130. The Synthesis of an *O*-2-Isooxacephem

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Summary

The synthesis of an iso-oxacephem is described. Reaction of methanesulfonyl chloride with hydroxyalkylmalonates can form sulfones or sulfonates, their ratio varying with the basicity of the tertiary amine used in the sulfonation.

Previously [1], we described the low-yield conversion of the styrylazetidinone **1a** to the hydroxymethylazetidinone **2**. We now describe the conversion of compounds of type **2** to iso-oxacephems **10**, which might have interesting antibacterial activity.

Our first approach involved cyclizations of type **9**→**11**, and required transformation of the hydroxy group in **2** to a methanesulfonate function. Reaction of **2** with one equivalent each of methanesulfonyl chloride and triethylamine (MsCl/Et_3N) in methylene chloride gave, surprisingly, a mixture of sulfone **5** and methanesulfonate **6**. Treatment of sulfone **5** with triethylamine gave a low yield of methanesulfonate **6**. Reaction of **2**, **5** or **6** with the appropriate amount of MsCl/Et_3N gave the methanesulfonate **3**. In order to confirm that triethylamine indeed generated a malonate carbanion which reacts with MsCl to give a sulfone, the styrylazetidinone **1a** was subjected to the action of MsCl/Et_3N. The sulfone **4** was obtained in excellent yield. Ozonolysis of **4**, followed by sodium borohydride reduction [2], gave the hydroxymethylazetidinone **5** in good yield, indicating that the low yield in the conversion **1a**→**2** is probably due to oxidative cleavage of an enolized form of the malonate **1a**.

Because of the low yield in the ozonolysis **1a**→**2**, the azide function of **1b** was reduced (H_2S/triethylamine [3]) to the corresponding amine, which was immediately acylated to the two amides **7a** and **7b**. Ozonolysis, followed by reductive workup of **7a** and **7b** gave the corresponding alcohols **8a** and **8b** in 70–80% yield. This large difference of yields from ozonolysis in the two series is not explained, but has been noticed previously [4]. The methanesulfonate **9b** was prepared in excellent yield, when pyridine was used rather than the much more basic triethylamine. All attempts to carry out the cyclization **9b**→**11c** failed, giving instead the compound **12**. However, the desired cyclization could be achieved in good yield

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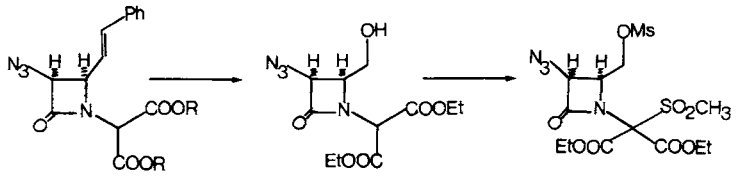
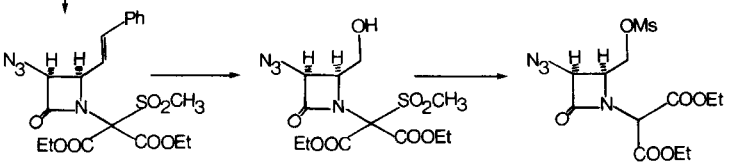


1a R = Et
1b R = CH_2Ph

2

3



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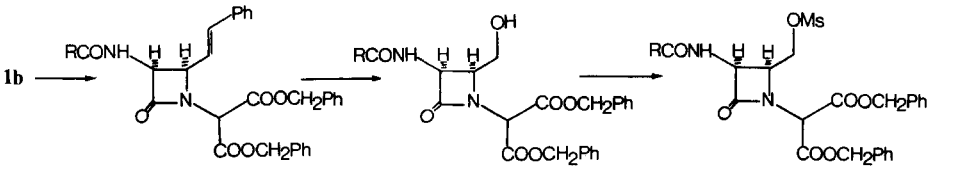
5

