CROATICA CHEMICA ACTA CCACAA **69** (4) 1367–1376 (1996)

ISSN-0011-1643
CCA–2381

Original Scientific Paper

A New Stereoselective Route to Preparing Optically Active 2-Imino-penam Derivatives[†]

Jure J. Herak and Mladen Vinković*

PLIVA Research Institute, Prilaz baruna Filipovića 25, HR-10000 Zagreb, Croatia

Received April 17, 1996; revised May 27, 1996; accepted June 8, 1996

A novel and simple procedure for preparation of (5*R*,6*S*)-2-benzylimino-6-bromo-3-isopropylidene-penam **2** and (5*R*,6*S*)-2-benzylimino-3-isopropylidene-penam **8** is described. The 2-imino-penam derivatives are prepared by modification of the Cooper reductive rearrangement of 3α-benzylamide of penicillanic acid sulfoxides. The absolute configurations of starting sulfoxides and imino-products are assigned on the basis of ^{1}H-NMR spectroscopic studies and verified by X-ray structure analysis of sulfoxide **3b** and imino-penam **8**.

INTRODUCTION

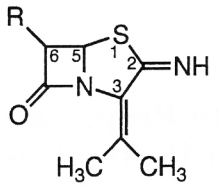
The reductive Cooper rearrangement,[1] is a well known procedure for the synthesis of thiazoline-azetidinone from penicillin. In its original form, the reductive rearrangement is performed on penicillin G sulfoxide with trimethyl phosphite. This type of rearrangement requires the use of carboxylic acid protective groups, such as esters, and the active 6-amido side-chains. When the formation of thiazoline-azetidinone is precluded or inhibited, other kinds of products are predominant.[2]

As a continuation of our research on the reactivity of the amide of penicillanic acid, and their cyclization to 2-azacepham derivatives,[3–5] we would like to report a new type of cyclization by modified Cooper rearrange-

[†] Dedicated to the memory of the late Professor Stanko Borčić.

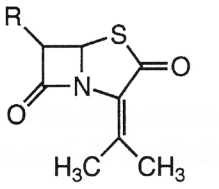
* Author to whom correspondence should be addressed.

ment, which involves a simple procedure for the preparation of novel 2-imino-penams **A**, as 2-*N*-analogs of the corresponding anhydropenicillins **B**.



2-imino-penams

A



anhydropenicillins

B

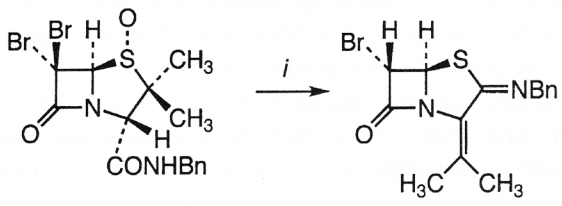
The rearrangement was performed by the action of phosphorous compounds like triethyl phosphite or triphenylphosphine onto 3α-benzylamide of penicillanic acid sulfoxides.

RESULTS AND DISCUSSION

Preparation of penicillanate sulfoxides has been intensively studied. Conversion of sulfides into sulfoxides may be carried out by many oxidizing agents. However, only a few of them allow selective oxidation. Recently, it was found that oxidation of 3α-amide- and 3α-benzylamide of penicillanic acid with *m*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane produced solely the (*R*)-sulfoxide.[6]

We have found that the enantiomerically pure (1*R*,5*R*)-3α-benzylamido-6,6-dibromopenicillanic acid sulfoxide **1**[6] under the Cooper rearrangement conditions (triethyl phosphite in benzene at boiling point, 13 h) led to the 2-imino-penam **2** in a one-pot process but in less than 10% yield (Scheme 1).

