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SYNTHESIS, REACTIONS AND BIOLOGICAL ACTIVITY OF DERIVATIVES OF OXIMES OF FOUR-MEMBERED HETEROCYCLES

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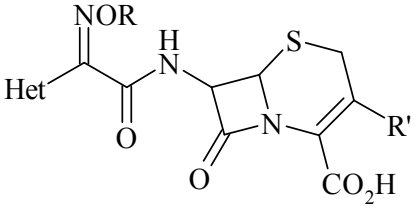
Abstract:
Literature data on the synthesis and structure of oximes of four-membered heterocycles with one heteroatom were reviewed. Synthesis of novel heterocycles from oximes of four-membered heterocycles was described. Biological activity of these oximes was also reviewed.

Keywords: oximes, four-membered heterocycles, azetidines, oxetanes, thietanes, biological activity

Introduction

The oximes of four-membered heterocycles with one heteroatom are widely used as intermediates in fine organic synthesis. In this review the principal methods for the production of aldoximes, ketoximes and amidoximes of four-membered heterocycles (such as azetidines, oxetanes and thietanes) and their derivatives are summarized. The principal methods for the investigation of structure the oximes of four-membered heterocycles are examined briefly with due to regard isomerism. The reactions and biological activity of the oximes of four-membered heterocycles will be examined in the last parts of the review. Among four-membered oxime derivatives lot of publications and reviews were dedicated to penicillin and cephalosporin antibiotics (for example, compounds of type **1**) [1]. Therefore, synthesis, reactions and biological activity of penicillin and cephalosporin derivatives was not included in this review.

This work were carried out in continuation of series of our reviews connected to synthesis, reactions and biological activity of heterocyclic oximes (such as, furan and thiophene oximes [IIa], indole and isatin oximes [IIb], pyridine oximes [IIc], pyrrole oximes [IId], quinoline oximes [IIe], oximes of five-membered heterocyclic compounds with two [IIf, IIg] and three [IIh, IIi] heteroatoms, oximes of six-membered heterocyclic compounds with two and three heteroatoms [IIj, IIk], oximes of seven-membered heterocyclic compounds containing one [IIIa] and two heteroatoms [IIIb], oximes of six-membered oxygen heterocycles [IIIc] and oximes of three-membered heterocycles [IIId]).



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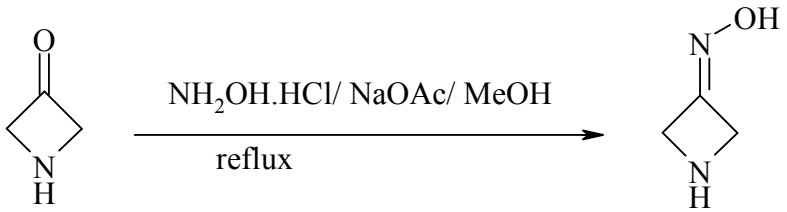
This part is the last in series of reviews dedicated to heterocyclic oximes.

1. SYNTHESIS OF OXIMES OF FOUR-MEMBERED HETEROCYCLES

1.1. Synthesis of azetidine oximes

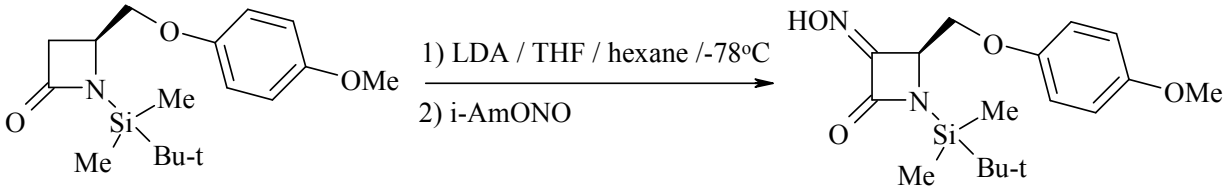
The classical method for the synthesis of azetidine oximes [IV] is based on the reaction of corresponding aldehydes or ketones with hydroxylamine hydrochloride (or free hydroxylamine) in the systems CH_2Cl_2 / n-PrOH [V], CH_2Cl_2 / DMF [VI], DMF [VII], pyridine [VIII, IX], CH_2Cl_2 / pyridine MeOH / NaOMe [X], MeOH / pyridine [XI], EtOH / pyridine [XII], Et_3N / MeOH [XIII], NaOAc / MeOH [XIV-XVI] and KOH / EtOH / H_2O [XVII]. Thus, reflux of azetidin-3-one derivative with $NH_2OH \cdot HCl$ in methanol afforded oxime **2** in 74% [XV].



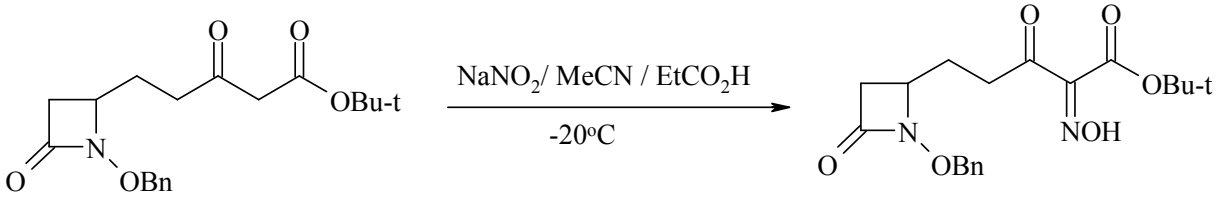
74%

2

The second group of methods of synthesis azetidine oximes is based on the nitrosation of corresponding heterocycles [XVIII] in the systems t-BuONO / LDA, LiHMDS or t-BuOK / THF [XIX], n-BuONO / NaOMe/ MeOH [XX], i-AmONO / KNH_2 [XXI] and i-AmONO / LDA [XXII]. For example, treatment of azetidine (S)-**3** with LDA and then with i-AmONO lead to oxime (S)-**4** in 60% yield [XXIII]. Interestingly, that azetidine ketoester derivative **5** in the system $NaNO_2$ / MeCN/ propanoic acid afforded only side chain nitrosation product **6** in 67% yield [XXIV].