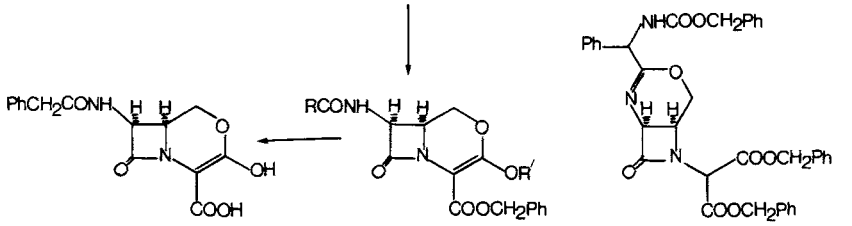
6



7a R = CH_2Ph
7b R = CH(Ph)NHCOOCH$_2$Ph

8a R = CH_2Ph
8b R = CH(Ph)NHCOOCH$_2$Ph

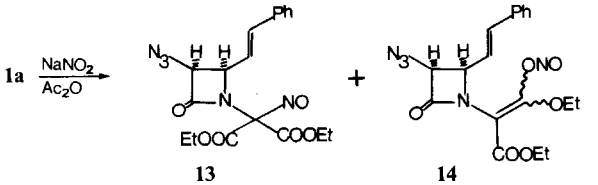
9a R = CH_2Ph
9b R = CH(Ph)NHCOOCH$_2$Ph



10

11a R = CH_2Ph, R′ = H
11b R = CH(Ph)NHCOOCH$_2$Ph, R′ = H
11c R = CH(Ph)NHCOOCH$_2$Ph, R′ = CH_2Ph

12



13

14

when **8a** or **8b** were treated with trifluoroacetic acid/methylene chloride 1:1 for 13–22 h at r.t.

Hydrogenolysis of **11a** with Pd/C in ethyl acetate at 40 psi failed, and only starting material was recovered. However, when palladium chloride was used as catalyst, the bicyclic derivative **10** was obtained in 45% yield. In the case of **11b**, we were not able to selectively remove the benzyl protecting group without hydrogenolyzing the amine function of the side-chain, so that the only clean product isolated was compound **10**.

However a cyclization of type **9b** → **11c** could be reasonably expected, since model studies on the styrylazetidinone **1a** with electrophiles showed the possibility of such reactions. Thus, treatment of **1a** with sodium nitrite/acetic anhydride, which is a known source of «NO^+» [5], gave a (1:1)-mixture of the nitrosomalonate **13** and the enenitrite **14** in excellent yield.

Experimental Part

General procedures: see [4]. Abbreviations: CI.-MS. = chemical ionization mass spectra. EI.-MS. = electron impact mass spectra.

Preparation of ethyl (3-azido-2-oxo-4-styryl-1-azetidinyl)mesylmalonate (**4**). Triethylamine (0.11 g, 1.08 mmol) was added to **1a** (0.372 g, 1 mmol) in 25 ml dry CH_2Cl_2. Methanesulfonyl chloride (0.115 g, 1.08 mmol) in 5 ml dry CH_2Cl_2 was added dropwise over 3 min at 0°. After 1 h, the solution was evaporated to dryness and ether was added. The ethereal solution was washed with water, dried and evaporated to give the crude product, which was chromatographed on silica gel with CH_2Cl_2 to give a quantitative yield of **4** as an oil. – IR. (CH_2Cl_2): 2100 (N_3), 1770 (β-lactam), 1755 (ester). – NMR. ($CDCl_3$): 1.20–1.39 (*2t*, J = 6 Hz, 6 H, 2 CH_3); 3.40 (*s*, 3 H, SO_2CH_3); 4.21–4.40 (2 *qa*, J = 6 Hz, 4 H, 2 CH_2); 4.90–5.30 (*m*, 2 H, $CHCHN_3$); 6.20 (*d* × *d*, J = 8 and 16 Hz, 1 H, C*H*=CHPh); 6.71 (*d*, J = 16 Hz, 1 H, CH=C*H*Ph); 7.20–7.40 (*m*, 5 H, Ph). – CI.-MS.: 451 ($M^+ + 1$), 422 ($M^+ - N_2$), 371 ($M^+ - SO_2CH_3$), 367 ($M^+ - N_3CH{=}C{=}O$).

