HL **ISSN: 2231 – 3087(print) / 2230 – 9632 (Online)**
http://heteroletters.org **Vol. 3: (2), 2013, 229-245**

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

Edgars Abele

Latvian Institute of Organic Synthesis, 21 Aizkraukles Street, Riga, LV-1006, Latvia,
E-mail: abele@osi.lv

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

Keywords: oximes, three-membered heterocycles, aziridines, oxiranes, thiiranes, biological activity

Introduction

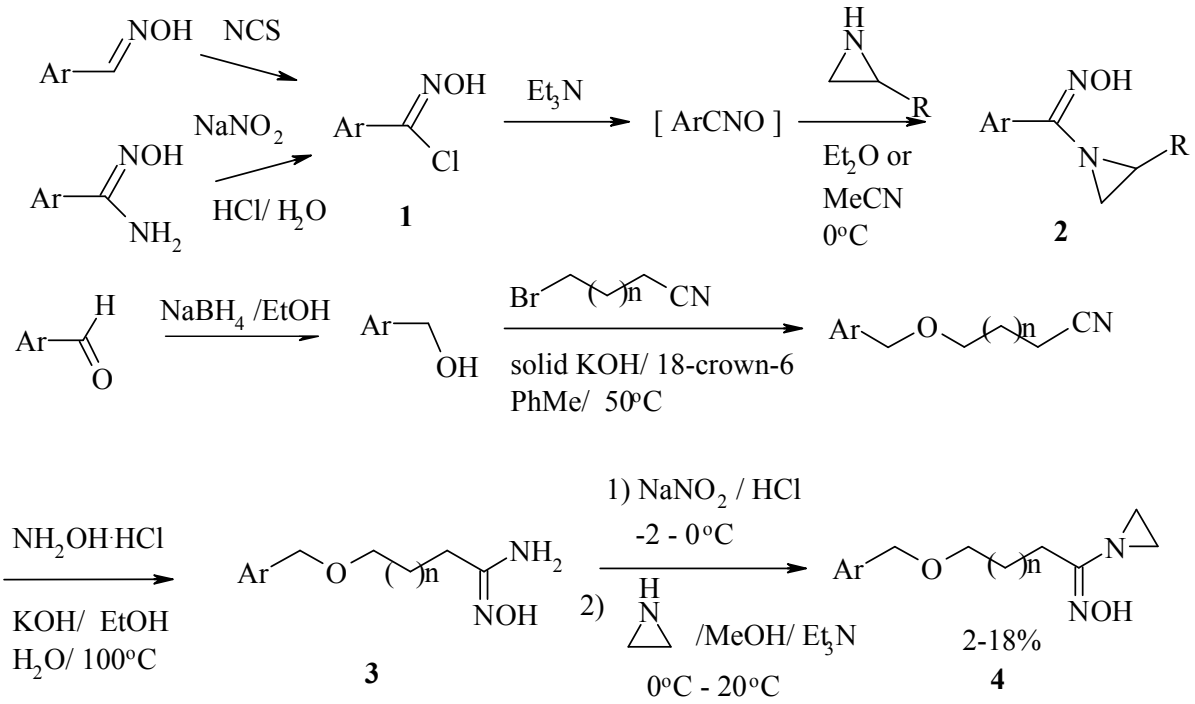
The oximes of three-membered heterocycles with one heteroatom are widely used as intermediates in fine organic synthesis. In this review the principal methods for the production of aldoximes, ketoximes and amidoximes of three-membered heterocycles (such as aziridine, oxirane and thiirane) and their derivatives are summarized. The principal methods for the investigation of structure the oximes of three-membered heterocycles are examined briefly with due to regard isomerism. The reactions and biological activity of the oximes of three-membered heterocycles will be examined in the last parts of the 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 [Ia], indole and isatin oximes [Ib], pyridine oximes [Ic], pyrrole oximes [Id], quinoline oximes [Ie], oximes of five-membered heterocyclic compounds with two [If, Ig] and three [Ih, Ii] heteroatoms, oximes of six-membered heterocyclic compounds with two and three heteroatoms [Ij, Ik], oximes of seven-membered heterocyclic compounds containing one [IIa] and two heteroatoms [IIb] and oximes of six-membered oxygen heterocycles [IIc]).

1. SYNTHESIS OF OXIMES OF THREE-MEMBERED HETEROCYCLES

1.1. Synthesis of aziridine oximes

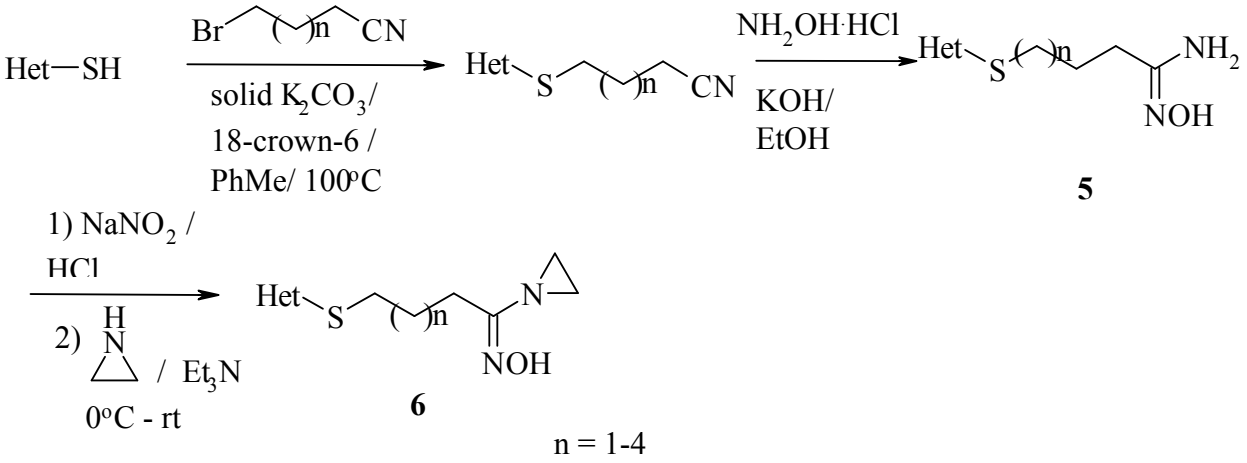
The classical method for the synthesis of aziridine oximes [III-V] is reaction of corresponding hydroximoyl chlorides, generated from aldoximes or amidoximes, with aziridines in the systems E_3N / Et_2O [V-VII], Et_3N / MeCN [VIII], Et_3N / MeOH [IX] or Et_3N / EtOH [Vb]. Typically, aldoximes or amidoximes were halogenated or diazotated in HCl forming hydroximoyl chlorides

1, which undergo further reaction with triethylamine and aziridines forming aziridine oximes **2** [V-VIII]**.** 1-Aziridin-1-yl-ω-[aryl(or hetaryl)oxy]-alkan-1-one oximes **4** were prepared in the four step process starting from corresponding aryl or hetaryl aldehydes. The last step of synthesis included reaction of amidoximes **3** with $NaNO_2$ / HCl / H_2O at 0°C, drying reaction mixtures at temperatures below 25°C, and treatment of crude intermediate with aziridine in the presence of triethylamine.