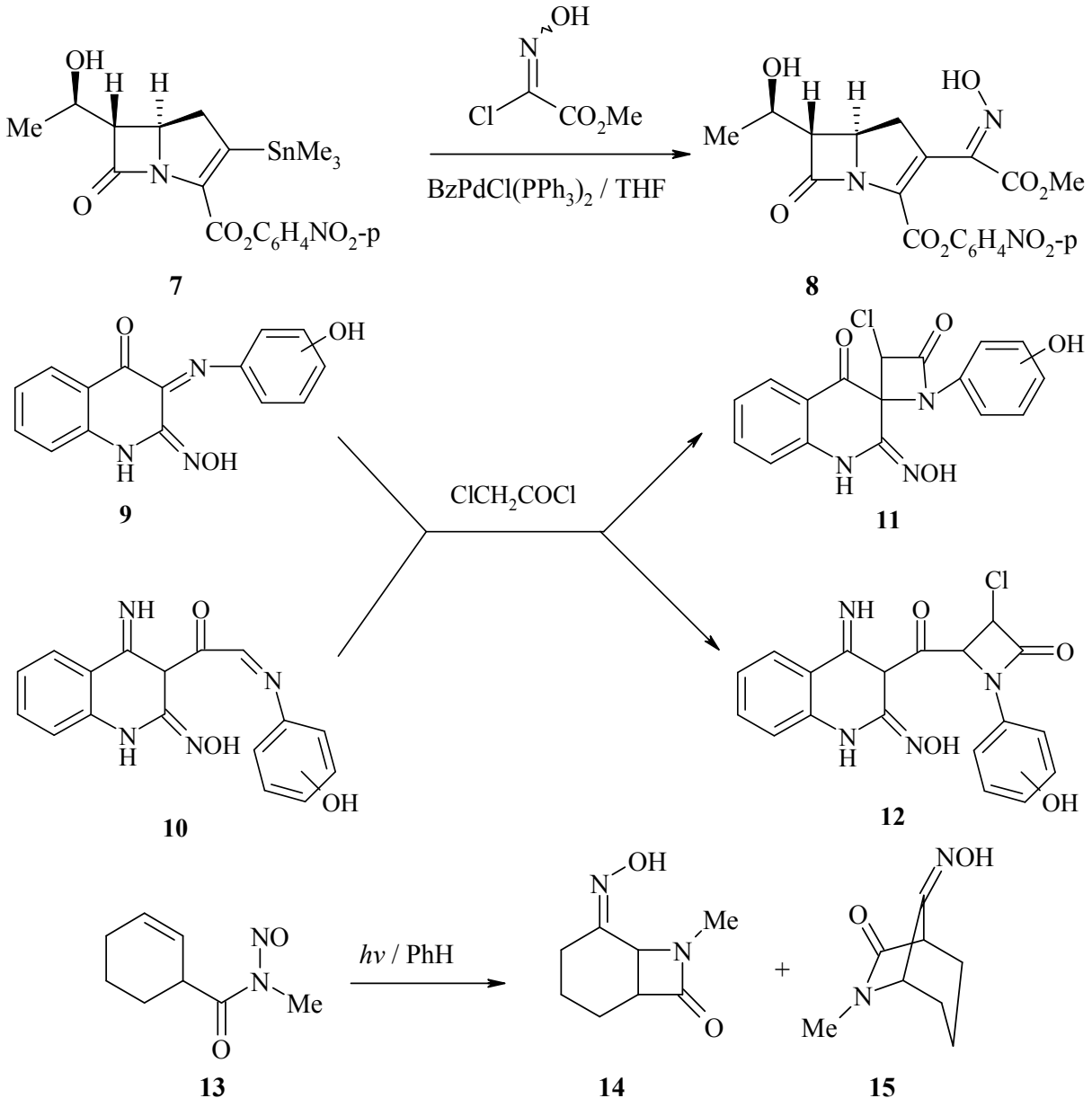
3 **4**



5 **6**

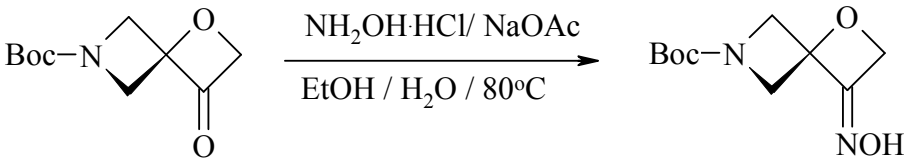
Antibacterial oxime derivative **8** were successfully obtained in the palladium-catalyzed Stille-type coupling reaction of stannane **7** and $ClC(=NOH)CO_2Me$ [XXV]. Beside this, cyclization of quinoline oxime derivatives **9** and **10** in the presence of chloroacetyl chloride leads to azetidine derivatives **11** and **12** in yields up to 58% [XXVI, XXVII]. Finally, photolysis of N-nitroso-

N-methyl-2-cyclohexene-1-carboxamide (**13**) under nitrogen gave syn-β-lactam oxime **14** (44% yield) and the corresponding keto-β-lactam **15** (7%) [XXVIII].



1.2. Synthesis of oxetane oximes

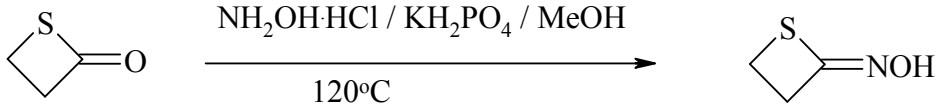
Oxetane oximes [XXIX] (e.g., oxime **17**) were obtained in the reaction of ketones (for example, compound **16**) with hydroxylamine hydrochloride in the system NaOAc /EtOH / H_2O [XXX].



16 **17**

1.3. Synthesis of thietane oximes

Thiethane oximes 1,1-dioxide oxime derivative [XXXI] and thietanone oxime [XXXII] was prepared from corresponding carbonyl compounds and hydroxylamine. For example, heating of thietanone **18** with $NH_2OH \cdot HCl$ in the system KH_2PO_4 / MeOH at 120°C for 12h in autoclave gives oxime **19** in 90% yield.



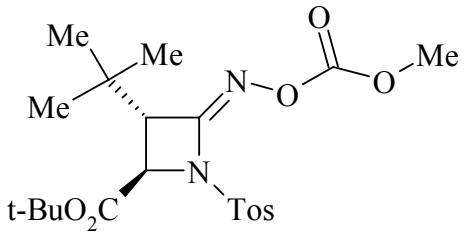
18 (E)-**19**

2. STRUCTURE

One of the most reliable methods for determining of the structure of isomeric oximes of four-membered heterocycles with one heteroatom is NMR spectroscopy. The ^1H NMR spectra of oximes of azetidine [III, XVI, XVIII], oxetane [XXX] and thietane [XXXI] have been investigated in details. Beside this, investigation of both E- and Z-isomers of compound **4** using ^1H NMR spectroscopic method was carried out [XXIII]. Detailed ^1H and ^{13}C NMR spectral characteristics of cis-1-(4-methoxyphenyl)-3-substituted-4-methoxyiminomethyl-4-methylsulfanylazetidin-2-ones were presented too [XXXIII].

IR spectroscopy was also used to study the structure of azetidine oximes [XIV, XV].

Structure S-4-tert-butyl 3-tert-butyl-4-methoxycarbonyloxyimino-1-(tosyl)azetidin-2-carboxylate (**20**) [XXXIV] was confirmed by X-ray crystallographic analysis.



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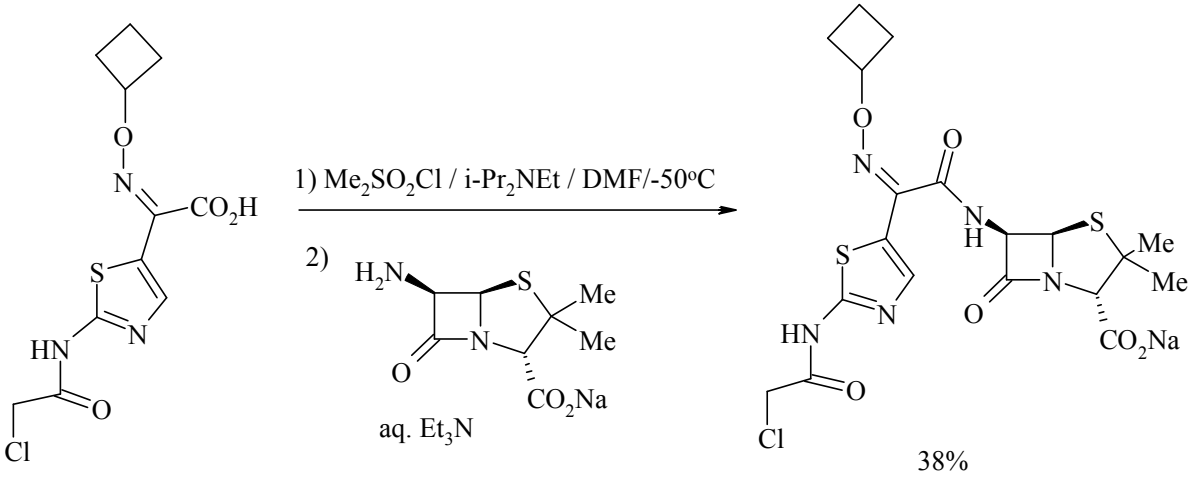
3. REACTIONS OF OXIMES OF FOUR-MEMBERED HETEROCYCLES

