Supporting Information

S-Alkyl Dithioformates as 1, 3-Dipolarophiles. Generation of *C(2)*-Unsubstituted Penems

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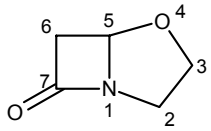
General

All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen. All chemicals were purchased from Acros, Aldrich, Avocado, Fluka or Lancaster and used as such unless stated otherwise. Anhydrous solvents were dried by passage through a column of anhydrous alumina using equipment from Anhydrous Engineering based in the University of Bristol School of Chemistry (see Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996,** *15*, 1518-1520). Microwave-assisted reactions were conducted in screw cap pressure tubes or in open vessel (100mL-round bottom flask equipped with a condenser) using a CEM *Discover* apparatus. Reactions were monitored by thin layer chromatography (TLC) with aluminum plates coated with Merck 60H-F_{254} silica gel, visualized with UV light or permanganate stain. Solvents were evaporated under reduced pressure using a Büchi rotary evaporator below 40 °C. 'Petroleum ether' refers to the fraction of petroleum ether boiling in the range 40-60 ^{o}C. Column chromatography was carried out using Merck 60 silica (40 - 62 μm). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. Infra-red spectra were recorded on a Perkin Elmer FT-IR spectrometer as a neat compound compressed onto a diamond window. Selected absorption maxima are quoted to the nearest wavenumber. Low resolution (EI or CI-with ammonia as CI reagent gas) and high resolution mass spectra were performed at the ESPRC Mass Spectrometry Service of the University of Swansea respectively on a Quattro II triple

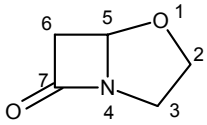
quadrupole and on a Finnigan MAT900XLT instruments and were calibrated with polyethyleneimine prior to data acquisition. Elemental analysis was performed by the Microanalysis service at the University of Bristol. Melting points were measured on a Reichert melting point apparatus and uncorrected.

^{1}H NMR (400MHz) and ^{13}C NMR (100.62MHz) were recorded on an Eclipse 400 spectrometer. Where spectroscopic assignments have been made, these are based specifically on ^{1}H-^{1}H and ^{1}H-^{13}C correlation spectroscopy. The data are being reported as (s = singlet, d = doublet, dd double doublet t = triplet, m = multiplet or unresolved, br = broad signal). Chemical shifts are quoted in parts per million (δ) downfield from internal tetramethylsilane TMS (1H, 0.0 ppm) or $CDCl_3$ (^{13}C, 77ppm) Coupling constants (*J*) are expressed in Hertz.

All β-lactam-containing compounds are named using IUPAC nomenclature with numbering from the β-lactam nitrogen atom and NMR assignments for bicyclic compounds are carried out using the traditional penam numbering protocol. For long range coupling $^{5}J_{3,6}$, $^{5}J_{2,6}$ see Bachi, M. D.; Breiman, R.; Meshulam, H. *J. Org. Chem.* **1983,** *48*, 1439-1444.



Numbering for Naming of bicyclic derivatives



Numbering for NMR Assignments of bicyclic derivatives

Exo and Endo assignment of the dithioformate cycloadducts **8a-c** described below was based on earlier work on related cycloadducts: Kirby, G. W.; Lochead, A. W. *J. Chem. Soc. (C), Chem. Comm.* **1983**, 1325-1327 ; Vedejs, E.; Stults, J. S.; Wilde, R. G. *J. Am. Chem. Soc*. **1988**, *110*, 5452-5460.

3-(Methylsulfanyl)-2-thiabicyclo[2.2.1]hept-5-ene (8a) : To a solution of CS_2 (0.5mL, 8 mmol) in 15 mL of anhydrous THF under nitrogen atmosphere, was added dropwise a 1M solution of $LiBEt_3H$ (8mL, 8 mmol). After stirring at room

temperature for 0.5h, MeI (1mL, 16 mmol) was added dropwise to the orange mixture. After 0.5h, NMR analysis of an aliquot confirmed the formation of methyl dithioformate **7a** (δ_H 11.33 (s) as reported by Gandhi, T.; Nethaji, M.; Jagirdar, B. R. *Inorg. Chem.* 2003, **42**, 4798-4800).