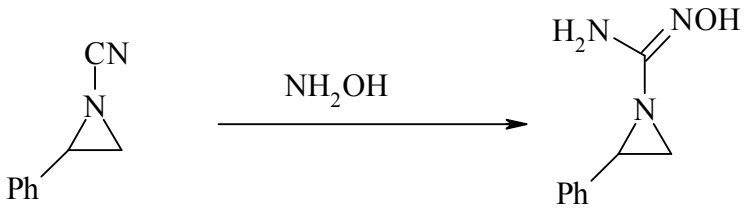


Ar = Ph, subst. Ph, pyridyl, quinolinyl; n = 1-3

1-Aziridin-1-yl-ω-(hetarylsulfanyl)-alkan-1-one oximes **6** were prepared in the three step process from corresponding thiols. The last step of reaction – treatment of amidoximes **5** subsequently with $NaNO_2$ / HCl and aziridine / Et_3N afforded desired aziridine oximes **6** in 2-40% yields. The process of synthesis of aziridine oximes **6** from amidoximes were strongly influenced by hetaryl substituent. Thus, treatment of pyridine, pyrimidine and quinoline substituted N-hydroxy-ω-(hetaryl-ylsulfanyl)-heptanamidines **5** with $NaNO_2$ / HCl and then with aziridine/ Et_3N in dry methanol afforded desired products **6** in only 2-20% yields. However, 1-aziridin-1-yl-ω-(2-benzothiazolylsulfanyl)-alkan-1-one oximes **6** were isolated in 20-40% yields [IX].



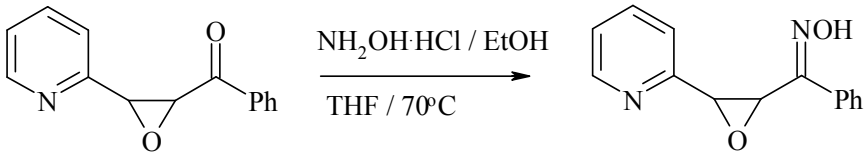
Treatment of N-cyanophenylaziridine **7** with hydroxylamine afforded aziridine oxime **8** [X].



7 **8**

1.2. Synthesis of oxirane oximes

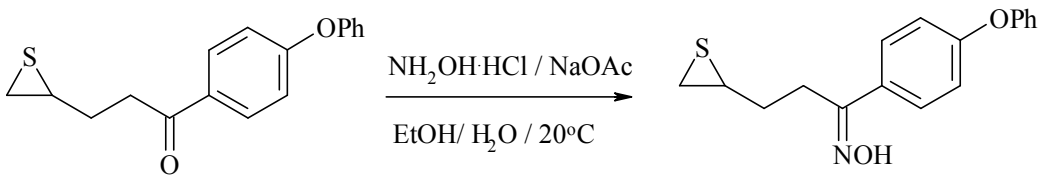
The classical method for the synthesis of oxirane oximes [XI-XIX] is based on the reaction of corresponding aldehydes or ketones with hydroxylamine hydrochloride (or sulphate) in the systems $NaHCO_3$ /Et_2O / H_2O [XX], $NaHCO_3$ / H_2O [XXI], KOAc / AcOH (pH 6) [XXII], NaOAc (^{13}C) / MeOH / [XXIII] NaOAc / H_2O / MeCN [XXIV], Et_3N / EtOH [XXV] or in the pyridine [XXVI], AcOH [XXVII], THF / EtOH [XXVIII] or H_2O [XXIX]. Thus, treatment of ketone (**9**) with $NH_2OH·HCl$ in the mixture of EtOH / THF at 70°C afforded corresponding oxime **10** as single products [XXVIII].



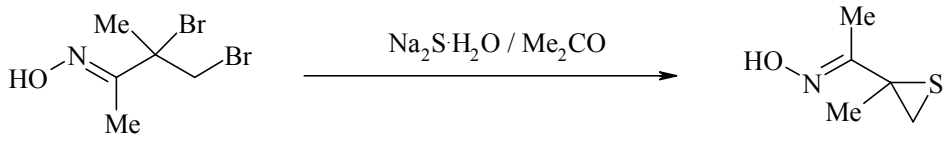
9 **10**

1.3. Synthesis of thiirane oximes

There are two methods dedicated to the synthesis of thiirane oximes. At first, thiirane oxime **12** was obtained by treatment of ketone **11** with $NH_2OH·HCl$ in the presence of NaOAc / EtOH / H_2O [XXX]. Beside this, reaction of 3,4-dibromo-3-methyl-2-hydroxyiminobutane (**13**) with $Na_2S·H_2O$ in acetone afforded 2-(α-hydroxyiminoethyl)-2-methylthiirane (**14**) in 40% yield [XXXI].



11 **12**



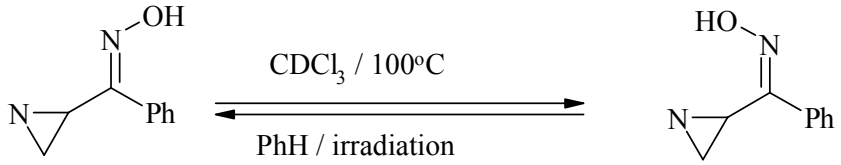
13 **14**

2. STRUCTURE

One of the most reliable methods for determining of the structure of isomeric oximes of three-membered heterocycles with one heteroatom is NMR spectroscopy. The ^{1}H NMR spectra of oximes of aziridine [V, VII, VIII, XXXII, XXXXIII], oxirane [XXXIV] and thiirane [XXXI] have been investigated in details.

IR spectroscopy was also used to study the structure of aziridine [V, VII, VIII, XXXII, XXXXIII], oxirane [XXXIV] and thiirane [XXXI] oximes.

Izomerization of aziridine oximes in details was studied in article [XXXII]. Interestingly, that E-isomer of aziridinylbenzaldoxime **15** in $CDCl_3$ solution at 100°C afforded Z-isomer **16**. However, Z-isomer **16** in benzene undergoes reversible photoisomerization to corresponding E-isomer **15**.



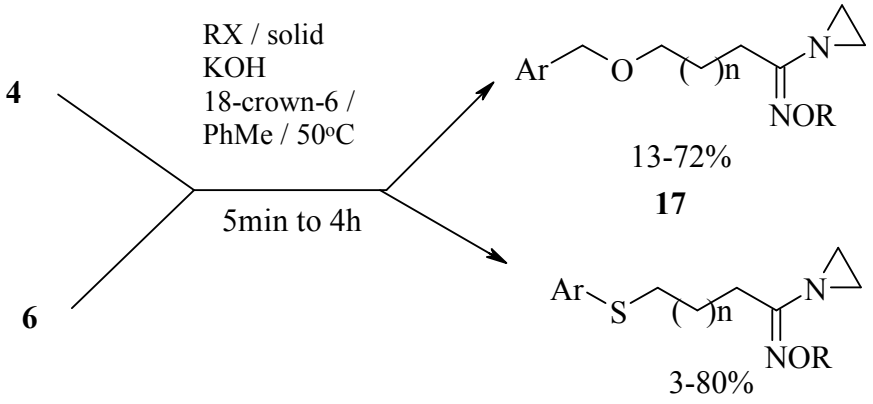
E-**15** Z-**16**

3. REACTIONS OF OXIMES OF THREE-MEMBERED HETEROCYCLES

3.1. Synthesis of O-alkyl derivatives of oximes of three-membered heterocycles

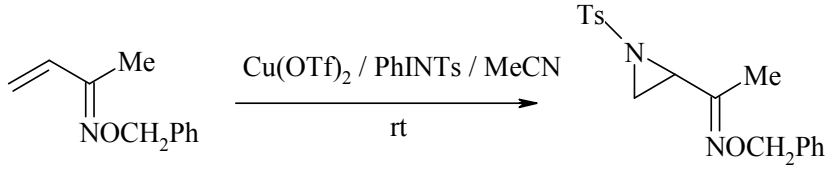
3.1.1. Synthesis of O-alkyl derivatives of aziridine oximes

The principal method for the preparation of aziridine oxime O-ethers is alkylation of corresponding oximes **4** and **6** with alkyl halides in the phase transfer catalytic system solid KOH / 18-crown-6 / PhMe at 50°C. Products were isolated in yields up to 80%. Interestingly, that E and Z isomers of benzothiazole O-methyloximes **18** were easily separated by column chromatography [IX].