3.1. Synthesis of O-alkyl derivatives of oximes of azetidine oximes

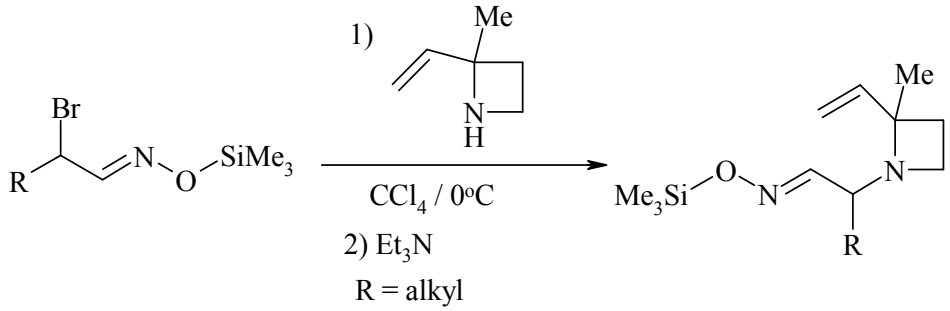
The principal methods for the preparation of azetidine oxime O-ethers [XXXV] are condensation of corresponding azetidine carbonyl compounds with alkoxyamines [XXXVI-XXXVIII] or reaction of azetidine oximes with alkyl halides [XXXIX]. Penicillin antibiotic intermediate **22** was prepared from 6-aminopenicillanic acid and oxime derivative **21** in the system Me_2SO_2Cl / i-

Pr_2NEt (then aq. Et_3N) [XL]. Similar methods were widely used in the preparation of β-lactam antibiotics [XXXV].



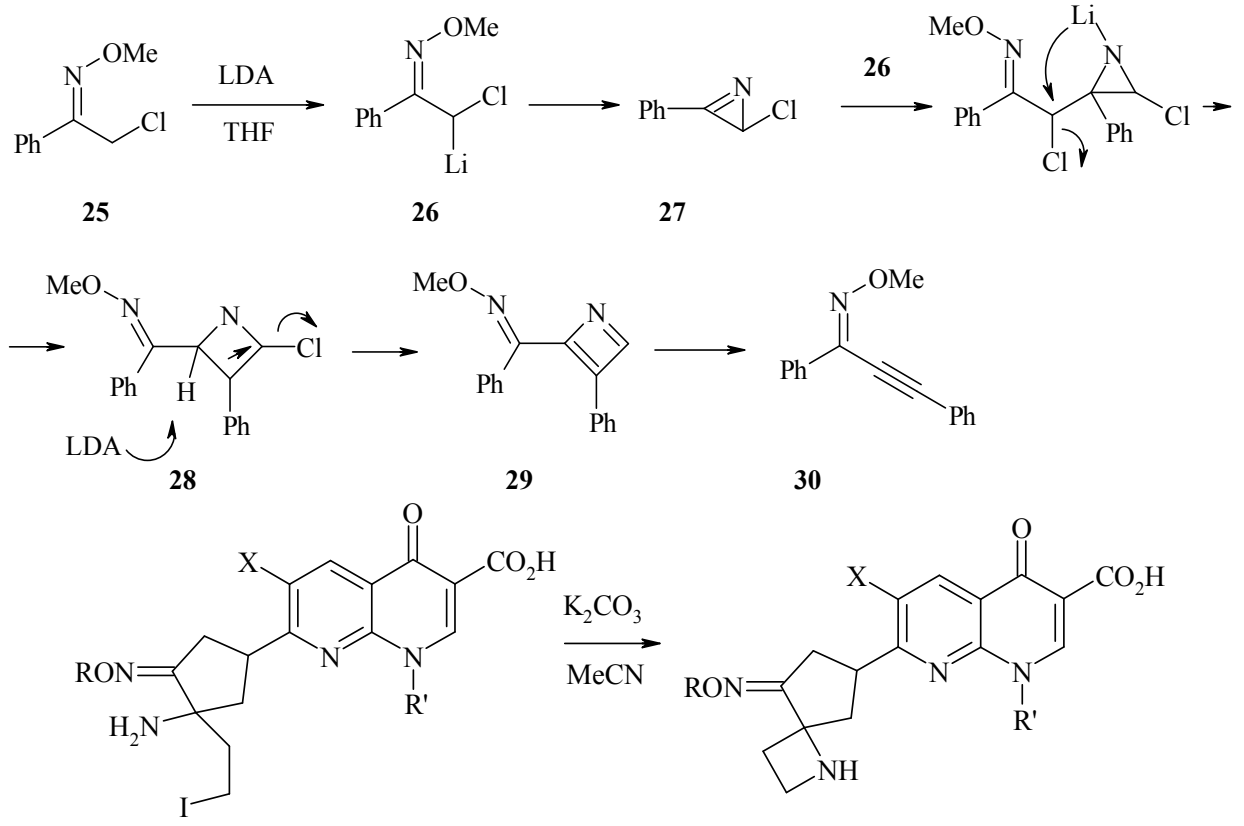
21 **22**

2-(2'-Methyl-2'-vinyl-1-azetidinyl)alkanal O-(trimethylsilyl)oximes (**24**) were prepared from O-silyl α–bromo aldoximes **23** and 2-methyl-2-vinylazetidine in methylene chloride at room temperature [XLI, XLII].



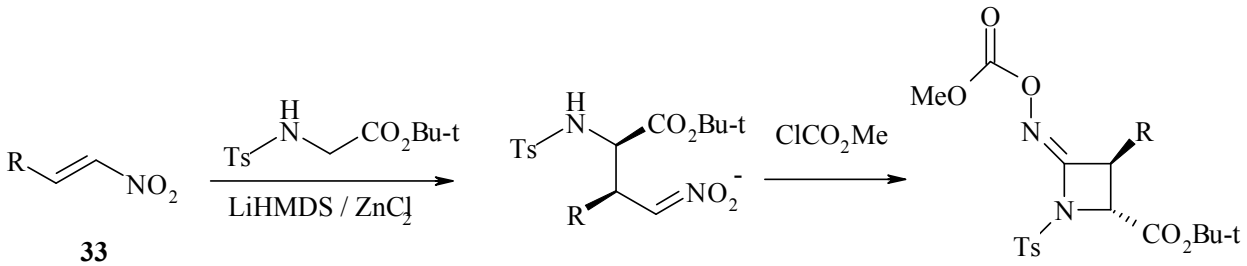
23 **24**

Some methods of synthesis of O-ethers of azetidine oximes were based on the formation of azetidine ring by cyclization of oxime ether derivatives. Thus, deprotonation of oxime **25** by LDA leads to Neber-type highly reactive intermediates **27** via .lithio oxime **26**. The reaction of compound **27** with oxime **26** leads to intermediate **28**. Removal of an α-proton of **28** with LDA leads to highly unstable azacyclobutadiene derivative **29**. The [2+2] cycloreversion of **29** yields alkynyl oxime ethers **30** [XLIII]. Cyclization of oxime derivatives **31** in the presence of K_2CO_3 afforded antibacterial azetidine oxime derivatives **32** [XLIV].