$C_{19}H_{22}N_4O_7S$	Calc.	C 50.66	H 4.88	N 12.44	S 7.11%
(450.24)	Found	„ 50.48	„ 4.81	„ 12.60	„ 7.31%

Preparation of ethyl (3-azido-4-hydroxymethyl-2-oxo-1-azetidinyl)mesylmalonate (**5**). Compound **4** (0.9 g, 2 mmol) in 50 ml dry CH_2Cl_2 was saturated with N_2 at −78°. Then a mixture of O_3/N_2 was bubbled in for 20 min. The excess ozone was removed by a stream of N_2; then 5 equiv. dimethyl sulfide was added, and after 1 h, $NaBH_4/Al_2O_3$ (0.5:5 g) were added [2]. The reaction mixture was stirred for 1 h at r.t. Filtration and evaporation gave the crude product, which was purified on silica gel with $CHCl_3$ to give 0.53 g (70%) of **5** as a foam. – IR. (CH_2Cl_2): 3600 (OH), 2100 (N_3), 1780 (β-lactam), 1750 (ester). – NMR. ($CDCl_3$): 1.25 (*t*, J = 6 Hz, 6 H, 2 CH_2CH_3); 3.41 (*s*, 3 H, SO_2CH_3); 3.40–3.70 (br., 4 H, $CHCH_2OH$); 4.31–4.38 (2 *qa*, J = 6 Hz, 4 H, 2 CH_2CH_3); 5.20 (*d*, J = 5 Hz, 1 H, CHN_3). – EI.-MS.: 305 ($M^+ - COOEt$), 295 ($M^+ - N_3CH{=}C{=}O$).

Preparation of ethyl (3-azido-4-mesyloxymethyl-2-oxo-1-azetidinyl)malonate (**6**). Compound **5** (0.1 g, 0.27 mmol) in 15 ml dry CH_2Cl_2 was treated with NEt_3 (0.303 g, 3 mmol). The solution was stirred at r.t. for 2 h then washed with water, dried and evaporated. The residue was chromatographed on silica gel using $CHCl_3$ to give 0.025 g (25%) of **6** as an oil. – IR. (CH_2Cl_2): 2110 (N_3), 1770 (β-lactam), 1740 (ester). – NMR. ($CDCl_3$): 1.35 (*t*, J = 6 Hz, 6 H, 2 CH_3); 2.98 (*s*, 3 H, OSO_2CH_3); 3.90–4.51 (*m*, 7 H, 2 CH_2 and $CHCH_2O$); 4.82 (*d*, J = 5 Hz, 1 H, CHN_3); 5.1 (*s*, 1 H, CH). – EI.-MS.: 333 ($M^+ - OEt$), 283 ($M^+ - OMs$). – CI.-MS.: 379 ($M^+ + 1$).

Preparation of ethyl (3-azido-4-mesyloxymethyl-2-oxo-1-azetidinyl)mesylmalonate (**3**). Compounds **2**, **5**, and **6** were separately treated in dry CH_2Cl_2 at 0° with methanesulfonyl chloride in presence of 2 equiv., 1 equiv. and 1 equiv. NEt_3 respectively. After 1 h the mixture were washed with water, dried and evaporated to give compound **3**, which was purified by column chromatography with $CHCl_3$, to give in each case a quantitative yield of **3** as a foam. – IR. (CH_2Cl_2): 2105 (N_3), 1795 (β-lactam), 1755 (ester). – NMR. ($CDCl_3$): 1.33 (*t*, J = 7 Hz, 6 H, 2 CH_3); 3.00 (*s*, 3 H, O–SO_2CH_3); 3.38 (*s*, 3 H,

C–SO_2CH_3); 4.20–4.81 (*m*, 7 H, 2 CH_2 and $CHCH_2O$); 5.08 (*d*, *J* = 5 Hz, 1 H, CHN_3). – CI.-MS.: 457 ($M^+ + 1$, S-cluster), 429 ($M^+ + 1 - N_2$), 384 ($M^+ + 1 - COOEt$), 377 ($M^+ - SO_2CH_3$), 361 ($M^+ - OSO_2CH_3$), 374 ($M^+ + 1 - N_3CH{=}C{=}O$).

$C_{13}H_{20}N_4O_{10}S_2$	Calc.	C 34.21	H 4.32	N 12.28	S 14.03%
(456.14)	Found	„ 33.98	„ 4.29	„ 12.37	„ 13.89%

