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REVIEW ARTICLE

2-Amino-4-thiazolidinones: synthesis and reactions

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Methods for the synthesis of 2-amino-4-thiazolidinones and their chemical properties are reviewed for the first time. 2-Amino-4-thiazolidinones are synthetically versatile substrates, as they can be used for the synthesis of a large variety of biologically active compounds, such as thiazolodihydropyrazoles, thiazolotriazines, and thiazolotetrahydropyrimidones, and as a raw material for drug synthesis. The high reactivity of amino and active methylene groups next to the carbonyl of the thiazolidin ring represents useful targets for many organic reactions.

Keywords: thiazolidine; 5-ones; synthesis; reactions; applications

1. Introduction

Amino-4-thiazolidinones, or their tautomeric forms, named pseudothiohydantoin have encountered a prominent place in heterocyclic chemistry, due to the high practical value of these compounds, and the broad spectrum of their biological activities. For example, 2,4-dioxothiazolidine derivatives are useful as hypoglycemics and hypolipidemic agents (*1*), and as intermediates in the synthesis of antidiabetic drugs (*2*). Other compounds derived from 2-amino-4-thiazolidinones are used as anticancer agents (*3, 4*), antiproliferative (*5*), antiinflammatory (*6*), cardiotonic (*7*), tuberculostatic (*8, 9*) and as dual 5-lipoxygenase and cyclooxygenase inhibitors with antiinflammatory activity (*10*). Despite this versatile importance, 2-amino-4-thiazolidinones have not been previously reviewed. The main purpose of this review is to present a survey of the chemistry of 2-amino-4-thiazolidinones and provide useful and up-to-date data for medicinal chemists.

2. Synthesis of 2-amino-4-thiazolidinones

2.1. *From α-halo carboxylic acid derivatives*

2-Imino-4-thiazolidone HCl **1** was synthesized from ethyl chloroacetate and thiourea in 95% ethanol, neutralization in sodium acetate solution under reflux gave 2-imino-4-thiazolidone **2**

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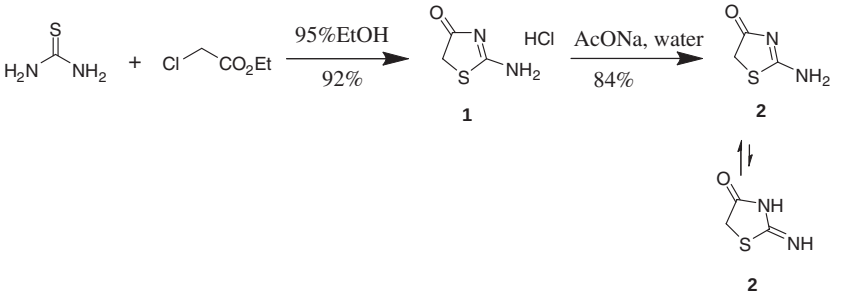
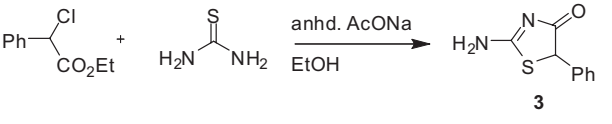
(Scheme 1) (*11–15*).



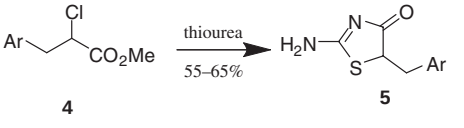
Scheme 1. Synthesis of 2-imino-4-thiazolidone.

5-Phenyl-2-amino-4-thiazolinone **3** has been synthesized from ethyl 2-chloro-2-phenylacetate, thiourea, and anhydrous sodium acetate in ethanol (Scheme 2) (*16*).



Scheme 2. Route to 5-Phenyl-2-amino-4-thiazolinone.

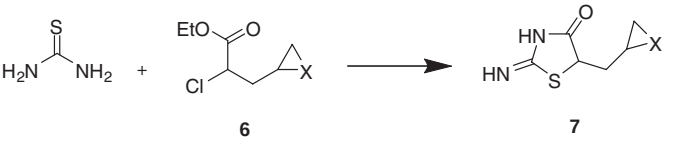
Treatment of 2-chloroesters **4** with thiourea afforded 2-aminothiazolidin-4-ones **5** (Scheme 3) (*17, 18*).



Ar=[2,4-$(OEt)_2$; 3,4-Me_2; 4-Cl-3-MeO; 3,5-$(MeO)_2$; 4-NHCOMe,3-MeO]phenyl

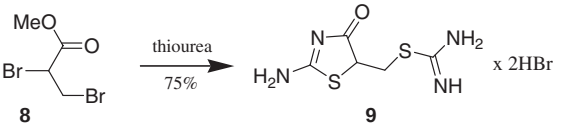
Scheme 3. Synthesis of 2-aminothiazolidin-4-ones.

Oxiranyl- and thiiranyl-substituted 2-imino-thiazolidine-4-ones **7** (Scheme 4) were prepared by refluxing thiourea with ethyl 2-chloro-3-(oxiran-2-yl)propanoate (**6**, X=O) or ethyl 2-chloro-3-(thiiran-2-yl)propanoate (**6**, X=S) (*19*).



Scheme 4. Synthesis of substituted 2-imino-thiazolidine-4-ones.

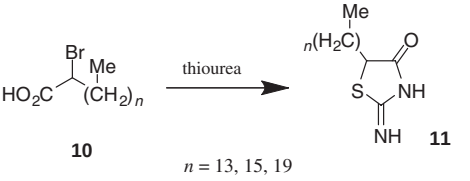
2-[(2-Amino-4,5-dihydro-4-oxothiazol-5-yl)methyl]isothiourea **9** was obtained upon treatment of methyl 2,3-dibromopropanoate **8** with thiourea (Scheme 5) (*19*).



8 **9**

Scheme 5. Synthesis of isothiourea.

Long-chain-substituted 2-imino-4-thiazolidinones and 2,4-thiazolidinediones **11** were prepared in about 80% yield by condensation of α-bromo-carboxylic acids **10** with thiourea (Scheme 6) (*20*).

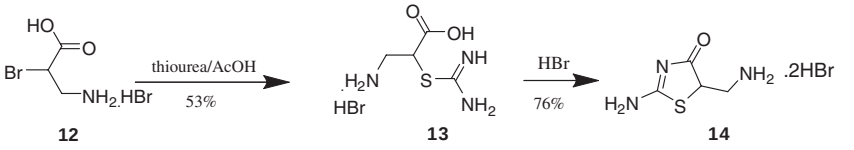


10 **11**

n = 13, 15, 19

Scheme 6. Synthesis of 2-imino(oxa)-4-thiazolidinones.

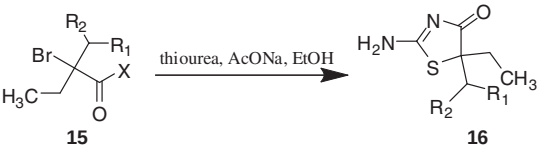
Reaction of 2-bromo-3-aminopropionic acid **12** with thiourea in AcOH gave 53% thiourea derivative **13**, which upon treatment with HBr gave 76% thiazoline derivative **14** (Scheme 7) (*21*).



12 **13** **14**

Scheme 7. Synthesis of thiazoline derivative.

5,5-Dialkyl-2-imino-4-thiazolidones **16** were prepared by condensing thiourea with dialkyl-substituted bromoacetic acids or the acid chlorides **15** (Scheme 8) (*22*).

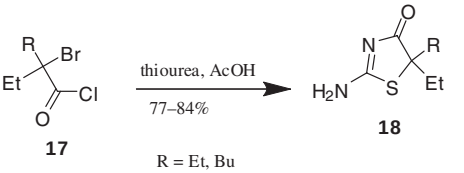


15 **16**

X = OH, Cl; R_1/R_2 = Et/Et, Et/Pr, Et/iso-Bu, Et/sec-Bu, ethyl/1-methylbutyl

Scheme 8. Synthesis of 5,5-dialkyl-2-imino-4-thiazolidones.

5,5-Disubstituted-2-imino-4-thiazolidones **18** were prepared by refluxing of α-bromoacid chlorides **17** with thiourea in glacial acetic acid (Scheme 9) (*23*).

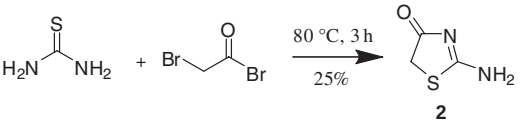


17 **18**

R = Et, Bu

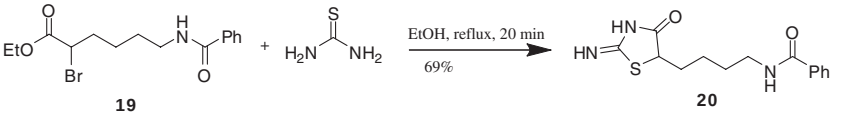
Scheme 9. Synthesis of 5,5-disubstituted-2-imino-4-thiazolidones.

Reaction of α-bromo acetyl bromide and thiourea afforded 2-amino-4-thiazolidinone **2** in 25% yield (Scheme 10) (*24*).



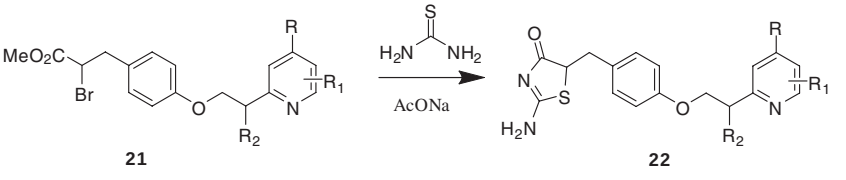
Scheme 10. Route to 2-amino-4-thiazolidinone **2**.

Refluxing ethyl 6-(benzamido)-2-bromohexanoate **19** with thiourea in ethanol gave the iminothiazolidinone **20** (Scheme 11) (*25*).



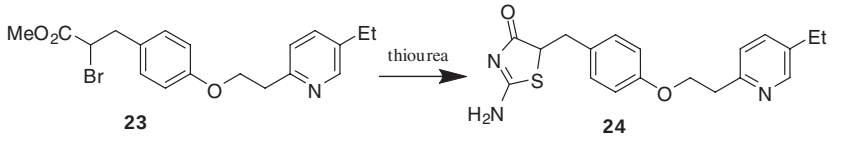
Scheme 11. Synthesis of iminothiazolidinone.

The synthesis of 5-[4-(pyridylalkoxy)benzyl]-2,4-thiazolidinediones **22**, which have hypoglycemic and hypolipidemic activities, was described. Thus treatment of α-bromoesters **21** with thiourea in the presence of sodium acetate afforded 2-amino-4-thiazolidinones **22** (Scheme 12) (*26*).



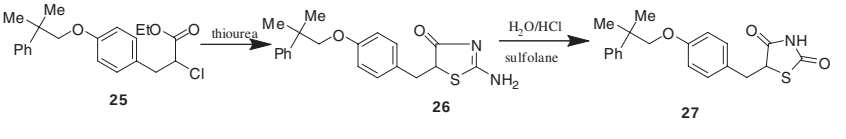
Scheme 12. Synthesis of 2-amino-4-thiazolidinones.

α-Bromoester **23** underwent cyclocondensation with thiourea to give the imino compound **24** (Scheme 13) (*27*).



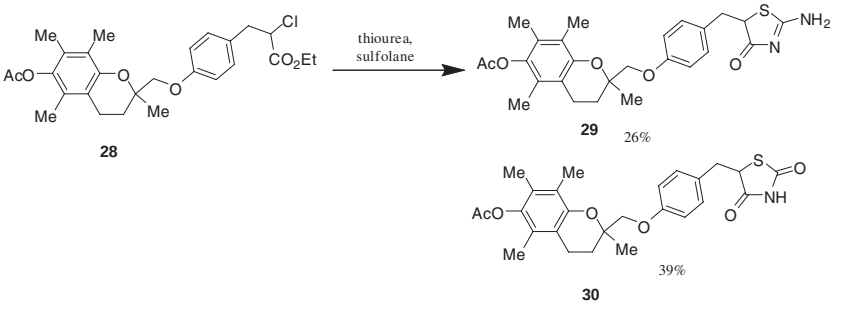
Scheme 13. Synthesis of imino compound.

Ethyl 2-chloro-3-[4-(2-methyl-2-phenylpropoxy)phenyl]propionate **25** was condensed with thiourea followed by hydrolysis using HCl to give 5-[4-(2-methyl-2-phenylpropoxy)benzyl] thiazolidine-2,4-dione **27** which possess hypoglycemic and hypolipidemic activities (Scheme 14) (*28*).



Scheme 14. Synthesis of (AL-321).

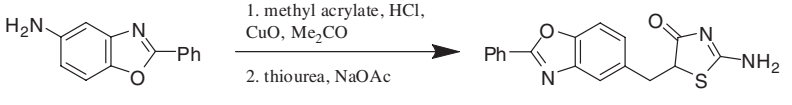
Reaction of α-haloester **28** with thiourea in the presence of sulfolane afforded 2-((4-((2-amino-4-oxo-4,5-dihydrothiazol-5-yl)methyl)phenoxy)methyl)-2,5,7,8-tetramethylchroman-6-yl acetate **29** and 2-((4-((2,4-dioxothiazolidin-5-yl)methyl)phenoxy)methyl)-2,5,7,8-tetramethylchroman-6-yl acetate **30** in 26% and 39% yields, respectively (Scheme 15) (*29*).



28 **29** **30**

Scheme 15. Synthesis of tetramethylchroman-6-yl acetates.

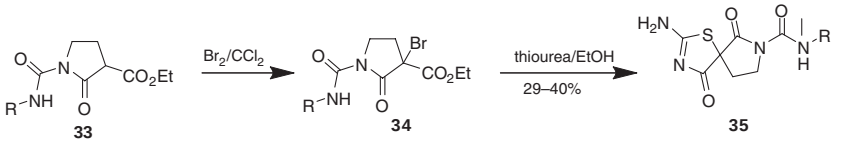
2-Phenylbenzo[*d*]oxazol-5-amine **31** was converted to 2-amino-5-((2-phenylbenzo[*d*]oxazol-5-yl)methyl)thiazol-4(5*H*)-one **32**, upon treatment with methyl acrylate followed by reaction with thiourea (Scheme 16) (*30*).



31 **32**

Scheme 16. Synthesis of thiazol-4(5*H*)-one.

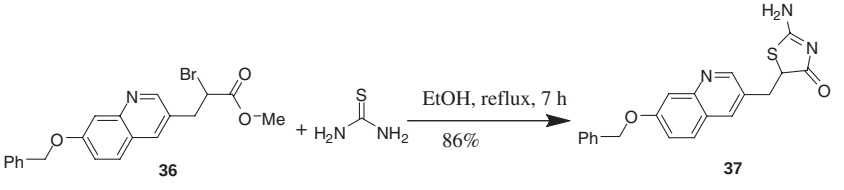
1-Carbaniloyl-2-oxo-3-pyrrolidinecarboxylates **33** were brominated to give **34**. These underwent substitution and cyclization reactions with thiourea to give spiro[pyrrolidinethiazolidine] **35** in 29–40% yields (Scheme 17) (*31*).



33 **34** **35**

Scheme 17. Synthesis of spiro[pyrrolidinethiazolidine].