Formation of 3α-benzylamido-6α-bromo-penicillanic acid sulfoxides **3a** and **3b**, as products of 6β-monodehalogenation, was observed as isolable in-



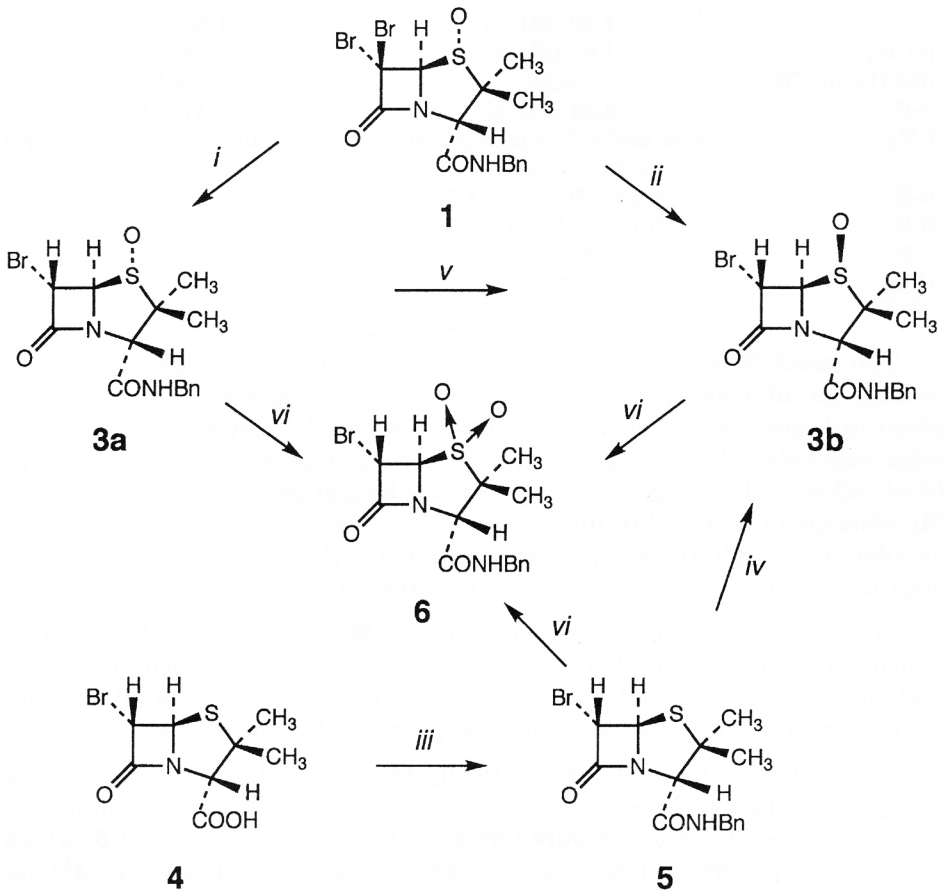
1 **2**

Scheme 1. Reagents and conditions: *i*, P(OEt)3/benzene/refl./13 h.

termediates in the first step of these procedure (Scheme 2). It was found that the stereochemical excess of the given sulfoxides was strongly influenced by the type of the phosphorous compound used.

Thus, treatment of (*R*)-sulfoxide **1** with triethyl phosphite in dichloromethane at low temperature (0 °C) for 15 minutes provided almost exclusively the less polar sulfoxide **3a**,[7] isolated in a pure state by short-column chromatography and crystallization from diethyl ether (Scheme 2).

On the other hand, the reaction of 6β-monodehalogenation of (1*R*,5*R*)-**1** with triphenylphosphine under the same reaction conditions occurred with complete inversion of the configuration at sulfur and gave the (1*S*,5*R*)-**3b**[7] in 60% yield.



Scheme 2. Reagents and conditions: *i*, $P(OEt)_3/CH_2Cl_2/0$ °C/15 min.; *ii*, $P(Ph)_3/CH_2Cl_2/0$ °C/15 min.; *iii*, $EtOCOCl/Et_3N/BnNH_2/5$ °C/2 h.; *iv*, *m*-CPBA/CH_2Cl_2/r.t./2 h.; *v*, benzene/refl./30 h.; *vi*, $KMnO_4$/EtOAc.