Freshly distilled cyclopentadiene was added (2mL, 24 mmol, 3equiv.) and the mixture was stirred at room temperature for 3h before being concentrated to a small volume. The crude mixture was then purified by flash chromatography (petroleum ether/ dichloromethane 5/1 to 2/1) to give the cycloadducts **8a** (440mg, 35%yield, diastereomeric mixture *exo/endo* 1.6:1 as judged by ^{1}H NMR – exo/endo assignments described below are based on COSY analysis) as a yellow oil (ATTENTION! STENCH and IRRITANT); **endo 8a** δ_H 6.40 (dd, 1H, $J_{5,6}$ 5.5, $J_{1,6}$ 2.8, H-6), 5.92 (dd, 1H, $J_{5,6}$ 5.5, $J_{4,5}$ 3.3, H-5), 4.09 (m, 1H, H-1), 3.76 (s, 1H, H-3), 3.35 (m, 1H, H-4), 2.28 (s, 3H, SMe), 1.94 (m, 1H, $J_{7,7}$ 9.5, H-7), 1.72 (dt, 1H, $J_{7,7}$ 9.5, $J_{1,7} = J_{4,7}$ 2.2, H-7) δ_C 139.00 (C-6), 131.7 (C-5), 56.5 (C-3), 51.6 (C-1), 50.8 (C-4), 48.0 (C-7), 16.9 (SCH_3); ***exo* 8a** δ_H 6.45 (dd, 1H, $J_{5,6}$ 5.5, $J_{1,6}$ 2.9, H-6), 5.97 (dd, 1H, $J_{5,6}$ 5.5, $J_{4,5}$ 3.2, H-5), 4.77 (d, 1H, $J_{3,4}$ 3.7, H-3), 4.14 (m, 1H, H-1), 3.60 (m, 1H, H-4), 2.19 (s, 3H, SMe), 1.76 (dt, 1H, $J_{7,7}$ 9.3, $J_{1,7}$= $J_{4,7}$ 2.2, H-7), 1.64 (m, 1H, H-7) δ_C 137.00 (C-6), 130.0 (C-5), 58.2 (C-3), 53.1 (C-1), 51.5 (C-7), 50.0 (C-4), 16.2 (SMe); ν_{max} /cm^{-1} 2912, 1435, 1423, 1336, 1327, 1271, 1255, 1246, 1194, 797 cm^{-1} ; MS(CI$^+$) m/z $[M+H]^+$ 159.0 ; HRMS calculated for $C_7H_{11}S_2$ $[M+H]^+$ 159.0297; found 159.0298.

N.B. The use of 1.1 or 5 equiv. of cyclopentadiene gave the same result (% yield and exo/endo ratio).

3-(4-Bromobenzylsulfanyl)-2-thiabicyclo[2.2.1]hept-5-ene (8b) : To thioformate **9** (1g, 4.32 mmol) in anhydrous toluene (40 mL) was added Lawesson's reagent (875mg, 0.5 equiv.) and the mixture was stirred and heated at reflux for 1.5h. At this stage, a TLC (petroleum ether/dichloromethane 2/1) showed that the thionation was complete. After cooling, freshly distilled cyclopentadiene (1.8mL, 5 equiv.) was added and after stirring for 1h at room temperature a TLC (petroleum ether/dichloromethane 2/1) showed complete disappearance of the putative dithioformate. The mixture was diluted with petroleum ether, filtered through Celite® and the filtrate was concentrated under reduced pressure. The crude yellow oil was purified by flash chromatography (petroleum ether/ethyl acetate 20/1 to 15/1) to give

the cycloadducts **8b** (300mg, 23%, NMR ratio *exo/endo* 0.6:1 as a yellow oil. Diastereomers were not separated (and assignments are based on COSY analysis) and the product was also contaminated by a small amount of an unidentified by-product derived from Lawesson's reagent which hampered complete characterisation. **endo 8b** δ_H 7.46-7.20 (m, 4H, Ar-H), 6.37 (dd, 1H, $J_{5,6}$ 5.4, $J_{1,6}$ 2.7, H-6), 5.83 (dd, 1H, $J_{5,6}$ 5.4, $J_{4,5}$ 3.3, H-5), 4.09 (m, 1H, H-1), 3.88, 3.82 (2d, 2 H, *J* 13.5, SCH_2), 3.66 (s, 1H, H-3), 3.22 (m, 1H, H-4), 1.94 (d, 1H, $J_{7,7}$ 9.5, H-7), 1.71 (m, 2H, H-7endo+exo); **exo 8b** δ_H 7.46-7.20 (m, 8H, Ar-H),6.45 (dd, 1H, $J_{5,6}$ 5.7, $J_{1,6}$ 3.2, H-6), 5.91 (dd, 1H, $J_{5,6}$ 5.7, $J_{4,5}$ 3.3, H-5), 4.62 (d, *J* 3.6, H-3), 4.11 (m, 1H, H-1), 3.77, 3.69 (2d, 2 H, *J* 13.5, SCH_2), 3.41 (m, 1H, H-4), 1.71 (m, 2H, H-7endo+exo), 1.56 (d, 1H, H-7) ; δ_C (exo+endo assignments are made where COSY analysis enabled this to be done) 139.1, 137.2, 137.0, 137.0, 131.8, 131.8, 131.7, 130.7, 130.5, 130.5, 130.4, 130.0, 121.0, 120.9, 55.6 (C-3exo), 54.1 (C-3endo), 53.2 (C-1exo), 51.9 (C-1endo), 51.5 (C-7exo), 51.1 (C-4endo), 50.0 (C-4exo), 48.4 (C-7endo), 37.6, 36.9, 35.7 (SCH_2); ν_{max} (cm^{-1})1669, 1485, 1070, 1011, 818, 804, 729 ; MS(CI^+) m/z $[M]^+$ 313; *Because of an impurity which could not be removed, a meaningful HRMS determination was not possible and we were unable to obtain CHN data for this compound within the usual limits of accuracy.*

