ACTA SCIENTIFICA NATURALIS

SPECIAL ISSUE
Dedicated to our colleague and friend Prof. Valerij Christov on the occasion of his 60th anniversary

VOLUME 2/2015

Dobromir D. Enchev, Editor

ISSN 2367-5144

Content

Regioisomeric hydroxynaphthadehydes derived chiral 1-phenylethylimines as auxiliaries in *trans-β*-lactam formation *via* Staudinger cycloaddition. Influence of the hydroxyl group position on the reaction output.

Vanya Kurteva[1]*, Atanas Kurutos[1,2], Boris Shivachev[3], Rositsa Nikolova[3]

[1] *Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Acad. G. Bonchev str., bl. 9, 1113 Sofia, Bulgaria*

[2] *Sofia University "St. Kliment Ohridski", Faculty of chemistry and pharmacy, 1, blv. J. Bourchier, 1164 Sofia, Bulgaria*

[3] *Institute of Mineralogy and Crystallography "Acad. Ivan Kostov", Bulgarian Academy of Sciences, Acad. G. Bonchev str., bl. 107, 1113 Sofia, Bulgaria*

E-mail: vkurteva@orgchm.bas.bg

Dedicated to our colleague and friend Prof. Valerij Christov on the occasion of his 60th anniversary

***Abstract:** The efficiency of enantiomeric 1-phenylethylamines and regioisomeric 2- and 4-hydroxynaphthadehydes derived imines as auxiliaries in trans-β-lactam formation via Staudinger cycloaddition was studied. The structures were assigned by 1D and 2D NMR techniques including variable temperature experiments. The influence of the hydroxyl group position on the reaction output is discussed. The absolute configurations of the products were determined by NMR spectra and confirmed by single crystal X-ray diffraction.*

***Keywords:** trans-β-lactams, Staudinger cycloaddition, regioisomeric hydroxynaphthaldehydes, 1-phenylethylamine, NMR, single crystal XRD.*

Introduction

β-Lactam antibiotics are among the most prescribed classes antimicrobial agents till nowadays [1]. As their therapeutic properties are strongly dependent on the ring stereochemistry [2], extraordinary efforts are devoted to stereoselective azetidinone ring construction [3]. Staudinger [2+2] ketene-imine cycloaddition is a fundamental protocol for *β*-lactam synthesis [4]. The asymmetric version is usually achieved by applying chiral auxiliary to induced chirality [5]; mainly chiral ketene precursors.

Recently, we reported on the chiral amine induced stereoselectivity in *trans-β*-lactam formation *via* Staudinger cycloaddition [6]. The products were obtained diastereoselectively as pairs of *trans*-C_3,C_4-configuration with moderate "enantioselectivity" in respect to azetidinone ring, diastereoselectivity in fact as the chiral auxiliary configuration is constant, up to 54 % *de*. It was found that the selectivity is dependent both on the chiral auxiliary and aldehyde components of the imine. The best results were obtained by aldehydes with oxygen containing substituents; methoxy or bulky *O*-acyl group. In an attempt to improve the selectivity, several elements are varying, chiral amine, ketene precursor and aromatic aldehyde.

Herein, the chiral auxiliary efficiency of imines composed of enantiomeric 1-phenylethylamines and regioisomeric hydroxynaphthadehydes in *trans-β*-lactam formation *via* Staudinger cycloaddition is presented.

Materials and Methods

All reagents were purchased from Sigma-Aldrich and were used without any further purification. The deuterated solvents were purchased from Deutero GmbH. The HPLC grade solvents were purchased from Labscan. Fluka silica gel (TLC-plates 60778 with fluorescent indicator 254 nm) were used for TLC chromatography. Merck Silica gel 60 (0.040-0.063 mm) was used for flash chromatography purification of the products. The NMR spectra were recorded on a Bruker Avance II+ 600 spectrometer (Rheinstetten,

Germany) at 25°C; the chemical shifts were quoted in ppm in δ-values against tetramethylsilane (TMS) as an internal standard. The assignment of the signals was confirmed by applying 2D techniques. The spectra were recorded as $3x10^{-2}$ M solutions in order to avoid intermolecular interactions in NOESY experiments. The spectra were processed with Topspin 2.1 program.