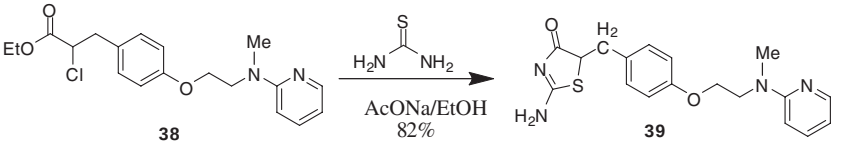
Methyl 3-(7-(benzyloxy)quinolin-3-yl)-2-bromopropanoate **36** was cyclocondensed with thiourea in the presence of AcONa in ethanol under reflux for 7 h to give 86% 2-imino-5-[(7-benzyloxy-3-quinolyl)methyl]thiazolidin-4-one **37** which has an antihyperglycemic effect (Scheme 18) (*32*).



36 **37**

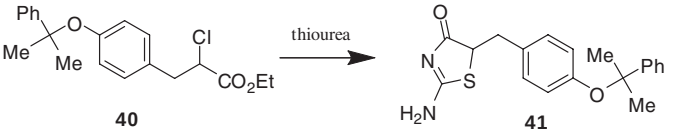
Scheme 18. Synthesis of thiazolidin-4-one.

2-Aminothiazol-4(5*H*)-one **39** was prepared in 82% by reaction of α-chloro-ester **38** with thiourea in ethanol in the presence of sodium acetate (Scheme 19) (*33*).



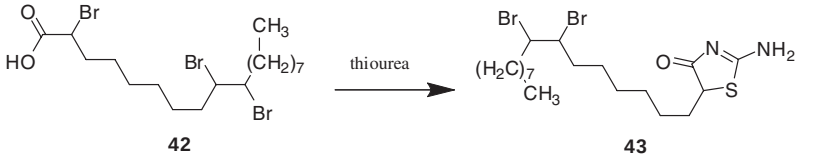
Scheme 19. Synthesis of 2-aminothiazol-4(5*H*)-one.

Thiazolidin-4-one **41** of hypoglycemic and hypolipidemic properties was prepared by treatment of ethyl 2-chloro-3-(4-(2-phenylpropan-2-yloxy)phenyl)propanoate **40** with thiourea (Scheme 20) (*34*).



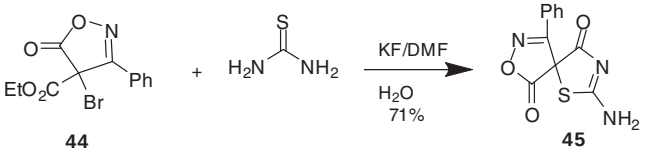
Scheme 20. Synthesis of thiazolidin-4-one.

Reaction between 2,9,10-tribromostearic acid **42** and thiourea afforded amino thiazolidinone **43** (Scheme 21) (*35*).



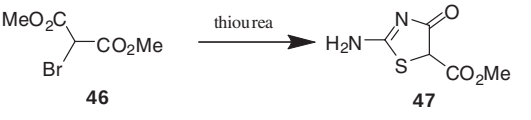
Scheme 21. Synthesis of aminothiazolidinone.

Reaction of ethyl 4-bromo-5-oxo-3-phenyl-4,5-dihydroisoxazole-4-carboxylate **44** with thiourea afforded 2-amino-9-phenyl-7-oxa-1-thia-3,8-diazaspiro[4.4]nona-2,8-diene-4,6-dione **45** (Scheme 22) (*36*).



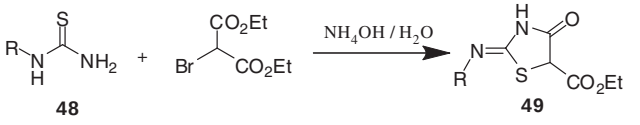
Scheme 22. Synthesis of 3,8-diazaspiro[4.4]nona-2,8-diene-4,6-dione.

α-Bromocarbonyl compound **46** reacted with thiourea to give thiazole derivative **47** (Scheme 23) (*37*).



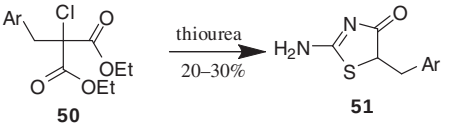
Scheme 23. Synthesis of thiazole derivative.

2-Alkyl/arylimino-5-carbethoxythiazolidin-4-ones **49** have been synthesized by the interaction of thiocarbamides **48** with diethyl bromomalonate (Scheme 24) (*38*).



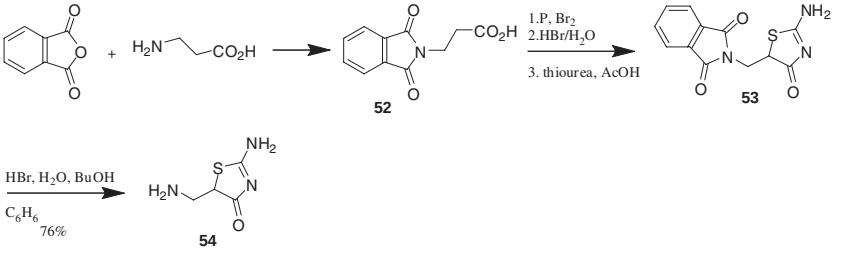
Scheme 24. Synthesis of 2-subs.imino-5-carbethoxythiazolidin-4-ones.

Condensation of diethyl 2-chloro-2-arylmethylmalonates **50** with thiourea afforded 2-aminothiazolidin-4-one derivatives **51** (Scheme 25) (*17*).



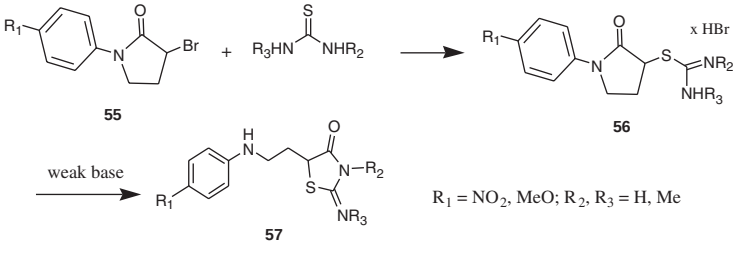
Scheme 25. Synthesis of 2-aminothiazolidin-4-one derivatives.

Phthalic anhydride was allowed to react with 3-aminopropanoic acid to give 3-(1,3-dioxoisoindolin-2-yl)propanoic acid **52**, which upon bromination followed by reaction with thiourea afforded 2-[(2-amino-4-oxo-4,5-dihydrothiazol-5-yl)methyl]isoindoline-1,3-dione **53**. Hydrolysis of **53** in the presence of hydrobromic acid gave 2-amino-5-(aminomethyl)thiazol-4(5*H*)-one **54** (Scheme 26) (*21*).



Scheme 26. Synthesis of 2-amino-5-(aminomethyl)thiazol-4(5*H*)-one.

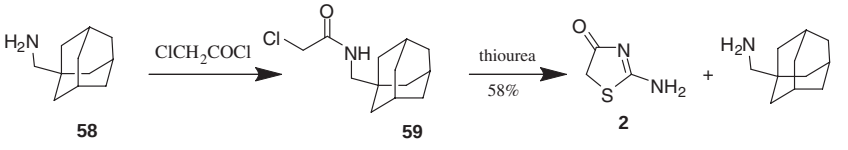
Substituted S-(1-phenylpyrrolidin-2-on-3-yl)isothiuronium salts **56** in weakly basic media underwent intramolecular recyclization reaction in which the γ-lactam cycle is split and a thiazolidine cycle **57** is formed (Scheme 27) (*39–41*).



Scheme 27. Synthesis of thiazolidine.

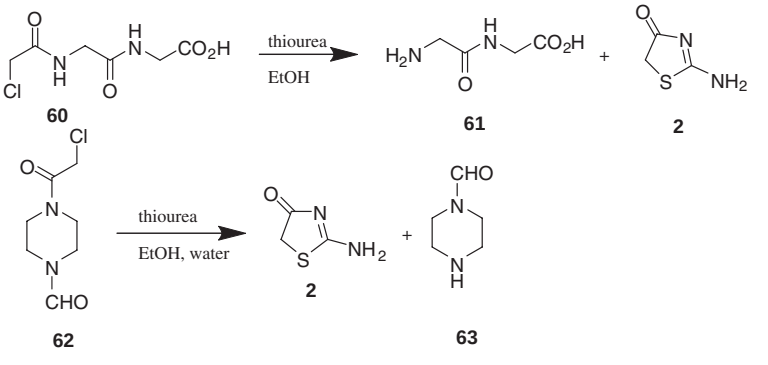
2.2. *From chloroacetamides*

Method for the removal of chloroacetyl groups is used for the preparation of 2-imino-4-thiazolidinone. Thus, 1-adamantyl methyl amine **58** was acylated with chloroacetyl chloride to give the corresponding amide **59**, which was then treated with thiourea to give 2-aminothiazol-4(5*H*)-one **2** in addition to the recovering of the starting material as a by-product (Scheme 28) (*42*).



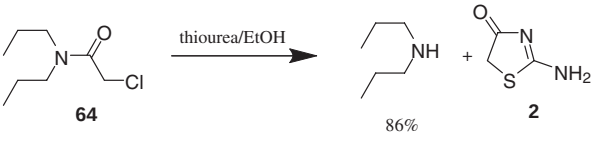
Scheme 28. Pathway to 2-aminothiazol-4(5*H*)-one.

2-(2-(2-Chloroacetamido)acetamido)acetic acid **60** was treated with thiourea to give a mixture of 2-(2-aminoacetamido)acetic acid **61** and 2-aminothiazol-4(5*H*)-one **2**. While 4-(2-chloroacetyl)piperazine-1-carbaldehyde **62** gave a mixture of piperazine-1-carbaldehyde **63** and 2-aminothiazol-4(5*H*)-one **2** (Scheme 29) (*43*).



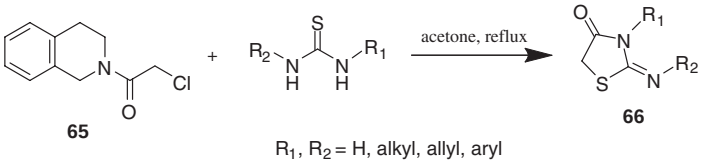
Scheme 29. Synthesis of 2-aminothiazol-4(5*H*)-one.

Condensation of 2-chloro-*N*,*N*-dipropylacetamide **64** with thiourea in ethanol gave 2-amino-4-thiazolidinone **2** as a side product (Scheme 30) (*44*, *45*).



Scheme 30. Synthesis of amino-4-thiazolidinone.

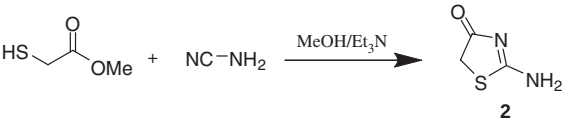
2-Imino-4-thiazolidinones **66** were prepared by reaction of thiourea derivatives with *N*-(2-chloroacetyl)tetrahydroisoquinoline **65** (Scheme 31) (*46*).



Scheme 31. Synthesis of 2-Imino-4-thiazolidinones.

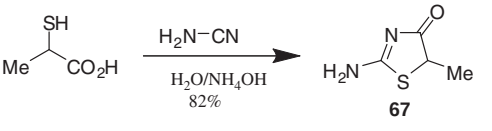
2.3. *From cyanamide*

Cyclocondensation of methyl 2-mercaptoacetate with cyanamide in methanol containing triethylamine afforded 2-amino-4-thiazolidinone **2** (Scheme 32) (*47*).



Scheme 32. Synthesis of 2-amino-4-thiazolidinone.

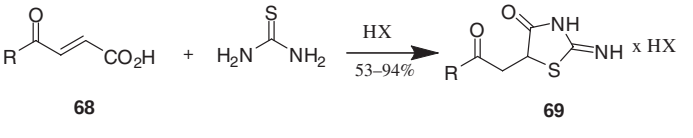
Heating thiolactic acid with cyanamide in water/ammonium hydroxide gave NH_3 gas and a precipitate of 82% 2-imino-4-oxo-5-methylthiazolidine **67** (Scheme 33) (*48*).



Scheme 33. Synthesis of 2-imino-4-oxo-5-methylthiazolidine.

2.4. *From α,β-unsaturated carboxylic acids*

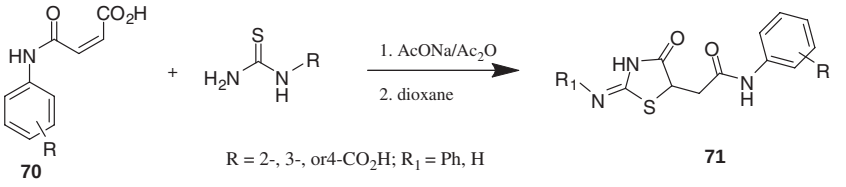
Single-stage synthesis of 5-aroylmethyl-2-iminothiazolidin-4-ones **69** was achieved by reaction between β-aroylacrylic acids and thiourea. Thus, hydrochlorides, hydrobromides, and sulfates of **69** were prepared in good yields by cyclocondensation of β-aroylacrylic acids **68** with thiourea in the presence of the appropriate HX (Scheme 34) (*49*).



R = Ph, *p*-MeC_6H_4, *p*-BrC_6H_4, *p*-ClC_6H_4, 5,6,7,8-tetrahydro-2-naphthyl; X= Br, Cl, HSO_4

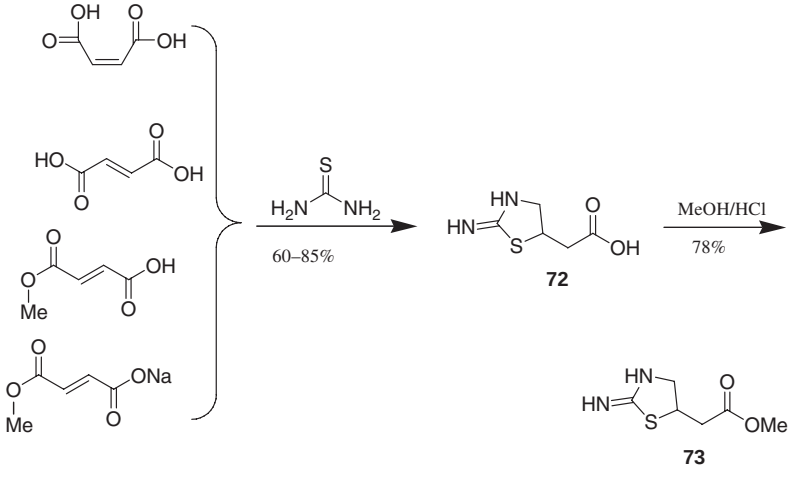
Scheme 34. Synthesis of sulfates.

N-(maleoylamino)benzoic acids **70** were treated with thiourea derivatives to give thiazolidines **71** (Scheme 35) (*50*).



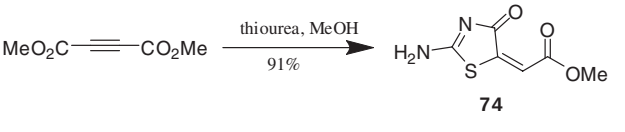
Scheme 35. Synthesis of thiazolidines.