3-(Naphthalen-1-ylmethylsulfanyl)-2-thiabicyclo[2.2.1]hept-5-ene (8c). The thionation procedure described above was also applied to **10** (530mg, 2.6mmol). After flash chromatography (petroleum ether/dichloromethane 2/1), two fractions were isolated: the endo product was obtained with 90% purity (as judged by ^{1}H NMR) (70mg, 10%) followed by the *exo* product (containing 7% of endo) (150mg, 20%). Repeating this reaction with 2.41g of thioformate **10** provided endo/exo mixture in a combined yield of 38%. ***endo* 8c** δ_H 8.20 (d, 1H, *J* 8.8, Ar-H), 7.90-7.81 (m, 2H, Ar-H), 7.62-7.39 (m, 4H, Ar-H), 6.38 (dd, 1H, $J_{5,6}$ 5.5, $J_{1,6}$ 2.7, H-6), 5.82 (dd, 1H, $J_{5,6}$ 5.5, $J_{4,5}$ 3.2, H-5), 4.44 and 4.33 (2d, 2H, *J* 13.4, SCH_2), 4.10 (m, 1H, H-1), 3.80 (s, 1H, H-3), 3.23 (m, 1H, H-4), 1.99 (d, 1H, $J_{7,7}$ 9.5, H-7), 1.72 (m, 1H, *J* 9.4, H-7); δ_C 138.9 (C-6), 131.6 (C-5), 128.7 128.2, 126.1, 125.8, 125.1, 124.0 (Ar), 54.8 (C-3), 51.8 (C-1), 51.2 (C-4), 48.4 (C-7), 36.0 (SCH_2); **exo 8c** δ_H 8.16-8.13 (m, 1H), 7.89-7.87 (m, 1H), 7.81-7.79 (m, 1H), 7.59-7.39 (m, 4H), 6.44 (dd, 1H, $J_{5,6}$ 5.5, $J_{1,6}$ 2.7, H-6), 5.86 (dd, 1H, $J_{5,6}$ 5.5, $J_{4,5}$ 3.1, H-5), 4.74 (d, 1H, $J_{3,4}$ 3.6, H-3), 4.33 and 4.18 (2d,

2H, *J* 13.5, SCH_2), 4.25 (m, 1H, H-1), 3.36 (m, 1H, H-4), 1.68 (ddd, 1H, $J_{7,7}$ 9.3, $J_{1,7}$ and $J_{4,7}$ 2.4, H-7), 1.56 (m, 1H, H-7) δ_C 136.9 (C-6), 130.2 (C-5), 128.8, 128.2, 126.1, 125.9, 125.1, 124.1 (Ar), 56.4 (C-3), 53.1 (C-1), 51.6 (C-7), 50.0 (C-4), 35.2 (SCH_2); ν_{max}(cm^{-1}) 1595, 1510, 1016, 777 ; MS(EI^+) m/z $[M+H]^+$ 285, $[HC(S)SCH_2Ar]^+$ 218; HRMS calculated for $C_{17}H_{17}S_2$ $[M+H]^+$ 285.0771; found 285.0770; Anal. Calcd for $C_{17}H_{16}S_2$: C,71.78; H, 5.67; S, 22.54; found C, 72.32; H, 5.65; S, 22.52. HRMS and microanalytical data were obtained on a mixture of exo and endo diastereomers.

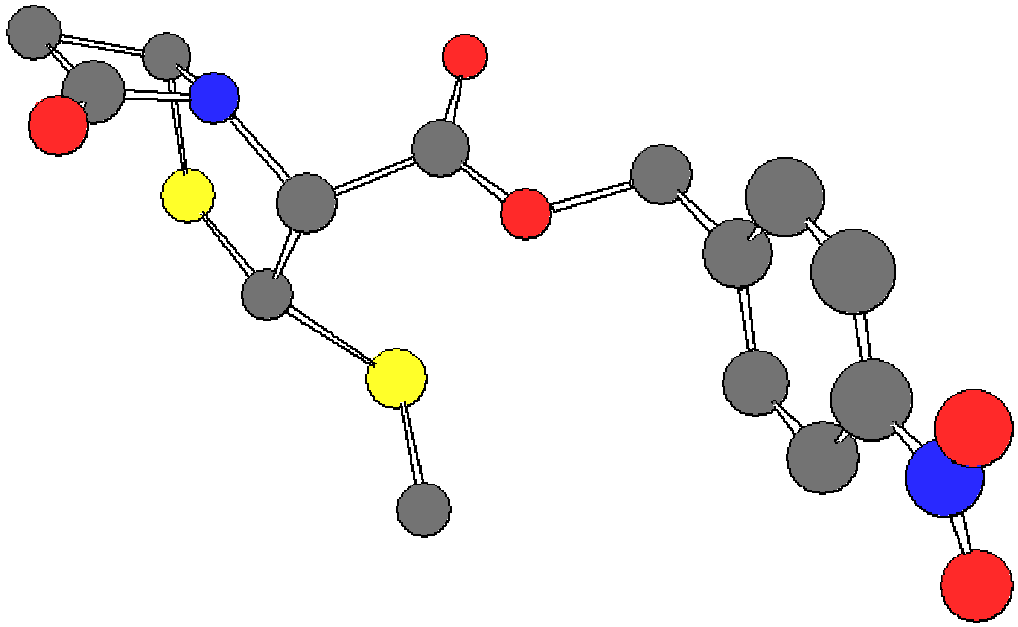
N.B . When NMR ^1H ($CDCl_3$, 270 MHz) on an aliquot of the thionation reaction mixture before addition of cyclopentadiene, showed signals for dithioformate **7c**: δ_H 11.32 (s, 1H, CHS), 5.02 (s, 2H, SCH_2).