The high performance liquid chromatography (HPLC) separations were performed on an Agilent 1100 System fitted with diode array detector and manual injector with a 20 µl injection loop. A stainless-steel Nucleosil Chiral-2 column (Macherey-Nagel GmbH &Co. KG, Düren, Germany) was used; 250x4 mm, particle size 5 µm, pore size 100 Å, chiral selector *N*-(3,5-dinitrobenzoyl)-*D*-phenylglycine. The analyses were performed at 25°C with a flow rate of 1.0 ml/min.

The azetidinones **4** were obtained *via* the following synthetic protocol:

A mixture of 2- or 4-naphthaldehyde (1 mmol) and 1-phenylethylamine (1 mmol) was grinded in a mortar. The solid phase formed was triturated with hexane and dried in desiccator to give imines **3** in quantitative yields.

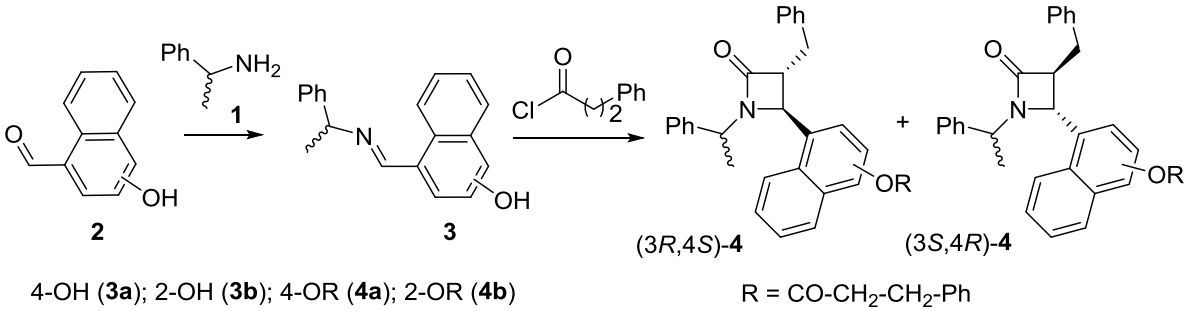
To a refluxing solution of imine **3** (1 mmol) and Et_3N (3 mmol) in xylene (15 ml) 3-phenylpropionyl chloride (2 mmol) was added and the mixture was refluxed for 3 h. The products were partitioned between water and xylene. The organic phase was washed with brine, dried over Na_2SO_4, evaporated to dryness, and purified by flash chromatography on silica gel. The results are summarized on Table 1.

The crystal of (*S*)-(3*R*,4*S*)-**4b** was mounted of on a glass capillary and all geometric and intensity data were taken from this crystal [7]. Crystallographic measurements were taken on an Agilent Supernova Dual diffractometer equipped with an Atlas CCD detector using micro-focus Mo Kα radiation (λ = 0.71073 Å) at room temperature. The determinations of the unit cell parameters, data collection and reduction were performed with Crysalispro software [8]. The structure was solved by direct methods and refined by the full-matrix least-squares method on F^2 with ShelxS and ShelxL 2013 programs [9]. All non-hydrogen atoms, were located successfully from Fourier maps and were refined anisotropically. Hydrogens adjoining were generated geometrically. Most important crystallographic and refinement indicators are listed on Table 3.

Results and Discussion

The title compounds were designed based on two main features. First, we already found that a bulky acyl substituent at *o*-position, obtained from o-vaniline hydroxyl and acyl chloride, led to moderate selectivity; 44 % *de* [6a]. Second, the compounds offer unlimited possibilities for *O*-derivatization after acyl group hydrolysis.

