{1}H NMR and ^{13}C NMR. IR ($CHCl_3$): 2957, 1759, 1640, 1471, 1394, 1256, 835 cm^{-1}. MS (EI): *m/z* = 320 [M^+ - ^{t}Bu]. HRMS (EI): *m/z* = 320.0585 calcd. for $C_{12}H_{22}NO_2SeSi$, found 320.0562.



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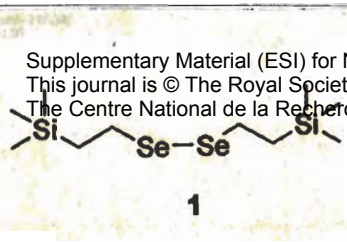

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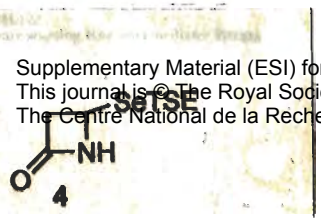

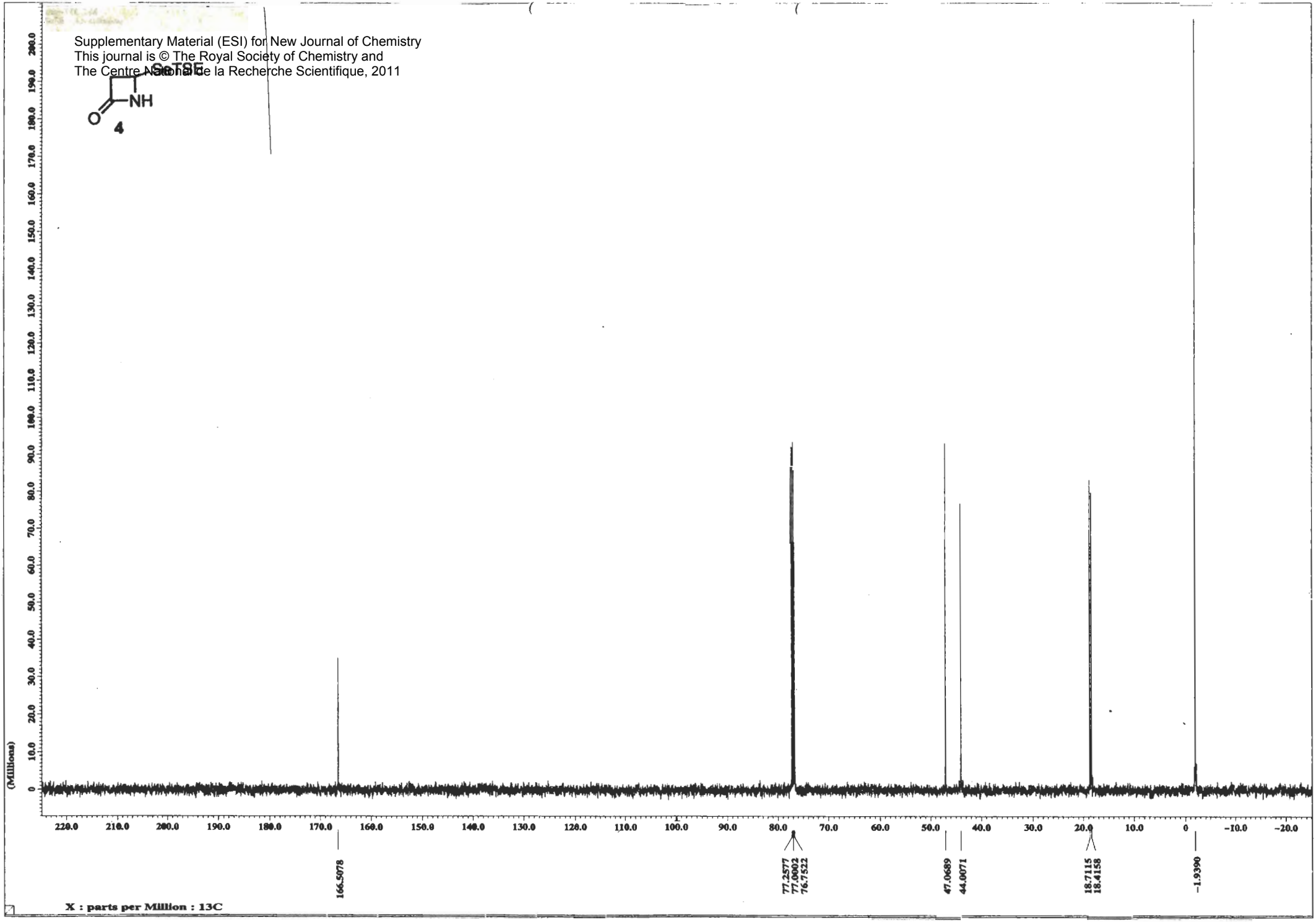

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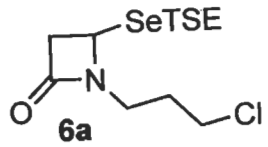