25 **26** **27** **28** **29** **30** **31** **32**

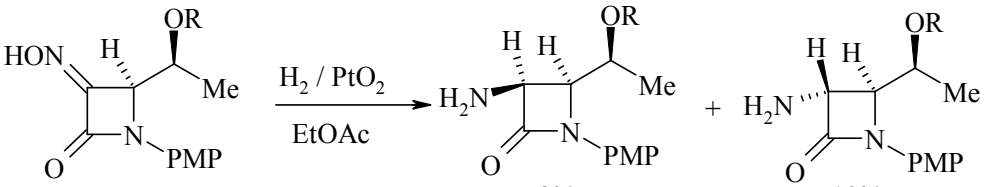
Addition/cyclization reaction of Ts-GlyOBu-t to nitroalkenes **33** in the system LiHMDS / $ZnCl_2$ (then $ClCO_2Me$) leads to azetidine oxime esters **34** in 47-52 % yields [XXXIV]. Finally, kinetics and theoretical study of 4-exo ring closure of carbamoyl radicals to azetidine benzyloxyaminyl radicals was described in article [XLV].



33 **34**

3.2. Transformation of oximes of four-membered heterocycles

Reduction of azetidine oximes to corresponding amino derivatives was realized in presence $LiAlH_4$ [XLVI, XLVII], aluminium reductants / $HgCl_2$ / THF / H_2O [XIX], Ac_2O / AcONa / H_2 / PtO_2 [XVI] or H_2 / PtO_2 / H_2O [XXIII]. Hydrogenation of chiral azetidine oxime **35** in the system PtO_2 / EtOAc leads to mixture of isomeric products **36** and **37** [XXII]. Oxetane oximes were reduced to corresponding oxetane amino derivatives by H_2 / Raney Ni [XXX].

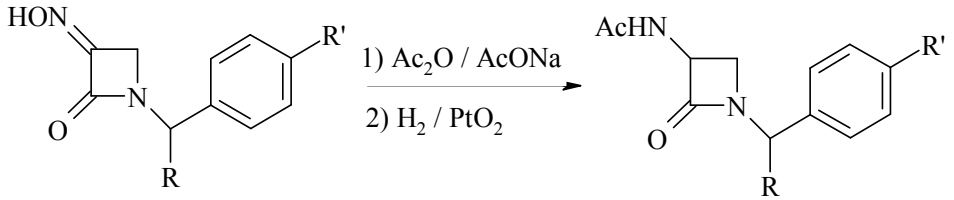


35 **36** **37**

R = H, Me

Some articles were dedicated to reduction of azetidine oximes to corresponding hydroxylamine derivatives of azetidine using BH_3·pyridine [XXXVII] or BH_3·THF [VII].

Reductive amidation of azetidine oximes to corresponding azetidine amides were described in some articles [IX, X, XX, XLVIII]. Thus, treatment of oximes **38** with Ac_2O/ AcONa and then with H_2 / PtO_2 afforded acetamides **39** in yields up to 28% [X].

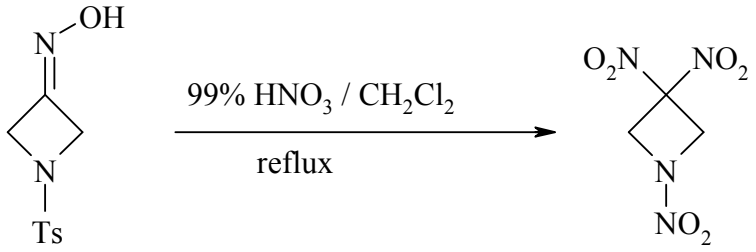


38 **39**

R, R' = H, CO_2Bn, OCH_2Ph

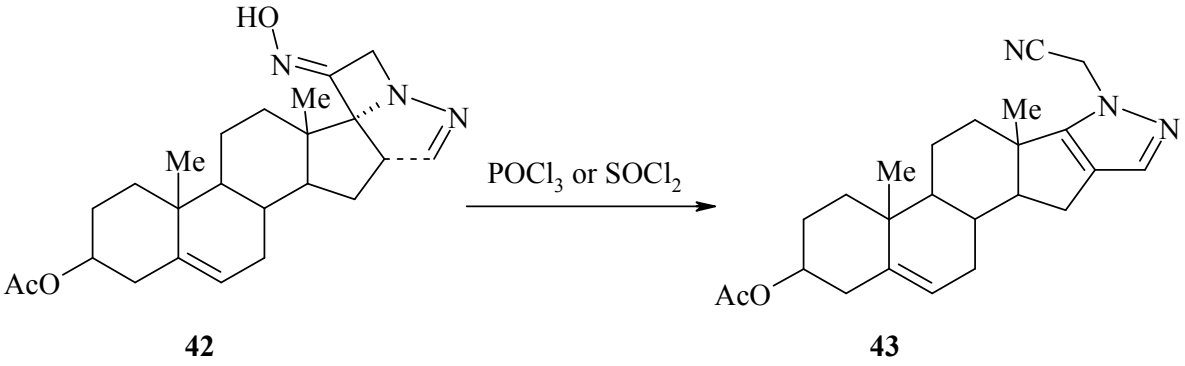
Azetidine oxime derivatives were readily converted to corresponding nitriles in the presence of SeO_2 in propanol [V]. Beside this, 1-(diphenylmethyl)-azetidine-3-carboxaldehyde was transformed to corresponding nitrile in 92% yield by treatment with NH_2OH·HCl in DMSO at 80°C. The above reaction proceeded via azetidine 3-aldoxime intermediate [XLIX].

3,3-Dinitro- and 1,3,3-trinitroazetidines were also prepared from azetidine oximes [XIV, XVII, L, LI]. Thus, treatment of N-tosylated oxime **40** with 99% HNO_3 in refluxing methylene chloride to produce the desired 1,3,3-trinitroazetidine **41** in yields up to 50% [L]. Interestingly, that N-alkylated azetidine 3-aldoximes under similar conditions afforded 3,3-dinitroazetidines [XVII, LI].

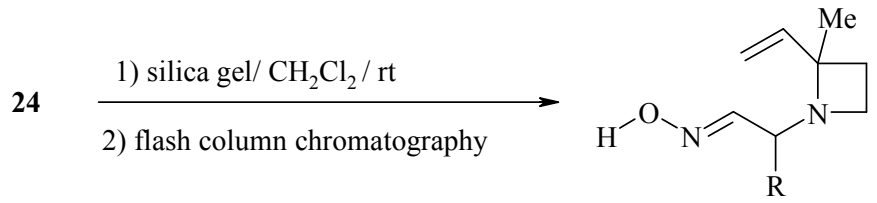


40 **41**

Finally, steroidal azetidine oxime derivative **42** in the presence of $POCl_3$ or $SOCl_2$ undergoes second-order Beckmann rearrangement leading to nitrile derivative **43** in 70% yield [LII]. Stirring of silyl ether **24** with silica gel in methylene chloride at room temperature, followed by flash column chromatography, afforded desilylated oxime **44** [XLII].



42 **43**



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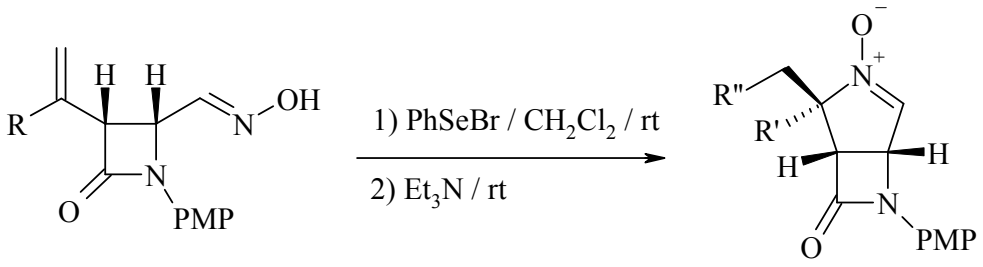
3.3. Synthesis of novel heterocyclic compounds from oximes of three-membered heterocycles

Recent advances in the synthesis of heterocyclic systems from oximes were described in reviews [LIII, LIV]. In this chapter specific reactions involving cyclization of oximes of three-membered oxygen heterocycles will be set out in details.