The desired *β*-lactams **4** were obtained by two step protocol as shown on Scheme 1. Enantiomeric 1-phenylethylamines **1**, one of the cheapest chiral amines on the market, were converted quantitatively into imines **3** by grinding with 2- or 4-hydroxynaphthaldehyde (**2**) in the absence of solvent. Staudinger cycloaddition was carried out in refluxing xylene with 3-phenylpropionyl chloride as a ketene precursor and triethylamine as a base. The acyl chloride was used in two-fold excess due to the presence of free hydroxyl group in **3**.



Scheme 1. Synthesis of azetidinones **4**.

The reaction was fast and efficient. The starting imines were fully consumed after 3 h reflux. The target 1,3,4-trisubstituted azetidin-2-ones possessing bulky *O*-3-phenylpropionyl substituent in naphthalene unit were obtained in good to excellent yields, 73-93 % after flash chromatography purification. As seen on Table 1, **3b** was more efficient than **3a** in the reaction studied; 89-93 % *vs* 73 %, respectively.

Table 1. Synthesis of azetidinones **4**.

Imine	**Azetidin-2-one**			
	Compd.	**Ring configuration**[a]	**Yield, %**[b]	***de*, %**[c]
(*S*)-**3a**	**4a**	(3*R*,4*S*)+(3*S*,4*R*)	73	26
(*S*)-**3b**	**4b**	(3*R*,4*S*)+(3*S*,4*R*)	89	52
(*R*)-**3b**	**4b**	(3*S*,4*R*)+(3*R*,4*S*)	93	52

[a]The major less polar diastereoisomer is given first; [b]Isolated yields after flash chromatography; [c]Determined from the ^{1}H NMR spectra of the crude reaction mixtures.

The configuration of the products and, respectively, the cycloaddition diastereoselectivety were determined by NMR spectra. The assignment of the signals was achieved by applying 2D techniques. In the case of **4b**, the spectra at room temperature showed characteristic pattern for exchange between two sites due to the steric hindrance around C_3-naphthyl bond caused by the bulky *O*-substituent. For that reason, variable temperature experiments were performed in DMSO-d_6 and finally, 1D and 2D spectra were recorded at 100°C (373K), where almost all signals are coalesced. Selected proton resonances are listed on Table 2.

Table 2. Selected ^{1}H NMR data for the isomeric azetidin-2-ones **4a** ($CDCl_3$, 298K) and **4b** (DMSO-d_6, 373K).

Azetidin-2-one	**C*H*-3 (m)**	**C*H*-4 (d), J**	**C*H*-CH$_3$ (q), J**	**C*H$_3$*-CH (d), J**
(*S*)-(3*R*,4*S*)-**4a**	3.282	4.684, 2.0	4.188, 7.2	1.660, 7.2
(*S*)-(3*S*,4*R*)-**4a**	3.336	4.673, 2.0	4.795, 7.2	1.304, 7.2
(*S*)-(3*R*,4*S*)/(*R*)-(3*S*,4*R*)-**4b**[a]	3.765	4.901, 2.2	4.098, 7.1	1.559, 7.1
(*S*)-(3*S*,4*R*)/(*R*)-(3*R*,4*S*)-**4b**[a]	3.761	5.029, 2.2	4.740, 7.2	1.051, 7.1

[a] Enantiomeric couple.

The diastereoselectivities were determined from the integral intensities of signals in areas free of other signals in proton NMR spectra of the crude reaction mixtures. In the case of **4b** where the signals are broad at room temperature, the isomeric ratios were additionally estimated by HPLC on chiral stationary phase. The conditions were varied and excellent separation was achieved, t_R-1 16.69 min and t_R-2 25.58 min, by using hexane/iso-propanol 95/5 as a mobile phase with a flow rate of 1.0 ml/min. The results were in full agreement with those obtained by NMR. As seen on Table 1, good selectivities were achieved for 2-hidroxynaphthaldehyde derived *β*-lactams **4b**, while (*S*)-**3a** was almost ineffective as chiral auxiliary. For that reason, combined with the fact that we have never detected significant differences in the efficiency of both enantiomers of the chiral auxiliary [6], the transformation was performed only with (*R*)-**3b**.