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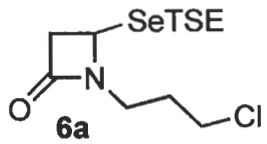

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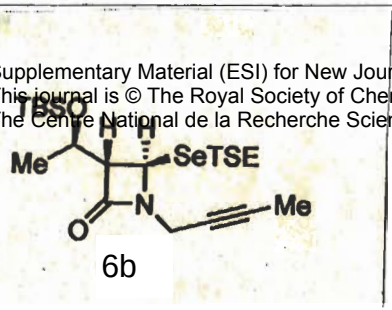

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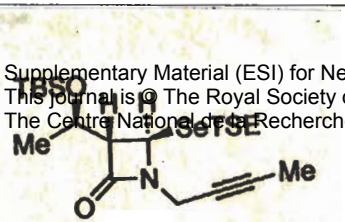

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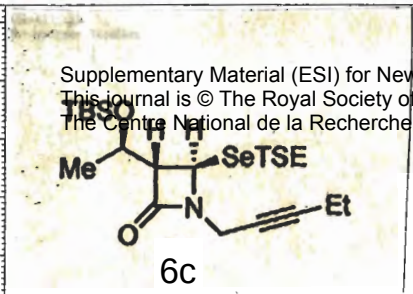

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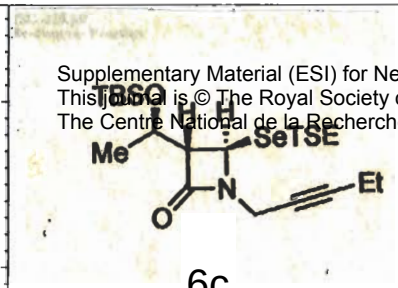

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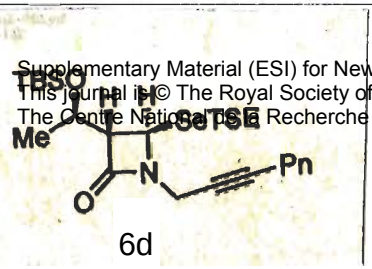

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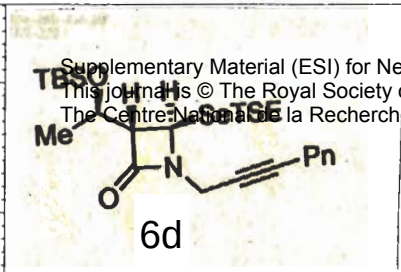

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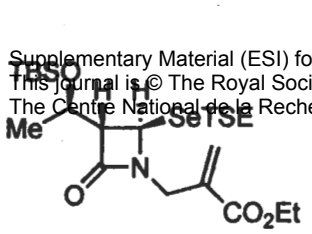