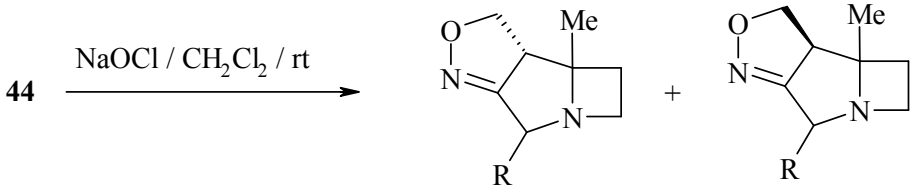
Reaction of unsaturated azetidine oximes **45** with phenyselenyl bromide in dichloromethane at room temperature in the presence of Et_3N leads to bicyclic nitrones **46** in 26-58% yields [LV, LVI].



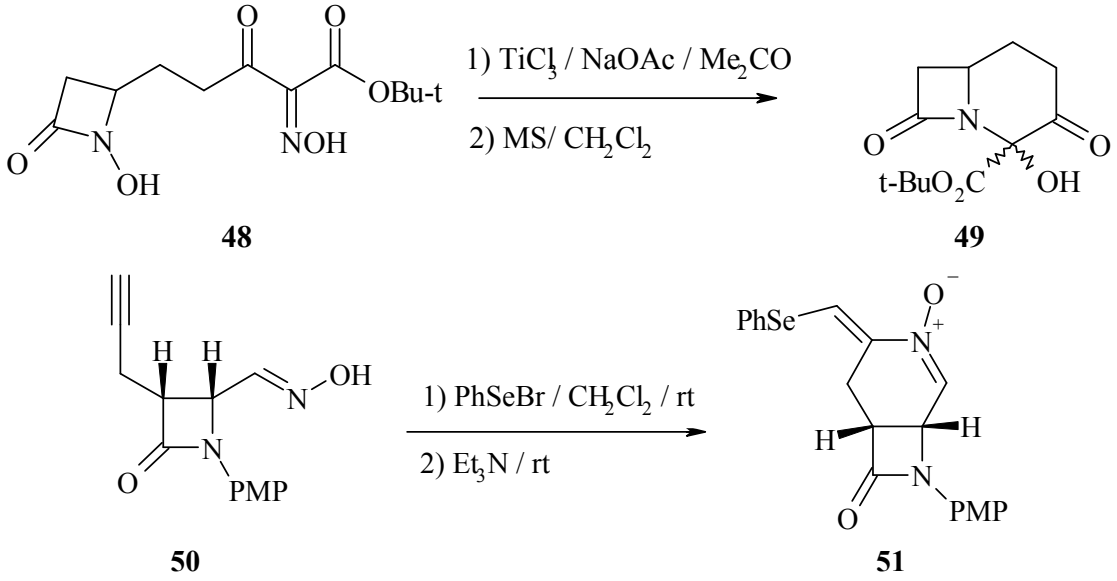
45 **46**

R = H, Me; R' - H, Me, SePh; R" = H, Me, SePh

Intramolecular cycloaddition of unsaturated oximes **44** in the system NaOCl / CH_2Cl_2 at 0^oC afforded 4',5'-dihydroisoxazolino[4,3-c]azetidino[1,2-a]-2,5-dimethylpyrrolidines **47** in yields up to 52% [XLII].



Cylization of azitidine ketooxime **48** in the system $TiCl_3$ / NaOAc / molecular sieves / acetone at pH 5 gives lactam **49** in 31% yield [XXIV]. Alkynyl derivative of azetidine oxime **50** and phenyselenyl bromide in dichloromethane at room temperature in the presence of Et_3N leads to fused pyridine derivative **51** in 83% yield [LV].

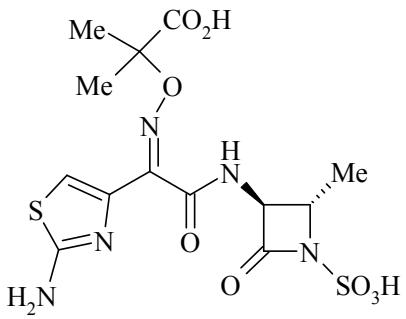


4. BIOLOGICAL ACTIVITY OF OXIMES OF FOUR-MEMBERED HETEROCYCLES

4.1. Antibacterial and anticancer activities

Among four-membered oxime derivatives lot of publications and reviews were dedicated to penicillin and cephalosporin antibiotics (for example, compounds of type **1**) [1]. Therefore, biological activity of penicillin and cephalosporin derivatives was not included in this review.

β-Lactam antibiotics (including simple, not fused azetidine ring) was also widely used in the treatment of different types bacterial infections [XI, XVIII, XXXV, LVII-LIX]. Among these compounds necessary to mention Aztreonam (**52**), Carumonam (**53**), Nocardicin-A (**54**), as well as, some new derivatives of β-lactam antibiotics **55-58**.



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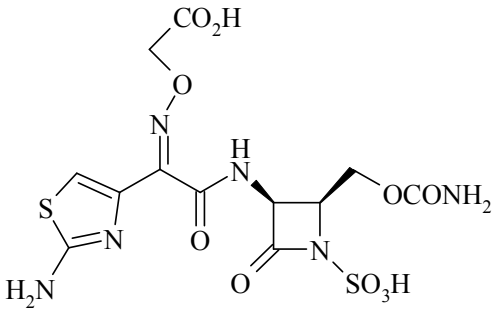

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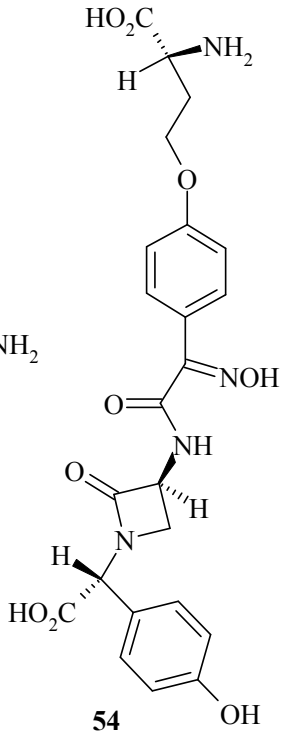

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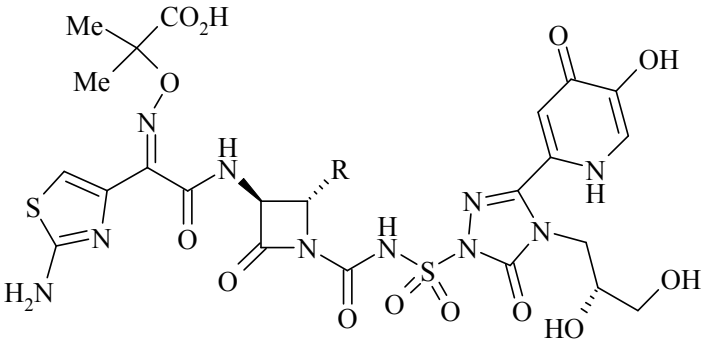
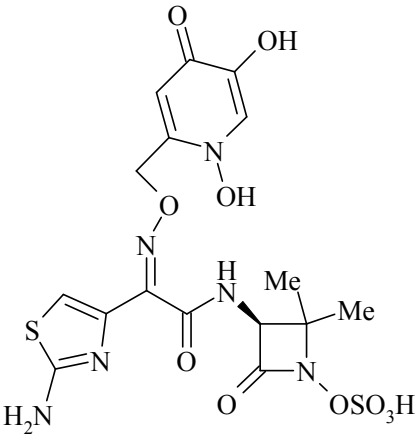