A variety of experiments were carried out in order to determine the optimum reaction conditions for the preparation of sulfoxides **3**. Thus, we found that an excess of phosphorous compound (*ca.* 2 mole) in dichloromethane provided the best results.

The relative stereochemical assignment for the sulfoxides **3a** and **3b** was deduced from their ^{1}H-NMR spectroscopy. The data are summarized in Table I.

TABLE I.

^{1}H-NMR data for sulfoxides **3a** and **3b**

Position	**3a**	**3b**
α-CH_3	1.39 (3H, s)	1.24 (3H, s)
β-CH_3	1.67 (3H, s)	1.78 (3H, s)
(β-CH_3)-(α-CH_3)	**0.28**	**0.54**
2-H	**4.34** (1H, s)	**4.47** (1H, s)
CH_2	4.40 and 4.50 each (1H, dd)	4.37 and 4.57 each (1H, dd)
	J = 5.5, 6.5 and 14.5	J = 6.0, 6.5 and 14.5
6-H	4.64 (1H, d, J = 1.5)	4.97 (1H, d, J = 1.5)
5-H	5.14 (1H, d, J = 1.5)	5.12 (1H, d, J = 1.5)
NH	6.90 (1H, br)	6.90 (1H, br)
C_6H_6	7.27–7.40 (5H, m)	7.23–7.38 (5H, m)

The small (5-H)-(6-H) coupling constant (J = 1.5 Hz) assigned *trans*-geometry, *i.e.* alfa-configuration at C-6 which was consistent with the data given in literature.[8] In accord with literature results concerning penicillins ester sulfoxides,[9,10] the larger shift difference for the geminal methyl groups (0.54) allowed the assignment of the (*S*)-configuration at the sulfur atom in **3b**, whereas in **3a** the shift differences for the same methyl groups are much smaller, (0.28) indicating a (*R*)-configuration. On the other hand, a downfield shift for 3-H due to a *syn*-axial effect is observed in the case of (*S*)-isomer.[11]

The X-ray structure analysis of sulfoxide **3b** (Figure 1, Table II) established the conformation of thiazolidine ring with *syn*-axial position for 3-H and, at the same time, determined the absolute configuration of all four chiral centers and confirmed structure **3b** proposed by the ^{1}H-NMR studies.[12]

An identical sample of the kinetically favoured sulfoxide **3b**[13] was also obtained through a three step synthesis. The process included a mild oxidation of 3α-benzylamide of pure (5*R*,6*S*)-6-bromopenicillanic acid **5**, which was prepared starting from pure (5*R*,6*S*)-6-bromopenicillanic acid **4**[14] *via* mixed anhydride according to a method described earlier for the preparation of sulfoxide **1**.[6] The structure of the two epimeric sulfoxides **3a** and **3b** was additionally confirmed by oxidation with $KMnO_4$, giving the same sulfone **6** in both cases.

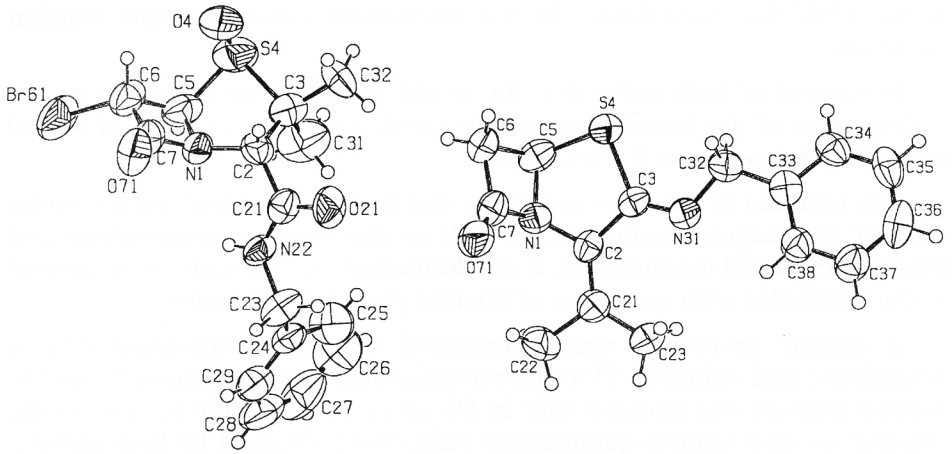


Figure 1. The TEP views of (2*S*,4*S*,5*R*,6*S*)-2-benzylcarbamoyl-6-bromo-3,3-dimethyl--7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-4-oxide (**3b**) and (5*R*)-3-benzylimino-2-isopropylidene-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane (**8**).