(±)-4-Nitrobenzyl (2S*, 5R*)-3-methylsulfanyl-7-oxo-4-thia-1-aza-bicyclo[3.2.0]heptane-2-carboxylate (11a) : Oxazolidinone **3** (75mg, 0.25 mmol) and **8a** (65mg, 1.7 equiv.) in anhydrous and degassed toluene (5mL) under nitrogen was placed in an adapted sealed tube, and the mixture was submitted to microwave irradiation (150W for 5 min, temp. max 150°C then 55W for 60min, temp. max 200°C). After this time the mixture was concentrated under reduced pressure and purified by flash chromatography (petroleum ether/ethyl acetate 4/1 to 2/1) to provide **11a** (66mg, 76%, *exo/endo* 2.5:1 as judged by ^1H NMR). as a light yellow solid.

The *exo* product recrystallised as colorless needles from petroleum ether/ethyl acetate and an X-ray structure was obtained (see below). ν_{max} (cm^{-1}) 1747, 1530, 1346, 1183, 1172 ; MS(CI^+) m/z $[M+NH_4]^+$ 372.1; HRMS calculated for $C_{14}H_{15}N_2O_5S_2$. $[M+H]^+$ 372.0682; found 372.0683. **e*xo* 11a:** ; m.p. 111-112°C; δ_H 8.25 and 7.58 (2m, 4H, Ar-H), 5.34 (dd, 1H, $J_{5,6\alpha}$ 4.2, $J_{5,6\beta}$ 1.7, H-5), 5.34 and 5.29 (2d, 2H, *J* 13.2, OCH_2), 5.13 (d, 1H, $J_{2,3}$ 6.8, H-3), 5.08 (d, 1H, $J_{2,3}$ 6.8, H-2), 3.61 (dd, 1H, $J_{6,6}$ 15.8, $J_{5,6\alpha}$ 4.2, H-6α), 3.10 (dd, 1H, $J_{6,6}$ 15.8, $J_{5,6\beta}$ 1.7, H-6β), 2.22 (s, 3H, SMe) δ_C 171.5 (CO), 166.4 (CO ester), 147.6, 142.0, 128.9, 123.8 (Ar), 65.9 (OCH_2), 65.4 (C-3), 62.1 (C-2), 61.6 (C-5), 46.9 (C-6), 16.9 (SMe); Anal. Calcd for $C_{14}H_{14}N_2O_5S_2$: C, 47.45; H, 3.98; N, 7.90; found C, 47.46; H, 3.88; N, 7.97; ***endo* 11a** (data extracted from the spectrum of the diastereomeric mixture) δ_H 8.23 and 7.54 (2m, 4H, Ar-H), 5.33 and 5.29 (2d, 2H, *J* 13.4, OCH_2), 5.34 (dd, 1H, $J_{5,6\alpha}$ 4.3, $J_{5,6\beta}$ 2.0, H-5), 5.07 (dd, 1H, $J_{2,3}$ 1.7, H-3), 5.06 (d, 1H, $J_{2,3}$ 1.7, H-2), 3.66 (ddd, 1H, $J_{6,6}$ 16.1, $J_{5,6\alpha}$ 4.3, $J_{2,6\alpha}$ 0.7, H-6α), 3.29 (ddd, 1H, $J_{6,6}$ 16.1, $J_{5,6\beta}$ 2.0, $J_{3,6\beta}$ 0.7, H-6β), 2.24 (s, 3H, SMe) ; δ_C 172.1 (CO), 166.9 (CO

ester), 147.7, 141.8, 128.6, 123.6 (Ar), 66.6 (C-3), 66.0 (OCH_2), 62.8 (C-2), 61.7 (C-5), 49.1 (C-6), 16.0 (SMe).

Ortep view of penam **11a.**



(±)-4-Nitrobenzyl (2S*,5R*)-3-(4-bromobenzylsulfanyl)-7-oxo-4-thia-1-aza-bicyclo[3.2.0]heptane-2-carboxylate (11b) : A solution of oxazolidinone **3** (175mg, 0.57 mmol) and cyclopentadiene adduct **8b** (266mg, 1.5 equiv.) in anhydrous and degassed toluene (15 mL) was prepared. Using an open vessel apparatus (flask +condenser,\under nitrogen), the mixture was submitted to microwave irradiation (200W) for 4h (temp. max 130°C). The mixture was concentrated under reduced pressure and purified by flash chromatography (petroleum ether/ethyl acetate 4/1 to 2/1). The less polar product was the *exo* diastereomer (65mg, 20%) and continued elution gave a mixture of the *exo* and *endo* cycloadducts (75mg, 25%, 1:1 *exo/endo* as judged by ^{1}H NMR). This corresponds to an isolated yield of 45% of a 2.8: 1 mix of *exo/endo* isomers.