55 R = H
56 R = Me



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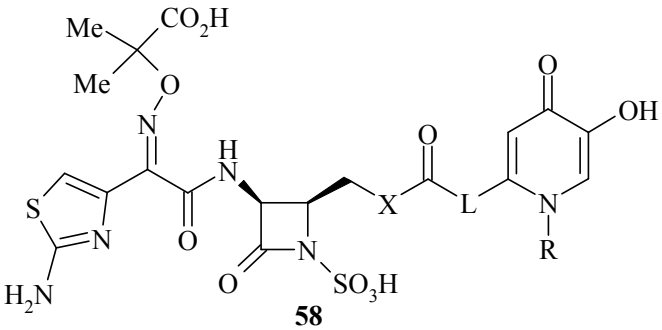
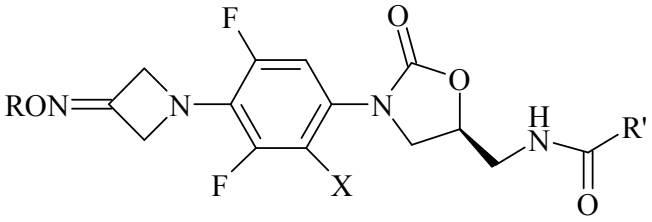


58

X= O, NH; R = H, OH; variable (for example, heterocycle)

Among non-β-lactam antibcterial agents necessary to mention acridinone oxime **59** [LX] and naphthyridine containing oxime derivatives (for example, oximes **32**) [XLIV, LXI].



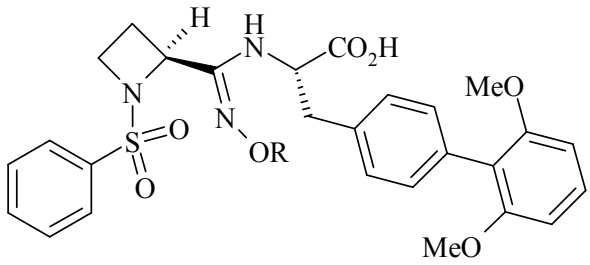
59

R = H, alkyl; R' = alkyl, O-alkyl

Beside this, azetidine oximes were used as intermediates in the synthesis of MEK kinase inhibitors. These compounds were used in the treatment of proliferative diseases and cancer [LXII].

4.2. VLA-4 antagonists

Azetidine oxime derivatives **60** are tested as VLA-4 (very late activating antigen-4, $\alpha_4\beta_1$, CD49d/CD29) antagonists. These compounds plays important role in inflammation by promoting leukocyte attachment and extravasation from the vasculature into peripheral tissues [XIII].



60

R = H, Me

References

I. (a) The Merck Index. An encyclopedia of chemicals, drugs and biologicals, 40th Ed., Whitehouse Station, NJ, USA, 2006; (b) Ashgate Handbook of Anti-infective Agents, Ed. G. W. A. Milne, Ashgate Publishing Company, Vermont, USA, 2000; (c) Antibacterial Chemotherapeutic Agents, Blackie Academic & Professional, UK, 1997; (d) B. Alcaide, C. Aragoncillo and P. Almendros, In Comprehensive Heterocyclic Chemistry III, A.R. Katritzky, C.A. Ramsden and E.F.V. Scriven, R.J.K. Taylor Ed.; Elsevier: Oxford, 2008; Vol. 2, pp 111-171; (e) Y. Aharonowitz, G. Cohen and J.F. Martin, Ann. Rev. Microbiolog. 46, 461 (1992); (f) C.J. Harrison and D. Bratcher, Pediatrics in Review 29, 264 (2008).

II. (a) E. Abele and E. Lukevics, Chem. Heterocycl. Comp. 37, 141 (2001); (b) E. Abele, R. Abele, O. Dzenitis and E. Lukevics, Chem. Heterocycl. Comp. 39, 3 (2003); (c) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 39, 825 (2003); (d) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 40, 1 (2004); (e) E. Abele, R. Abele, K. Rubina and E. Lukevics, Chem. Heterocycl. Comp. 41, 137

(2005); (f) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 43, 387 (2007); (g) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 43, 945 (2007); (h) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 44, 637 (2008); (i) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 44, 769 (2008); (j) E. Abele, R. Abele and E. Lukevics, Chem. Heterocycl. Comp. 45, 1420 (2009); (k) E. Abele, R. Abele, L. Golomba, J. Visnevska, T. Beresneva, K. Rubina and E. Lukevics, Chem. Heterocycl. Comp. 46, 905 (2010);

III. (a) E. □bele, R. □bele, □. Golomba, J. Viš□evska, T. Beres□eva and K. Rubina, Latvian J. Chem. 50, 205 (2011); (b) E. Abele, Latvian J. Chem. 51, 83 (2012); (c) E. Abele, Heterocycl. Lett. 2, 515 (2012); (d) E. Abele, Heterocycl. Lett. 3, 229 (2013).

IV. A. Singh, N. Sikder and A.K. Sikder, Indian J. Chem., Sec. B, 44B, 2560 (2005).

V. A. Furlenmeier, W. Hofheinz, C.N. Hubschwerlen and H.P. Isenring, US Pat. 4816582 (1989).

VI. D. Hagiwara, K. Sawada, T. Ohnami and M. Hashimoto, Chem. Pharm. Bull. 30, 3061 (1982).

VII. S.R. Ganta, S. Perumal, S.R.R. Pagadala and O. Samuelson, Bioorg. Med. Chem. Lett. 19, 1618 (2009).

VIII. R. Lysek, Z. Urbanczyk-Lipkowska and M. Chmielewski, Tetrahedron 57, 1301 (2001).

IX. K. Chiba, M. Mori and Y. Ban, J. Chem. Soc., Chem. Commun. 770 (1980).

X. K. Chiba, M. Mori and Y. Ban, Tetrahedron 41, 387 (1985).

XI. M. Ihara, Y. Haga, M. Yonekura, T. Ohsawa, K. Fukumoto and T. Kametani, J. Am. Chem. Soc. 105, 7345 (1983).

XII. J.A. Moore, W.F. Holton and E.L. Wittle, J. Am. Chem. Soc. 84, 390 (1962).

XIII. T.M. Kamenecka, Y.-J. Park. L.S. Lin, S. de Laszlo, E.D. McCauley, G. Van Riper, L. Egger, U. Kidambi, R.A. Mumford, S. Tong, W. Tang, A. Colletti, Y. Teffera, R. Stearns, M. MacCoss, J.A. Schmidt and W.K. Hagmann, Bioorg. Med. Chem. Lett. 14, 2323 (2004).