The products were obtained diastereoselectively as pairs of isomers with the desired *trans*-C_3,C_4-configuration; J_{34} 2.0-2.2 Hz. No *cis*-azetidinone formation was observed. So, two diastereoisomers of **4a** with (*S*)-(3*S*,4*R*) and (*S*)-(3*R*,4*S*) configuration and both enantiomeric couples of *trans*-azetidinone **4b**,

(*S*)-(3*S*,4*R*)/(*R*)-(3*R*,4*S*) and (*S*)-(3*R*,4*S*)/(*R*)-(3*S*,4*R*), were obtained. In all cases, the less polar compound was predominant. The isomeric ratios (Table 1) show that the presence of a bulky *O*-acyl group at *o*-position in naphthyl rings possesses significant superiority over its *p*-regioisomer in both conversion and selectivity; 73 % with 26 % *de vs* 89-93 % with 52 % *de*. The diastereoselectivities in **4b** formation, 52 % *de*, were identical with those achieved from 2,4,6-trimethoxybenzaldehyde derived imines [6a], the best results till now. However, **4b** were obtained in better yields than the corresponding 2,4,6-trimethoxybenzyl compounds, which makes 2-hydroxynaphthaldehyde a good candidate for further studies.

The absolute configurations of the products were assigned from their NMR spectra. In all cases, characteristic up-fielding of the quartet for C*H*-CH_3 and down-fielding of the doublet for CH_3-CH of the chiral auxiliary in the less polar isomers were observed independently on the solvent and temperature (Table 2, Figure 1).

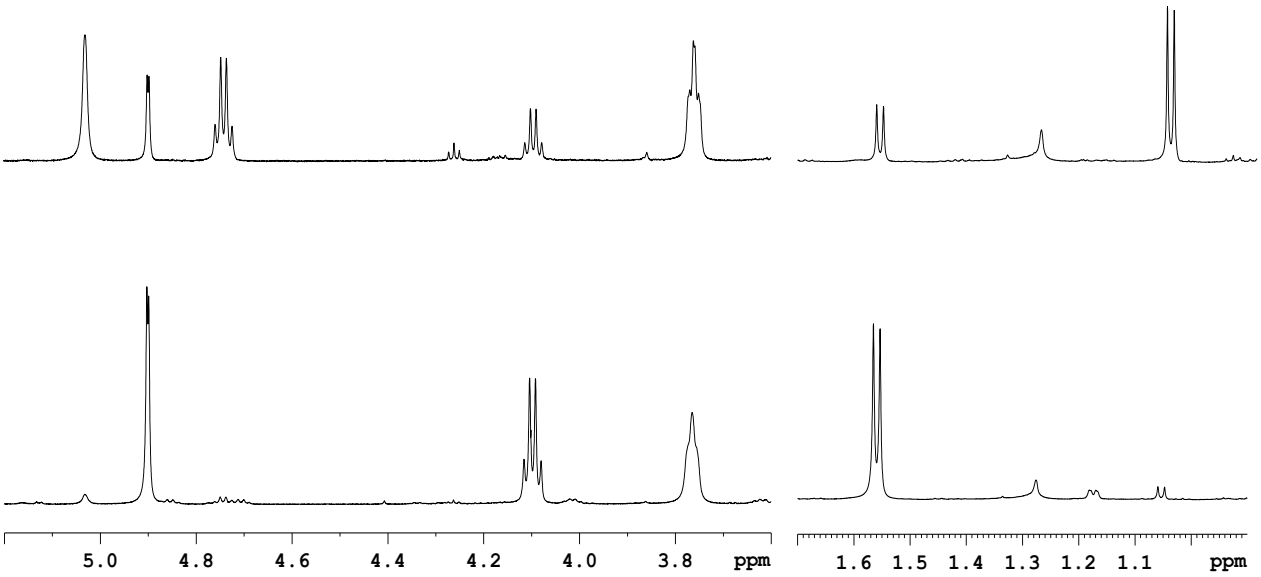


Figure 1. Parts of ^{1}H NMR spectra of less polar isomer (down) and enriched to more polar isomer fraction (up) of **4b** in DMSO-d_6 at 373K.