Reactions of thiourea with, maleic acid, fumaric acid, methyl hydrogen fumarate, or its sodium salt give 2-imino-2,3,4,5-tetrahydro-1,3-thiazol-5-acetic acid **72**, its methyl ester **73** was prepared by heating in methanol in the presence of concentrated HCl (Scheme 36) (*51*).



Scheme 36. Synthesis of methyl 1,3-thiazol-5-acetic acid ester.

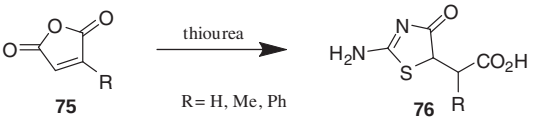
Dimethyl acetylene-dicarboxylic esters (DMADCs) have been treated with thiourea to give (*E*)-methyl 2-(2-amino-4-oxothiazol-5(4*H*)-ylidene)acetate **74** (Scheme 37) (*52, 53*).



Scheme 37. Synthesis of (*E*)-methyl 2-(2-amino-4-oxothiazol-5(4*H*)-ylidene)acetate.

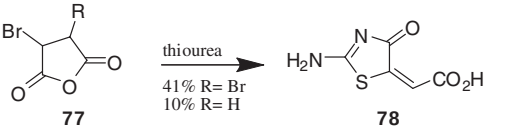
2.5. *From anhydrides or imides*

Maleic anhydrides **75** reacted with thiourea to give 1,3-thiazolidine **76** (Scheme 38) (*51*).



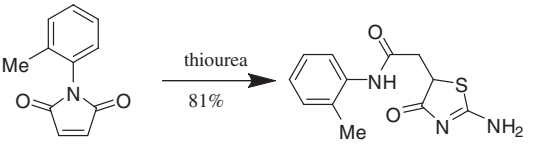
Scheme 38. Synthesis of 1,3-thiazolidine.

Reaction of 2,3-dibromosuccinic anhydride or bromomaleic anhydride **77** and thiourea gave (*E*)-2-(2-amino-4-oxothiazol-5(4*H*)-ylidene)acetic acid **78** (Scheme 39) (*54*).



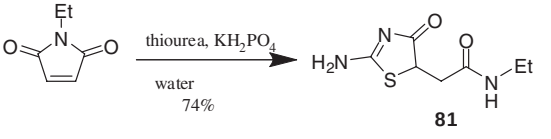
Scheme 39. Synthesis of (*E*)-2-(2-amino-4-oxothiazol-5(4*H*)-ylidene)acetic acid.

1-*o*-Tolyl-1*H*-pyrrole-2,5-dione **79** was reacted with thiourea to give 2-(2-amino-4-oxo-4,5-dihydrothiazol-5-yl)-*N*-*o*-tolylacetamide **80** in good yield (Scheme 40) (*51*).



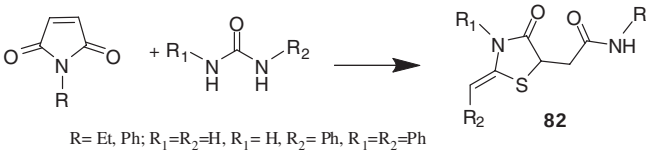
Scheme 40. Synthesis of 2-(2-amino-4-oxo-4,5-dihydrothiazol-5-yl)-*N*-*O*-tolylacetamide.

When a buffer solution of *N*-ethylmaleimide and thiourea was left for 2 days at room temperature, *N*-ethyl-α-(2-imino-4-oxothiazolidin-5-yl)acetamide **81** was obtained (Scheme 41) (*55*).



Scheme 41. Synthesis of *N*-ethyl-α-(2-imino-4-oxothiazolidin-5-yl)acetamide.

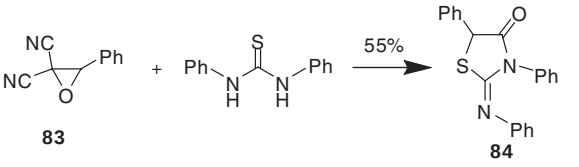
N-substituted maleimides were condensed with thiourea derivatives to give 4-thiazolidone derivatives **82** in 46–71% yields (Scheme 42) (*56*).



Scheme 42. Synthesis of 4-thiazolidone derivatives.

2.6. *From epoxides*

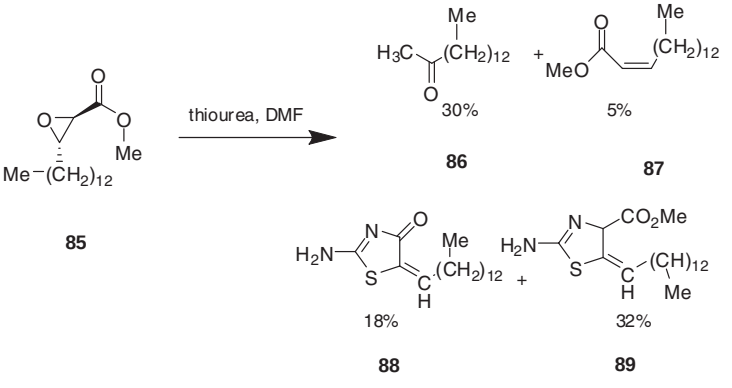
The nucleophilic ring opening of gem-dicyano epoxides by N-substituted or N,N′-disubstituted thioureas leads to 2-imino-4-thiazolidinones, via postulated cyanocarbonyl intermediates. Thus, reaction of 2,2-dicyano-3-phenyloxirane **83** and diphenylthiourea gave 55% diphenylthiazolidinone **84** (Scheme 43) (*57*).



83 **84**

Scheme 43. Synthesis of diphenylthiazolidinone.

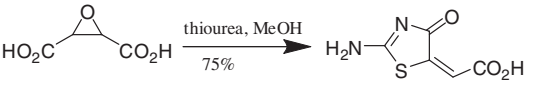
Methyl *E*-2,3-epoxyhexadecanoate **85** reacted with thiourea to give aminotridecylthiazolinecarboxylate **88** and tridecylmethylenethiazolinone **89** along with *Z*- and *E*-**86** and **87** (Scheme 44) (*58*).



85 **86** **87** **88** **89**

Scheme 44. Synthesis of thiazolinecarboxylate and thiazolinone.

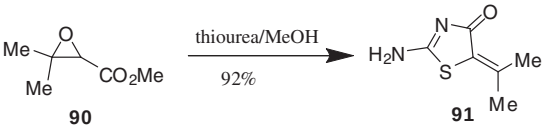
The reaction of *Z*-methylepoxysuccinic acid with thiourea gave 2-imino-4-oxothiazolidine **78** (Scheme 45) (*59*).



78

Scheme 45. Synthesis of 2-imino-4-oxothiazolidine.

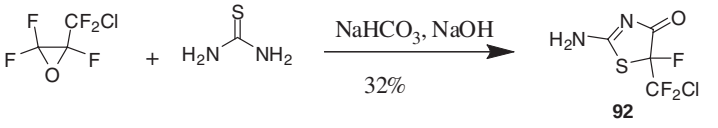
Ethylene oxide **90** and thiourea in MeOH, kept for 2 weeks at 30 °C, gave 2-amino-4-keto-5-isopropylidene-2-thiazoline **91** in 92% yield (Scheme 46) (*60*).



90 **91**

Scheme 46. Synthesis of 2-amino-4-keto-5-isopropylidene-2-thiazoline.

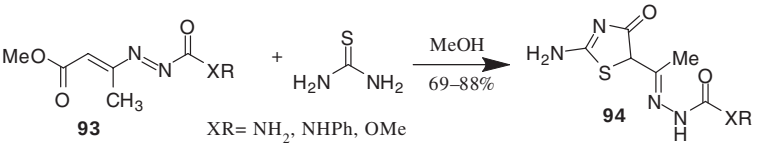
Reactions of 3-chloropentafluoropropene-1,2-oxide with thiourea gave 2-amino-5-(chlorodifluoromethyl)-5-fluorothiazol-4(5*H*)-one **92** (Scheme 47) (*61*).



Scheme 47. Synthesis of 5-fluorothiazol-4(5*H*)-one.

2.7. *From azoalkenes*

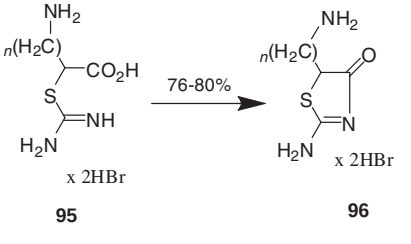
Thiourea easily reacted under very mild conditions with some conjugated azoalkenes **93** in a one-pot reaction to give 39–88% of substituted thiazolinones **94** that frequently exhibited hydrazono-hydrazino tautomerism in the chain at position 5 of the ring. The chemical structure was confirmed by x-ray diffraction (Scheme 48) (*62*).



Scheme 48. Synthesis of substituted thiazolinones.

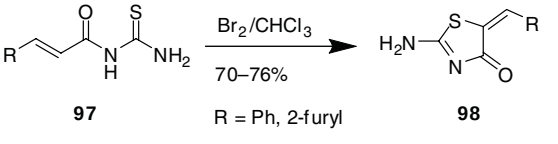
2.8. *From isothiourea derivatives*

2-Amino-4-oxy-5-aminomethyl(ethyl)thiazolines, which have radioprotective activity, were synthesized. 2-Amino-4-oxo-5-aminomethyl-2-thiazoline dihydrobromide (**96**, $n = 0$) and 2-amino-4-oxo-5-aminoethyl-2-thiazoline dihydrobromide (**96**, $n = 1$) were prepared by cyclization of *S*-(1-carboxy-2-aminoethyl)isothiourea (**95**, $n = 0$) and *S*-(1-carboxy-3-aminopropyl)isothiourea (**95**, $n = 1$), respectively (Scheme 49) (*63*).



Scheme 49. Synthesis of 2-thiazoline.

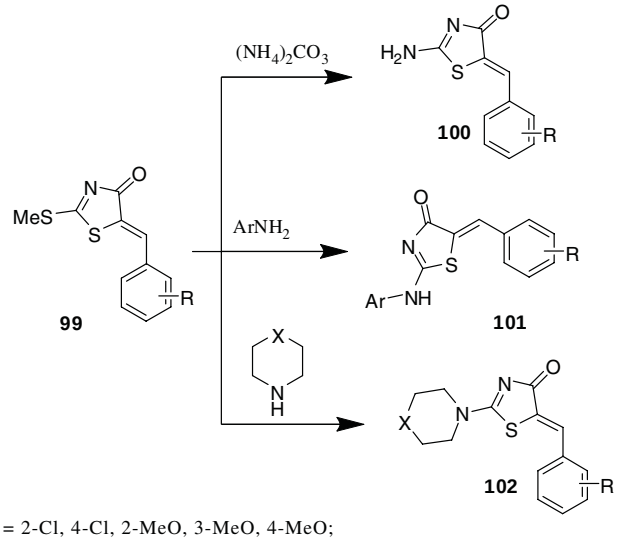
Synthesis of 2-substituted *E*-5-arylidenethiazolin-4-ones **98** from α,β-unsaturated acyl isothiocyanates was reported. Thus, propenoylthioureas **97** were oxidized with bromine in chloroform to *E*-5-arylidenethiazolin-4-ones **98** (Scheme 50) (*64*).



Scheme 50. Synthesis of *E*-5-arylidenethiazolin-4-ones.

2.9. *From 2-(alkylthio)-2-thiazolin-4-ones*

Reactions of *E*-5-(arylmethylene)-2-(alkylthio)-2-thiazolin-4-ones **99** with ammonium carbonate were reported to give **100** while reaction with aromatic primary amine and secondary amines afforded **101** and **102** (Scheme 51) (*65*).

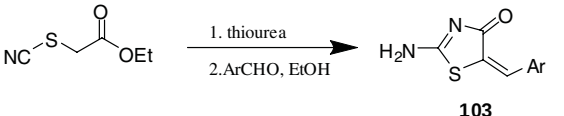


R = 2-Cl, 4-Cl, 2-MeO, 3-MeO, 4-MeO;
Ar = H, 4-MeC$_6$H4, 4-MeOC$_6$H$_4$, PhCH2, 4-MeC$_6$H$_4$CH$_2$, 4-MeOC$_6$H$_4$CH$_2$; X= CH$_2$, O

Scheme 51. Synthesis of *E*-5-(arylmethylene)-2-thiazolin-4-ones.

2.10. *Miscellaneous methods*

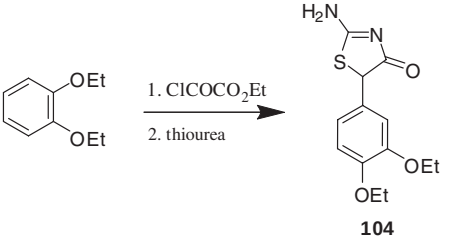
Reaction of ethyl thiocyanoacetate with aromatic aldehydes in the presence of thioureas afforded *E*-5-arylidene-2-imino-4-thiazolidinones **103** (Scheme 52) (*66*).



(*p*-Me, *o*-MeO, *p*-NMe$_2$)C$_6$H$_4$

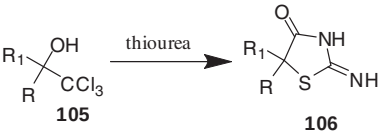
Scheme 52. Synthesis of *E*-5-arylidene-2-imino-4-thiazolidinones.

2-Iminothiazolidin-4-one **104** derivative was prepared in two steps. 1,2-Diethoxybenzene was condensed with ethyl (chlorocarbonyl)formate followed by thiourea (Scheme 53) (*67*).



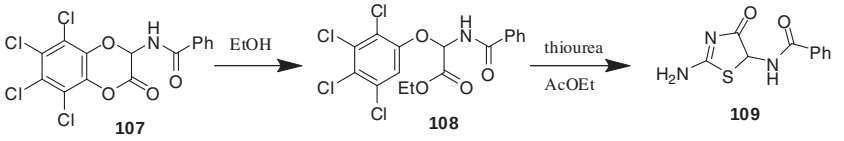
Scheme 53. Synthesis of 2-iminothiazolidin-4-one.

The reaction of ethyl-, vinyl-(trichloromethyl)carbinols **105** with aqueous thiourea was reported. Thus, **105** and alkaline thiourea gave 27–66% of the corresponding 2-imino-4-thiazolidinones **106** (Scheme 54) (*68*).



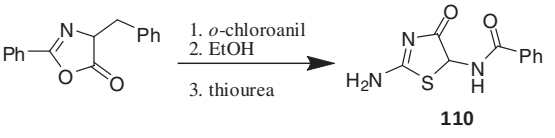
Scheme 54. Synthesis of 2-imino-4-thiazolidinones.

Tetrachlorobenzodioxinone **107** reacted with ethanol to give ethyl 2-benzamido-2-(2,3,4,5-tetrachlorophenoxy)acetate **108** and reacted with thiourea to give *N*-(2-amino-4-oxo-4,5-dihydrothiazol-5-yl)benzamide **109** (Scheme 55) (*69*).



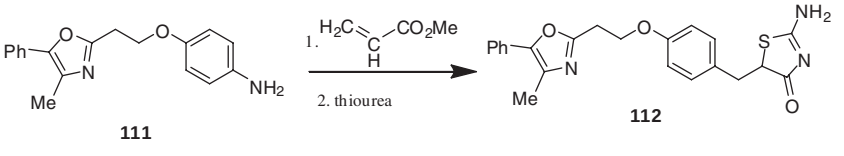
Scheme 55. Synthesis of 4,5-dihydrothiazol-5-yl)benzamide.