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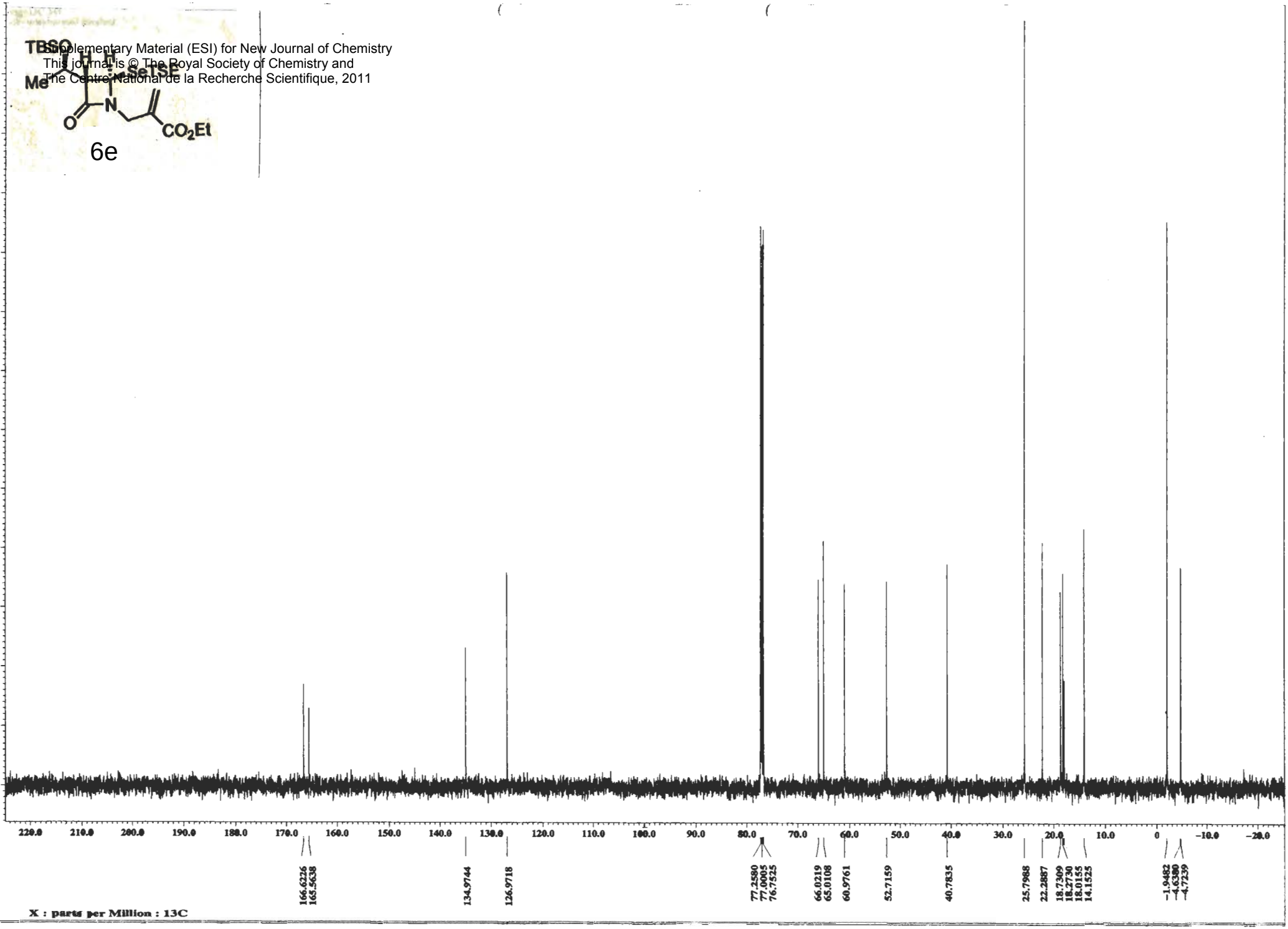