***exo* 11b** δ_H 8.25, 7.55, 7.43, 7.13 (4m, 8H, Ar-H), 5.33 (dd, 1H, $J_{5,6\alpha}$ 4.3, $J_{5,6\beta}$ 1.7, H-5), 5.31 and 5.26 (2d, 2H, *J* 13.5, OCH_2), 5.01 (d, 1H, $J_{2,3}$ 6.7, H-3), 4.90 (d, 1H, $J_{2,3}$ 6.7, H-2), 3.81 and 3.77 (2d, 2H, *J* 13.2, SCH_2), 3.60 (dd, 1H, $J_{6,6}$ 16.1, $J_{5,6\alpha}$ 4.3, H-6α), 3.07 (dd, 1H, $J_{6,6}$ 16.1, $J_{5,6\beta}$ 1.7, H-6β); δ_C 171.4 (CO), 166.2 (CO ester), 147.9, 141.8, 134.0, 131.9, 130.5, 128.8, 123.8, 121.7, 65.9 (OCH_2), 65.0 (C-3), 61.5 (C-5),

59.4 (C-2), 46.6 (C-6), 37.4 (SCH_2) ; ***endo* 11b** (data extracted from spectra of a 1/1 mixture) δ_H 8.24, 7.55, 7.47, 7.16 (4m, 8H, Ar-H), 5.23 (bs, 2H, OCH_2), 5.21 (dd, 1H, $J_{5,6\alpha}$ 4.3, $J_{5,6\beta}$ 2.2, H-5), 5.04 (d, 1H, $J_{2,3}$ 1.0, H-3), 4.77 (d, 1H, $J_{2,3}$ 1.0, H-2), 3.80 (m, 2H, SCH_2), 3.66 (ddd, 1H, $J_{6,6}$ 16.1, $J_{5,6\alpha}$ 4.3, $J_{2,6\alpha}$ 0.7, H-6α), 3.32 (ddd, 1H, $J_{6,6}$ 16.1, $J_{5,6\beta}$ 2.2, $J_{3,6\beta}$ 1.0, H-6β) δ_C 172.4 (CO), 166.6 (CO ester), 147.8, 141.6, 135.1, 131.8, 130.6, 128.5, 123.9, 121.3 (Ar), 67.0 (C-3), 66.2 (OCH_2), 61.7 (C-5), 60.1 (C-2), 49.8 (C-6), 37.6 (SCH_2) ; ν_{max} (cm^{-1}) 1777, 1746, 1607, 1519, 1486, 1344, 1289, 1172 ; MS(EI^+) m/z $[^{81}BrM]^+$ 510 $[^{79}BrM]^+$ 508; HRMS Calcd for $C_{20}H_{16}{}^{79}BrN_2O_5S_2$ $[M-H]^+$ 507.9757; Found 507.9767.

(±)-4-Nitrobenzyl (2S*, 5R*) (naphthalen-1-ylmethylsulfanyl)-7-oxo-4-thia-1-aza-bicyclo[3.2.0]heptane-2-carboxylate (11c) : A solution of oxazolidinone **3** (75 mg, 0.25 mmol), **8c** (104mg, 1.5 equiv.) and ionic liquid ([emim]PF6, 6mg, 10%) in anhydrous and degassed toluene (5 mL) under nitrogen in an adapted sealed tube was submitted to microwave irradiation (150W for 2min, temp. max 150°C then 55W for 60min, temp. max 200°C). The mixture was then concentrated under reduced pressure and purified by flash chromatography (petroleum ether/ethyl acetate 4/1 to 2/1). This gave the less polar product *exo* diastereomer (10mg, 8%) and a mixture of the *exo* and *endo* cycloadducts (50mg, 40%). This corresponds to an isolated yield of 48% of a 2: 1 mixture of *exo/endo* isomers.

***exo* 11c** δ_H 8.09-8.01 (m, 3H, Ar-H), 7.89-7.81 (m, 2H, Ar-H), 7.53-7.48 (m, 3H, ArH), 7.42-7.30 (m, 3H, Ar-H), 5.34 (dd, 1H, $J_{5,6\alpha}$ 4.4, $J_{5,6\beta}$ 1.7, H-5), 5.20 and 5.00 (2d, 2H, *J* 13.0, OCH_2), 5.03 (d, 1H, $J_{2,3}$ 6.8, H-3), 4.96 (d, 1H, $J_{2,3}$ 6.8, H-2), 4.37 and 4.26 (2d, 2H, *J* 13.2, SCH_2), 3.59 (dd, 1H, $J_{6,6}$ 16.1, $J_{5,6\alpha}$ 4.4, H-6α), 3.08 (dd, 1H, $J_{6,6}$ 16.1, $J_{5,6\beta}$ 1.7, H-6β) ; δ_C 171.7 (CO), 166.2 (CO ester), 147.7, 141.7, 134.2, 131.5, 131.2, 129.0, 128.7, 128.6, 127.4, 126.3, 126.1, 125.2, 123.7, 123.7 (Ar), 65.8 (OCH_2), 65.2 (C-3), 61.4 (C-5), 60.6 (C-2), 46.2 (C-6), 36.0 (SCH_2) ; ***endo* 11c** δ_H 8.21-7.29 (m, 11H, Ar-H), 5.22 (dd, 1H, $J_{5,6\alpha}$ 4.3, $J_{5,6\beta}$ 2.1, H-5), 5.20 and 5.00 (2d, 2H, *J* 13.0, OCH_2), 5.11 (d, 1H, $J_{2,3}$ 1.7, H-3), 4.85 (bs, 1H, H-2), 4.32 (s, 2H, SCH_2), 3.66 (ddd, 1H, $J_{6,6}$ 16.5, $J_{5,6\alpha}$ 4.3, $J_{2,6\alpha}$ 0.8, H-6α), 3.35 (ddd, 1H, $J_{6,6}$ 16.5, $J_{5,6\beta}$ 2.1, $J_{3,6\beta}$ 0.8, H-6β) ppm. δ_C 172.5 (CO), 166.7 (CO ester), 147.8, 141.7, 134.1, 131.4, 131.2, 128.8, 128.7, 128.3, 127.4, 126.4, 126.1, 125.0, 123.8, 123.7 (Ar), 67.1 (C-3),