Preparation of benzyl (2-oxo-3-phenylacetamido-4-styryl-1-azetidinyl)malonate (**7a**). To a solution of **1b** (2.48 g, 0.005 mol) in 70 ml dry CH_2Cl_2 at 0° was added NEt_3 (0.6 g, 0.006 mol). H_2S was bubbled in for 20 min. The solution was allowed to stand for 2 h at r.t. Evolution of N_2 was observed. N_2 was bubbled in for 30 min, then (1.5 g, 0.018 mol) pyridine was added, followed by dropwise addition of (0.9 g, 0.006 mol) phenylacetyl chloride in 10 ml CH_2Cl_2. The solution was stirred for 2 h at 25°, then washed with 5% HCl, 10% $NaHCO_3$- and NaCl-solutions, dried ($MgSO_4$) and evaporated to give impure amide, which was chromatographed on silica gel. CH_2Cl_2 eluted impurities, and $CHCl_3$ gave 2.5 g (84%) of **7a** as an oil. – IR. (CH_2Cl_2): 3400 (NH), 1770 (β-lactam), 1750 (ester), 1680 (amide). – NMR. ($CDCl_3$): 3.41 (*s*, 2 H, CH_2); 4.75 (*d*×*d*, *J* = 5 and 8 Hz, 1 H, C*H*CH=C); 5.00–5.21 (*m*, 5 H, 2 CH_2Ph and H–C(2)); 5.5 (*d*×*d*, *J* = 5 and 8 Hz, 1 H, C*H*NH); 5.85 (*d*×*d*, *J* = 8 and 16 Hz, 1 H, C*H*=CHPh); 6.45 (*d*, *J* = 16 Hz, 1 H, CH=C*H*Ph); 6.61 (*d*, *J* = 8 Hz, 1 H, NH); 7.00–7.40 (*m*, 20 H, 4 Ph). – CI.-MS.: 589 ($M^+ + 1$), 454 ($M^+ + 1 - COOCH_2Ph$), 414 ($M^+ + 1 - PhCH_2CONHCH{=}C{=}O$).

$C_{36}H_{32}N_2O_6$ (588.18) Calc. C 73.46 H 5.44 N 4.76% Found C 73.41 H 5.41 N 4.81%

Preparation of benzyl [3-(α-benzyloxycarbonylamino-α-phenylacetamido)-2-oxo-4-styryl-1-azetidinyl]-malonate (**7b**). Compound **1b** (2.48 g, 0.005 mol) was treated with H_2S by the procedure described for **7a**. After N_2 was bubbled in, the solution was washed with water, dried and evaporated. The crude product was dissolved in 40 ml dry CH_2Cl_2. D(–)-α-benzyloxycarbonyl amino-α-phenylacetic acid (1.44 g, 0.005 mol) and *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (1.24 g, 0.005 mol) were added [6]. The solution was stirred at r.t. for 4 h, washed with 10% HCl, saturated $NaHCO_3$-solution and water, then dried and evaporated to give impure amide which was chromatographed on silica gel and eluted with $CHCl_3$ to give 2.7 g (72%) of **7b** as a foam. – IR. (CH_2Cl_2): 3300–3400 (NH), 1770 (β-lactam), 1745 (ester), 1727 (carbamate), 1685 (amide). – NMR. ($CDCl_3$): 4.70–5.30 (*m*, 9 H, 3 CH_2O and 3 CH); 5.40–5.63 (br., 1 H, C*H*NH); 5.81–6.90 (*m*, 4 H, CH=CH and 2 NH); 7.20–7.41 (*m*, 25 H, 5 Ph).

$C_{44}H_{39}N_3O_8$ (737.00) Calc. C 71.64 H 5.29 N 5.69% Found C 71.29 H 5.40 N 5.48%

Preparation of benzyl (4-hydroxymethyl-2-oxo-3-phenylacetamido-1-azetidinyl)malonate (**8a**) *and benzyl [3-(α-benzyloxycarbonylamino-α-phenylacetamido)-4-hydroxymethyl-2-oxo-1-azetidinyl]malonate* (**8b**). Both β-lactams **7a** and **7b** were treated identically. The spectra of **8a** and **8b** were similar except for variations due to amide side-chains.

β-Lactam **7a** (2.94 g, 0.005 mol) in 50 ml dry CH_2Cl_2 was saturated with N_2 at – 78°. Then a mixture of O_3/N_2 was bubbled in until KI/starch paper showed excess ozone (16 min). The excess ozone was removed by passing a stream of N_2 for 10 min. Dimethyl sulfide (1.6 g, 5 eq.) was added, and the temperature allowed to rise to 25° over 1 h, following which 4 g $MgSO_4$ was added. After a few minutes, $NaBH_4/Al_2O_3$ 1:10 (*g*/*g*) were added while stirring. After 1 h the solution was filtered and evaporated to give the impure product, which was chromatographed on silica gel. Impurities were eluted with CH_2Cl_2 and **8a** was eluted with $CHCl_3$, 2 g (76%). – IR. (CH_2Cl_2): 3250–3550 (NH, OH), 1769 (β-lactam), 1735 (ester), 1685 (amide). – NMR. ($CDCl_3$): 3.50 (*s*, 2 H, CH_2); 5.60–4.18 (*m*, 4 H, $CHCH_2OH$); 5.10 (*s*, 4 H, CH_2O); 5.38 (*s*, 1 H, CH); 5.58 (*d*×*d*, *J* = 5 and 9 Hz, 1 H, C*H*NH); 7.00 (br., 1 H, NH); 7.20 (*s*, 15 H, 3 Ph).