The same pattern was observed in the spectra of analogues 1-phenylethylamine derived azetidinones [6a] with known configuration. Methylene resonances at 4.08-4.32 ppm and 4.80-4.94 ppm and methyl group signals at 1.53-1.71 ppm and 1.19-1.33 ppm were registered for (*S*)-(3*S*,4*R*)/(*R*)-(3*R*,4*S*) and (*S*)-(3*R*,4*S*)/(*R*)-(3*S*,4*R*) compounds, respectively. Based on this obvious similarity, it can be assumed that less polar isomers possess (*S*)-(3*R*,4*S*) and (*R*)-(3*S*,4*R*) configuration, while more polar are (*S*)-(3*S*,4*R*) and (*R*)-(3*R*,4*S*) isomers.

This suggestion was confirmed by single crystal X-ray diffraction. Appropriate crystal phase of less polar (*S*)-**4b** isomer was grown by slow evaporation of benzene solution. The core of the molecule of **4b** is an azetidine (actually azetidin-2-one) cycle that supports four distinct aromatic fragments; toluene (substituent at position 3), ethylbenzene (side-chain 1-phenyl ethyl), 2-oxonaphthalene (2-oxoacylnaphthalene at position 4) and 3-phenylpropanal (naphthalene substituent). Thus the produced molecule is relatively voluminous with a sphere of enclosure of 7.6 Å (Figure 2).

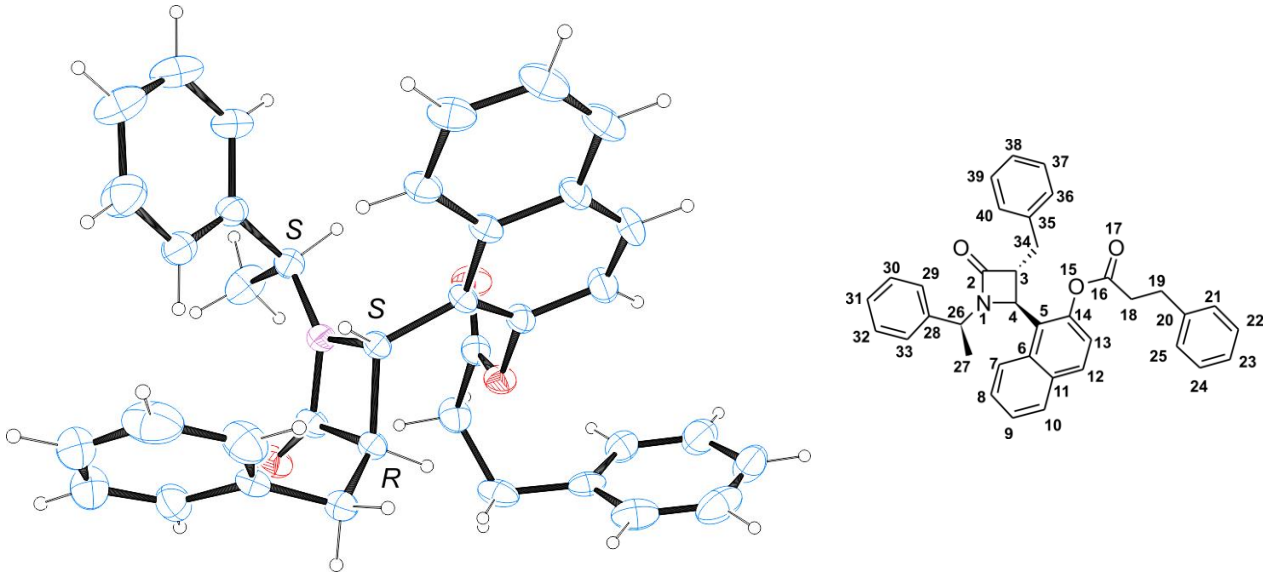


Figure 2. ORTEP view of (*S*)-(3*S*,4*R*)-**4b** and the atomic numbering scheme; ellipsoids are drawn at 50% probability, hydrogen atoms are shown as small spheres with arbitrary radii.