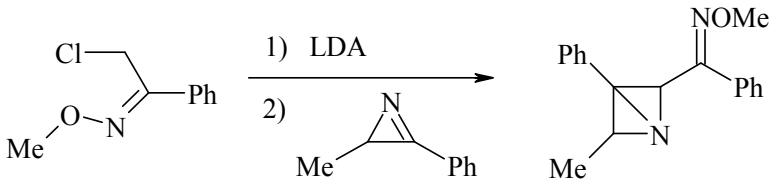


n =1-4; R = Me, CH_2Ph, $(CH_2)_3SiMe_3$

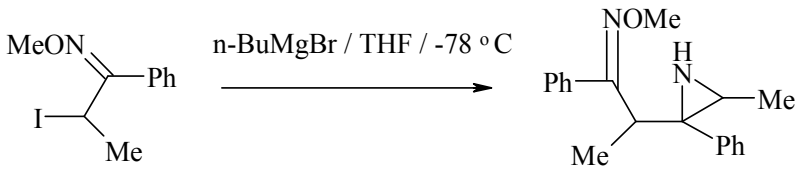
O-Alkyl derivatives of aziridine oximes were also obtained by the formation of novel aziridine ring in the oxime ether derivatives. Thus, direct aziridination of methyl vinyl ketone O-benzyloxime **19** in the system $Cu(OTf)_2$ / PhINTs / MeCN leads to 2-(1-benzyloxyiminoethyl)aziridine **20** (yield 46-60%). Beside this, formation of product **20** proceeds stereoselectively [XXXV]. Metalation of oxime derivative **21** with LDA, following by treatment of the reaction mixture with 2-methyl-3-phenyl-2H-azirine, leads to oxime methyl ether **22** [XXXVI]. Dimerization of 1-phenyl-2-iodo-1-metoxyiminopropane (**23**) in the presence of n-butyl magnesium bromide at -78°C afforded aziridine oxime ether **24** in 41% yield [XXXVII].



19 **20**



21 **22**

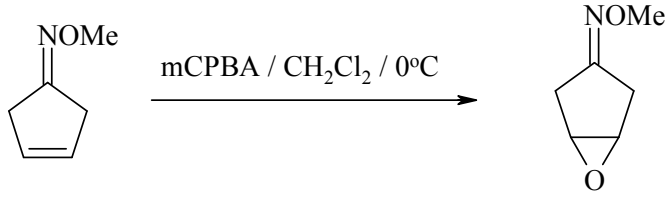


23 **24**

Beside this aziridine oximes easily undergo O-acylation in the presence of acylating agents (Ac_2O, aryl isocyanates or acyl chlorides) leading to corresponding O-acyl derivatives [VII].

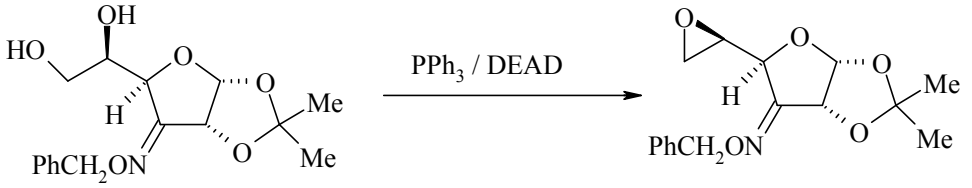
3.1.2. Synthesis of O-alkyl derivatives of oxirane oximes

O-Ethers of oxirane oximes [XXXVIII-XL] usually were obtained by treatment of corresponding carbonyl compounds with O-alkylhydroxylamines in the systems EtOAc / AcOH [XLI], AcONa / MeOH [XLII] or MeOH / pyridine [XXXIV]. Oxirane oxime O-ethers were also obtained in the epoxidation of unsaturated oxime O-ethers in the presence of m-chloroperbenzoic acid (m-CPBA) [XLIII, XLIV]. Thus, treatment of methoxyiminocyclopentene **25** with mCPBA (m-chloroperoxybenzoic acid) in CH_2Cl_2 at 0°C leads to oxime ether **26** in 72% yield [XLIV].



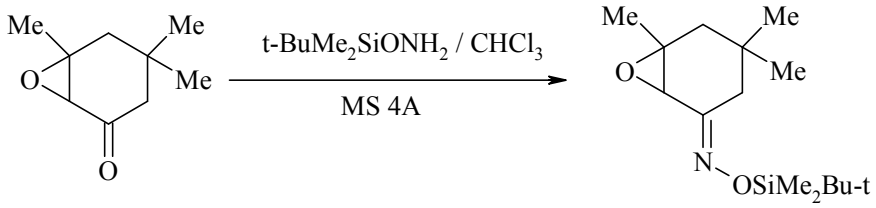
25 **26**

Oxirane derivatives **28** were successfully prepared from 1,2-diol **27** in the presence of PPh_3 / DEAD under Mitsunobu-type conditions [XLV]. Mixture of E and Z-isomeric silyl oxime ethers **30** was obtained in the silylation of 2,3-epoxy-2,5,5-trimethylcyclohexan-1-one oxime (**29**) with O-(tert-butyldimethylsilanyl)hydroxylamine in $CHCl_3$ in the presence of molecular sieves 4Å [XIII].



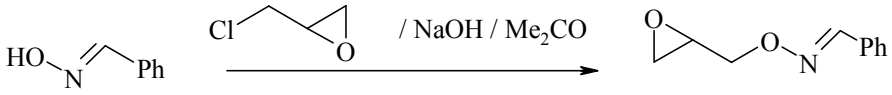
67%

27 **28**



29 **30**

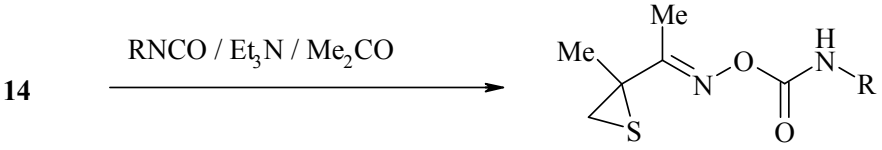
Large group of methods were dedicated to synthesis of O-(2,3-epoxypropyl)oximes by alkylation of corresponding oximes with 2,3-epoxy-1-halogenopropanes [XLVI-LIII]. Typically, treatment of benzaldehyde oxime **31** with 2,3-epoxy-1-chloropropane in the system NaOH / Me_2CO at 56-65°C afforded oxime ether **32** in 65% yield [L].



31 **32**

3.1.3. Synthesis of O-alkyl derivatives of thiirane oximes

Reaction of thiirane oxime **14** with cyclohexyl- and phenyl-isocyanates in the presence of Et_3N in acetone provides O-carbamoyl derivatives **33** in 69-76% yields [XXXI].

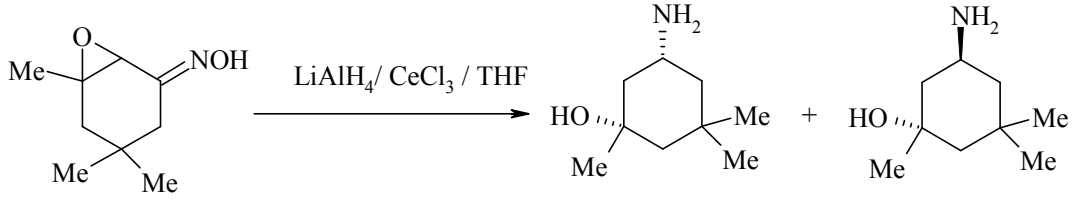


33

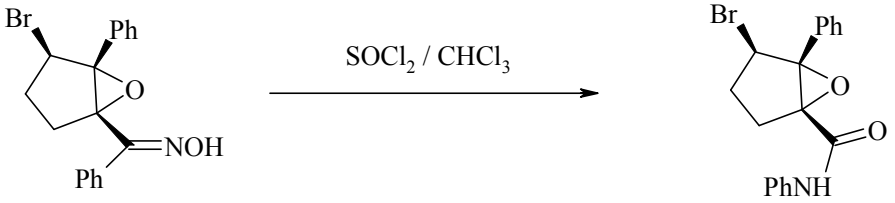
Reaction of oximes with thioepichlorohydrin in the presence of NaOH in acetone afforded oxime ethers of type RR'C=$NOCH_2$(Thiirane) [LIV].