Next, we wanted to check if the kinetically favoured sulfoxide **3b** was also thermodynamically more stable. Therefore, we thermally treated enantiomerically pure samples of **3a** and **3b**. It was found that (*R*)-sulfoxide **3a** almost completely epimerized to thermodynamically more stable (*S*)-sulfoxide **3b** at the boiling point of dry benzene for 30 hours. At higher temperature (reflux of toluene), the epimerization of **3a** completely occurred after 2

TABLE II.

Summary of some essential crystallographic data for sulfoxide **3b** and imino-penam **8** derivative[a]

	3b	8
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
a/Å	9.798(3)	5.295(6)
b/Å	18.752(4)	11.559(8)
c/Å	19.246(2)	11.698(11)
β/deg	90	90.64(8)
V/Å^3	3536.1(14)	715.9(12)

[a] X-ray diffraction data were measured on a Phillips PW 1100 diffractometer modified by Stoe & Cie with Mo-Kα radiation and graphite monochromator. For further details of the crystal structure determinations see Ref. 12.

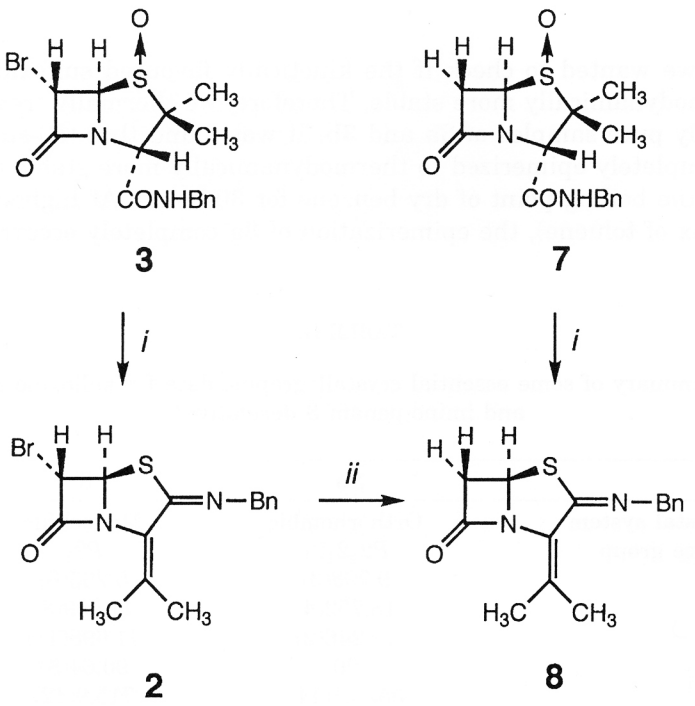
hours, while the (*S*)-sulfoxide **3b** was unchanged under the same reaction conditions.

Treatment of both sulfoxides (**3a** or **3b**) with triethyl phosphite at the boiling point of dry benzene or toluene (with azeotropic removal of water) leads to 2-imino-penam **2** (Scheme 3).

The outcome of the rearrangement was highly dependent on the molar ratio of the reagents employed, as well as the reaction temperature and time. After careful optimization, **2** was formed in *ca.* 70% yield by treatment of the sulfoxides with an excess of triethyl phosphite (5 moles).