The bond distances and angles (Table 4) are similar to the values reported in the literature for such type of molecules and ring systems [6*a*,10]. The aromatic rings are nearly planar with *rms* for the mean plane of 0.052, 0.008, 0.016 and 0.006 Å for C5/C6/C7/C8/C9/C10/C11/C12/C13/ C14, C20/C21/C22/C23/C24/C25, C28/C29/C30/C31/C32/C33 and C35/C36/C37/C38/C39/C40 rings, respectively. As no typical hydrogen bond donors and acceptors are present in **4b** the crystal packing is stabilized by weak C-H…O interactions. The most interesting one is the intramolecular C3-H3…O15 (Table 5) as it is directly related to the *R* center in the molecule. A hypothetical *S* center would shift the toluene and thus the C3-H3…O15 interaction will be hampered.

Table 3. Crystal data and structure refinement for **4b**.

Empirical formula	$C_{37}H_{33}NO_3$
Formula weight	539.64
Temperature/K	290
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a/Å	8.0544(8)
b/Å	12.5271(14)
c/Å	29.558(3)
α/°	90
β/°	90
γ/°	90

Volume/Å^3	2982.3(5)
Z	4
ρ_{calc} g.cm^{-3}	1.202
μ/mm^{-1}	0.076
$F_{(000)}$	1144.0
Crystal size/mm^3	0.35 × 0.30 × 0.28
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.76 to 50.042
Index ranges	-9 ≤ h ≤ 8, -14 ≤ k ≤ 14, -34 ≤ l ≤ 35
Reflections collected	12173
Independent reflections	4931 [R_{int} = 0.1153, R_{sigma} = 0.1070]
Data/restraints/parameters	4931/0/371
Goodness-of-fit on F^2	1.007
Final R indexes [$I>=2\sigma\ (I)$]	R_1 = 0.0863, wR_2 = 0.2143
Final R indexes [all data]	R_1 = 0.1521, wR_2 = 0.3079
Largest diff. peak/hole / e Å^{-3}	0.64/-0.798

Table 4. Selected bond lengths and angles for **4b**

Bond	**Distance [Å]**	**Angle**	**[^{o}]**
C3-C2	1.520(10)	C2-C3-C4	85.5(5)
C3-C4	1.567(8)	C34-C3-C2	119.4(6)
N1-C2	1.373(8)	C34-C3-C4	118.4(5)
N1-C4	1.482(9)	C2-N1-C4	94.4(5)
N1-C26	1.440(10)	C2-N1-C26	138.1(6)
O6-C2	1.213(8)	C26-N1-C4	127.3(6)
C6-C5	1.440(8)	O6-C2-N1	131.0(7)
C5-C4	1.515(9)	C6-C5-C4	119.8(6)
C26-C27	1.532(12)	N1-C26-C28	112.0(6)

C3-C34	1.513(10)	N1-C26-C27	110.8(6)
C35-C34	1.488(10)	C28-C29-C30	118.4(10)
Torsion angle [^{o}]			
C4-C3-C2-N1	3.4(5)	C4-C3-C34-C35	51.7(8)
C4-N1-C2-O6	178.0(8)	C4-N1-C26-C28	-60.4(9)
C10-C11-C12-C13	-176.4(9)	C4-N1-C26-C27	175.2(7)
C33-C32-C31-C30	-5.3(19)	C29-C28-C26-N1	146.9(7)
C24-C23-C22-C21	-2.3(17)	C40-C35-C36-C37	-0.3(13)

Table 5. Weak interactions for **4b**.