3.2. Transformation of oximes of three-membered heterocycles

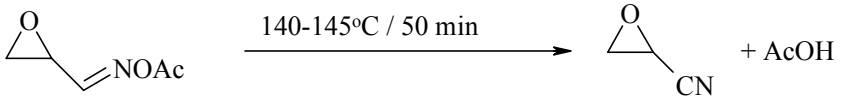
Reduction of oxirane oxime **34** to corresponding isomeric aminoalcohols **35** and **36** was realized in presence $LiAlH_4$ / $CeCl_3$ / THF [LV]. Beckman type rearrangement of oxime **37** in $SOCl_2$ / $CHCl_3$ afforded corresponding amide **38** as a single product [XV]. Glycidaldehyde oxime acetate **39** undergoes thermal elimination of acetic acid leading to nitrile **40** [XX]. Interestingly, that thiirane oxime **14** in the presence of triphenylphosphine in $CHCl_3$ gives product of desulfuration H_2C=CMe-C(Me)=NOH [XXXI].



34 **35** **36**

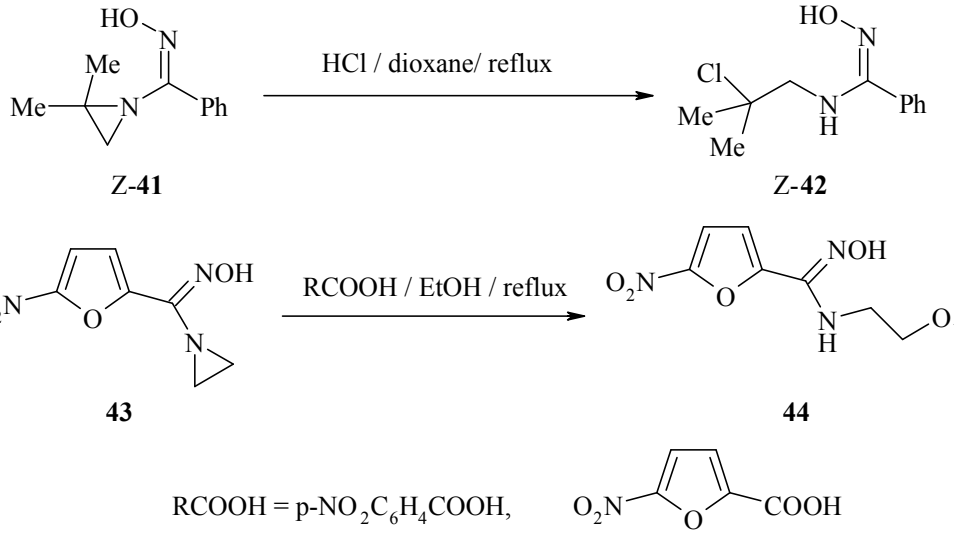


37 **38**

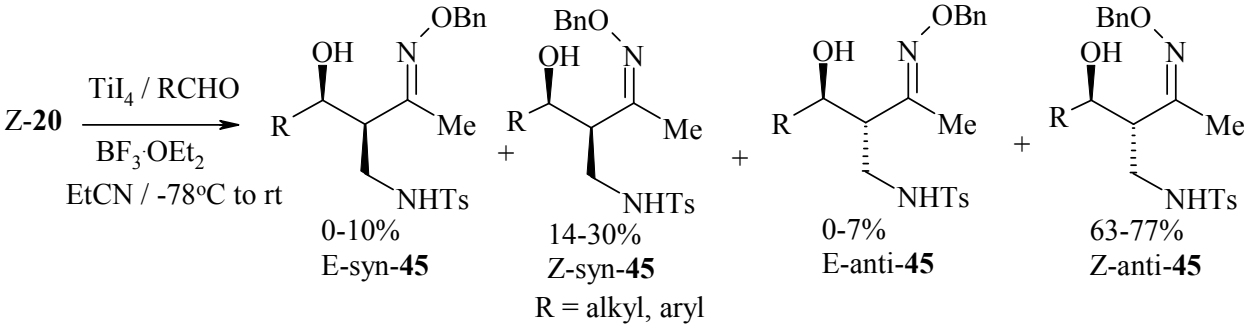


39 **40**

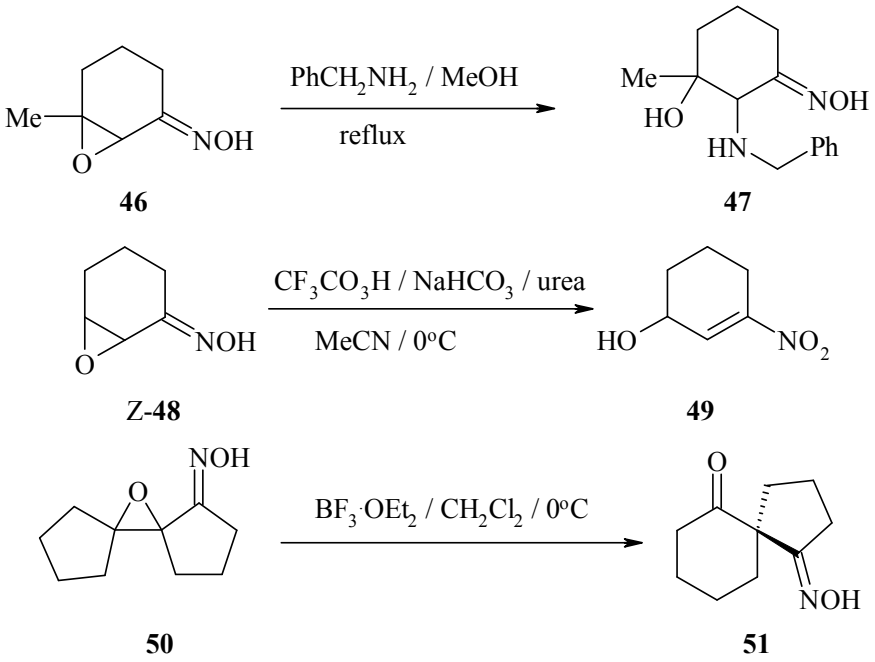
Aziridine oximes readily undergo aziridine ring opening leading to acyclic amino derivatives [VII, XXXIII, XXXV]. Thus, heating of (2,2-dimethylaziridin-1-yl)-phenyl-methanone oxime (**41**) with HCl in dioxane afforded chloro derivative **42** in 93% yield [XXXIII]. Reaction of oxime **43** with carboxylic acids leads to esters **44** [VII].



Reductive ring-opening 2-(1-benzyloxyiminoethyl)aziridines **20** with TiI_4 in the presence of aldehydes and $BF_3 \cdot OEt_2$ was studied in the details in article [XXXV]. Aza-aldol products **45** were isolated in good yields with high diastereoselectivities.



Oxirane ring opening in the corresponding oxime derivatives were widely presented in the literature [XIV, XVIII, XXI, XLII, XLV, LVI, LVII]. Typically, heating of 2,3-epoxy-3-methylcyclohexanone oxime (**46**) with benzylamine in methanol leads to 3-hydroxy-3-methyl-2-phenylmethylaminocyclohexanone oxime (**47**). Sometimes epoxide ring opening was followed by transformation of oxime group or cyclopentanone ring transformations. Thus, interaction of oxime **48** with peroxytrifluoroacetic acid, $NaHCO_3$ and urea in acetonitrile gives 3-nitro-2-cyclohexen-1-ol (**49**) in 72 % yield [XIIa]. Rearrangement of epoxide oxime **50** in the system $BF_3 \cdot OEt_2$ / CH_2Cl_2 afforded E-spiro[4,5]decan-6,10-dione-6-oxime (**51**) in 86% yield [XVIII].