N-(2-amino-4-oxo-4,5-dihydrothiazol-5-yl)benzamide **110** was prepared by reaction of 4-benzyl-2-phenyloxazol-5(4*H*)-one with chloroanil followed by thiourea (Scheme 56) (*69*).



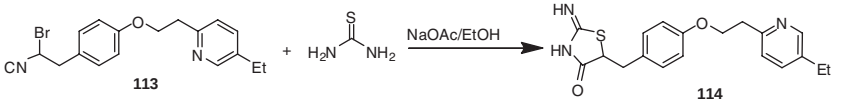
Scheme 56. Synthesis of *N*-(4,5-dihydrothiazol-5-yl)benzamide.

5-(4-Hydroxybenzyl)-2,4-dioxothiazolidine derivatives, which are useful as hypoglycemic and hypolipidemic agents, were prepared. Thus 4-(2-(4-methyl-5-phenyloxazol-2-yl)ethoxy)aniline **111** was reacted with methyl acrylate and thiourea to give aminothiazolidinone **112** (Scheme 57) (*1*).



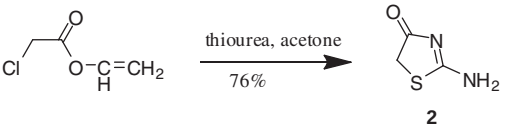
Scheme 57. Synthesis of aminothiazolidinone.

2-Bromo-3-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]propionitrile **113** was refluxed for 6 h with thiourea and sodium acetate in ethanol to give 59% yield of 5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2-imino-4-thiazolidinone **114** (Scheme 58) (*70*).



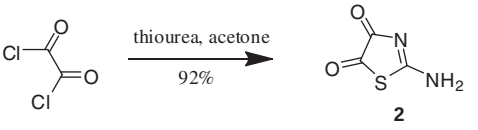
Scheme 58. Synthesis of 2-imino-4-thiazolidinone.

Vinyl 2-chloroacetate underwent nucleophilic displacement with thiourea to give 2-aminothiazol-4(5*H*)-one **2** (Scheme 59) (*71*).



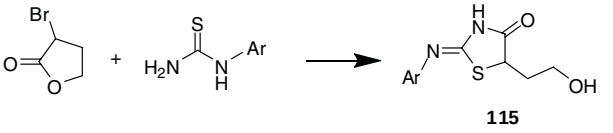
Scheme 59. Reaction of vinyl 2-chloroacetate with thiourea.

The reaction of thiourea with oxalyl chloride permits the preparation of 2-aminothiazolidin-4-one **2** (Scheme 60) (*72*).



Scheme 60. Reaction of thiourea with oxalyl chloride.

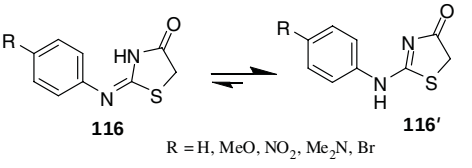
The synthesis of substituted 5-(2-hydroxyethyl)-2-phenylimino-1,3-thiazolidin-4-ones **115** is described, starting from phenylthioureas and 3-bromotetrahydrofuran-2-one under mild conditions (Scheme 61) (*73*).



Scheme 61. Synthesis of 1,3-thiazolidin-4-ones.

3. Imino-amino tautomerism

Ramsh *et al.* (*74*) reported that 2-imino-4-thiazolinone and its 2-aryl derivatives **116** exist in the crystal state as the amino tautomers (Scheme 62).

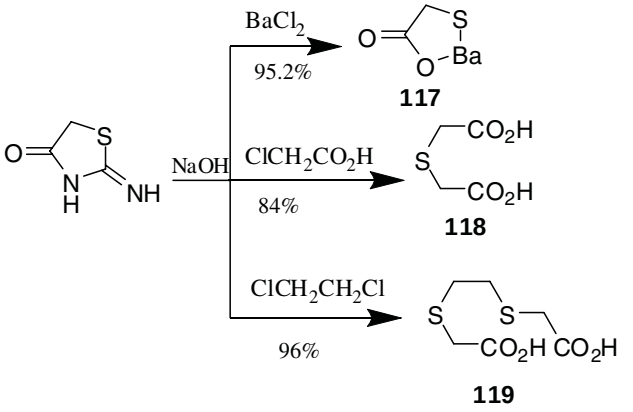


Scheme 62. Tautomerization of 2-imino-4-thiazolinone.

4. Reactions

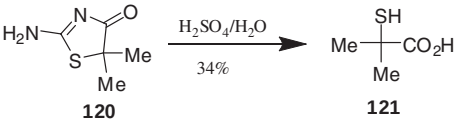
4.1. *Ring cleavage*

2-Imino-4-thiazolidinone **2** was cleaved with aqueous sodium hydroxide. Treatment of the product with barium chloride, chloroacetic acid, or 1,2-dichloroethane gave barium 2-sulfidoacetate **117**, 2,2'-thiodiacetic acid **118**, and 2,2'-(ethane-1,2-diylbis(sulfanediyl))diacetic acid **119**, respectively (Scheme 63) (*75*).



Scheme 63. Reactivity of **2** towards barium chloride, chloroacetic acid, and 1,2-dichloroethane.

2-Amino-5,5-dimethylthiazol-4(5*H*)-one **120** underwent ring cleavage when heated with aqueous sulfuric acid to give 2-mercapto-2-methylpropanoic acid **121** (Scheme 64) (*76*).



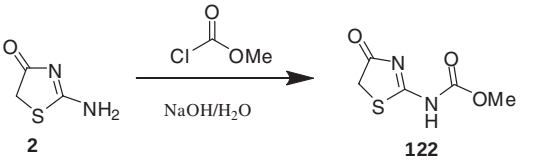
Scheme 64. Hydrolysis of 2-amino-5,5-dimethylthiazol-4(5*H*)-one.

4.2. *Hydrolysis*

2-Amino-5-ethylidenethiazol-4(5*H*)-ones underwent acid hydrolysis to give thiazolidin-2,4-dione which showed diverse biological activities (*1, 11, 68, 77–88*).

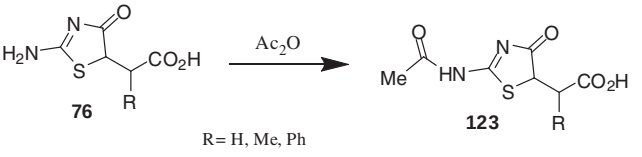
4.3. *Acylation*

Thiazolidinone **2** was acylated with methyl chloroformate to yield methyl 4,5-dihydro-4-oxothiazol-2-ylcarbamate **122** (Scheme 65) (*89*).



Scheme 65. Reaction of **2** with methyl chloroformate.

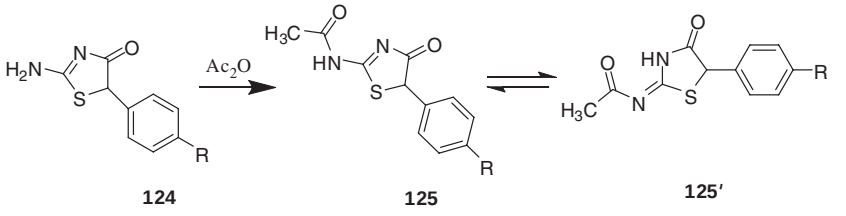
Acetylation of 2-aminothiazolidin-4-one **76** with acetic anhydride gave *N*-acetyl derivative **123** (Scheme 66) (*90*).



76 **123**

Scheme 66. Acetylation of 2-aminothiazolidin-4-one.

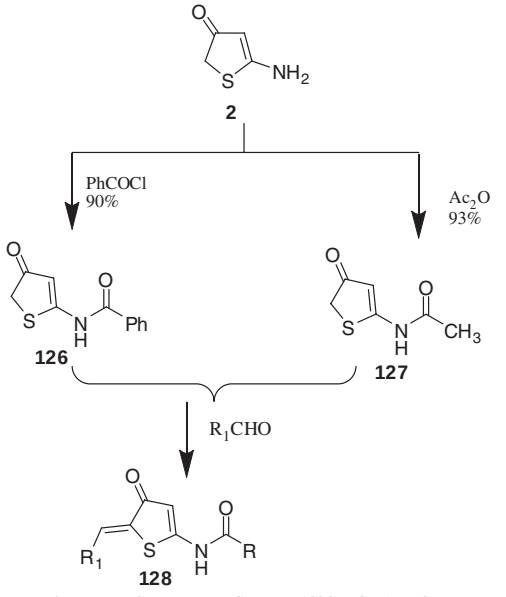
Acetyliminothiazolidinones **125** were prepared in high yields by acetylation of **124**, which exist in tautomeric equilibrium with 2-amino-4-hydroxythiazolines **125** (Scheme 67) (*91*).



124 **125** **125′**

Scheme 67. Formation of 2-amino-4-hydroxythiazolines.

Acetylation or benzoylation of pseudothiohydantoin gave **126** and **127**. The reaction of **127** with the corresponding aldehyde gave **128** that had tuberculostatic activity (Scheme 68) (*8, 9*).

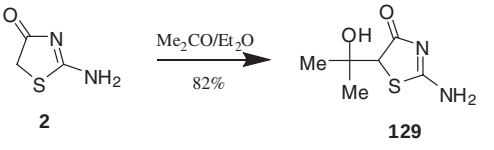


2 **126** **127** **128**

Scheme 68. Acylation of pseudothiohydantoin.

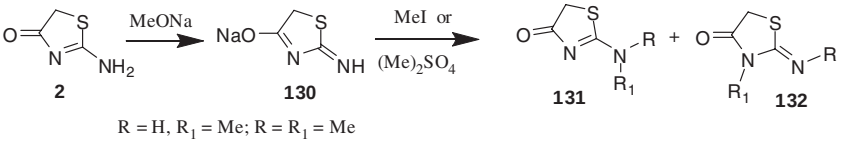
4.4. *Alkylation*

2-Amino-5-(2-hydroxypropan-2-yl)thiazol-4(5*H*)-one **129** was prepared in 82% yield by alkylation of 2-amino-4-thiazolidinone **2** with acetone (Scheme 69) (*92*).



Scheme 69. Alkylation of **2** with acetone.

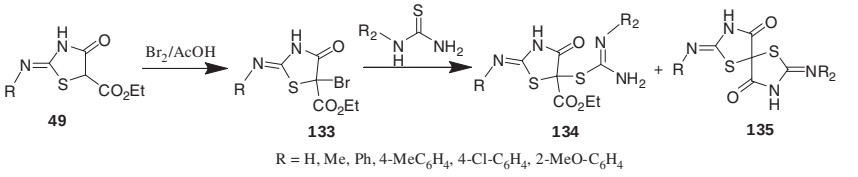
Methylation of 2-aminothiazol-4(5*H*)-one has been reported. Treatment of 2-amino-4-thiazolidinone **2** with sodium methoxide gave **130** which underwent alkylation with methyl iodide or dimethyl sulfate to give a mixture of **131** and **132** (Scheme 70) (*93*).



Scheme 70. Methylation of 2-amino-4-thiazolidinone **2** .

4.5. *Bromination*

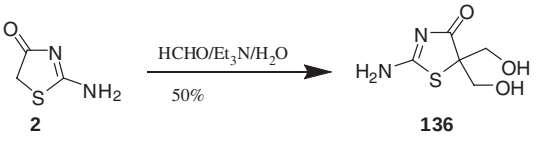
Bromination of 2-alkyl/arylimino-5-carbethoxythiazolidin-4-ones **49** afforded 5-bromo derivatives **133**, which reacted with thiocarbamides to give 2-alkyl/arylimino-5-carbethoxy-5-isothiocarbamidothiazolidin-4-ones **134** and 2,7-dialkyl/arylimino-3,8-diaza-1,6-dithiaspiro[4.4] nonane-4,9-diones **135** (Scheme 71) (*94*).



Scheme 71. Bromination of **49**.

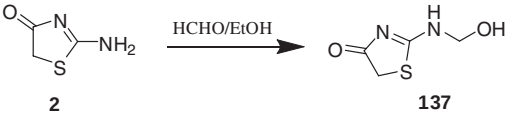
4.6. *Reaction with formalin*

2-Amino-5,5-bis(hydroxymethyl)-4-thiazolinone **136** was synthesized in 50% yield by treating pseudothiohydantoin **2** with formalin in the presence of catalytic amount of triethylamine (Scheme 72) (*95*).



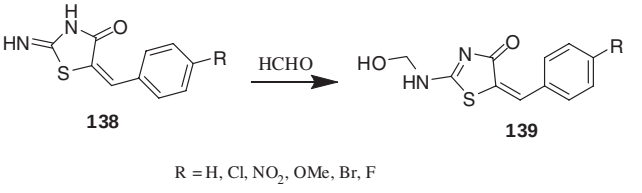
Scheme 72. Formation of 2-Amino-5,5-bis(hydroxymethyl)-4-thiazolinone.

2-[(Hydroxymethyl)amino]-4-thiazolinone **137** was prepared by reaction of 2-aminothiazol-4(5*H*)-one **2** with formalin (Scheme 73) (*96*).



Scheme 73. Formation of 2-[(Hydroxymethyl)amino]-4-thiazolinone **137**.

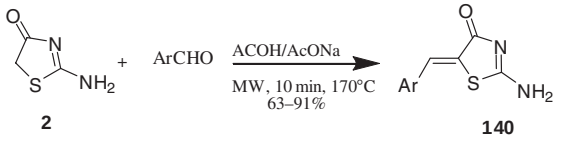
The hydroxymethylation of 2-imino-5-arylidenethiazolidin-4-ones **138** has been reported to give (*E*)-5-arylidene-2-(hydroxymethylamino)thiazol-4(5*H*)-ones **139** (Scheme 74) (*97, 98*).



Scheme 74. Formation of (*E*)-5-arylidene-2-(hydroxymethylamino)thiazol-4(5*H*)-ones.

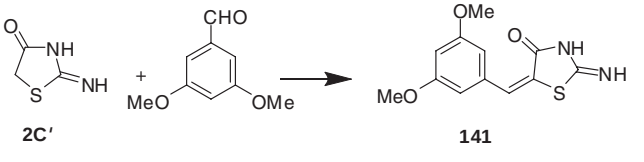
4.7. *Knoevenagel condensation*

5-Arylidene-2-imino-4-thiazolidinone derivatives **140** were synthesized, in 10 min with 63–91% yields, by the cross-aldol condensation of aromatic aldehydes with 2-amino-4-thiazolidinone **2** in sodium acetate/acetic acid under microwave irradition (Scheme 75) (*99*).



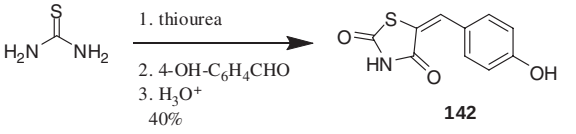
Scheme 75. Formation of 5-Arylidene-2-imino-4-thiazolidinone derivatives.

5-[(3,5-Dimethoxyphenyl)methylene]-2-imino-4-thiazolidinone **141** as an anti-inflammatory agent was synthesized from 3,5-dimethoxybenzaldehyde and **2′** *via* Knoevenagel condensation (Scheme 76) (*6*).