A similar procedure was investigated to convert 6,6-unsubstituted penicillanic acid sulfoxide **7**[3] to the corresponding 2-imino-penam **8**, but the desired product was isolated only in 5% yield. Much better results on the preparation of **8** (almost quantitative yield) were obtained by hydrodehalogenation of the imino-penam **2** in the presence of 10% Pd/C catalyst.

The structure of thus obtained imino-penams were unambiguously established through the X-ray diffraction study of a suitable single crystal of imino-penam **8** and the TEP plot is shown in Figure 1 (Table II).



Scheme 3. Reagents and conditions: *i*, $P(OEt)_3$/benzene/refl./13 h.; *ii*, H_2/Pd/C/EtOAc/r.t./2 atm.

In conclusion, this work describes a simple route to the diastereoselective synthesis of penicillanic acid sulfoxides **3a** and **3b**. These compounds exhibit a peculiar chemical and spectroscopic behaviour and can be easily transformed through intramolecular cyclization into enantiomerically pure 2-imino-penam derivatives which are potentially valuable intermediates for further transformation to chiral 4-acetoxy-2-azetidinone or to other nonclassical β-lactams.

EXPERIMENTAL

M.p. were determined by a Fisher-Johns apparatus and were uncorrected. IR spectra were recorded using a Perkin-Elmer Model 257 G spectrometer. ^{1}H-NMR spectra were recorded using Jeol FX 90Q and Varian Xl-GEM 300 spectrometers. Chemical shifts δ_H were in ppm downfield from Me_4Si, and J values were given in Hz. Specific rotations were recorded at 589 nm [sodium D line] on a Jasco DIP-360 polarimeter using a 1 dm cell. TLC was run on Merck Kieselgel HF_{254} plates and spots were visualized under UV light or I_2 vapour adsorption. Column chromatography was performed on Merck Kieselgel 60 (70-230 mesh ASTM) activated at 105 °C.

(2S,4R,5R,6S)-2-Benzylcarbamoyl-6-bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptane-4-oxide ***(3a)***

A solution of sulfoxide **1** (232 mg, 0.5 mmol) triethyl phosphite (167 mg, 1 mmol) in dry dichloromethane (30 mL) was stirred at 0 °C. After 15 minutes the TLC analysis showed that the starting sulfoxide was not present in the reaction mixture. Cold water (20 mL) was then added to the resulting mixture. The layers were separated and the organic layer was quickly washed with aq. sodium hydrogen carbonate (10 mL) and with water. Evaporation of the dry (Na_2SO_4) organic layer under reduced pressure gave an oily residue, which after purification by silica gel column chromatography eluted with dichloromethane-ethyl acetate 2 : 1, gave sulfoxide **3a** (104 mg, 54.4%). Crystallization from diethyl ether afforded a white crystalline solid: m.p. 134–135 °C; R_f = 0.40 [dichloromethane-ethyl acetate (2 : 1, v/v)]; $[\alpha]_D^{20}$ = + 179 (c = 1, CH_2Cl_2); IR (KBr) ν_{max}/cm^{-1}: 3295s, 2980m, 1790vs, 1655 s, 1530m, 1280m, 1240m, 1050s.

Anal. Calcd. for $C_{15}H_{17}BrN_2O_3S$ (M_r = 385.27): C 46.76, H 4.45, N 7.27, S 8.32; found: C 46.45, H 4.50, N 7.15, S 8.10 %.

(2S,5R,6S)-2-Benzylcarbamoyl-6-bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]-heptane ***(5)***

To a cooled solution (0 °C) of carboxylic acid **4**[14] (1400 mg, 5 mmol), triethylamine (616 mg, 6.1 mmol) and dichloromethane (15 mL), the solution of ethyl chloroformate (620 mg, 5.7 mmol) in dichloromethane (5 mL) was added dropwise. After being stirred for 30 minutes, a solution of benzylamine (5%) in dry dichloromethane was added dropwise until the pH was adjusted to 7.5. The mixture was allowed to warm to room temperature and stirred for a further hour, then washed with water and with diluted hydrochloric acid (10 mL). The organic phase was washed with water once more and dried (Na_2SO_4). Evaporation of the organic layer under reduced pressure gave an amorphous residue which was purified by silica gel chromatogra-