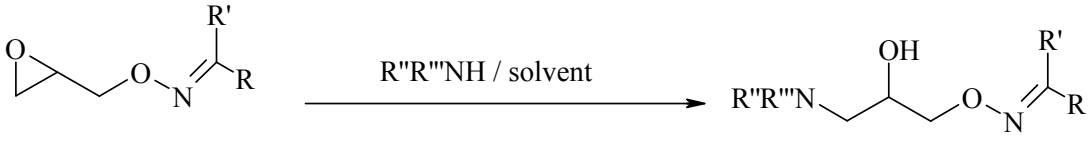


46 **47**

Z-48 **49**

50 **51**

O-(2,3-Epoxypropyl)oximes also easily react with different nucleophiles (for example, amines, azides etc.) leading to products of epoxide ring opening [LVIII]. Treatment of these O-(2,3-epoxypropyl)oximes with amine nucleophiles usually leads to substituted O-(3-amino-2-hydroxypropyl)oximes which are valuable biologically active substances [LII, XLVII, LIX]. Typically, treatment of oxime ethers **52** with primary or secondary amine in protic (EtOH) or aprotic (for example, benzene) solvent afforded O-(3-amino-2-hydroxypropyl)oximes **53.**



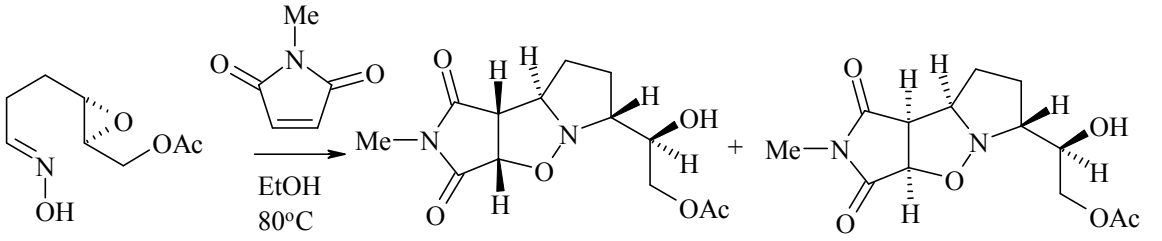
52 **53**

R-R'" = H, alkyl, aryl, hetaryl

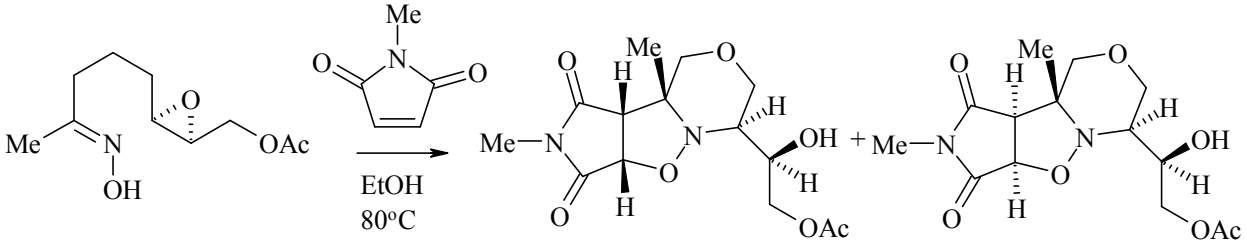
3.3. Synthesis of novel heterocyclic compounds from oximes of three-membered heterocycles

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

Cycloaddition cascade reactions of epoxide oximes with N-methylmaleimide (NMM) leading to compounds with fused pyrrolidine ring were described in details in the article [XXIV]. Thus, heating of oxime **54** in ethanol in the presence of NMM resulted in 2-exo-tet epoxide cleavage, followed by in situ cycloaddition, which leads to a 1:1 mixture of exo- and endo-cycloadducts **55** and **56** (overall yield 73%). Epoxide **57** under similar conditions afforded 2:1 mixture of cycloadducts **58** and **59** (60%).

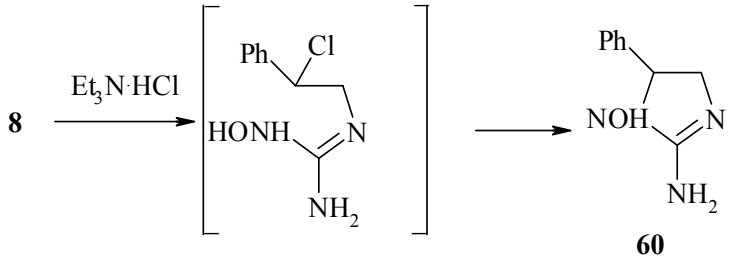


54 **55** **56**



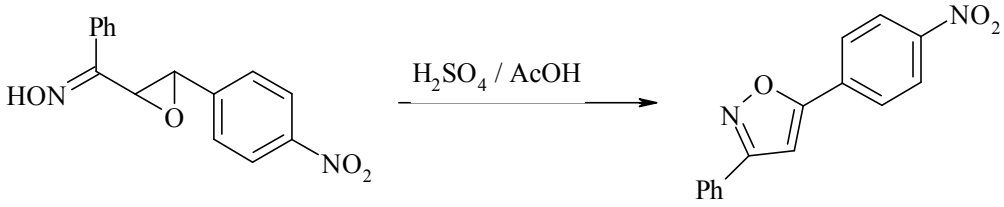
57 **58** **59**

Ring expansion of aziridine oxime **8** in the presence of triethylamine hydrochloride leads to N-hydroxyimidazoline (**60**) [X]



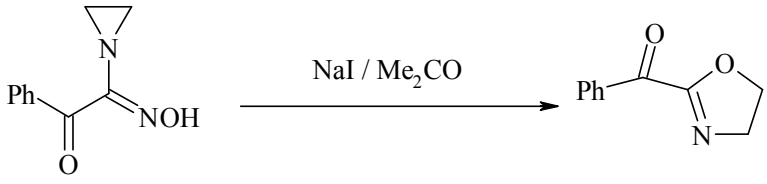
60

Synthesis of novel isoxazole ring by rearrangement of oxirane oximes under acidic conditions [XXVIII, XXIX, LXII-LXV] or in the presence of sulfonium ylide [LXVI] was widely presented in the literature. Thus, heating of oxime **61** in a mixture of acetic and sulfuric acids afforded isoxazole **62** [XXVIII].



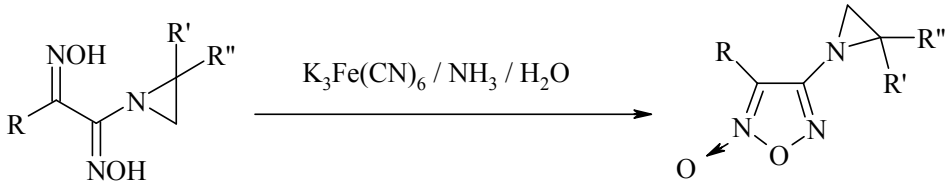
61 **62**

Thermal rearrangement of aziridine oxime **63** in the system NaI / acetone gives 2-benzoyloxazoline **64** in 25% yield [VI].



63 **64**

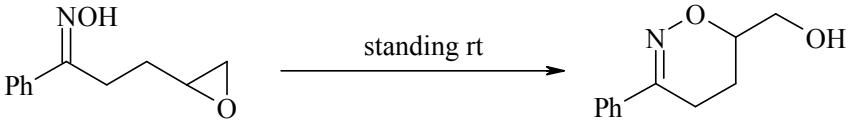
Oxidation of aziridine dioxime **65** in the system $K_3Fe(CN)_6$ / NH_3 / H_2O leads to furoxan derivatives **66** [V]. Beside this, three step synthesis of 1,2,4-oxadiazoles from aziridine oximes were also presented in literature [XXXIII].