D	**H**	***A***	**d(*D*-H) [Å]**	**d(H-A) [Å]**	**d(D-A) [Å]**	**D-H-A [°]**
C4	-H4…	O1	0.98	2.30	2.902(8)	118.9
C20	-H20A…	O6^i	0.97	2.60	3.483(11)	151.6

Symmetry code: (i) *-2-x,1/2+y,-1/2-z*

Conclusions

Stereoselective *trans-β*-lactam formation *via* Staudinger cycloaddition was achieved by applying imines composed of enantiomeric 1-phenylethylamines and regioisomeric 2- and 4-hydroxynaphthadehyde as chiral auxiliaries. The title compounds with *O*-3-phenylpropionyl substituent in naphthalene unit were obtained diastereoselectively as pairs of *trans*-isomers in good to excellent yields and low to moderate enantioselectivity in respect to azetidinone ring. It was found that the presence of a bulky *O*-acyl group at *o*-position in naphthyl ring possess significant superiority over its p-regioisomer in both yield and selectivity. The absolute configurations of the products were assumed on the comparison of chiral auxiliary signals in proton NMR spectra with those of already obtained in the group compounds with known configurations and were confirmed by single crystal XRD analysis.

Acknowledgements

The financial support by The Bulgarian Science Fund, project "Development of Advanced and Effective Research Infrastructure for NMR Analysis of Bio- and Nanomaterials" and infrastructure projects UNA-17/2005, DRNF-02-13/2009 and DRNF-02-01/2009, is gratefully acknowledged. We also thank Dr. Nikolay Vassilev from IOCCP-BAS for carrying out the high temperature NMR experiments.

References

[1]. (a) Cimarusti, C. M.; Sykes, R. B., *Med. Res. Rev.* **1984**, *4*, 1-24. (b) *Beta-Lactam Antibiotics for Clinical Use*, Eds., S. F. Queener, J. A. Webber, S. W. Queener, Clinical Pharmacology, Marcel Deccer, Inc.: New York, **1986**; Vol. 4. (c) Nathwani, D.; Wood, M. J., *Drugs* **1993**, *45*, 866-894. (d) Drawz, S. M.; Bonomo, R. A., *Clin. Microbiol. Rev.* **2010**, *23*, 160-201. (e) *Heterocyclic Scaffolds I. β-Lactams*, Ed., B. K. Banik, *Topics in Heterocyclic Chemistry*, Series Ed., B. U. W. Maes, Springer-Verlag: Berlin Heidelberg, Germany, **2010**; Vol. 22. (f) *Lactams - Advances in Research and Application*, Ed., A. A.