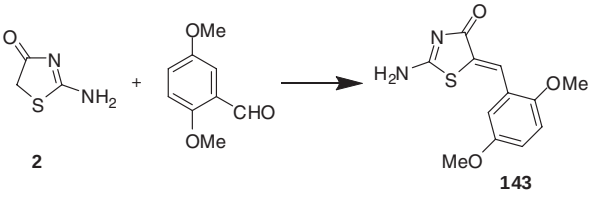
Scheme 76. Formation of 5-[(3,5-dimethoxyphenyl)methylene]-2-imino-4-thiazolidinone.

5-[(4-Hydroxy)-benzylidene]thiazolidine-2,4-dione **142** (an intermediate in synthesis of antidiabetic agents) was prepared from thiourea in four steps with overall yield of 40% (Scheme 77) (*2*).



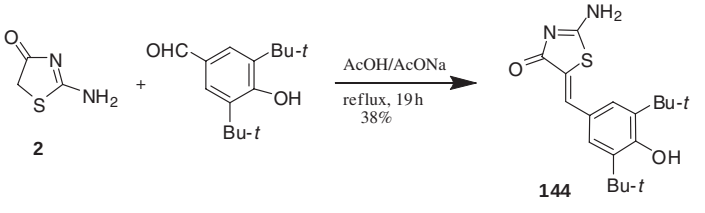
Scheme 77. Formation of 5-[(4-Hydroxy)-benzylidene]thiazolidine-2,4-dione **142** .

Treatment of 2-amino-4-thiazolidinone **2** with 2,5-dimethoxybenzaldehyde afforded the potential cardiotonic Knoevenagel product **143** in 70% yield (Scheme 78) (*7*).



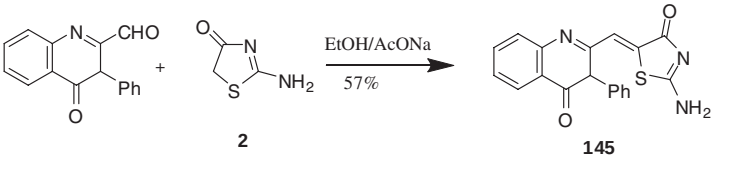
Scheme 78. Formation of Knoevenagel product **143**.

(5Z)-5-(3,5-Di-tert-butyl-4-hydroxybenzylidene)-2-aminothiazol-4(5*H*)-one **144** was prepared by Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with 2,6-di-*tert*-butyl-4-formylphenol (Scheme 79) (*100*).



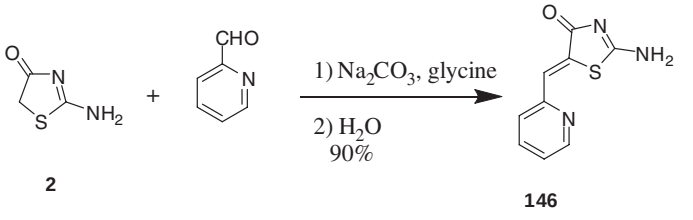
Scheme 79. Reaction of **2** with 2,6-di-*tert*-butyl-4-formylphenol.

Quinazolin-4(3)-ones bearing different 2-amino-4-thiazolidinone as potential antiinflammatory agent were reported. Thus the Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with 3,4-dihydro-4-oxo-3-phenylquinoline-2-carbaldehyde led to (*Z*)-2-amino-5-((4-oxo-3-phenyl-3,4-dihydroquinolin-2-yl)methylene)thiazol-4(5*H*)-one **145** (Scheme 80) (*101*).



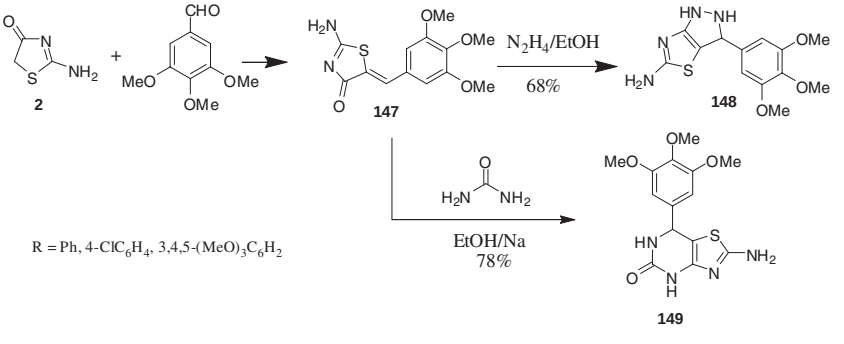
Scheme 80. Reaction of **2** with 3,4-dihydro-4-oxo-3-phenylquinoline-2-carbaldehyde.

Chowdhry *et al*. (*102*) reported the synthesis of bidentate ligand (*Z*)-2-amino-5-(pyridin-2-ylmethylene)thiazol-4(5*H*)-one **146** by condensation of 2-aminothiazol-4(5*H*)-one **2** with picolinaldehyde (Scheme 81).



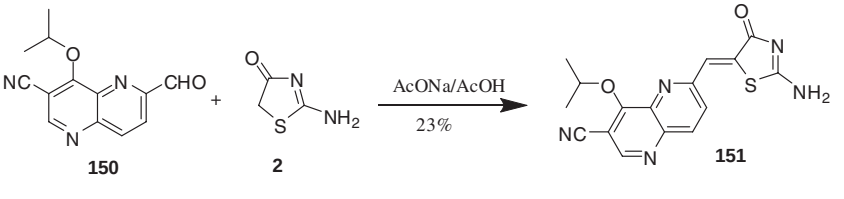
Scheme 81. Reaction of **2** with picolinaldehyde.

The arylidene derivatives **147** were also prepared through reaction of **2** with aromatic aldehydes. **147** Reacted with hydrazine hydrate and urea to give thiazolodihydropyrazole **148** and thiazolotetrahydropyrimidone **149**, respectively (Scheme 82) (*102*).



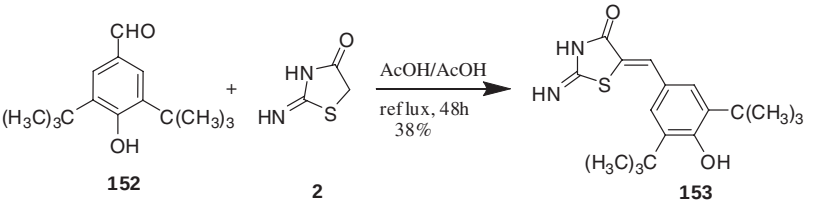
Scheme 82. Formation of thiazolodihydropyrazole and thiazolotetrahydropyrimidone.

Substituted 1,5-naphthyridine thiazolinones **151** reported to have antiproliferative and anticancer activities. 6-Formyl-4-isopropoxy-1,5-naphthyridine-3-carbonitrile **150** was condensed with 2-amino-4-thiazolidinone **2** to afford the Knoevenagel product **151** in 23% yield (Scheme 83) (*5*).



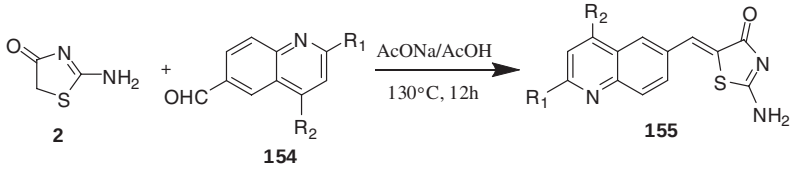
Scheme 83. Formation of 1,5-naphthyridine thiazolinones.

(Z)-5-[[3,5-Bis(1,1-dimethylethyl)-4-hydroxyphenyl]-methylene]-2-imino-4-thiazolidinone **153** is useful as dual 5-lipoxygenase and cyclooxygenase inhibitors with antiinflammatory activity, and was prepared in 38% yield by reaction of 2-imino-4-thiazolidinone **2** with 3,5-di-tert-butyl-4-hydroxybenzaldehyde **152** (Scheme 84) (*10*).



Scheme 84. Reaction of **2** with 3,5-di-tert-butyl-4-hydroxybenzaldehyde.

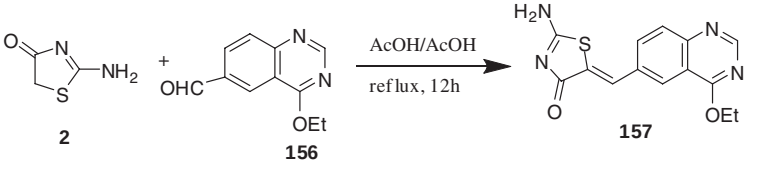
Quinolinyl-methylene-thiazolinones have been reported as potent and selective cyclin-dependent kinase 1 (CDK1) inhibitors. Thus, the Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with quinoline-6-carbaldehyde derivatives **154** led (*Z*)-2-amino-5-((2,4-dialkylquinolin-6-yl)methylene)thiazol-4(5*H*)-one **155** (Scheme 85) (*103, 104*).



R_1=R_2 = H; R_1 =NHAc, R_2= OEt

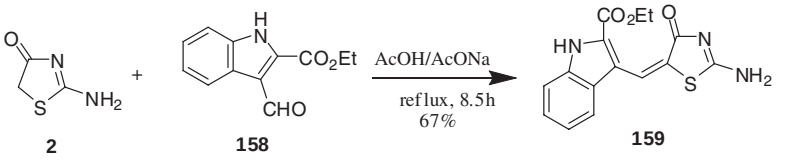
Scheme 85. Reaction of **2** with quinoline-6-carbaldehyde derivatives.

Quinazolinylmethylene thiazolinones as CDK1 inhibitors were prepared. Thus, the Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with 4-ethoxyquinazolin-6-carbaldehyde **156** afforded stereo-selectively, (5*Z*)-2-amino-5-((4-ethoxyquinazolin-6-yl)methylene)thiazol-4(5*H*)-one **157** (Scheme 86) (*105*).



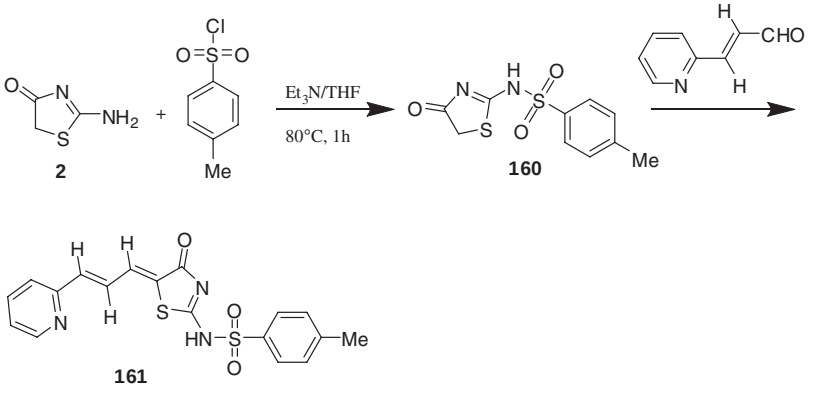
Scheme 86. Reaction of **2** with 4-ethoxyquinazoline-6-carbaldehyde.

Stereoselective synthesis of ethyl 3-[(9E)-(2-amino-4-oxothiazol-5(4*H*)-ylidene)methyl]-1*H*-indole-2-carboxylate **159** was achieved in 67% yield by condensation of ethyl 3-formyl-1*H*-indole-2-carboxylate **158** with 2-amino-4-thiazolidinone **2** under Knoevenagel conditions (Scheme 87) (*106*).



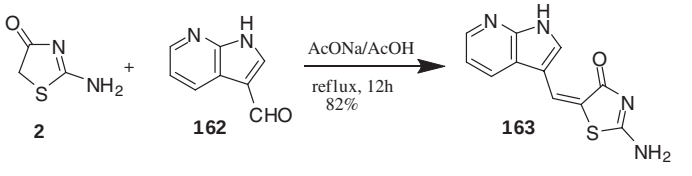
Scheme 87. Reaction of ethyl 3-formyl-1*H*-indole-2-carboxylate.

Thiazolone-based sulfonamides were prepared as inhibitors of nonstructural protein 5B polymerase. Thus, 4-methylbenzene-1-sulfonyl chloride was condensed with 2-amino-4-thiazolidinone **2** to afford sulfonamide **160**, that condensed with (*E*)-3-(pyridin-2-yl)acrylaldehyde under the Knoevenagel condition to give compound **161** (Scheme 88) (*14*).



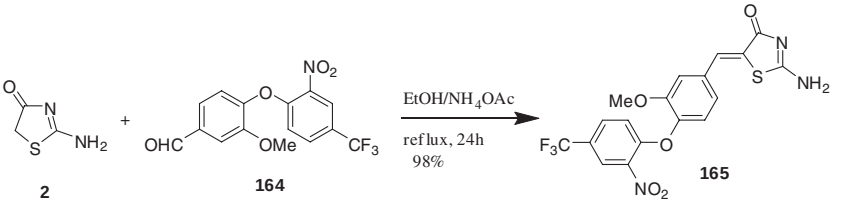
Scheme 88. Reaction of **2** with 4-methylbenzene-1-sulfonyl chloride.

(5*E*)-5-((1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene)-2-aminothiazol-4(5*H*)-one **163** was prepared in 82% yield as anti-cancer agent by the Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with 1*H*-pyrrolo[2,3-*b*]pyridine-3-carbaldehyde **162** (Scheme 89) (*3*).



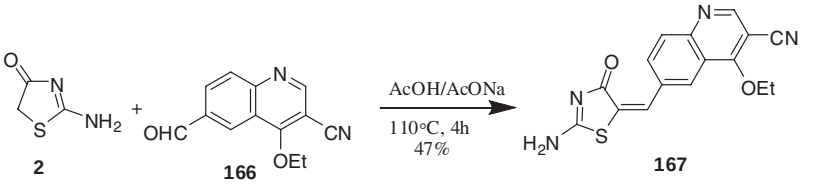
Scheme 89. Reaction of **2** with 1*H*-pyrrolo[2,3-*b*]pyridine-3-carbaldehyde.

Heterocyclic arylidene aryl ether compounds are useful for treating diseases or disorders mediated through modulation of estrogen-related alpha receptors. The Knoevenagel condensation of 2-amino-4-thiazolidinone **2** with 4-(4-(trifluoromethyl)-2-nitrophenoxy)-3-methoxybenzaldehyde **164** afforded (5*Z*)-5-(4-(4-(trifluoromethyl)-2-nitrophenoxy)-3-methoxybenzylidene)-2-aminothiazol-4(5*H*)-one **165** (Scheme 90) (*107*).



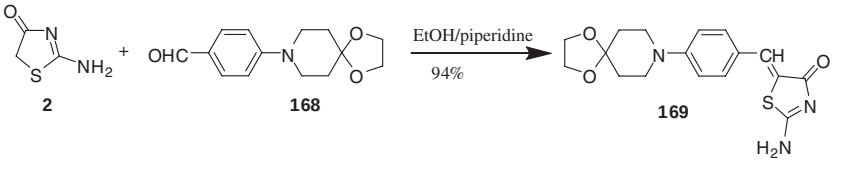
Scheme 90. Reaction of **2** with 4-(4-(trifluoromethyl)-2-nitrophenoxy)-3-methoxybenzaldehyde.

Thiazolinone 3,4-disubstituted quinolines as CDK1 inhibitors for treating cancer was reported. 6-((15*E*)-(2-Amino-4-oxothiazol-5(4*H*)-ylidene)methyl)-4-ethoxyquinoline-3-carbonitrile **167** was prepared by reaction of 2-amino-4-thiazolidinone **2** with 4-ethoxy-6-formylquinoline-3-carbonitrile **166** (Scheme 91) (*4*).