66.1 (OCH_2), 61.7 (C-5), 60.9 (C-2), 49.7 (C-6), 35.9 (SCH_2) ; ν_{max} /cm^{-1} 1779, 1748, 1607, 1520, 1345, 1290, 1173 ; MS (EI^+) m/z [M^+] 480; HRMS calcd for $C_{24}H_{20}N_2O_5S_2$ 480.0808; found 480.0822.

(±)-4-Nitrobenzyl 7-oxo-4-thia-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (12). To cycloadduct **11a** (250mg, 0.70 mmol) in dichloromethane (12mL) was added dropwise at 0°C a solution of MCPBA (182mg, 70-75%, 1.05 equiv.) in dichloromethane (12mL) and then the mixture was let to warm up to room temperature overnight. The mixture was then quenched by saturated aqueous solution of $NaHCO_3$, the organic phase was washed with brine, dried using magnesium sulfate and concentrated under reduced pressure. The residual oil was diluted with dichloromethane (6 mL) and triethylamine (0.2 mL, 2 equiv.) was added. The mixture was either submitted to microwave irradiation (25W, 15min, temp. max 50°C with instant cooling) or allowed to stand at room temperature for 2h. After concentration under reduced pressure, the mixture was washed with a saturated aqueous solution of $NaHCO_3$, the organic phase is washed with brine, dried over magnesium sulfate and concentrated under reduced pressure. The product was then be obtained by precipitation using petroleum ether/dichloromethane to give penem **12** (150mg, 70%) as a pale brown solid. Alternatively, **12** could be isolated in 40 % yield following chromatography (petroleum ether/ ethyl acetate 3/1). Penem **12** decomposed above 115°C and no satisfactory mp was obtained. δ_H 8.24 and 7.58 (2m, 4H, Ar-H), 7.36 (dd, 1H, $J_{2,6\beta}$ 1.2, $J_{2,6\alpha}$ 1.0, H-2), 5.82 (dd, 1H, $J_{5,6\alpha}$ 4.2, $J_{5,6\beta}$ 2.0, H-5), 5.41 and 5.28 (2d, 2H, J 13.5, OCH_2), 3.89 (ddd, 1H, $J_{6,6}$ 16.6, $J_{5,6\alpha}$ 4.2, $J_{2,6\alpha}$ 1.0, H-6α), 3.62 (dd, 1H, $J_{6,6}$ 16.6, $J_{5,6\beta}$ 2.0, $J_{2,6\beta}$ 1.2, H-6β) ; δ_C 173.0 (CO), 158.3 (CO ester), 148.0 (C-3), 142.6 (C-2), 137.4 (C-3), 131.5, 128.3, 128.8, 65.5 (OCH_2), 64.1 (C-5), 50.5 (C-6); ν_{max} /cm^{-1} 1790, 1697, 1517, 1348, 1214 ; MS(EI^+) m/z $[M]^+$ 306 ; HRMS Calcd for $C_{13}H_{10}N_2O_5S$ 306.0305; Found 306.0305.

Benzyl (5R, 6S, 8R) 6-[1-(*tert*-butyldimethylsilanyloxy)ethyl]-3-methylsulfanyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (14a): To the 4-benzyl diazomalonate-6-[1-(*tert*-butyldimethylsilanyloxy)ethyl]azetidinone (129mg, 0.29 mmol) in an adapted sealed tube and in degassed anhydrous toluene (5mL) was added $Rh_2(OAc)_4$ (3mg, 2.5 mol%) under nitrogen. The mixture was then stirred under

microwave irradiation (100W) for 10min (max temp 140°C). A TLC (petroleum ether/ ethylacetate 2/1) shows the reaction was then complete and the oxazolidinone **13** has been formed, and this material was used without further purification.

To this crude product was added cycloadduct **8a** (80mg, 1.75 equiv.) in toluene (1mL) and this mixture was then stirred under nitrogen under microwave irradiation (150W then 55W) for 1h (max temp 160°C). After this time, the solution was concentrated under reduced pressure, and the crude mixture was purified by flash chromatography (petroleum ether/ethyl acetate 20/1 to 10/1). This gave the less polar *endo* product (11mg, 7%) followed by the *exo* cycloadduct (14mg, 10%) both as pale yellow oils.