$C_{29}H_{28}N_2O_7$ (516.14) Calc. C 67.44 H 5.42 N 5.42% Found C 67.34 H 5.49 N 5.44%

Preparation of benzyl (4-mesyloxymethyl-2-oxo-3-phenylacetamido-1-azetidinyl)malonate (**9a**) *and benzyl [3-(α-benzyloxycarbonylamino-α-phenylacetamido)-4-mesyloxymethyl-2-oxo-1-azetidinyl]malonate* (**9b**). Both **9a** and **9b** were prepared identically from **8a** and **8b** in quantitative yield. Their spectra were similar except for variations due to amide side-chains.

To **8a** (1.72 g, 3.3 mmol) in 30 ml dry CH_2Cl_2, pyridine (0.53 g, 6.6 mmol) was added, followed by dropwise addition of methanesulfonyl chloride (0.72 g, 6.6 mmol) in 5 ml CH_2Cl_2. The solution was stirred at RT. for 24 h, washed with water, dried and evaporated to give the crude product, which was chromatographed on silica gel with $CHCl_3$ to give **9a** quantitatively.

Data of **9a**. M.p. 105–106°. – IR. (CH_2Cl_2): 3400 (NH), 1770 (β-lactam), 1750 (ester), 1680 (amide). – NMR. ($CDCl_3$): 2.80 (*s*, 3 H, OSO_2CH_3); 3.60 (*s*, 2 H, CH_2); 4.21–4.58 (br., 3 H, $CHCH_2O$); 5.20 (*s*, 4 H, 2 CH_2O); 5.31 (*s*, 1 H, CH); 5.41 (*d* × *d*, J = 5 and 8 Hz, 1 H, C*H*NH); 7.02 (*d*, J = 8 Hz, 1 H, NH); 7.41 (*s*, 15 H, Ph).

$C_{30}H_{30}N_2O_9S$	Calc.	C 60.60	H 5.05	N 4.71	S 5.38%
(594.24)	Found	„ 60.78	„ 5.13	„ 4.83	„ 5.27%

Data of **9b**.

$C_{38}H_{37}N_3O_{11}S$	Calc.	C 61.37	H 4.98	N 5.65	S 4.30%
(743.50)	Found	„ 61.31	„ 5.01	„ 5.58	„ 4.41%

Preparation of dibenzyl 2-{2-[a-(benzyloxycarbonylamino)benzyl]-6-oxo-azetidino[3,2-d]-4a,6a-dihydro[1,3]oxazin-5-yl}malonale (**12**). MEt_3 (0.02 g, 0.2 mmol) was added to a solution of **9b** (0.1 g, 0.13 mmol) in 5 ml CH_2Cl_2. The solution was stirred at r.t. for 24 h, washed with water, dried and evaporated. The crude product was chromatographed on silica gel and eluted with $CHCl_3$ to give the bicyclic compound **12**, 20 mg (23%). – IR. (CH_2Cl_2): 3410 (NH), 1780 (β-lactam), 1750 (ester), 1725 (carbamate). – NMR. ($CDCl_3$): 4.31 (*m*, 2 H, $CHCH_2O$); 4.70–5.10 (*m*, 2 H, CHCHN); 5.11–5.40 (*m*, 8 H, 3 CH_2O and 2 CH); 7.20 (*s*, 21 H, 4 Ph and NH). – CI.-MS.: 513 ($M^+ + 1 - PhCH_2OC{=}O$).