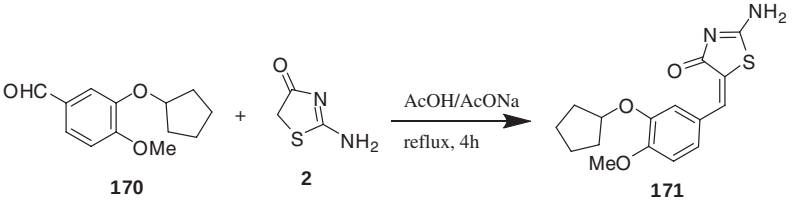
Scheme 91. Reaction of **2** with 4-ethoxy-6-formylquinoline-3-carbonitrile.

The Knoevenagel condensation between 4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)benzaldehyde **168** and pseudothiohydantoin **2** afforded (*Z*)-5-(4-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)benzylidene)-2-aminothiazol-4(5*H*)-one **169** in 94% yield as potent and selective human β3 agonists (Scheme 92) (*108, 109*).



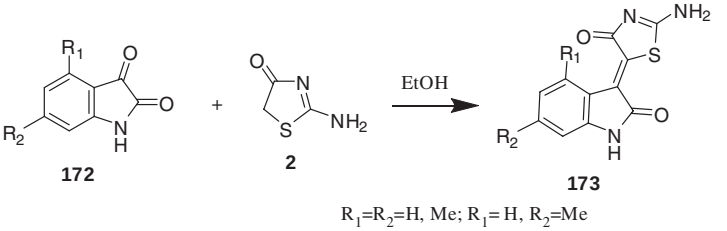
Scheme 92. Reaction of **2** with 4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)benzaldehyde.

Synthesis and *in vitro* activity of rhodanine-based phosphodiesterase-4 (PDE4) inhibitors has been described. Knoevenagel condensation of 2-imino-4-thiazolidinone **2** with 3-(cyclopentyloxy)-4-methoxybenzaldehyde **170** in sodium acetate/acetic acid under refluxing conditions for 4 h afforded 5-(3-(cyclopentyloxy)-4-methoxybenzylidene)-2-aminothiazol-4(5*H*)-one **171** (Scheme 93) (*110*).



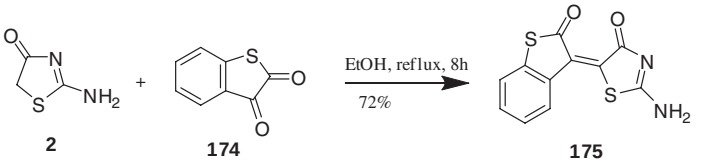
Scheme 93. Reaction of **2** with 3-(cyclopentyloxy)-4-methoxybenzaldehyde.

Condensation of isatin derivatives **172** with 2-aminothiazol-4(5*H*)-one **2** in refluxing ethanol afforded isatylidene derivatives **173** in good yields, and showed promising antibacterial activity (Scheme 94) (*111, 112*).



Scheme 94. Reaction of **2** with isatin derivatives.

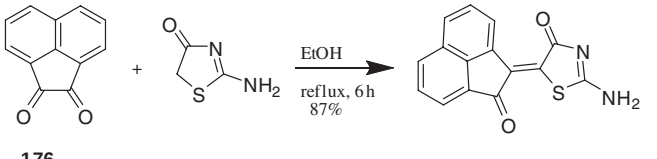
A facile synthesis of thiazolidinone **175** was described by the Knoevenagel-type condensation of benzo[*b*]thiophene-2,3-dione **174** (commonly known as thioisatin) with 2-amino-4-thiazolidinone **2** (Scheme 95) (*113*).



2 **174** **175**

Scheme 95. Condensation of **2** with benzo[b]thiophene-2,3-dione.

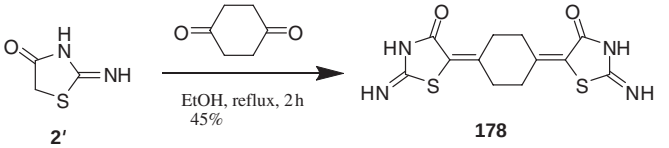
The synthesis of acenaphthylidene derivative **177** involved the Knoevenagel-type condensation of 2-amino-thiazolidin-4-one **2** with acenaphthylene-1,2-dione **176** (Scheme 96) (*114*).



176 **177**

Scheme 96. Condensation of **2** with acenaphthylene-1,2-dione.

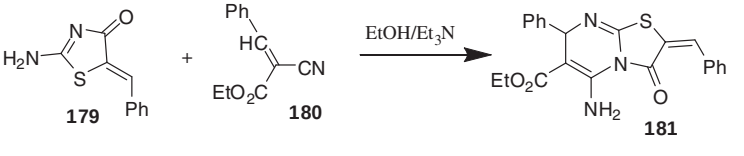
Condensation of 2-imino-4-thiazolidinone **2** with 1,4-cyclohexanedione gave 5,5′-(1,4-cyclohexanediylidene)bis[2-imino-4-thiazolidinone] **178** (Scheme 97) (*112*).



2′ **178**

Scheme 97. Condensation of **2** with 1,4-cyclohexanedione.

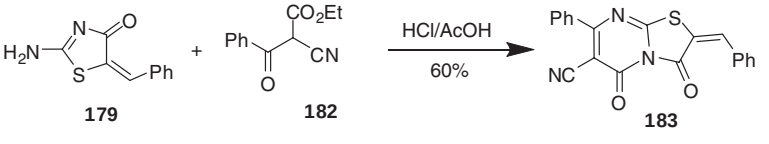
(*E*)-ethyl 5-amino-2-benzylidene-3-oxo-7-phenyl-3,7-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate **181** was obtained by reaction of (5*Z*)-2-amino-5-benzylidenethiazol-4(5*H*)-one **179** with ethyl 2-cyano-3-phenylacrylate **180** (Scheme 98) (*115*).



179 **180** **181**

Scheme 98. Formation of thiazolo[3,2-*a*]pyrimidine derivatives.

(*E*)-2-benzylidene-3,5-dioxo-7-phenyl-3,5-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidine-6-carbonitrile **183** was prepared by reaction of ethyl 2-cyano-3-oxo-3-phenylpropanoate **182** with 2-amino-5-benzylidenethiazol-4(5*H*)-one **179** in a mixture of acetic and hydrochloric acid (Scheme 99) (*116*).

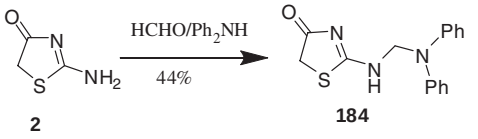


179 **182** **183**

Scheme 99. Reaction between **179** and ethyl 2-cyano-3-oxo-3-phenylpropanoate.

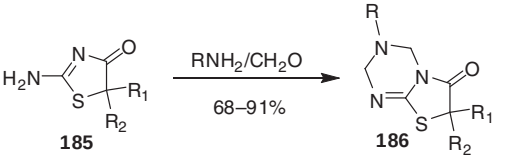
4.8. *Mannich reactions*

The Mannich reaction of aminothiazolidinone **2** with aqueous formaldehyde and diphenylamine gave 44% 2-((diphenylamino)methylamino)thiazol-4(5*H*)-one **184** (Scheme 100) (*117*).



Scheme 100. Formation of 2-((diphenylamino)methylamino)thiazol-4(5*H*)-one.

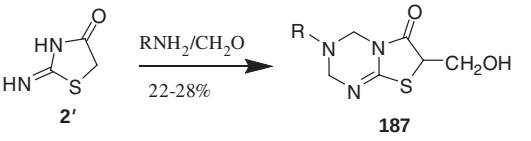
The aminomethylation of 2-iminothiazolidin-4-ones by aqueous formaldehyde and primary amines was studied. Thiazolotriazines **186** were prepared in 68–91% yields by the aminomethylation of iminothiazolidinones **185** with primary amines and aqueous formaldehyde (Scheme 101) (*118*).



R = Ph, 2-naphthyl; R_1=H, R_2=Et, Ph

Scheme 101. Formation of thiazolotriazines.

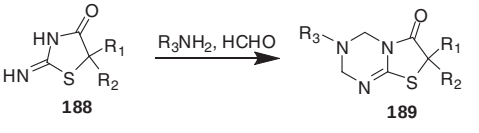
Similarly, iminothiazolidinone **2** gave 22 and 28% thiazolotriazines **187** with *t*-butylamine and benzylamine (Scheme 102) (*118*).



R = Me_3C, $PhCH_2$

Scheme 102. Mannich reaction with *t*-butylamine and benzylamine.

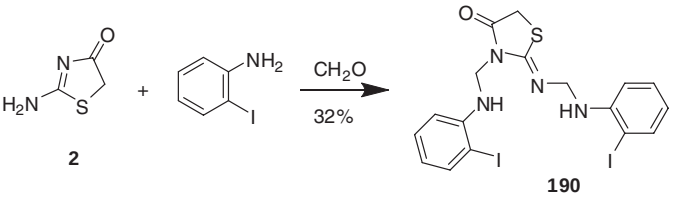
Thiazolotriazinones **189** were prepared in 42–90% yields by Mannich reactions of **188** with formaldehyde and primary amines (Scheme 103) (*119*).



R_1 = R_2 = H, R_3 = Me, Ph, *m*-, p-tolyl, *p*-$MeOC_6H_4$, *m*-ClC_6H_4, *m*-BrC_6H_4, *m*-$O_2NC_6H_4$, 2-$C_{10}H_7$;
R_1 = H, R_2 = Me,
R_3 = 2-$C_{10}H_7$; R_1R_2 = PhCH, *p*-ClC_6H_4CH, *p*-FC_6H_4CH, *p*-BrC_6H_4CH, R_3 = Me; R_1R_2 = PhCH, R_3 = Ph

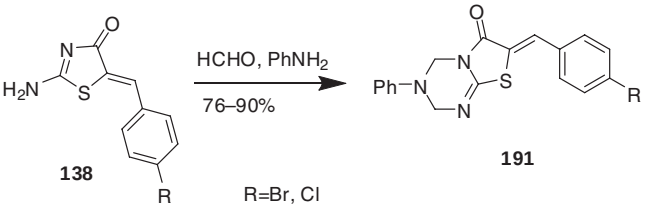
Scheme 103. Formation of thiazolotriazinones.

Additionally (*Z*)-3-((2-iodophenylamino)methyl)-2-((2-iodophenylamino)methylaimino) thiazolidin-4-one **190** was obtained in 32% yield through the aminomethylation of **2** with 2-iodoaniline (Scheme 104) (*118*).



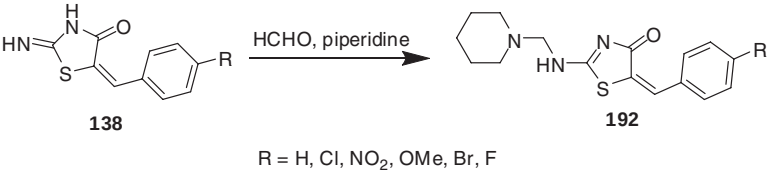
Scheme 104. Mannich reaction with 2-iodoaniline.

The aminomethylation of arylidene 2-aminothiazolidin-4-ones **138** by aqueous formaldehyde and aniline afforded thiazolotriazines **191** (Scheme 105) (*118*).



Scheme 105. Synthesis of thiazolotriazines.

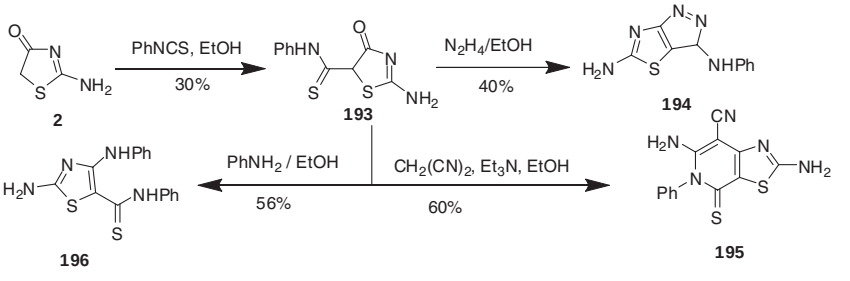
The aminomethylation of 2-imino-5-arylidenethiazolidin-4-ones **138** have been reported to give (*E*)-5-benzylidene-2-(piperidin-1-ylmethylamino)thiazol-4(5*H*)-ones **192** (Scheme 106) (*96*, *97*).



Scheme 106. Aminomethylation of 2-imino-5-arylidenethiazolidin-4-ones.

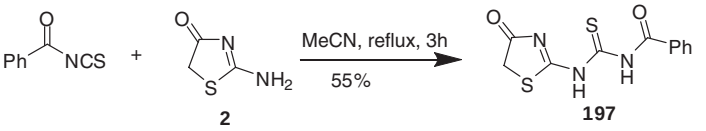
4.9. *Reaction with phenylisocyanate derivatives*

Thiazolidone **2** reacted with phenylisothiocyanate to give 2-imino-5-phenylaminothiocarboxamido-4-thiazolidone **193** which was converted to a thiazolopyrazole **194**, a thiazolopyridine **195**, and a (phenylamino)thiazoleamine **196** by reaction with hydrazine hydrate, malononitrile, and aniline (Scheme 107) (*120*).



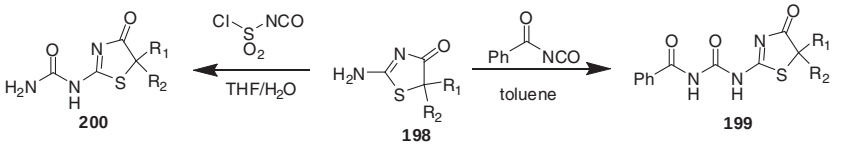
Scheme 107. Reaction of **2** with phenylisothiocyanate.

2-Amino-4-thiazolidinone **2** was reacted with benzoyl isothiocyanate in refluxing acetonitrile to give *N*-(4-oxo-4,5-dihydrothiazol-2-ylcarbamothioyl)benzamide **197** with 55% yield (Scheme 108) (*121*).



Scheme 108. Reaction of **2** with benzoyl isothiocyanate.

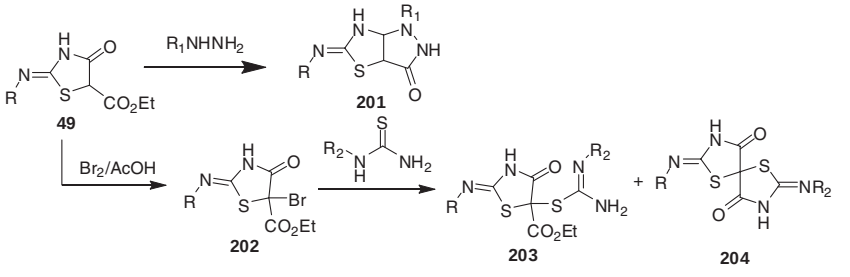
2-Aminothiazolidinone **198** reacted with benzoyl isocyanate and sulfurisocyanatidic chloride to give thiazolyl ureas **199** and thioureas **200**, respectively (Scheme 109) (*122*).



Scheme 109. Formation of thiazolyl ureas and thioureas.