XIV. T. Axenrod, C. Watnick, H. Yazdekhasti and P.R. Dave, J. Org. Chem. 60, 1959 (1995).

XV. A.P. Marchand, D. Rajagopal, S.G. Bott and T.G. Archibald, J. Org. Chem. 59, 1608 (1994).

XVI. M. Altamura, M. Giammaruco, M. Taddei and P. Ulivi, J. Org. Chem. 60, 8403 (1995).

XVII. A.R. Katritzky, D.J. Cundy and J. Chen, J. Heterocycl. Chem. 31, 271 (1994).

XVIII. H. Yamashita, N. Minami, K. Sakakibara, S. Kobayashi and M. Ohno, Chem. Pharm. Bull. 36, 469 (1988).

XIX. K. Kühlein and H. Jensen, Lieb. Ann. Chem. 369 (1974).

XX. J.J. Tufariello, D.J.P. Pinto, A.S. Milowsky and D.V. Reinhardt, Tetrahedron Lett. 28, 5481 (1987).

XXI. P. Wegner and H. Jensen, Ger. Pat. 2337448 (1975); Chem. Abstr. 82, 171003n (1975).

XXII. Y. Takahashi, H. Yamashita, S. Kobayashi and M. Ohno, Chem. Pharm. Bull. 34, 2732 (1986).

XXIII. L. Banfi, G. Cascio, C. Ghiron, G. Guanti, E. Manghisi, E. Narisano and R. Riva, Tetrahedron 50, 11983 (1994).

XXIV. C.M. Gasparski, A. Ghosh and M.J. Miller, J. Org. Chem. 57, 3546 (1992).
XXV. J.D. Hinks, E. Hunt and A.K. Takle, Tetrahedron Lett. 41, 2995 (2000).
XXVI. H.A. Suleiman, A.I.M. Koraiem and N.Y. Mahmoud, J. Chin. Chem. Soc. 51, 553 (2004).
XXVII. H.A. Suleiman, A.I.M. Koraiem and N.Y. Mahmoud, J. Chin. Chem. Soc. 52, 119 (2005).
XXVIII. Y.L. Chow and R.A. Perry, Can. J. Chem. 63, 2203 (1985).
XXIX. B.L. Murr, G.B. Hoey and C.T. Lester, J. Am. Chem. Soc. 77, 4430 (1955).
XXX. J.A. Burkhard, C. Guerot, H. Knust and E.M. Carreira, Org. Lett. 14, 66 (2012).
XXXI. J.E. Coates and F.S. Abbott, J. Org. Chem. 42, 3506 (1977).
XXXII. (a) K. Drauz, G. Knaup, S. Retzow, M. Schwarm and C. Weckbecker, US Pat. 5874121 (1999); (b) K. Drauz, G. Knaup, S. Retzow, M. Schwarm and C. Weckbecker, Ger. Pat. 19505933 (1996); Chem. Abstr. 125, 276577a (1996).
XXXIII. E. Grochowski and K. Pupek, Tetrahedron 47, 6759 (1991).
XXXIV. B. Mendler, U. Kazmaier, V. Huch and M. Veith, Org. Lett. 7, 2643 (2005).
XXXV. (a) M.C. Cook, G.I. Gregory and J. Bradshaw, Ger. Pat. 2223287 (1972); Chem. Abstr. 78, 72129g (1973); (b) Glaxo Laboratories Ltd. France Pat. 2204404 (1974); Chem. Abstr. 81, 169535m (1974); (c) H. Breuer and T. Denzel, Ger. Pat 3122795 (1982); Chem. Abstr. 125764g (1983); (d) G. Just, D. Dugat and W.Y. Liu, Can. J. Chem. 61, 1730 (1983); (e) K. Yoshioka, T. Miyawaki, S. Kishimoto, T. Matsuo and M. Ochiai, J. Org. Chem. 49, 1427 (1984); (f) U.D. Treuner, T. Denzel and H. Breuer, Eur. Pat. 68466 (1983); Chem. Abstr. 98, 197892v (1983); (g) M. Ochiai and T. Matsuo, Eur. Pat. 95764 (1983); Chem. Abstr. 100, 191649j (1984); (h) W.A. Slusarchyk, T. Dejneka and W.H. Koster, Belg. Pat. 904121 (1986); Chem. Abstr. 106, 4752b (1987); (i) U.D. Treuner, Ger. Pat. 3440845 (1985); Chem. Abstr. 103, 195946p (1985); (j) H. Straub, Ger. Pat. 3433676 (1985); Chem. Abstr. 103, 37287v (1985); (k) J.E. Sundeen, Eur. Pat. 229012 (1987); Chem. Abstr. 107, 236364a (1987).
XXXVI. A. Furlenmeier, W. Hofheinz, C.N. Hubschwerlen and H.P. Isenring, US Pat. 4652651 (1987).
XXXVII. D. Hagiwara, K. Sawada, T. Ohnami and M. Hashimoto, Chem. Pharm. Bull. 30, 3061 (1982).
XXXVIII. S. Ariga, S. Hata, D. Fukuda, T. Nishi, I. Hachiya and M. Shimizu, Heterocycles 86, 1187 (2012).
XXXIX. M. Hashimoto, M. Aratani, D. Hagiwara, K. Sawada and T. Onami, US Pat. 4369312 (1983).
XL. P. Brown, S.H. Calvert, P.C.A. Chapman, S.C. Cosham, A.J. Eglington, R.L. Elliot, M.A. Harris, J.D. Hinks, J. Lowther, D.J. Merrikin, M.J. Pearson, R.J. Ponsford and J.V. Syms, J. Chem. Soc., Perkin Trans. 1, 881 (1991).
XLI. A. Hassner and K.S. Keshava Murthy, Tetrahedron Lett. 28, 4097 (1987).
XLII. A. Hassner, K.S. Keshava Murthy, A. Padwa, W.H. Bullock and P.D. Stull, J. Org. Chem. 53, 5063 (1988).
XLIII. T. Tsuritani, K. Yagi, H. Shinokubo and K. Oshima, Angew. Chem., Int. Ed. 42, 5613 (2003).
XLIV. L.-S. Feng, M.-L. Liu, S. Wang, Y. Chai, K. Lv, G.-Z. Shan, J. Cao, S.-J. Li and H.-Y. Guo, Tetrahedron 67, 8264 (2011).