$C_{37}H_{33}N_3O_8$ (647.23) Calc. C 68.62 H 5.10 N 6.49% Found C 68.75 H 4.91 N 6.64%

Preparation of cis-*4-benzyloxycarbonyl-3-hydroxy-7-phenylacetamido and of* cis-*4-benzyloxycarbonyl-7-[2-(benzyloxycarbonylamino)-2-phenylacetamido]-3-hydroxy-isooxacephems* (**11a** and **11b**). Both β-lactams **11a** and **11b** were prepared by the same procedure from **8a** and **8b** and **11a** obtained in 50% yield after 13 h, while **11b** was obtained in 10% yield after 13 h and 50% starting material was recovered. After 22 h, **11b** was obtained in 30% yield, without recovery of starting material. Their spectra were similar except for variations due to the amide side-chain.

A mixture of trifluoroacetic acid/CH_2Cl_2 1:1 (10 ml) was added dropwise at 5° in 5 min to the hydroxymethyl-β-lactam **8a** (0.258 g, 0.5 mmol) in 1 ml dry CH_2Cl_2. The mixture was stirred at r.t. for 13 h then evaporated, CCl_4 (50 ml) was added, and the solution again evaporated. The crude product was chromatographed on silica gel and after elution of impurities with CH_2Cl_2 and $CHCl_3$, **11a** was eluted with AcOEt as a foam (0.102 g). – IR. (CH_2Cl_2): 3200–3500 (NH, OH), 1790 (β-lactam), 1755 (ester), 1735 (C=C), 1680 (amide). – NMR. ($CDCl_3$): 2.89 (br., 1 H, OH, exchanged with D_2O); 3.50 (*s*, 2 H, $PhCH_2$); 3.61–4.00 (*m*, 2 H, $CHCH_2O$); 4.09–4.51 (*m*, 2 H, C*H*CHNH); 5.10 (*s*, 2 H, $PhCH_2O$); 6.36 (*d*, J = 8 Hz, 1 H, NH); 7.39, 7.23 (2 *s*, 10 H, 2 Ph). – CI.-MS.: 391 ($M^+ + 1 - H_2O$), 233 ($M^+ - PhCH_2CONHCH{=}C{=}O$), 218 ($M^+ + 2 - OH - PhCH_2OOCC{=}C{=}O$).

$C_{22}H_{20}N_2O_6$ (408.06) Calc. C 64.70 H 4.90 N 6.86% Found C 64.93 H 5.06 N 7.06%

Data of **11b** (as a mixture of 2 diastereoisomers). – IR. (CH_2Cl_2): 3300–3450 (NH, OH), 1790 (β-lactam), 1754 (ester), 1730 ($O_2C{=}C$), 1715 (carbamate), 1689 (amide). – NMR. (200 MHz, $CDCl_3$): 3.51–3.92 (*m*, 3 H, $CHCH_2O$); 4.01 (br., 1 H, OH); 4.32 (*d* × *d*, J = 5 and 10 Hz, 1 H, C*H*NH); 5.01 (*d*, J = 1.5 Hz, 2 H, $NHCOOCH_2$); 5.13 (*s*, 2 H, CH_2O); 5.20 (*d*, J = 4 Hz, 1 H, C*H*Ph); 5.81 (*d*, J = 8 Hz, 1 H, NHCO); 6.22 (*d*, J = 5 Hz, 1 H, NHCOO); 7.32 (*m*, 15 H, Ph). – CI.-MS.: 540 ($M^+ + 1 - H_2O$), 234 ($M^+ + 1 - PhCH_2OCONHCH(Ph)CONHCH{=}C{=}O$), 367 ($M^+ + 2 - OH - PhCH_2OOCC{=}C{=}O$).

$C_{30}H_{27}N_3O_8$ (557.11) Calc. C 64.63 H 4.84 N 7.54% Found C 64.39 H 4.75 N 7.51%

Preparation of 4-carboxy-3-hydroxy-7-phenylacetamido-isooxacephem (**10**). Compound **11a** (0.20 g, 0.48 mmol) in 30 ml AcOEt with $PdCl_2$ (60 mg) was hydrogenated at r.t. at 40 psi for 3 h. The mixture was then filtered and evaporated to give the crude product as a foam. Crystallization from EtOAc/ether 1:10 gave 0.07 g (45%) of **10**, m.p. 128–130°. – IR. (Nujol): 3150–3650 (OH, NH, COOH), 1783 (β-lactam), 1725 (C=C), 1680 (amide). – NMR. (DMSO/$CDCl_3$/D_2O): 3.52 (*s*, 2 H, CH_2); 3.60–3.31 (*m*, 2 H, $CHCH_2O$); 4.10–4.60 (*m*, 2 H, CHCHND); 7.38 (*s*, 5 H, Ph). – CI.-MS.: 301 ($M^+ + 1 - H_2O$), 300 ($M^+ + 1 - H_2O - H$), 218 ($M^+ + 2 - OH - HOOCC{=}C{=}O$), 118 ($PhCH_2C{\equiv}\overset{+}{N}H$).