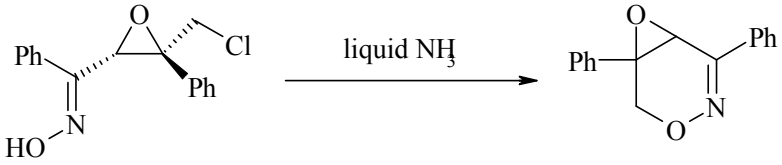
65 **66**

R = H, 1-aziridinyl; R' , R" = H, Me

Some works are connected with synthesis of 1,2-oxazine [XXII, LXIV, LXVII] and 1,3-dioxane [LXVIII] derivatives from oxirane oximes. Thus, oxime **67** standing at room temperature afforded oxazine **68** in quantitative yield [XXII]. (2RS,3RS)-4-Chloro-2,3-epoxy-1,3-diphenylbutan-1-one oxime (**69**) in liquid NH_3 gives bicyclic adduct **70** [LXIV].

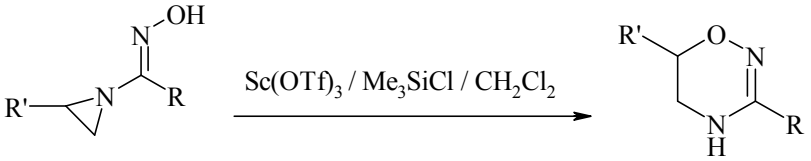


67 **68**



69 **70**

1,2,4-Oxadiazine ring was easily constructed from N-hydoxy-2-carboimidoyl-aziridines in the presence of HCl / H_2O [IIIc] or HCl / H_2O / acetone [Va, VII]. Recently novel and convenient route to 5,6-dihydro-4H-[1,2,4]oxadiazine **72** by rearrangement of aziridin-1-yl oximes **71** in the system $Sc(OTf)_3$ / Me_3SiCl / CH_2Cl_2 was described [LXIX].



25-81%

71 **72**

R = alkyl, aryl; R' = alkyl

4. BIOLOGICAL ACTIVITY OF OXIMES OF THREE-MEMBERED HETEROCYCLES

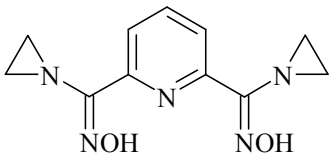
4.1. Cytotoxic, anticancer and antibacterial activities

Cytotoxic activity of selected 1-aziridin-1-yl-ω-[aryl(or hetaryl)oxy]-alkan-1-one and 1-aziridin-1-yl-ω-(hetarylsulfanyl)-alkan-1-one oximes **73-81** was tested *in vitro* on the monolayer

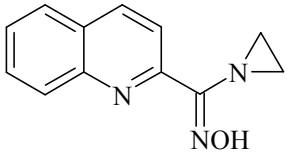
tumor cell lines: MG-22A (mouse hepatoma) and HT-1080 (human fibrosarcoma) (Table 1) [IX]. A preliminary analysis of the structure-activity relationship for the cytotoxic action clearly indicate the strong influence of substituent (Br or H) in the aromatic aziridine oximes **73** and **74** on toxic effects *in vitro*. Among these aromatic oximes compound **74** exhibits high cytotoxicity on the HT-1080 cell line (IC_{50} 5 μg/mL). Very high activity against both cancer lines exhibit benzothiazole amidoximes derivatives **75-78.** Interestingly, that only E-isomer of O-methyl oxime **76** show high activity on the MG-22A and HT-1080 cancer cell lines. 2-Pyridyl **79** (HT–1080; IC_{50} 2-3 μg/mL; MG-22A; IC_{50} 3 μg/mL) and both quinoline **80, 81** substituted oximes also exhibit high cytotoxicity against both cancer cell lines [IX].

Acute toxicity of synthesized compounds was tested on 3T3- Swiss Albino mice embrio fibroblasts**.** In general, the compounds **73-81** exhibit middle to high toxicity in the range of LD_{50} 154-512 mg/kg (Table 1) [IX].

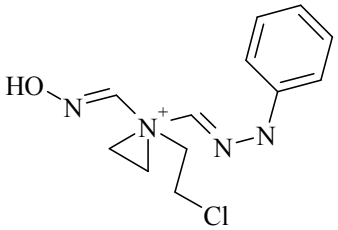
Very high cytotoxicity of heteroaromatic aziridine oximes **82** (HT-1080, IC_{50} = 0.4 μg/ml; MG-22A, IC_{50} = 0.9 μg/ml) and **83** (HT-1080, IC_{50} = 1.5 μg/ml; MG-22A, IC_{50} = 2 μg/ml) were presented in patent [LXX] and article [VIII]. Cytostatic properties of aziridine oxime salts **84** were also presented in the chemical literature [LXXI]. Beside this, oximes of three-membered heterocycles were included in the structure of cephalosporin antibiotics [LXXII].



82

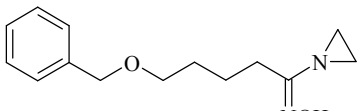
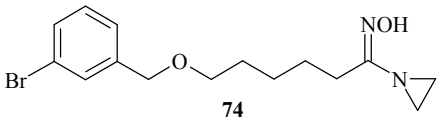
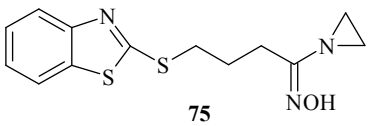
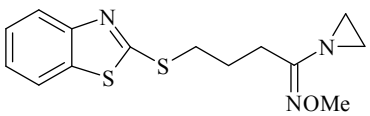


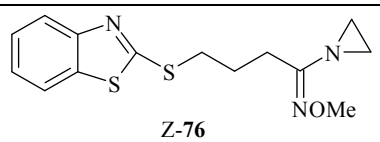
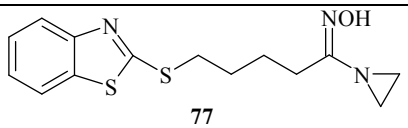
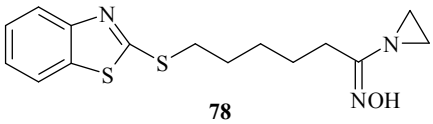
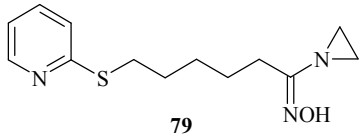
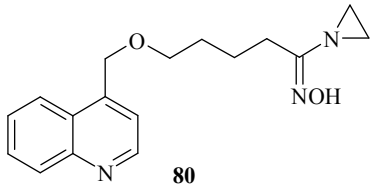
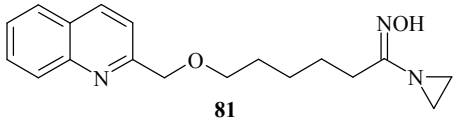
83



84

Table 1. Cytotoxicity of selected 1-aziridin-1-yl-ω-[aryl(or hetaryl)oxy]-alkan-1-one and 1-aziridin-1-yl-ω-(hetarylsulfanyl)-alkan-1-one oximes **73-81** IC_{50} (μg/ml)

Compound	HT-1080, IC_{50}	MG-22A, IC_{50}	3T3, LD_{50}
 **73**	8	14	472
 **74**	5	9	512
 **75**	**0.2**	**0.3**	176
 E-**76**	0.6	0.5	184

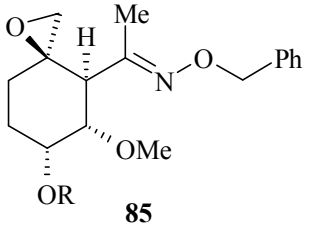
 Z-**76**	3	3	553
 **77**	**0.3**	**0.3**	154
 **78**	1	2	193
 **79**	2	3	265
 **80**	1	1	228
 **81**	2	2	313

4.2. Action on central nervous system

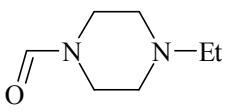
7-Chloro-5-(2-fluorophenyl)-2,3-dihydro-2-{[(methoxyimino)methyl]aziridinyl}-1,4-benzodiazepine 4-oxide was used as intermediate in the synthesis of sedative, muscle relaxant and anticonvulsant agents [LXXIII].