4.10. *Reaction with hydrazines*

The reaction of **49** with hydrazines afforded 2-arylimino-2,3,4,5-tetrahydropyrazolo[3,4-*d*]-thiazol-6(*H*)-ones **201**. Bromination of **49** afforded 5-bromo derivatives **202**, which upon reaction with thiocarbamides gave 2-alkyl/arylimino-5-carbethoxy-5-isothiocarbamidothiazolidin-4-ones **203** and 2,7-dialkyl/arylimino-3,8-diaza-1,6-dithiaspiro[4.4]nonane-4,9-diones **204** (Scheme 110) (*38*).

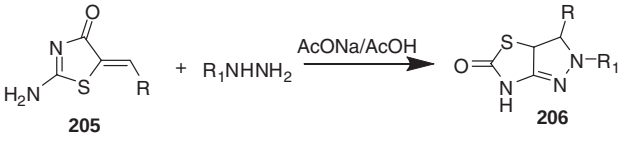


Scheme 110. Reaction with hydrazines and bromine.

Pyrazolinothiazolidin-2-ones **206** were prepared from rhodamine benzylidene derivatives **205** by condensation with phenylhydrazines, some of them showed antifungal activity (Scheme 111) (*123*).

4.11. *Formation of enaminones*

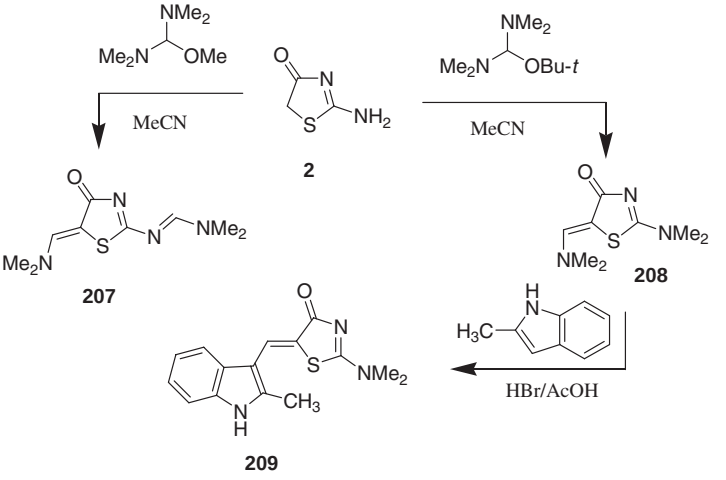
The enaminones of 2-aminothiazol-4(5*H*)-ones **207** and **208** were prepared by reaction of **2** with methoxy-*N*,*N*,*N*′,*N*′-tetramethylmethanediamine or *t*-butoxy-*N*,*N*,*N*′,*N*′-tetramethylmethanediamine in aceteonitrile. Thiooxoaplysinopsin derivative **209** was prepared



205 206

Scheme 111. Formation of Pyrazolinothiazolidin-2-ones.

by reaction of *N*-substituted thiohydantoin **208**, Bredereck's reagent, and 2-methylindole (Scheme 112) (*124, 125*).

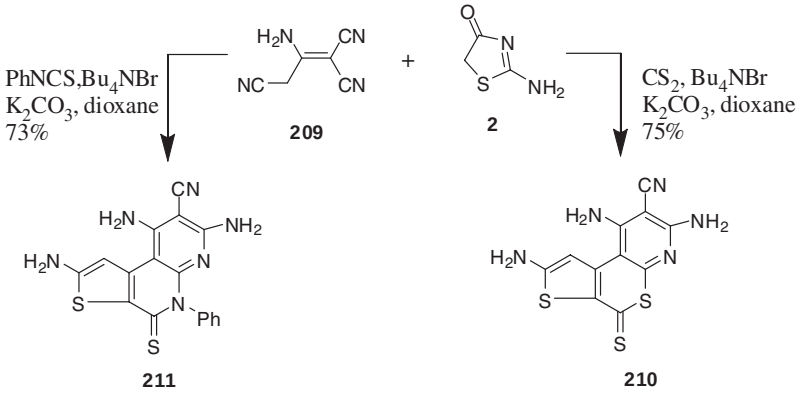


2 207 208 209

Scheme 112. Formation of enaminones.

4.12. *Different reactions*

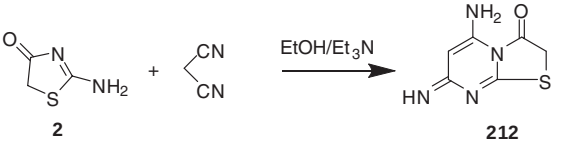
Ketoketene thioacetals, which were formed by treatment of 2-amino-1-propene-1,1,3-tricarbonitrile **210** with carbondisulphide or with phenylisothiocyanate, were allowed to react with 2-aminothiazol-4(5*H*)-one **2** under phase transfer catalytic (PTC) conditions to afford thiopyrano[2,3-*b*]pyridine or pyrido[2,3-*b*]pyridine derivatives **211** and **212**, respectively (Scheme 113) (*126*).



209 2 211 210

Scheme 113. Synthesis of pyrido[2,3-*b*]pyridine.

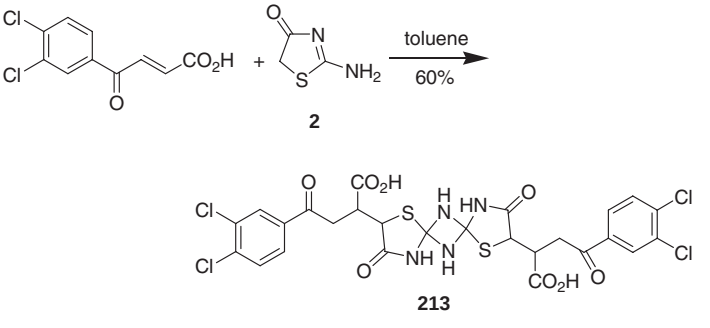
Thiazolo[3,2-*a*]pyrimidine **212** was prepared in one-pot reaction from 2-imino-4-thiazolidinone **2** and malononitrile (Scheme 114) (*116*).



2 **212**

Scheme 114. Reaction of **2** with malononitrile.

Dispiro[thiazolidine-2,2′-[1,3]diazetidine-4′,2"-thiazolidine]-5,5"-diacetic acid **213** was prepared in 60% yield by reaction of 3,4-dichlorocinnamic acid with pseudothiohydantoin **2** (Scheme 115) (*127*).

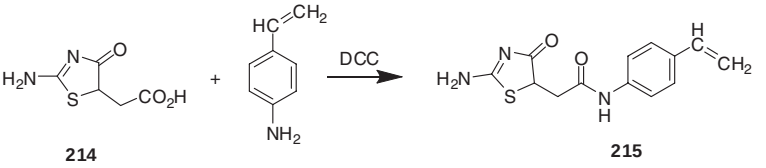


2

213

Scheme 115. Formation of dispiro compound.

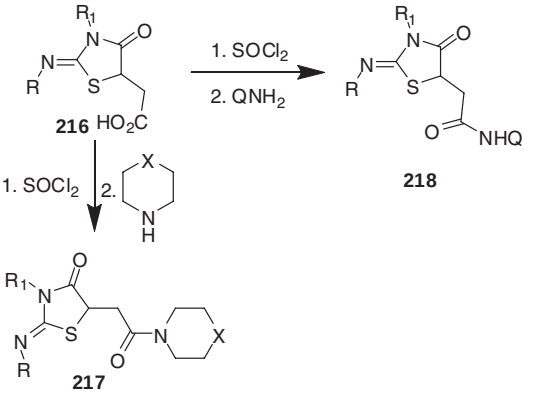
The reaction of 2-amino-4-oxothiazolidine-5-acetic acid **214** with *p*-aminostyrene in the presence of dicyclohexylcarbodiimide (DCC) gave a new monomer **215** which was obtained conveniently under mild conditions (Scheme 116) (*77*).



214 **215**

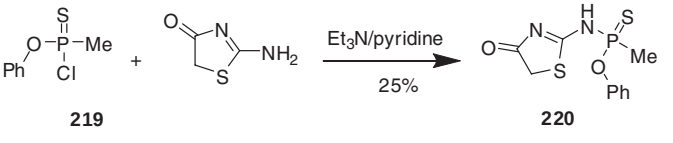
Scheme 116. Reaction with *p*-aminostyrene.

Thiazolidineacetic acids **216** which was amidated by first making the acid chloride then amination by morpholine, piperidine, aniline, phenylhydrazine, or prop-2-en-1-amine gave the corresponding amides **217** and **218**, respectively (Scheme 117) (*128*, *129*).



Scheme 117. Formation of amides.

Thiophosphorylation of thiazolidinone was achieved. Thiazolidine **220** was prepared in 25% yield by condensing **2** with *o*-phenyl methylphosphonochloridothioate **219** (Scheme 118) (*126*).



Scheme 118. Synthesis of thiazolidine.

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References

(1) Meguro, K.; Fujita, T. JP 61286376, 1986; *Chem. Abstr.* **1987**, *106*, 138436.
(2) Qi, G. *Huagong Shikan*, **2006**, *20*, 52–68; *Chem. Abstr.* **2007,** *149*, 104630.
(3) Chen, S.; Sidduri, A. PCT Int. Appl. WO 2006040049, 2006; *Chem. Abstr.* **2006,** *144*, 412492.
(4) Chen, L.; Chen, S.; Michoud, C. US Pat. Appl. Publ. US 20060004046, 2006; *Chem. Abstr.* **2006**, *144*, 108310.
(5) Liu, J.-J. US 2006223843, 2006; *Chem. Abstr*. **2006,** *145*, 397520.
(6) Zheng, L.-L.; Ao, G.; Li, Z. *Huaxue Yanjiu Yu Yingyong* **2007,** *19*, 1051–1055; *Chem. Abstr.* **2007,** *149*, 307734.
(7) Andreani, A.; Rambaldi, M.; Locatelli, A.; Leoni, A.; Bossa, R.; Chiericozzi, M.; Galatulas, I.; Salvatore, G. *Eur. J. Med. Chem.* **1993,** *28*, 825–829.
(8) Tsurkan, A.A.; Frolova, A.I.; Pospelov, N.I.; Dorofeeva, L.A. *Khimiko Farmatsevticheskii Zh*. **1975**, *9*, 12–15; *Chem. Abstr*. **1975,** *83*, 114278.
(9) Mameli, E.; Zorzi, L. *Farmaco*, **1954,** *9*, 691–704.
(10) Unangst, P.C.; Connor, D.T.; Cetenko, W.A.; Sorenson, R.J.; Kostlan, C.R.; Sircar, J.C.; Wright, C.D.; Schrier, D.J.; Dyer, R.D. *J. Med. Chem.* **1994,** *37*, 322–328.
(11) Wang, S.; Zhang, X.; Qi, Y. *Zhongguo Yaowu Huaxue Zazhi* **2000,** *10*, 291–292; *Chem. Abstr*. **2001,** *135*, 46132.
(12) Tsirul'nikova, N.V.; Gurevich, M.Z.; Karandeeva, I.V.; Danielyan, D.G. *Nauch. Tr. VNII Khim. Reaktivov i Osobo Chist. Khim. Veshchestv*, **1989,** *51*, 97–101; *Chem. Abstr.* **1990,** *113*, 191221.
(13) Zubenko, V.G. USSR SU 952844, 1982; *Chem. Abstr.* **1983,** *98*, 89349.