Acton, Scholarly Edition: Atlanta, Georgia, **2012**. (g) Lewis, K., *Nat. Rev. Drug. Discov.* **2013**, *12*, 371-387. (h) Qin, W.; Panunzio, M.; Biondi, S., *Antibiotics* **2014**, *3*, 193-215.
[2]. (a) Singh, G. S. *Mini Rev. Med. Chem.* **2004**, *4*, 69-92. (b) Singh, G. S. *Mini Rev. Med. Chem.* **2004**, *4*, 93-109. (c) Hou, J. P.; Poole, J. W., *J. Pharm. Sci.* **2006**, *60*, 503-532. (d) *β-Lactams: Unique Structures of Distinction for Novel Molecules*, Ed., B. K. Banik, *Topics in Heterocyclic Chemistry*, Series Ed., B. U. W. Maes, Springer-Verlag: Berlin Heidelberg, Germany, **2013**; Vol. 30.
[3]. (a) Hart, D. J.; Ha, D.-C., *Chem. Rev.* **1989**, *89*, 1447-1465. (b) *The Chemistry of β-Lactams*, Ed., M. I. Page, Chapman and Hall: London, **1992**. (c) *The Organic Chemistry of β-Lactams*, Ed., G. I. Georg, VCH: New York, **1993**. (d) De Kimpe, N., In *Comprehensive Heterocyclic Chemistry-II*; A, Eds., R. Katritzky, C. W. Rees, E. V. F. Scriven, A. Padwa, Pergamon: Oxford, **1996**; Vol. 1B, chapter 1.18, pp. 507-589. (e) *Tetrahedron* **2000**, *56*, 31st issue is devoted to *β*-lactam chemistry. (f) Alcaide, B.; Almendros, P., *Chem. Soc. Rev.* **2001**, *30*, 226-240. (g) Singh, G. S. *Tetrahedron* **2003**, *59*, 7631-7649. (h) Thompson, S.; Coyne, A. G.; Knipe, P. C.; Smith, M. D. *Chem. Soc. Rev.* **2011**, *40*, 4217-4231. (i) Singh, G. S.; Sudheesh, S., *Arkivoc* **2014**, *i*, 337-385. (j) Alcaide, B.; Almendros, P. in *Progress in Heterocyclic Chemistry*, G. W. Gribble, J. Joule, Eds.; Elsevier Ltd., 2011, Vol. 22, Chapter 4, 85-107. (k) Pitts, C. R.; Lectka, T., *Chem. Rev.* **2014**, *114*, 7930-7953.
[4]. (a) Staudinger, H., *Liebigs Ann. Chem.* **1907**, *356*, 51-123. (b) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M., *Eur. J. Org. Chem.* **1999**, 3223-3235. (c) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M., *Curr. Med. Chem.* **2004**, *11*, 1837-1872.
[5]. (a) Brandi, A.; Cicchi, S.; Cordero, F. M., *Chem. Rev.* **2008**, *108*, 3988-4035. (b) Xu, J., *Arkivoc* **2009**, *ix*, 21-44. (c) Konaklieva, M. I.; Plotkin, B. J., *Asymmetric Synthesis of β-Lactams via the Staudinger Reaction*, Ed., A. B. Hughes, *Amino Acids, Peptides and Proteins in Organic Chemistry: Protection Reactions, Medicinal Chemistry, Combinatorial Synthesis*, Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, **2011**: Vol. 4, pp. 293-319.
[6]. (a) Todorov, A. R.; Kurteva, V. B.; Bontchev, R. P.; Vassilev, N. G., *Tetrahedron* **2009**, *65*, 10339-10347. (b) Kurteva, V. B.; Todorov, A. R.; Stoylova-Dicheva, M., *Arkivoc* **2011**, *xi*, 198-212.
[7]. The crystallographic data for (*S*)-(3*R*,4*S*)-**4b** were deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 1402487. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; tel: +44 1223 762910; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk; http://www.ccdc.cam.ac.uk/deposit.
[8]. CrysAlis PRO, Agilent Technologies, UK Ltd, Yarnton, England, 2011.
[9].Sheldrick, G. M., *Acta Cryst. A* **2008**, *64*, 112-122.
[10]. (a) Tanaka, F.; Node, M.; Tanaka, K.; Mizuchi, M.; Hosoi, S.; Nakayama, M.; Taga, T.; Fuji, K., *J. Am. Chem. Soc.* **1995**, *117*, 12159-12171. (b) Ahn, M.; Tanaka, K.; Fuji, K., *J. Chem. Soc., Perkin Trans. 1* **1998**, 185-192. (c) Bonini, B. F.; Femoni, C.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A.; Varchi, G., *Synlett* **2001**, 1092-1096. (d) Benfatti, F.; Bottoni, A.; Cardillo, G.; Fabbroni, S.; Gentilucci, L.; Stenta, M.; Tolomelli, A., *Adv. Synth. Catal.* **2008**, *350*, 2261-2273. (e) Vaske, Y. S. M.; Mahoney, M. E.; Konopelski, J. P.; Rogow, D. L.; McDonald, W. J., *J. Am. Chem. Soc.* **2010**, *132*, 11379-11385. (f) Michalak, M.; Stodulski, M.; Stecko, S.; Woźnica, M.; Staszewska-Krajewska, O.; Kalicki, P.; Furman, B.; Frelek, J.; Chmielewski, M., *Tetrahedron* **2012**, *68*, 10806-10817. (g) Yoshimura, T.; Takuwa, M.; Tomohara, K.; Uyama, M.; Hayashi, K.; Yang, P.; Hyakutake, R.; Sasamori, T.; Tokitoh, N.; Kawabata, T., *Chem. Eur. J.* **2012**, *18*, 15330-15336. (h) Chen, Z.; Lin, L.; Wang, M.; Liu, X.; Feng, X., *Chem. Eur. J.* **2013**, *19*, 7561-7567. (i) Li, Y.; Tergaonkar, V., *Cancer Res.* **2014**, *74*, 1639-1644.