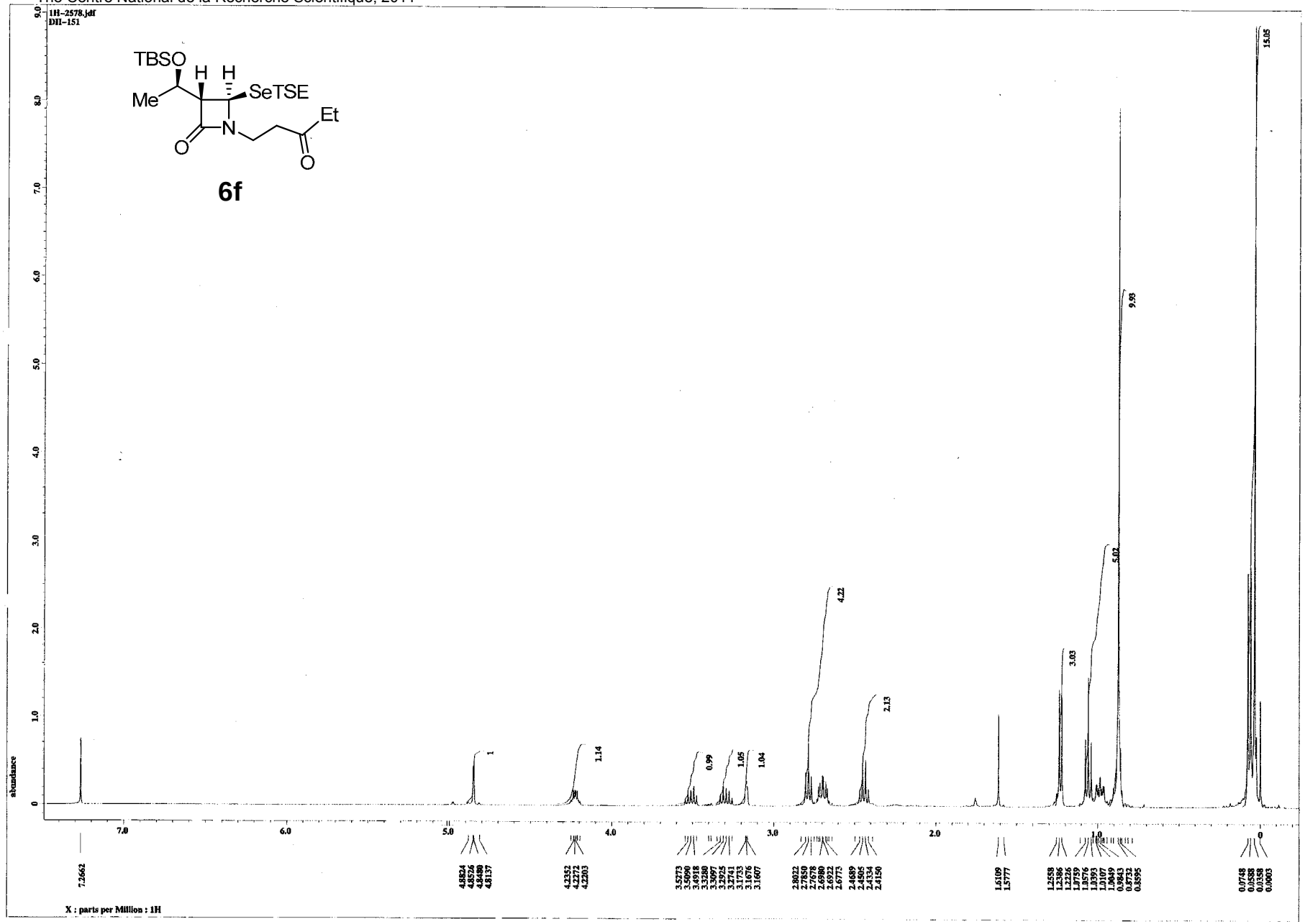

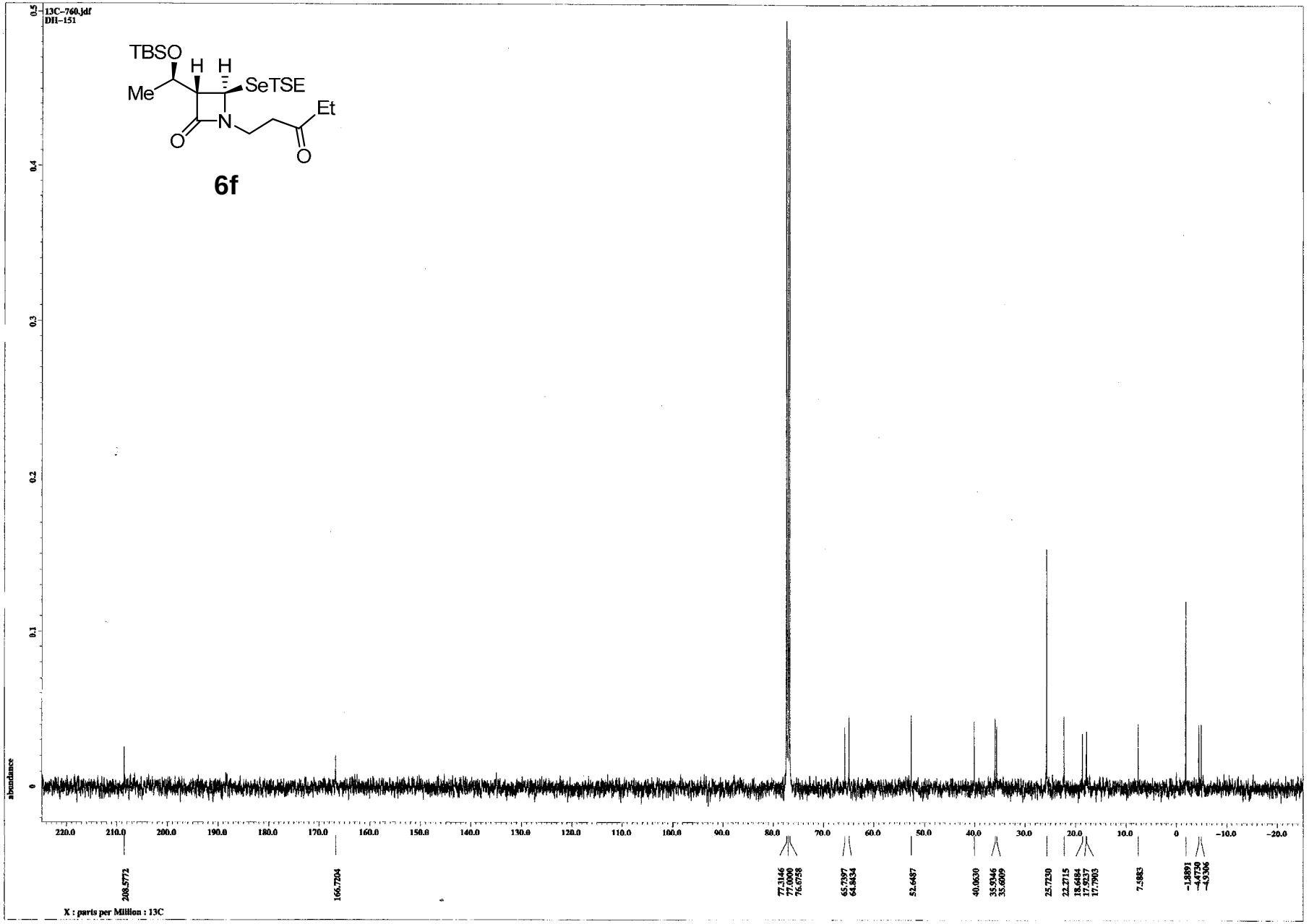

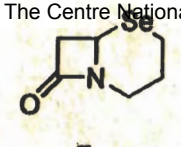

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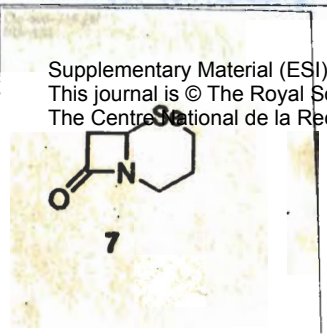

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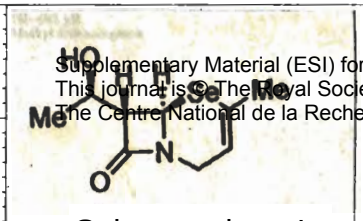
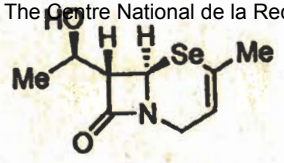


Selenacephem I



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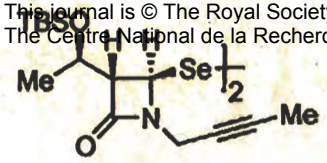

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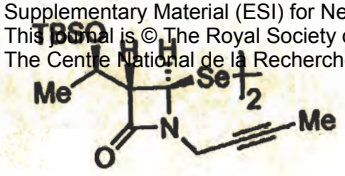

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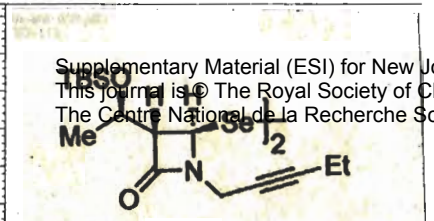