phy with dichloromethane-ethyl acetate (gradient elution) and gave amide **5** (1167 mg, 63.2 %) as white foam: R_f = 0.34 [dichloromethane-ethyl acetate (5 : 1, v/v)]; IR (film) ν_{max}/cm^{-1}: 3300m, 1785vs, 1660s, 1530s, 1450m, 1300m, 1230m; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.47 and 1.71(each 3 H, s, CMe_2), 4.35(1 H, s, 2-H), 4.35 and 4.49 each (1 H, dd, J = 6.0, 6.5 and 14.5, CH_2), 4.74(1 H, d, J = 0.5, 6-H), 5.24(1 H, d, J = 0.5, 5-H), 6.92(1 H, br, NH), 7.24–7.43(5 H, m, C_6H_5);

Anal. Calcd. for $C_{15}H_{17}BrN_2O_2S$ (M_r = 369.27): C 48.79, H 4.64, N 7.59, S 8.68; found: C 48.50, H 4.32, N 7.45, S 9.00 %.

(2S,4S,5R,6S)-2-Benzylcarbamoyl-6-bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptane-4-oxide ***(3b)***

(a): A solution of sulfoxide **1** (232 mg, 0.5 mmol) triphenylphosphine (262 mg, 1 mmol) in dry dichloromethane (20 mL) was stirred at 0 °C. for 15 minutes. Cold water (20 mL) was then added to the resulting mixture. The layers were separated and the organic layer was washed with aq. sodium hydrogen carbonate (10 mL) and with water. Evaporation of dry (Na_2SO_4) organic layer under reduced pressure gave a foamy residue which, after purification by silica gel chromatography eluted with dichloromethane-ethyl acetate 2 : 1, gave sulfoxide **3b** (115 mg, 60%). A small sample was recrystallized from diethyl ether giving an analytical sample as a white crystalline solid: m.p. 141–143 °C; R_f = 0.45 [dichloromethane-ethyl acetate (2 : 1, v/v)]; $[\alpha]_D^{20}$ = + 213 (c = 1, CH_2Cl_2); IR (KBr) ν_{max}/cm^{-1}: 3335m, 2980m, 1795vs, 1660 s, 1525m, 1275m, 1040m.

Anal. Calcd. for $C_{15}H_{17}BrN_2O_3S$ (M_r = 385.27): C 46.76, H 4.45, N 7.27, S 8.32; found: C 46.55, H 4.32, N 7.50, S 8.15%.

(b): A solution of penicillamide **5** (1849 mg, 5 mmol) and *m*-chloroperbenzoic acid (55%, 2510 mg, 8.0 mmol) in dichloromethane (50 mL) was stirred at room temperature for 2 hours. The reaction mixture was then washed with 5% aqueous $Na_2S_2O_5$ (40 mL), saturated aqueous $NaHCO_3$ (40 mL) and water. The dry (Na_2SO_4) organic layer was evaporated under reduced pressure which, after trituration with diethyl ether, gave sulfoxide **3b** (51.4%) of spectroscopic properties identical to those described above.

(2S,5R,6S)-2-Benzylcarbamoyl-6-bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]-heptane-4,4-dioxide ***(6)***