***endo* 14a** δ_H 7.40-7.32 (m, 5H, Ar-H), 5.21 (d, 1H, $J_{5,6}$ 2.2, H-5), 5.18 (s, 2H, OCH_2), 5.01 (d, 1H, $J_{2,3}$ 1.2, H-3), 4.99 (d, 1H, $J_{2,3}$ 1.2, H-2), 4.24 (qd, 1H, $J_{8,9}$ 6.4, $J_{6,8}$ 4.6, H-8), 3.46 (ddd, 1H, $J_{6,8}$ 4.6, $J_{5,6}$ 2.2, $J_{3,6}$ 1.0, H-6), 2.20 (s, 3H, SMe), 1.23 (d, 3H, $J_{8,9}$ 6.4, CH_3-9), 0.85 (s, 9H, $(CH_3)_3$), 0.06 and 0.05 (2s, 6H, $(CH_3)_2$) ; δ_C 173.3 (CO), 167.3 (CO ester), 134.9, 128.7, 128.6, 128.2 (Ar), 71.3 (C-6), 67.8 (OCH_2), 66.6 (C-3), 64.9 (C-8), 63.6 (C-5), 62.9 (C-2), 25.6 ($(CH_3)_3$), 22.3 (CH_3), 17.9 ($C(CH_3)_3$), 16.5 (SMe), -4.3, -5.1 ($Si(Me)_2$) ; ***exo* 14a** δ_H 7.41-7.32 (m, 5H, Ar-H), 5.29 (d, 1H, $J_{5,6}$ 2.0, H-5), 5.23 and 5.17 (2d, 2H, J 12.1, OCH_2), 5.07 (d, 1H, $J_{2,3}$ 7.0, H-3), 4.98 (d, 1H, $J_{2,3}$ 7.0, H-2), 4.21 (qd, 1H, $J_{8,9}$ 6.4, $J_{6,8}$ 4.7, H-8), 3.23 (dd, 1H, $J_{6,8}$ 4.7, $J_{5,6}$ 2.0, H-6), 2.18 (s, 3H, SMe), 1.22 (d, 3H, $J_{8,9}$ 6.4, CH_3-9), 0.84 (s, 9H, $(CH_3)_3$), 0.05 and 0.02 (2s, 6H, 2xCH_3) ; δ_C 171.7 (CO), 166.4 (CO ester), 134.9, 128.6, 128.5 (Ar), 69.3 (C-6), 67.4 (OCH_2), 65.1 (C-8), 64.5 (C-3), 63.7 (C-5), 61.4 (C-2), 25.6 ($(CH_3)_3$), 22.4 (CH_3), 17.9 ($C(CH_3)_3$), 16.8 (SMe), -4.3, -5.1 (($Si(Me)_2$) ; ν_{max} /cm^{-1} 2956, 2930, 1774, 1748, 1292, 1186 ; MS (ES^+) m/z $[M+Na]^+$ 490, HRMS (ES^+) Calcd for $C_{22}H_{34}NO_4S_2Si$ 468.1693, found 468.1694.

Benzyl (5R,6S,8R) 6-[1-(*tert*-butyldimethy-silanyloxy)ethyl]-3-(naphthalen-1-ylmethylsulfanyl)-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (14c): A solution of oxazolidinone **13** (105 mg, 0.25 mmol) (prepared as described above) and **8c** (107mg, 1.5 equiv.) in anhydrous and degassed toluene (5 mL) under nitrogen was placed in an adapted sealed tube, and submitted to microwave irradiation (150W for 4min, temp. max 150°C then 55W for 2h, temp. max 120°C). The mixture was concentrated under reduced pressure and purified by flash chromatography (petroleum ether/ethyl acetate 20/1 to 15/1). This gave the less polar *endo* product

(10mg, 7%) followed by the *exo* diastereomer (24mg, 18%). The diastereomeric ratio was 2:1 *exo/endo* as judged by ^{1}H NMR and these yields represent those obtained over two steps from the 4-diazomalonate precursor of **13**;

***endo* 14c** δ_H 8.06, 7.85, 7.74 (3d, 3H, Ar-H), 7.57-7.48 (m, 3H, Ar-H), 7.37-7.35 (m, 6H, Ar-H), 5.22 (d, 1H, $J_{5,6}$ 2.1, H-5), 5.13 (s, 3H, OCH_2 + H-3), 4.85 (s, 1H, H-2), 4.31 and 4.23 (2d, 2H, *J* 13.4, SCH_2), 4.26 (m, 1H, H-8), 3.49 (ddd, 1H, $J_{6,8}$ 4.4 Hz, $J_{5,6}$ 2.1, $J_{3,6}$ 1.0, H-6), 1.23 (d, 3H, $J_{8,9}$ 6.1, CH_3-9), 0.86 (s, 9H, $(CH_3)_3$), 0.06 and 0.05 (2s, 6H, $(CH_3)_2$) ; δ_C 173.6 (CO), 166.9 (CO ester), 145.9, 134.7, 134.1, 131.6, 131.2, 128.8, 128.7, 128.6, 128.5, 128.3, 126.3, 126.00, 125.1, 123.9 (Ar), 71.7 (C-6), 67.8 (OCH_2), 66.9 (C-3), 64.8 (C-8), 63.5 (C-5), 60.9 (C-2), 36.1 (SCH_2), 25.6 ($(CH_3)_3$), 22.3 (CH_3-9), 17.9 ($C(CH_3)_3$), -4.3, -5.1 ($Si(Me)_2$) ; MS(CI^+) m:z $[M\text{-}SiMe_2]^+$ 536;