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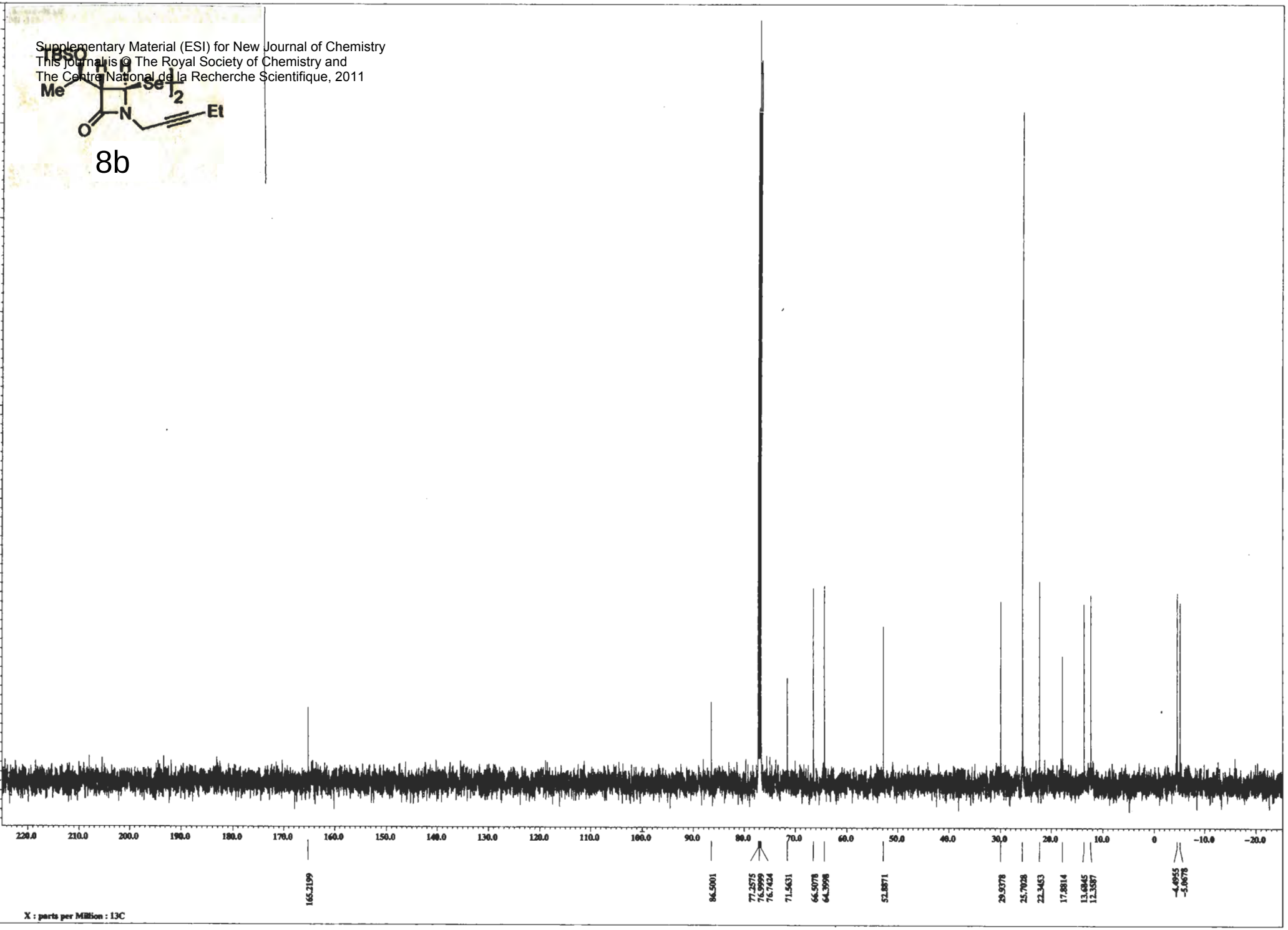

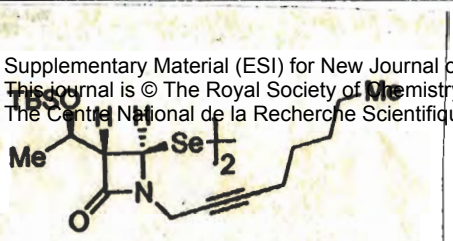

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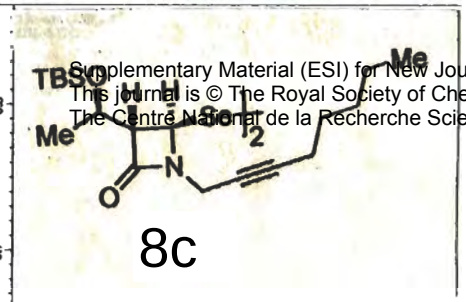

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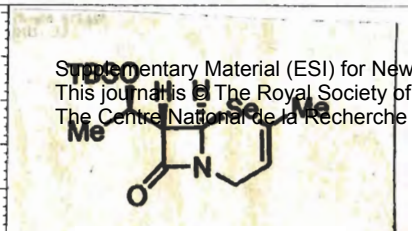

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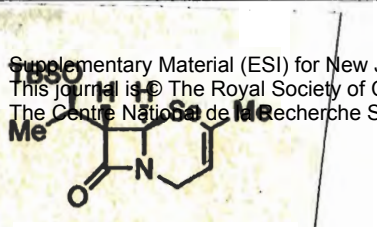