(a): Sulfoxide **3a** (192 mg, 0.5 mmol) was dissolved in 80% acetic acid (2 mL) and ethyl acetate (10 mL), cooled to 5 °C and the saturated aq. solution of $KMnO_4$ was added under cooling and stirring as long as the rose colour persisted. After addition of water (20 mL), the solution was discoloured by 30% solution of H_2O_2. The layers were separated and the organic layer was washed with water, saturated aq. solution of $NaHCO_3$, dried (Na_2SO_4) and filtered. After evaporation of the organic layer under reduced pressure, sulfone **6** (152 mg, 76%) was obtained as a white crystalline solid: m.p. 171–173 °C (ethanol); R_f = 0.53 [benzene-ethyl acetate (3 : 1, v/v)]; $[\alpha]_D^{20}$ = + 161 (c = 1, CH_2Cl_2); IR (KBr) ν_{max}/cm^{-1}: 3320s, 3290s, 1810vs, 1660vs, 1550m, 1490m, 1330s, 1320s, 1160m, 1115m; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.42 and 1.70 each (3 H, s, CMe_2), 4.23(1 H, s, 2-H), 4.39 and 4.59 each (1 H, dd, J = 5.5, 6.5 and 15.0, CH_2), 4.65(1 H, d, J = 1.5, 6-H), 5.22(1 H, d, J = 1.5, 5-H), 6.83(1 H, br, NH), 7.21–7.40(5 H, m, C_6H_5).

Anal. Calcd. for $C_{15}H_{17}BrN_2O_4S$ (M_r = 401.27); C 44.89, H 4.27, N 6.97; found: C 44.67, H 4.22, N 7.25 %.

(b): Sulfoxide **6** was also obtained by treatment of sulfoxide **3b** with a saturated aq. solution of $KMnO_4$ according to the above method *(a)*.

(c): Sulfoxide **6** was also obtained by treatment of sulfide **5** with a saturated aq. solution of $KMnO_4$ according to the above method *(a)*.

(5R,6S)-3-Benzylimino-6-bromo-2-isopropylidene-7-oxo-4-thia-1-azabicyclo[3.2.0]-heptane ***(2)***

(a): A suspension of sulfoxide **3a** (200 mg, 0.52 mmol) triethyl phosphite (432 mg, 2.7 mmol) in dry benzene (30 mL) was stirred and gradually warmed until at reflux. TLC analysis showed that the starting sulfoxide was not present in the reaction mixture after 13 hours. The residue was purified by silica gel column chromatography eluted with toluene to give the imino-penam **2** (129 mg, 71%) as a white crystalline solid: m.p. 64–66 °C (diethyl ether); R_f = 0.55 (toluene); $[\alpha]_D^{20}$ = + 85 (c = 1, CH_2Cl_2); IR (film) ν_{max}/cm^{-1} 2990w, 2910w, 1790vs, 1630vs, 1450w, 1350m, 1300s, 1160m, 1090m, 1030m; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.12 and 2.30 each (3 H, s, CMe_2), 4.50 and 4.57 each (1 H, d, J = 16.5, CH_2), 4.92(1 H, d, J = 1.0, 6-H), 5.29(1 H, d, J = 1.0, 5-H), 7.25–7.36(5 H, m, C_6H_5); MS m/z M^+ 351.

Anal. Calcd. for $C_{15}H_{15}BrN_2OS$ (M_r = 351.25): C 51.29, H 4.35, N 7.58, found: C 49.87, H 4.22, N 7.35 %.

(b): Imino-penam **2** was also obtained by the treatment of sulfoxide **3b** with triethyl phosphite according to the above method *(a)*.

(5R)-3-Benzylimino-2-isopropylidene-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane ***(8)***

(a): To a suspension of imino-penam **2** (200 mg, 0.57 mmol), sodium hydrogen carbonate (5% aq. solution, 15 mL) in ethyl acetate (20 mL), at room temperature 10% Pd-C catalyst (100 mg), was added. The reaction flask was evacuated and filled with hydrogen gas (2 atm) and the mixture was stirred until no further uptake of hydrogen was observed. The suspension was filtered through Celite, and the layers separated. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography with toluene to give the imino-penam **8** (148 mg, 95%) as a white crystalline solid: m.p. 73–74 °C (diethyl ether); R_f = 0.28 (toluene); $[\alpha]_D^{20}$ = + 233 (c = 1, CH_2Cl_2); IR (film) ν_{max}/cm^{-1}: 2960w, 2910w, 1780vs, 1630vs, 1450w, 1410m, 1350s, 1300vs, 1250m, 1220m, 1200m, 1150w, 1100m, 1010m; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.09 and 2.30 each (3 H, s, CMe_2), 3.27(1 H, d, J = 1.5, 6β-H), 3.73(1 H, d, J = 4.0, 6α-H), 4.51 and 4.57 each (1 H, d, J = 17, CH_2), 5.19(1 H, dd, J = 1.5 and 4.0, 5-H), 7.23–7.38(5 H, m, C_6H_5); MS m/z M^+ 272.