4.3. Angiogenesis inhibitors

Oxirane oxime derivatives **85** were tested as angiogenesis inhibitors [CLVI-CLIX]. These compounds exhibit a wide range of activity on the CNS, as well as, were used in the treatment of asthma, arthritis, psoriasis and allergy.

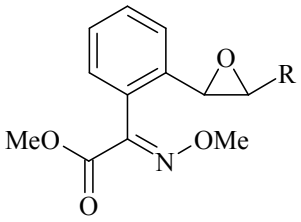


85

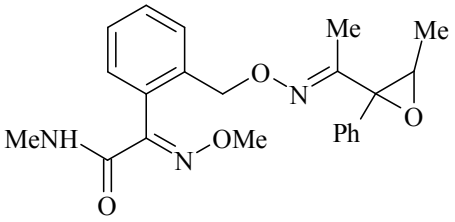
R = Ac, $CONH_2$, 

4.4. Oxirane oximes as fungicides and antifeedants

Derivatives of oxirane oximes **86** [LXXVI, LXXVII] and **87** [LXXVII] exhibit high fungicidal activity. Beside this, oxirane oximes were tested as antifeedants [LXXIX].



86



87

R = alkyl, aryl

References

I. (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, 825 (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);

II. (a) E. Ābele, R. Ābele, Ļ. Golomba, J. Višņevska, T. Beresņeva 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).

III. (a) F.W. Semmler, Chem. Ber. 37, 950 (1904); (b) J. Smrt, J. Beranek and J. Sicher, Czech.Pat. 87649 (1958); Chem. Abstr. 54, 8852g (1960); (c) P. Rajagopalan and C.N. Talaty, J. Am. Chem. Soc. 88, 5048 (1955).

IV. C. Plankiewicz, Bull. Acad. Pol. Sci., Ser. Sci. Chem. 25, 19 (1977).

V. (a) A.V. Eremeev, I.P. Piskunova, V.G. Andrianov and E.E. Liepinsh, Chem. Heterocycl. Comp. 18, 369 (1982); (b) V.G. Andrianov, V.G. Semenikhina and A.V. Eremeev, Russ. J. Org. Chem. 29, 877 (1993).

VI. T. Sasaki, T. Yoshioka and Y. Suzuki, Bull. Chem. Soc. Jpn. 44, 185 (1971)

VII. T. Sasaki and T. Yoshioka, Bull. Chem. Soc. Jpn. 42, 556 (1969).

VIII. A. Grigorjeva, A. Jirgensons, I. Domracheva. E. Yashchenko, I. Shestakova, V. Andrianov and I. Kalvinsh, Chem. Heterocycl. Comp. 45, 161 (2009).

IX. (a) E. Abele, R. Abele, V. Bridane, I. Domraceva, L. Golomba, A. Grigorjeva, E. Jascenko, A. Jirgensons, I. Kalvins and I. Sestakova, Latvia Pat. 14080 (B), (2010); (b) E. Abele, R. Abele, V. Bridane, I. Domraceva, L. Golomba, A. Grigorjeva, E. Jascenko, A. Jirgensons, I. Kalvins and I. Sestakova, Latvia Pat. 14081 (B) (2010); (c) E. Abele, R. Abele, V. Bridane, I. Domraceva, L. Golomba,

A. Grigorjeva, E. Jascenko, A. Jirgensons, I. Kalvins and I. Sestakova, Latvia Pat. 14082 (B), (2010).
X. M.M. Campbell, A. C. Campbell, A. Peace, J. Pick and G.F. Woods, J. Chem. Soc., Chem. Commun. 1164 (1985).
XI. S. Bodforss, Chem. Ber. 51, 192 (1918).
XII. (a) E.J. Corey and H. Estreicher, Tetrahedron Lett. 22, 603 (1981); (b) E.J. Corey and J.P. Dittami, J. Am. Chem. Soc. 107, 256 (1985).
XIII. S.E. Denmark and M.S. Dappen, J. Org. Chem. 49, 798 (1984).
XIV. E.J. Corey, E.S. Melvin, Jr. and M.F. Haslanger, Tetrahedron Lett. 3117 (1975).
XV. R.C. Fuson, H.H. Hully, J.F. McPherson and F.W. Spangler, J. Org. Chem. 7, 462 (1942).
XVI. O. Widman, Chem. Ber. 49, 477 (1916).
XVII. C.L. Stevens and V.J. Traynelis, J. Org. Chem. 19, 533 (1954).
XVIII. R.D. Bach, M.W. Tubergen and R.C. Klix, Tetrahedron Lett. 27, 3565 (1986).
XIX. A. Souto, J. Rodriguez and C. Jimenez, Tetrahedron Lett. 50, 7395 (2009).
XX. G.B. Payne, J. Am. Chem. Soc. 81, 4901 (1959).
XXI. B. Kasum, R.H. Prager and C. Tsopelas, Austr. J. Chem. 43, 355 (1990).
XXII. J.R. Donald, M.G. Edwards and R.J.K. Taylor, Tetrahedron Lett. 48, 5201 (2007).
XXIII. J.M. Richter, Y. Ishihara, T. Masuda, B.W. Whitefield, T. Llamas, A. Pohjakallio and P.S. Baran, J. Am. Chem. Soc. 130, 17938 (2008).
XXIV. H.A. Dondas, M. Frederickson, R. Grigg, J. Markandu and M. Thornton-Pett, Tetrahedron, 53, 14339 (1997).
XXV. J. Yamaguchi, M. Toyoshima, M. Shoji, H. Kakeya, H. Osada and Y. Hayashi, Angew. Chem. Int. Ed. 45, 789 (2006).
XXVI. G. Lazarevski, G. Kobrehel, S. Dokic, L. Kolacny-Babic and B. Kojic-Prodic, J. Antibiotics 47, 349 (1994).
XXVII. L. Reichel and A. Neubauer, Z. Chem. 4, 459 (1964); Chem Abstr. 62, 9085a (1965).
XXVIII. H.J. Roth and M. Schwarz, Arch. Pharm. 294, 769 (1961).
XXIX. J.-C. Cherton, M. Lanson, D. Ladjama, Y. Guichon and J.-J. Besselier, Can J. Chem. 68, 1271 (1990).
XXX. M. Lee, M. Ikejiri, D. Klimpel, M. Toth, M. Espahbodi, D. Hesek, C. Forbes, M. Kumarasiri, B.C. Noli, M. Chang and S. Mobashery, Med. Chem. Lett. 3, 490 (2012).
XXXI. V.P. Tashchi, T.I. Rukasov, Yu.G. Orlova, Yu.A. Putsykin and Yu.A. Baskakov, Chem. Heterocycl. Comp. 18, 566 (1982).
XXXII. J.E. Johnson, J.A. Maia, K. Tan, A. Ghafouripour, P. de Meester and S.S.C. Chu, J. Hetrocycl. Chem. 23, 1861 (1986).
XXXIII. J.E. Johnson, D. Nwoko, M. Hotema, N. Sanchez, R. Alderman and V. Lynch, J. Hetercycl. Chem. 33, 1583 (1996).
XXXIV. S. Coulton, P.J. O'Hanlon and N.H. Rogers, Tetrahedron 43, 2165 (1987).
XXXV. M. Shimizu, S. Nishiura and I. Hachiya, Heterocycles 74, 177 (2007).
XXXVI. T. Tsuritani, K. Yagi, H.Shinokubo and K. Oshima, Angew. Chem. Int. Ed. 42, 5613 (2003).
XXXVII. H. Kakiya, K. Yagi, H. Shinokubo and K. Oshima, J. Am. Chem. Soc. 124, 9032 (2002).