***exo* 14c** δ_H 8.06, 7.87, 7.79 (3d, 3H, Ar-H), 7.55-7.31 (2m, 9H, Ar-H), 5.29 (d, 1H, $J_{5,6}$ 2.0, H-5), 5.21 and 5.00 (2d, 2H, *J* 12.1, OCH_2), 4.97 and 4.91 (2d, 2H, $J_{2,3}$ 6.8, H-3 and H-2), 4.31 and 4.26 (2d, 2H, *J* 13.0, SCH_2), 4.19 (qd, 1H, $J_{8,9}$ 6.5, $J_{8,6}$ 4.6, H-8), 3.20 (dd, 1H, $J_{6,8}$ 5.4, $J_{5,6}$ 2.0, H-6), 1.21 (d, 3H, $J_{8,9}$ 6.5, CH_3-9), 0.83 (s, 9H, $(CH_3)_3$), 0.04 and 0.01 (2s, 6H, 2xCH_3) ; δ_C 171.7 (CO), 166.4 (CO ester), 134.8, 134.1, 131.8, 131.3, 128.9, 128.8, 128.5, 128.4, 127.4, 126.3, 126.0, 125.2, 123.8 (Ar), 69.0 (C-6), 67.3 (OCH_2), 65.1 (C-8), 64.3 (C-3), 63.5 (C-5), 59.5 (C-2), 35.9 (SCH_2), 25.6 ($(CH_3)_3$), 22.4 (CH_3-9), 17.9 ($C(CH_3)_3$), -4.3, -5.1 (($Si(Me)_2$) ; ν_{max} /cm^{-1} 2954, 1779, 1749, 1257 ; MS(CI^+) m:z $[M\text{-}SiMe_2]^+$ 536; MS (ES^+) m/z $[M+H]^+$ 594; HRMS (ES^+) Calcd for $C_{32}H_{43}N_2O_4S_2Si$ $[M+NH_4]^+$ 611.2428, found 611.2430.

Benzyl (5R,6S,8R) 6-[1-(*tert*-Butyldimethylsilanyloxy)ethyl]-7-oxo-4-thia-1-aza-bicyclo[3.2.0]hept-2-ene-2-carboxylate (15) : To **14c** (120mg, 0.20 mmol) in dichloromethane (3 mL)was added dropwise at 0°C a solution of MCPBA (52mg, 70-75%, 1.05 equiv.) in dichloromethane (3 mL). After stirring at room temperature overnight, the mixture was quenched by saturated aqueous $NaHCO_3$, the organic phase was washed with brine, dried over magnesium sulfate and concentrated under reduced pressure. The residual oil was diluted with dichloromethane (2 mL) and triethylamine (0.075 mL) was added. The mixture was submitted to microwave irradiation (25W, 15min, temp. max 50°C with instant cooling). After evaporation of solvents, the mixture was washed with a saturated aqueous solution of $NaHCO_3$, the organic phase was washed with brine, dried over magnesium sulfate and concentrated

under reduced pressure. Purification by flash chromatography (petroleum ether/ ethyl acetate 10/1) gave penem **15** (35 mg, 40%) as a viscous yellow oil; δ_H 7.41-7.29 (m, 5H, Ar-H), 7.22 (d, 1H, $J_{2,6}$ 1.0, H-2), 5.71 (d, 1H, $J_{5,6}$ 1.7, H-5), 5.23 (s, 2H, OCH_2), 4.24 (qd, 1H, $J_{8,9}$ 6.5, $J_{6,8}$ 4.6, H-8), 3.76 (ddd, 1H, $J_{6,8}$ 4.6, $J_{5,6}$ 1.7, $J_{2,6}$ 1.0, H-6), 1.25 (d, 3H, $J_{8,9}$ 6.5, CH_3-9), 0.86 (s, 9H, $(CH_3)_3$), 0.07 and 0.06 (2s, 6H, $(CH_3)_2$) ; δ_C 173.6 (CO), 158.7 (CO ester), 135.4 and 135.4 (C-2 and C-3), 128.5, 128.2, 128.2, 127.3, 72.4 (C-6), 66.9 (OCH_2), 66.1 (C-5), 65.2 (C-8), 25.8 ($Si(CH_3)_3$), 22.4 (CH_3-9), 17.9 ($C(CH_3)_3$), -4.4, -5.1 ($SiMe_2$) ; ν_{max} /cm^{-1} 2953, 2885, 1790, 1712, 1556, 1322, 1225, 1197, 1064. HRMS (ES^+) Calcd for $C_{21}H_{33}N_2O_4SSi$ $[M+NH_4]^+$ 437.1925, found 437.1920.