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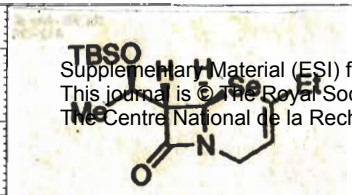

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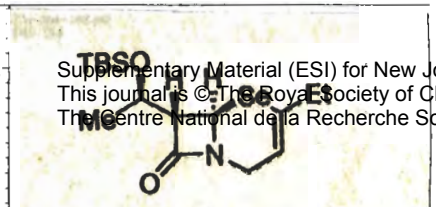

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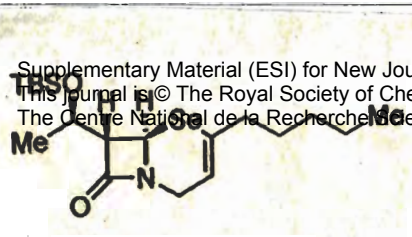

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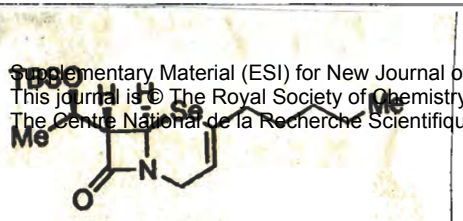

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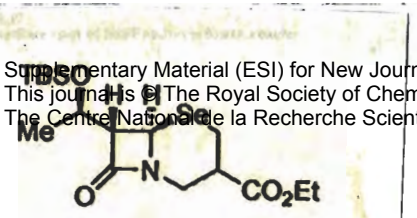

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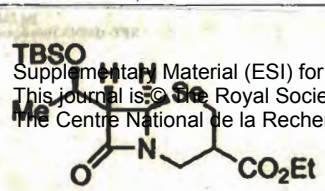

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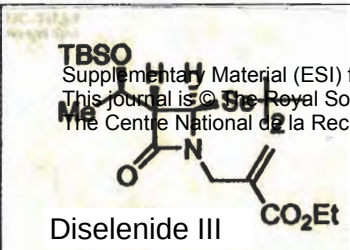

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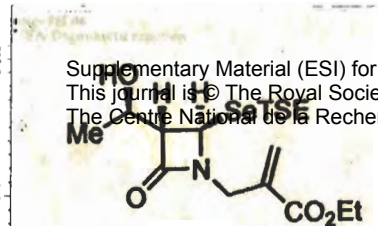

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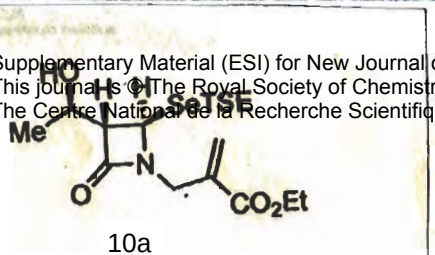

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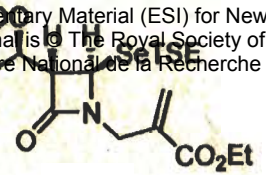

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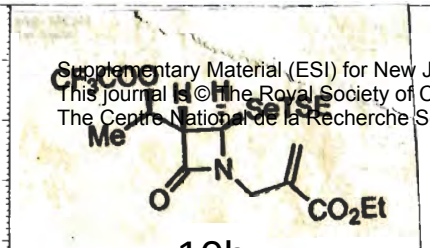