Treatment of **10** with CH_2N_2 gave the corresponding methyl ester as an oil. – IR. (CH_2Cl_2): 3200–3500 (OH, NH), 1790 (β-lactam), 1755 (ester), 1735 ($O_2C{=}C$), 1680 (amide). – CI.-MS.: 333 ($M^+ + 1$), 315 ($M^+ + 1 - H_2O$), 218 ($M^+ + 2 - OH - CH_3OOCC{=}C{=}O$).

*Preparation of diethyl 2-[*cis*-(3-azido-2-oxo-4-styryl-1-azedinyl)]-2-nitrosomalonate resp. 2-[*cis*-(3-azido-2-oxo-4-styryl-1-azedinyl)]-*O*-nitrosomalonate* (**13** and **14**). To the β-lactam **1a** (0.372 g, 1 mmol) in 3 ml DMF and acetic anhydride (0.510 g, 5 mmol) was added dropwise the solution of 0.350 g (5 mmol) $NaNO_2$ in 1 ml water. The mixture was stirred at r.t. for 15 h. The water (20 ml) was added, and the product was extracted with ether. The ethereal solution was washed 4 times with water, dried and evaporated to give **13** and **14** quantitatively. Chromatography on silica gel with CH_2Cl_2 gave **14**, 0.2 g (49%) as an oil. – IR. (CH_2Cl_2): 2105 (N_3), 1800 (β-lactam), 1765 (ester), 1759 (O_2C=C), 1679 (ON=O), 1585, 1340, 1220 and 970. – ^{1}H-NMR. ($CDCl_3$): 1.31, 1.39 (2*t*, *J* = 7 Hz, 6 H, 2 CH_3); 4.33, 4.41 (2 *qa*, *J* = 7 Hz, 4 H, 2 CH_2); 4.88–5.27 (*m*, 2 H, $CHCHN_3$); 6.05 (*d*×*d*, *J* = 7 and 16 Hz, 1 H, C*H*=CHPh); 6.79 (*d*, *J* = 16 Hz, 1 H, CH=C*H*Ph); 7.32 (*m*, 5 H, Ph). – ^{13}C-NMR. ($CDCl_3$ at 0.00 ppm): 87.28 (C=O), 81.46 (N–C=O), 81.24 (OCO), 75.69 (O_2C=*C*), 61.28–50.22 (Ph), 49.74 (*C*Ph), 43.21 (*C*=CPh), 19.10 (*C*–C=C), –9.01 (CN_3), –12.14 (OCH_2), –14.13 (O=C–O*C*H_2), –63.44 (OCH_2CH_3), –63.77 (O=C–OCH_2CH_3). – EI.-MS.: 401 (M^+), 318 ($M^+ - N_3CH$=C=O).

$C_{18}H_{19}N_5O_6$ (401.43) Calc. C 53.86 H 4.73 N 17.45% Found C 53.59 H 4.91 N 17.32%

Compound **13**, 0.2 g (49%) was eluted with $CHCl_3$. – IR. (CH_2Cl_2): 2105 (N_3), 1770 (β-lactam), 1755 (ester), 1210 and 965 (N=O). – NMR. ($CDCl_3$): 1.36 (*t*, *J* = 7 Hz, 6 H, 2 CH_3); 4.21 (*qa*, *J* = 7 Hz, 4 H, 2 CH_2); 4.80–5.08 (*m*, 2 H, $CHCHN_3$); 5.91–6.40 (*m*, 1 H, C*H*=CHPh); 6.61 (*d*, *J* = 16 Hz, 1 H, CH=C*H*Ph); 7.31 (*m*, 5 H, Ph). – EI.-MS.: 318 ($M^+ - N_3CH$=C=O), 288 ($M^+ - N_3CH$=C=O–N=O).

$C_{18}H_{19}N_5O_6$ (401.43) Calc. C 53.86 H 4.73 N 17.45% Found C 54.01 H 4.69 N 17.28%

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