XXXVIII. R.L. Mansell and E.W. Weiler, Phytochemistry, 19, 1403 (1980).
XXXIX. R.G. Kostyanovskii, A.V. Prosyanik, A.I. Mishchenko, G.V. Shustov, I.I. Chervin, N.L. Zaichenko, A.P. Pleshkova, P.N. Belov and V.I. Markov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 28, 1640 (1979).
XL. S. Su, D.E. Acquilano, J. Arumugasamy, A.B. Beeler, E.L. Eastwood, J.R. Giguere, P. Lan, X. Lei, G.K. Min, A.R. Yeager, Y. Zhou, J.S. Panek, J.K. Snyder, S.E. Schaus and J.A. Porco, Jr., Org. Lett. 7, 2751 (2005).
XLI. (a) X. Lei, N. Zaarur, M.Y. Sherman and J.A. Porco, Jr., J. Org. Chem. 70, 6474 (2005); (b) C. Li and J.A. Porco, Jr., J. Org. Chem. 70, 6053 (2005).
XLII. D. Sawada and M. Shibasaki, Angew. Chem. Int. Ed. 39, 209 (2000).
XLIII. J.B. Rodriguez, E.G. Gros and A.M. Stoka, Zeitsch. Naturforsch., B, 43, 1038 (1988).
XLIV. E.J. Corey, K. Niimura, Y. Konishi, S. Hashimoto and Y. Hamada, Tetrahedron Lett. 27, 2199 (1986).
XLV. M. Fernandez-Gonzalez and R. Alonso, J. Org. Chem. 71, 6767 (2006).
XLVI. J. Wolf, R. Polanowski and M. Krajewska, Pol. Pat. 53525; Chem. Abstr. 68, 49175d (1968).
XLVII. S.I. Sadykh-Zade and A.A. Eiynbov, Vop. Neftekhim. 3, 143 (1971); Chem. Abstr. 76, 140349q (1972).
XLVIII. P.L. Ferrarini, W. Badawneh, G. Saccomanni, V. Calderone, R. Grecco, A. Marinelli, R. Scatizzi, and P.L. Barilli, Eur. J. Med. Chem. 32, 955 (1997).
XLIX. S. Kurbatov, A. Sirit and N. Sen, Org. Prep. Proced. Int. 31, 681 (1999).
L. E. Gueler, N. Sen, S. Kurbanov and R. Nirzaoglu, Org. Prep. Proced. Int. 30, 195 (1998).
LI. B. Macchia, A. Balsamo, M.C. Breschi, G. Chiellini, M. Macchia, A. Martinelli, C. Martini, C. Nardini, S. Nencetti, A. Rossello and R. Scatizzi, J. Med. Chem. 37, 1518 (1994).
LII. M. Blanc, A. Tamir, S. Aubriot, M.C. Michel, M. Bouzoubaa, G. Leclerc and P. Demenge, J. Med. Chem. 41, 1613 (1998).
LIII. A. Kocak, S. Kurbanli and S. Malkandu, Synth. Commun. 37, 1155 (2007).
LIV. S.I. Sadykh-Zade and V.A. Dzhafarov, Uch. Zap. Azerb. Gos. Univ., Ser. Khim. Nauk 2, 33 (1972); Chem. Abstr. 83, 78986j (1975).
LV. R. Dresler and A. Uzarewicz, Pol. J. Chem. 74, 1581 (2000).
LVI. R. Das and D.N. Kirk, J. Chem. Soc., Perkin. Trans.1, 1821 (1984).
LVII. G. Saccomanni, M. Bodawneti, B. Adinolfi, V. Calderone, T. Cavallini, P.L. Ferrarini, R. Greco, G. Manera and L. Testai, Bioorg. Med. Chem. 11, 4921 (2003).
LVIII. A.K Sinha, S.N. Rastogi, G.K. Patnaik and R.C. Srimal, Indian J. Chem. Sec.B, 32B, 738 (1993).
LIX. (a) M. Bouzoubaa, G. Leclerc, N. Decker, J. Schwartz and G. Andermann, J. Med. Chem. 27, 1291 (1984); (b) A. Charaf, M. Bouzoubaa, A. Bouzoubaa, M. Blanc, G Leclerc, Eur. J. Med. Chem. 29, 69 (1994); (c) V.K. Tandon, M. Kumar, A.K. Awasthi, H.O. Saxena and G.K. Goswamy, Bioorg. Med. Chem. Lett. 14, 3177 (2004); (d) J. Stanek, J. Frei, H. Mett, P. Schneider and U. Regenass, J. Med. Chem. 35, 1339 (1992); (e) B. Jamart-Gregoire, P. Caubere, M. Blanc, J.P. Gnassounou and G. Advenier, J. Med. Chem. 32, 315 (1989); (f) A. Balsamo,

M.C. Breschi, G. Ghiellini, A. Lucacchini, M. Macchia, A. Martinelli, C. Martini, C. Nardini, E. Orlandini, F. Romagnoli and A. Rossello, Eur. J. Med. Chem. 29, 855 (1994).
LX. E. Abele and E. Lukevics, Heterocycles 53, 2285 (2000).
LXI. 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.
LXII. S. Ito and M. Sato, Bull. Chem. Soc. Jpn. 63, 2739 (1990).
LXIII. A.A. Jarrar, A.Q. Hussein and A.S. Madi, J. Heterocycl. Chem. 27, 275 (1990).
LXIV. C.L. Stevens and V.J. Traynelis, J. Org. Chem. 19, 533 (1954).
LXV. L.I. Klimova and N.N. Suvorov, Chem. Natural Comp. 2, 265 (1966).
LXVI. P. Bravo and G. Gaviraghi, Gazz. Chem. Ital. 102, 395 (1972).
LXVII. X. Wan, G. Doridot and M.M. Joullie, Org. Lett. 9, 977 (2007).
LXVIII. D. Sawada, M. Kanai and M. Shibasaki, J. Amer. Chem. Soc. 122, 10521 (2000).
LXIX. Y.S. Cho, S.K. Kang, J.H. Ahn, J.D. Ha and J.-K. Choi, Tetrahedron Lett. 47, 9029 (2006).
LXX. I. Kalvinsh, V. Andrianov, I. Shestakova, I. Kanepe and I. Domracheva, WO Pat. 0121585; Chem. Abstr. 134, 252268 (2001).
LXXI. I.A. Poplavskaya, R.G. Kurmangalieva, S.F. Khalilova, K.A. Abdullin and I.K. Kudrina, Pharm. Chem. J. 15, 231 (1981).
LXXII. M.W. Foxton, C.J. Latham, T.L. Gane and G. Smith, UK Pat.2168972; Chem. Abstr. 106, 32702d (1987).
LXXIII. A. Walser, US Pat. 4226768; Chem. Abstr. 94, 84183p (1981).
LXXIV. M. Fardis, H.-J. Pyun, J. Tario, H. Lin, C.U. Kim, J. Ruckman, Y. Lin, L. Green and B. Hicke, Bioorg. Med. Chem. 11, 5051 (2003).
LXXV. H.-J. Pyun, M. Fardis, J. Tario, C.Y. Yang, J. Ruckman, D. Henninger, H. Jin and C.U. Kim, Bioorg. Med. Chem. Lett. 14, 91 (2004).
LXXVI. R. Seele, F. Schuetz, H. Wingert, H. Sauter, E. Ammermann and G. Lorenz, Ger. Pat.3911724; Chem. Abstr. 114, 228705s (1991).
LXXVII. R. Seele, F. Schuetz, H. Wingert, H. Sauter, E. Ammermann and G. Lorenz, Eur. Pat.393428; Chem. Abstr. 114, 228706t (1991).
LXXVIII. W. Grammenos, H. Sauter, H. Bayer, T. Grote, A. Gypser, R. Kirstgen, B. Muller, A. Ptock, F. Rohl, R. Gotz, G. Lorenz, E. Ammermann, S. Strathmann and V. Harries, PCT Pat. 9847886; Chem. Abstr. 129, 316131a (1998).
LXXIX. G. Ruberto, A. Renda, C. Tringali, E.M. Napoli and M.S.J. Simmonds, J. Agricult. Food Chem. 50, 6766 (2002).

Received on January 14,2013.