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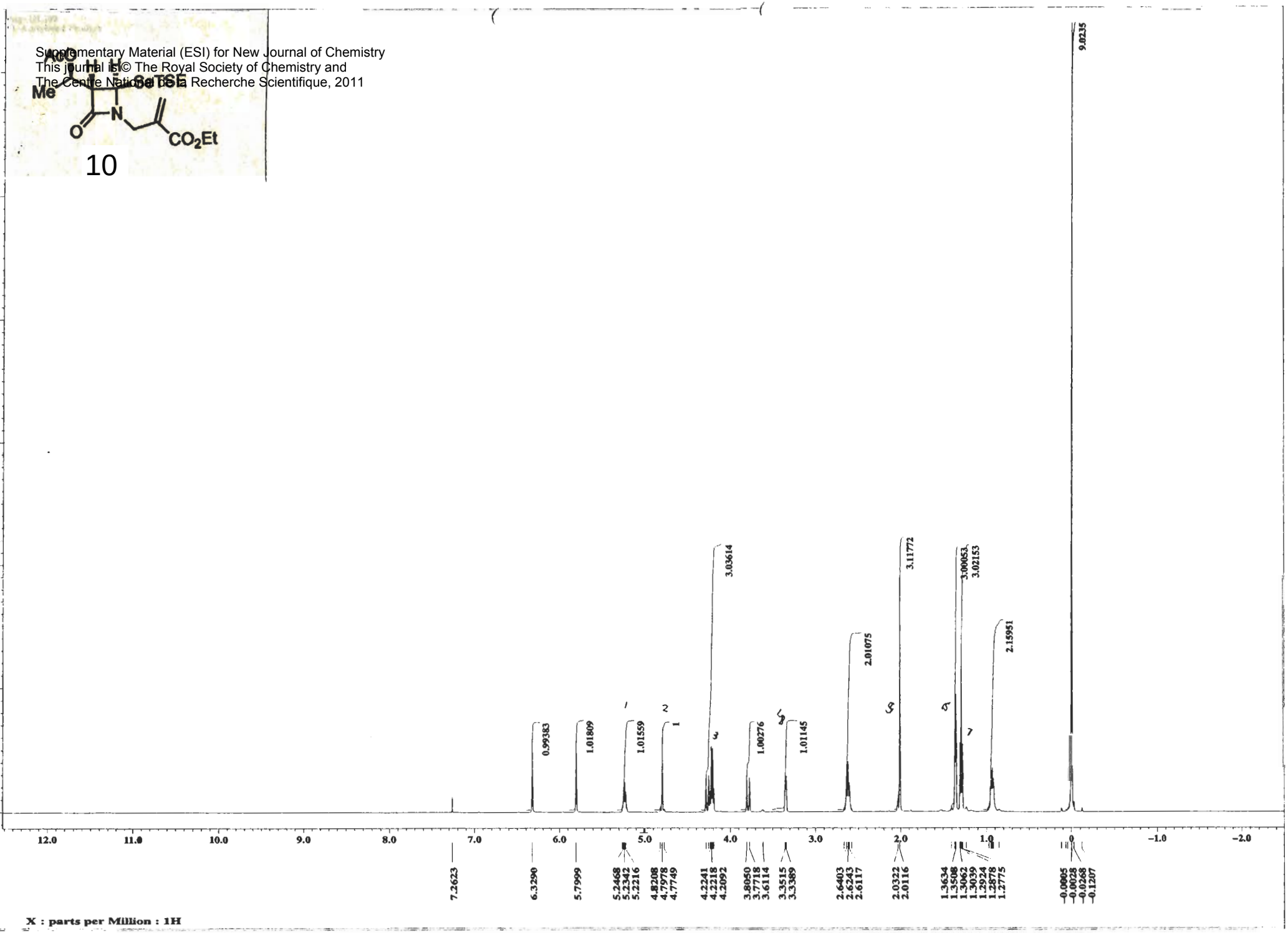

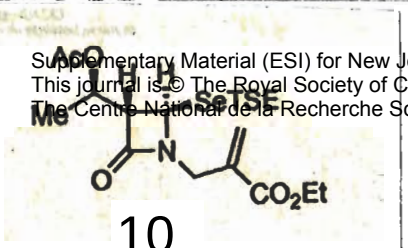

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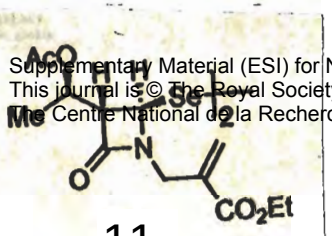

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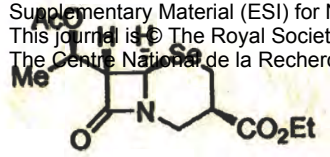

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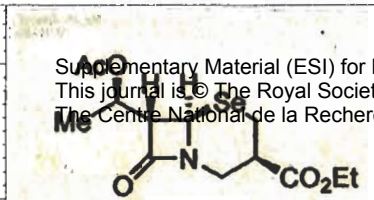

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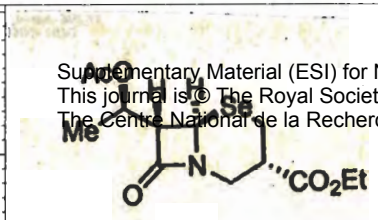

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