XLV. G.A. DiLabio, E.M. Scanian and J.C. Walton, Org. Lett. 7, 155 (2005).
XLVI. B. Li, T.V. Magee, R.A. Buzon, D.W. Widlicka, D.R. Bill, T. Brandt, X. Cao, M. Coutant, H. Dou, K. Granskog, M.E. Flanagan, C.M. Hayward, B. Li, F. Liu, W. Liu, T.-T. Nguyen, J.W. Raggon, P. Rose, J. Rainville, U.D. Reily, Y. Shen, J. Sun and G.E. Wilcox, Org. Proces. Res. Develop. 16, 788 (2012).
XLVII. C. Guerot, B.H. Tshitchanov, H. Knust and E.M. Carreira, Org. Lett. 13, 780 (2011).
XLVIII. J.J. Folmer, C. Acero, D.L. Thai and H. Rapoport, J. Org. Chem. 63, 8170 (1998).
XLIX. J.K. Augustine, A. Bombrun and R.N. Atta, Synlett 2223 (2011).
L. T. Axenrod, C. Watnick, H. Yazdekhasti and P.R. Dave, Tetrahedron Lett. 34, 6677 (1993).
LI. V.V. Nelel'ko, B.L. Korsunskii, N.N. Makhov, N.V. Chukanov, T.S. Larikova, I.V. Ovchinnikov and V.A. Tartakovsky, Russ. Chem. Bull. 58, 2028 (2009).
LII. T. Yamauchi and J.A. Moore, J. Org. Chem. 31, 42 (1966).
LIII. E. Abele and E. Lukevics, Heterocycles 53, 2285 (2000).
LIV. E. Abele and E. Lukevics, Synthesis of heterocycles from oximes in The Chemistry of Hydroxylamines, Oximes and Hydroxamic Acids, The Chemistry of Functional Groups, Z. Rappoport, J. F. Liebman (Eds.), Wiley, Chichester, 2009, Pt. 1, pp.233-302.
LV. B. Alcaide, P. Almendros, J.M. Alonso, M.F. Aly, C. Pardo, E. Saez and M.R. Torres, J. Org. Chem. 67, 7004 (2002).
LVI. N. Arumugam, R, Raghunathan, V. Shanmugaiah and N. Mathivanan, Bioorg. Med. Chem. Lett. 20, 3698 (2010).
LVII. (a) T. Kamiya, M. Hashimoto and O. Nakaguti, Ger. Pat. 2645085 (1977); Chem. Abstr. 87, 102148t (1977); (b) H. Brauer and T. Denzel, Ger. Pat. 3122793 (1082); Chem. Abstr. 98, 125763f (1983); (c) Takeda Chemical Industries, Jpn. Pat 57212179 (1982); Chem. Abstr. 98, 197886w (1983); (d) W.H. Kostner, Eur.Pat. 61765 (1982); Chem. Abstr. 98, 71823e (1983); (e) R. Heymes and A. Bonnet, Ger. Pat. 3239157 (1983); Chem. Abstr. 99, 53479p (1983); (f) C.M. Cimarusti, R.T. Fox, A.W. Fritz, W.H. Koster and J.L. Moniot, Eur. Pat. 86556; Chem. Abstr. 100, 6197x (1984); (g) W.A. Slusarchyk, T. Dejneka, W.H. Koster and E.M. Gordon, Ger. Pat 3334984 (1984); Chem. Abstr. 101, 130503f (1984); (h) Hoffannn-La Roche, F., and Co. A.-G. Jpn. Pat. 5921681 (1984); Chem. Abstr. 101, 23220q (1984); (i) Takeda Chemical Industries, Ltd. Jpn. Pat. 8534965 (1985); Chem. Abstr. 103, 22377a (1985); (j) Otsuka Chemical Co. Ltd. Jpn. Pat. 60112789 (1985); Chem. Abstr. 103, 215075j (1985); (k) Teikoku Hormone Mfg. Co. Ltd. Jpn. Pat. 6041675 (1983); Chem. Abstr. 103, 104787y (1985); (l) C. Yoshida, K. Tanaka, Y. Ochiai and J. Nakano, Jpn. Pat. 6110581 (1986); Chem. Abstr. 105, 97252f (1986); (m) H. Umezawa, M. Ono, H. Mori and H. Yamashita, Jpn. Pat. 60202882 (1985); Chem. Abstr. 104, 186240x (1986) (n) A. Heymes and A. Bonnet, France Pat. 2558467 (1985); Chem. Abstr. 105, 114820j (1986); (o) J.S. Skotnicki, T.J. Commons, R.W. Rees and J.L. Speth, J. Antibiot. 36,1201 (1983);
LVIII. (a) S. Nakagawa, F. Nakano, T. Mitomo, K Yamada and K. Matsuda, Jpn. Pat. 6153282 (1986); Chem. Abstr. 105, 133656b (1986); (b) N. Noguchi, H. Masuya, T. Sugawara, Y. Kawano and M. Ochiai, J. Antibiot. 38, 1387 (1985); (c) A. Furlenmeier, W. Hofheinz, C.N. Hubschwerlen and H.P. Isenring, US Pat. 4652651 (1987); Chem. Abstr. 154164w (1987); (d) M. Klich, J.G. Teutsch and J.F. Chantot,

Ger. Pat. 3617168 (1986); Chem. Abstr. 106, 138157v (1987); (e) R. Zahler, H. Breuer and G.A. Jacobs, Eur. Pat. 200159 (1986); Chem. Abstr. 106, 84276n (1987); (f) B.Magerlein and K.S. Kim, Eur. Pat. 246786 (1987); Chem. Abstr. 109, 92647m (1988); (g) R.E. Mewshaw and T.J. Commons, US Pat. 4709025 (1987); Chem. Abstr. 108,112071d (1988); (h) R. Heymes and A. Bonnet, France Pat. 2588867 (1987); Chem. Abstr. 109, 128714x (1988); (i) H. Yamashita, N. Minami, K. Sakakibara, S. Kobayashi, M. Ohno, M. Hamada and H. Umezawa, J. Antibiot. 40, 1716 (1987); (j) R.B. Sykes, W.L. Parker, C.M. Cimarusti, W.H. Koster and W.A. Slusarchyk, US Pat. 4775670 (1988); Chem. Abstr. 111, 194450n (1989); (k) M. Ono, N. Minami and H. Yamashita, Jpn. Pat. 63132886 (1988); Chem. Abstr. 23625m (1989); (l) J.E. Sundeen and P.H. Ermann, Eur. Pat. 342423 (1989); Chem. Absr. 113, 40326u (1990); (m) M.R. Barbachyn, S.J. Brickner and R.C. Thomas, Eur. Pat. 281289 (1988); Chem. Abstr. 112, 76796r (1990); (n) M. Ochiai, S. Kishimoto and T. Matsuo, US Pat. 4782147 (1988); Chem. Abstr. 112, 118534m (1990).

LIX. (a) U.D. Treuner, Eur. Pat. 336369 (1989); Chem. Abstr. 113, 40323r (1990); (b) H.A. Albrecht, D.D. Keith and F.M. Konzelman, US Pat. 4912214 (1990); Chem. Abstr. 113, 58789g (1990); (c) B.J. Magerlein, PCT Int. WO Pat. 9003376 (1990); Chem. Abstr. 113, 131871j (1990); (d) H.Y. Kang, A.N. Pae, H.Y. Koh and M.H. Chang, Bull. Korean Chem. Soc. 12, 75 (1991); (e) P.H. Ermann and H. Straub, Eur. Pat. 420069 (1991); Chem. Abstr. 115, 158831z (1991); (f) M.J. Miller, US Pat. 4992544 (1991); Chem. Abstr. 114, 247043r (1991); (g) J. Nieschalk and E. Schaumann, Lieb. Ann. 141 (1996); (h) J. Fetzar, F. Bertha, T. Czuppon, M. Kajtar-Peredy, M. Konkoly-Thege and K. Lempert, J. Chem. Res. (s), 446 (1995); (i).Y. Nagao, T. Kumagai, S. Kobayashi, S. Tamai, K. Ohta, Y. Inoue and I. Kishi, Heterocycles 46, 193 (1997); (j) E.L. Setti, S.N. Malti, O.A. Phillips, A.V.N. Reddy, R.G. Micetich, F. Higasitani, C. Kunugita, K. Nishida and T. Uji, PCT Int. WO Pat. 9910324 (1999); Chem. Abstr. 130, 209544c (1999); (k) E. Desarbre and M.G.P. Page, PCT Int. WO Pat. 2008116813 (2008); Chem. Abstr. 149, 417684t (2008); (l) J.J. Tufariello and D.J.P. Pinto, Tetrahedron Lett. 28, 5485 (1987); (m) M.J. Mitton-Fry, J.T. Arcari, M.F. Brown, J.M. Casavant, S.M. Finegan, M.E. Flanagan, H. Gao, D.M. George, B.S. Gerstenberger, S. Han, J.R. Hardink, T.M. Harris, T. Hoang, M.D. Huband, R. Irvine, M.S. Lall, M.M. Lemmon, C. Li, J. Lin, S.P. McCurdy, J.P. Mueller, L. Mullins, M. Niosi, M.C. Noe, D. Pattavina, J. Penzien, M.S. Plummer, H. Risley, B.P. Schuff, V. Shanmugasundaram, J.T. Starr, J. Sun, J. Winton and J.A. Young, Bioorg. Med. Chem. Lett. 22, 5989 (2012).

LX. VK.V.N. Josyula and R.B. Renslo, PTC Int. WO Pat. 20074049 (2007); Chem. Abstr. 146, 142631p (2007).

LXI. K. Lv, Y. Sun, L. Sun, Z.Wei, H. Gao, J. Wu and M. Liu, ChemMedChem, 7, 1230 (2012).

LXII. A. Aay, N.K Anand, O.J. Bowles, J. Bussenius, S. Costanzo, J.K. Curtis, L. Dubenko, A.A. Joshi, A.R. Kennedy, A.I. Kim, E. Koltun, J.-C.L. Manalo, C.J. Peto, K.D. Rice and T.H. Tsang, PCT Int. Appl. WO Pat. 200744515 (2007); Chem. Abstr. 146, 441655f (2007).

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