Anal. Calcd. for $C_{15}H_{16}N_2OS$ (M_r = 272.35): C 66.07, H 5.92, N 10.26, found: C 66.14, H 5.92, N 10.29%.

(b): Imino-penam **8** was also obtained by the treatment of sulfoxide **7**[3] with triethyl phosphite according to the method for preparation **2** in very poor yield (5%).

Acknowledgment. – The authors thank M. Kovačević, D. Sc., and I. Lukić, M. Sc., for their valuable discussions and help in preparing this manuscript. This work was supported by the Ministry of Science and Technology of the Republic of Croatia.

REFERENCES

1. R. D. G. Cooper and F. L. Jose, *J. Am. Chem. Soc.* **92** (1970) 2575–2576.
2. R. D. G. Cooper and D. O Spry, *Rearrangements of Cephalosporins and Penicillins*, in: E. H. Flynn (Ed.), *Cephalosporins and Penicillins*, Academic Press, New York, 1972, p 201.
3. J. J. Herak, M. Vinković, and I Lukić, *Tetrahedron* **51** (1995) 5083–5092.
4. J. J. Herak, M. Vinković, Z. Mandić, I. Lukić, M. Tomić, and M. Kovačević, *Tetrahedron: Asymmetry* **5** (1994) 1605–1612.
5. J. J. Herak, *Sulfur Reports* **18** (1996) 379–396.
6. D. U. Belinzoni, E. L. Setti, and O. A. Mascaretti, *J. Chem. Research* (1988) (*S*), 176–177; (*M*) 1501–1533.
7. Judged from the ^{1}H-NMR spectrum and TLC of the crude reaction mixture.
8. P. V. DeMarco and R. Nagarajan, in: E. H. Flynn (Ed.), *Cephalosporins and Penicillins*, Academic Press, New York, 1972, p. 330.
9. R. D. G. Cooper, P. V. DeMarco, J. C. Cheng, and N. D. Jones, *J. Am. Chem. Soc.* **91** (1969) 1408–1415.
10. A. J. Vlietinck, E. Roets, H. Vanderhaeghe, and S. Toppet, *J. Org. Chem.* **39** (1974) 441–444.
11. R. A. Archer and P. V. DeMarco, *J. Am. Chem. Soc.* **91** (1969) 1530–1532.
12. M. Vinković and J. J. Herak, to be published
13. Similar data were given for 6α-halopenicillinates: P. J. Claes, H. Vanderhaeghe, E. Roets, J. Thomis F. DeMeester, and J. L. Piette *J. Antibiotics* **38** (1985) 75–82.
14. G. Cignarella G. Piffieri, and E. Testa *J. Org. Chem.* **27** (1962) 2668–2669

SAŽETAK

Novi stereoselektivni put priprave optički aktivnih derivata 2-imino-penama

Jure J. Herak i Mladen Vinković

Opisan je jednostavan postupak za pripravu (5*R*,6*S*)-3-benzilimino-6-bromo-2-izopropiliden-7-okso-4-tia-1-azabiciklo[3.2.0]heptana **2** and (5*R*,6*S*)-3-benzilimino-2-izopropiliden-7-okso-4-tia-1-azabiciklo[3.2.0]heptana **8**. Derivati 2-imino-penama su priređeni modificiranom Cooper-ovom reduktivnom pregradnjom sulfoksida 3α-benzilamida penicilanske kiseline. Apsolutne konfiguracije polaznih sulfoksida i imino-produkata su određene na osnovi ^{1}H-NMR spektroskopske studije i potvrđene rentgenskom strukturnom analizom sulfoksida **3b** i imino-penama **8**.