(14) Frank, R.; Kless, A.; Jostock, R. PCT Int. Appl. WO 2006122777, 2006; *Chem. Abstr.* **2006,** *146,* 7948.
(15) Danielyan, D.G.; Tsirul'nikova, N.V.; Temkina, V.Y. *Trudy IREA* **1984,** *46,* 3–6; *Chem. Abstr.* **1985,** *103,* 104522.
(16) Najer, H.; Giudicelli, R.; Morel, C.; Menin, J. *Bull. Soc. Chim. Fr*. **1963,** *5,* 1018–1022.
(17) Sohda, T.; Mizuno, K.; Hirata, T.; Maki, Y.; Kawamatsu, Y. *Chem. Pharm. Bull*. **1983,** *31,* 560–569.
(18) Kawamatsu, Y.; Shoda, T.; Hirata, T. Eur. Pat. Appl. EP 32128, 1981; *Chem. Abstr.* **1981,** *95,* 169176.
(19) Mekhtieva, I.R.; Magerramov, A.M.; Khalilova, A.Z.; Mamedova, S.G. *Kimya Problemlari J.* **2004,** *3,* 32–37; *Chem. Abstr.* **2005,** *143,* 347091.
(20) Mukarram, M.; Ahmad, I.; Farooqi, J.A.; Ahmad, M. *Fette, Seifen, Anstrichmittel*, **1986,** *88,* 224–226; *Chem. Abstr.* **1987,** *106,* 138316.
(21) Golubev, A.A.; Semenenko, M.N.; Mandrugin, A.A.; Fedoseev, V.M. *Khim. Geterotsikl. Soedin.* **1986,** *12,* 1687–1689; *Chem. Abstr.* **1987,** *107,* 236584.
(22) Doran, W.J.; Shonle, H.A. *J. Org. Chem.* **1938,** *3,* 193–197.
(23) Skinner, G.S.; Elmslie, J.S.; Gabbert, J.D. *J. Am. Chem. Soc.* **1959,** *81,* 3756–3759; *Chem. Abstr.* **1960,** *54,* 2269.
(24) Tjiptasurasa. *Majalah Farmasi Indones.* **2005,** *16,* 182–185; *Chem. Abstr.* **2006**, *146,* 481969.
(25) Witkowski, S.; Czerepko, K.; Roszkowska, W.; Worowski, K. *Acta Poloniae Pharm.* **1983,** *40,* 309–312; *Chem. Abstr*. **1984,** *101,* 23384.
(26) Sohda, T.; Momose, Y.; Meguro, K.; Kawamatsu, Y.; Sugiyama, Y.; Ikeda, H. *Arzneim. Forsch.* **1990,** *40,* 37–42; *Chem. Abstr.* **1990,** *113,* 23750.
(27) Meguro, K.; Fujita, T. Eur. Pat. Appl. EP 193256, 1986; *Chem. Abstr.* **1986,** *105,* 226543.
(28) Takashi, S.; Katsutoshi, M.; Hiroyuki, T.; Yasuo, S.; Takeshi, F. *Chem. Pharm. Bull.* **1982,** *30,* 3563–3573.
(29) Yoshioka, T.; Fujita, T.; Kanai, T.; Aizawa, Y.; Kurumada, T.; Hasegawa, K.; Horikoshi, H. *J. Med. Chem.* **1989,** *32,* 421–428.
(30) Iijima, I.; Ozeki, M.; Okumura, K.; Inamasu, M. Eur. Pat. Appl. EP 283035, 1988; *Chem. Abstr.* **1989,** *110,* 57657.
(31) Gailius, V.; Stamm, H. *Chemiker Zeitung* **1985,** *109,* 119–120; *Chem. Abstr.* **1985,** *103,* 123400.
(32) Sakuma, S.; Endo, T. PCT Int. Appl. WO 2000073273, 2000; *Chem. Abstr.* **2000,** *134,* 29324.
(33) Wang, E.-S.; Wang, J.-C.; Jiang, Z.-H.; Wang, J.-P. *Jilin Daxue Ziran Kexue Xuebao* **2000,** *3,* 68–72; *Chem. Abstr.* **2000,** *134,* 222652.
(34) Kauramatsu, Y.; Fujita, T. Eur. Pat. Appl. EP 8203, 1980; *Chem. Abstr.* **1980,** *93,* 114506.
(35) Amat-Guerri, F. *An. Quim.* **1975,** *71,* 325–327; *Chem. Abstr.* **1975,** *83,* 131516.
(36) Chande, M.S.; Bhat, U.S. *Indian J. Chem.* **2000,** *39B,* 68–70; *Chem. Abstr.* **2000,** *133,* 135293.
(37) Lloyd, D.; Millar, R.W. *Tetrahedron* **1980,** *36,* 2675–2679.
(38) Chande, M.S.; Ambhaikar, S.B. *Indian J. Chem.* **1996,** *35B,* 373–376; *Chem. Abstr.* **1996,** *124,* 289343.
(39) Sedlák, M.; Hejtmankova, L.; Hanusek, J.; Machacek, V. *J. Heterocycl. Chem.* **2002,** *39,* 1105–1107.
(40) Sedlák, M.; Hanusek, J.; Hejtmánková, L.; Kašparová, P. *Org. Biomol. Chem.* **2003,** *1,* 1204–1209.
(41) Hanusek, J.; Hejtmánková, L.; Sterba, V.; Sedlák, M. *Org. Biomol. Chem.* **2004,** *16,* 1756–1763.
(42) Plakhotnik, V.M.; Kovtun, V.Yu.; Leont'eva, N.A.; Petrova, I.G.; Pushkarskaya, N.L.; Yashunskii, V.G. *Khim. Farm. Zh.* **1982,** *16,* 1060–1063; *Chem. Abstr.* **1982,** *97,* 215613.
(43) Masaki, M.; Kitahara, T.; Kurita, H.; Ohta, M. *J. Am. Chem. Soc.* **1968,** *90,* 4508–4509.
(44) Speziale, A.J.; Hamm, P.C. *J. Am. Chem. Soc.* **1956,** *78,* 5580–5584.
(45) Libermann, D.; Himbert, J.; Hengl, L. *Bull. Soc. Chim. Fr.* **1948,** 1120–1124; *Chem. Abstr.* **1949,** *43,* 19924.
(46) Zhang, D.; Xu, Y.; Hua, W. Preparation 2-imino-4-thiazolidinones. CN 1556106, 2004; *Chem. Abstr.* **2005,** *143,* 229832.
(47) Ried, W.; Kuhnt, D. *Liebigs Ann. Chem.* **1986,** 780–784.
(48) Kretov, A.E.; Bespalyi, A.S. *Zh. Obshch. Khim.* **1963,** *33,* 3323–3325; *Chem. Abstr.* **1964,** *60,* 30883.
(49) Khachikyan, R.S.; Safaryan, E.V.; Grigoryan, G.V.; Agbalyan, S.G.; Atashyan, S.M. *Armyanskii Khim. Zh.* **1984,** *37,* 490–493; *Chem. Abstr.* **1985,** *102,* 24538.
(50) Augustin, M.; Mueller, W. *J. Prakt. Chem. (Leipzig)* **1985,** *327,* 789–798.
(51) Balasubramaniyan, V.; Balasubramaniyan, P.; Wani, M.J. *Indian J. Chem.* **1990,** *29B,* 1092–1096; *Chem. Abstr.* **1991,** *114,* 143210.
(52) Liu, K.-C.; Tuan, J.Y.; Shih, B.-J. *J. Chin. Chem. Soc.* **1977,** *24,* 65–70.
(53) Hendrickson, J.B.; Rees, R.; Templeton, J.F. *J. Am. Chem. Soc.* **1964,** *86,* 107–111.
(54) Jurgevica, I.; Mikstais, U. *Latv. PSR Zinat. Akad. Vestis Kim. Ser.* **1982,** *3,* 364–366; *Chem. Abstr.* **1982,** *97,* 144832.
(55) Bethell, J.R.; Maitland, P. *J. Chem. Soc.* **1961,** 5211–5216; *Chem. Abstr.* **1962,** *56,* 66875.
(56) Marrian, D.H. *J. Chem. Soc.* **1949,** 1797–1799; *Chem. Abstr.* **1950,** *44,* 7558.
(57) Le Marechal, A.M.; Robert, A.; Leban, I. *Tetrahedron* **1990**, *46,* 453–464.
(58) Ansari, M.H.; Ahmad, M.S.; Ahmad, M. *Indian J. Chem.* **1987,** *26B,* 146–149; *Chem. Abstr.* **1988,** *108,* 21772.
(59) Choughuley, A.S.U.; Chadha, M.S. *Indian J. Chem.* **1963,** *1,* 437–440; *Chem. Abstr.* **1964,** *60,* 23349.
(60) Culvenor, C.C.J.; Davies, W.; Maclaren, J.A.; Nelson, P.F.; Savige, W.E. *J. Chem. Soc. Abstr.* **1949,** 2573–2577; *Chem. Abstr.* **1950,** *44,* 14947.
(61) Kvicala, J.; Hovorkova, P.; Paleta, O. *J. Fluor. Chem.* **2001,** *108,* 1–5.
(62) Attanasi, O.A.; De Cresentini, L.; Foresti, E.; Galarini, R.; Sanmteusanio, S.; Serra-Zanetti, F. *Synthesis* **1995,** 1397–1400.
(63) Mandrugin, A.A.; Rodyunin, A.A.; Fedoseev, V.M.; Konstantinova, M.M.; Dontsova, G.V.; Rakhmanina, O.N. *Khim. Farm. Zh.* **1989,** *23,* 832–834; *Chem. Abstr.* **1989,** *111,* 190468.
(64) Kutschy, P.; Dzurilla, M.; Kristian, P.; Kutschyova, K. *Collect. Czech. Chem. Commun.* **1981,** *46,* 436–445.

(65) Omar, M.T.; Sherif, F.A. *J. Prak. Chem. (Leipzig)* **1980,** *322,* 835–842.
(66) Kambe, S.; Hayashi, T. *Bull. Chem. Soc. Jpn.* **1972,** *45,* 3192–3195.
(67) Takeda Chemical Industries, Ltd., Japan; Senju Pharm. Co., Ltd. JP 57188579, 1982; *Chem. Abstr.* **1983,** *98,* 198200.
(68) Reeve, W.; Steckel, T.F. *Can. J. Chem.* **1980,** *58,* 2784–2788.
(69) Sato, M.; Stammer, C.H. *J. Heterocycl. Chem.* **1977,** *14,* 149–151.
(70) Halama, A.; Hejtmankova, L.; Lustig, P.; Richter, J.; Srsnova, L.; Jirman, J. PCT Int. Appl. WO 2002088120, 2002; *Chem. Abstr.* **2002,** *137,* 353010.
(71) Hauser, M. *J. Org. Chem.* **1962,** *27,* 43–46.
(72) Ulrich, H.; Sayigh, A.A.R. *Angew. Chem.* **1966,** *78,* 761–769.
(73) Váňa, J.; Hanusek, J.; Ržička, A.; Sedlák, M. *J. Heterocycl. Chem.* **2009,** *46,* 635–639.
(74) Ramsh, S.M.; Smorygo, N.A.; Khrabrova, E.S. *Kh. Geterotsikl. Soedin.* **1985,** *1,* 32–37; *Chem. Abstr.* **1985,** *102,* 166208.
(75) Danielyan, D.G.; Tsirul'nikova, N.V.; Temkina, V.Ya. *Trudy IREA* **1984**, *46,* 3–6; *Chem. Abstr.* **1985,** *103,* 104522.
(76) Skinner, G.S.; Bicking, J.B.; Lovett, J.R. *J. Org. Chem.* **1959,** *24,* 1587–1588.
(77) Takemoto, K.; Kanaoka, K.; Miyata, M. *Revue Roum. Chim.* **1980,** *25,* 1097–1100; *Chem. Abstr.* **1981,** *94,* 1347.
(78) Mukarram, M.; Ahmad, I.; Farooqi, J.A.; Ahmad, M. *Fette Seifen Anstrichmittel* **1986,** *88,* 224–226; *Chem. Abstr.* **1987,** *106,* 138316.
(79) Iijima, I.; Ozeki, M.; Okumura, K.; Inamasu, M. Eur. Pat. Appl. EP 283036, 1988; *Chem. Abstr.* **1989,** *110,* 75529.
(80) Hasler, H.; Kaufmann, F.; Pirson, W.; Schneider, F. *Eur. J. Med. Chem.* **1987,** *22,* 559–567; *Chem. Abstr.* **1988,** *109,* 48224.
(81) York, B.M. US 4864028, 1989; *Chem. Abstr.* **1990,** *112,* 158249.
(82) York, B.M. US 4717725, 1988; *Chem. Abstr.* **1988,** *109,* 129010.
(83) Yoshioka, T.; Kitazawa, E.; Kurumada, T.; Yamazaki, M.; Hasegawa, K. Jpn Kokai Tokkyo Koho JP 61036284, 1986; *Chem. Abstr.* **1986,** *104,* 207256.
(84) Sankyo Co., Ltd., Japan. Jpn Kokai Tokkyo Koho JP 60051189, 1985; *Chem. Abstr.* **1985,** *103,* 54068.
(85) Sohda, T.; Momose, Y.; Meguro, K.; Kawamatsu, Y.; Sugiyama, Y.; Ikeda, H. *Arzneim. Forsch.* **1990,** *40,* 37–42; *Chem. Abstr.* **1990,** *113,* 23750.
(86) Meguro, K.; Fujita, T. Eur. Pat. Appl. EP 193256, 1986; *Chem. Abstr.* **1986,** *105,* 226543.
(87) Sohda, T.; Mizuno, K.; Tawada, H.; Sugiyama, Y.; Fujita, T. *Chem. Pharm. Bull.* **1982,** *30,* 3563–3573; *Chem. Abstr.* **1983,** *98,* 125944.
(88) Yoshioka, T.; Fujita, T.; Kanai, T.; Aizawa, Y.; Kurumada, T.; Hasegawa, K.; Horikoshi, H. *J. Med. Chem.* **1989,** *32,* 421–428.
(89) Valls, N.; Segarra, V.M.; Alcalde, E.; Marin, A.; Elguero, J. *J. Prak. Chem. (Leipzig)* **1985,** *327,* 251–260.
(90) Balasubramaniyan, V.; Balasubramaniyan, P.; Wani, M.J. *Indian J. Chem.* **1990,** *29B,* 1092–1096; *Chem. Abstr.* **1991,** *114,* 143210.
(91) Le Marechal, A.M.; Robert, A.; Leban, I. *Tetrahedron* **1990,** *46,* 453–464.
(92) Brown, R.A. *Proc. Natl Inst. Sci. USA* **1961,** *47,* 465–469.
(93) Basova, Yu.G.; Ramsh, S.M.; Ginak, A.I. *Khim. Geterotsikl. Soedin.* **1981,** *8,* 1046–1049; *Chem. Abstr.* **1982,** *96,* 68880.
(94) Chande, M.S.; Ambhaikar, S.B. *Indian J. Chem.* **1996,** *35B,* 373–376; *Chem. Abstr.* **1996,** *124,* 289343.
(95) Ramsh, S.M.; Ivanenko, A.G. *Chem. Heterocycl. Compd.* **2003,** *39,* 1541–1542.
(96) Ramsh, S.M. *Khim. Geterotsikl. Soedin.* **1986,** *5,* 672–678; *Chem. Abstr.* **1986,** *105,* 190237.
(97) Ramsh, S.M.; Solov'eva, S.Yu.; Ginak, A.I. *Khim. Geterotsikl. Soedin.* **1983,** *7,* 928–932; *Chem. Abstr.* **1983,** *99,* 157478.
(98) Solov'eva-Yavits, S.Yu.; Ramsh, S.M.; Smorygo, N.A.; Ginak, A.I.; Sochilin, E.G. *Khim. Geterotsikl. Soedin.* **1980,** *7,* 929–932; *Chem. Abstr.* **1980,** *93,* 204518.
(99) Zhou, J.-F.; Sun, X.-J.; Zhu, F.-X.; Li, Y.-L.; Gong, G.-X. *Synth. Commun.* **2008,** *38,* 4182–4187.
(100) Qu, H.; Zhao, D.; Cheng, M. *Zhongguo Yaowu Huaxue Zazhi* **2004,** *14,* 298–300; *Chem. Abstr.* **2005,** *145,* 9998.
(101) Ibrahim, E.S.A.; Khalil, M.A.; Hassan, A.M.; Abdel-Ghany, Y.S.; Hazzaa, A.A.; El-Sayed, A.E. *Alex. J. Pharm. Sci.* **2007,** *21,* 17–24; *Chem. Abstr.* **2007,** *148,* 517661.
(102) Chowdhry, M.M.; Mingos, D.M.P.; White, A.J.P.; Williams, D.J. *Perkin 1* **2000,** *20,* 3495–3504.
(103) Chen, S.; Chen, Li; Le, N.T.; Zhao, C.; Sidduri, A.; Lou, J.P.; Michoud, C.; Portland, L.; Jackson, N.; Liu, J.-J.; Konzelmann, F.; Chi, F.; Tovar, C.; Xiang, Q.; Chen, Y.; Wen, Y.; Vassilev, L.T. *Bioorg. Med. Chem. Lett.* **2007,** *17,* 2134–2138.
(104) Chen, L.; Chen, S.; Michoud, C. PCT Int. Appl. WO 2006029863, 2006; *Chem. Abstr.* **2006,** *144,* 331426.
(105) Chen, L.; Chen, S.; Liu, J.-J. WO 2006040050, 2006; *Chem. Abstr.* **2006,** *144,* 412525.
(106) Jakse, R.; Bevk, D.; Golobic, A.; Svete, J.; Stanovnik, B. *Z. Naturforsch. B* **2006,** *61,* 413–419; *Chem. Abstr.* **2006,** *146,* 402130.
(107) Player, M.R.; Pottorf, R.S.; Rentzeperis, D.; De, D. US Pat. Appl. Publ. US 20060014812, 2006; *Chem. Abstr.* **2006,** *144,* 150121.
(108) Hu, B.; Malamas, M.; Ellingboe, J. *Heterocycles* **2002,** *57,* 857–870.
(109) Hu, B.; Malamas, M.; Ellingboe, J.; Largis, E.; Han, S.; Mulvey, R.; Tillett, J. *Bioorg. Med. Chem. Lett.* **2001,** *11,* 981–984.
(110) Irvine, M.W.; Patrick, G.L.; Kewney, J.; Hastings, S.F.; MacKenzie, S.J. *Bioorg. Med. Chem. Lett.* **2008,** *18,* 2032–2037.

(111) Pardasani, P.; Pardasani, R.T.; Sherry, D.; Chaturvedi, V.; Saxena, A. *Indian J. Heterocycl. Chem.* **2000,** *10,* 129–134; *Chem. Abstr.* **2001,** *134,* 326451.
(112) Pardasani, R.T.; Pardasani, P.; Ojha, C.K.; Sherry, D.; Chaturvedi, V.; Sharma, I. *Phosphorus Sulfur Silicon Relat. Elem.* **2002,** *177,* 2435–2443.
(113) Londhe, A.; Gupta, B.; Khatri, P.; Pardasani, P.; Pardasani, R.T. *Indian J. Heterocycl. Chem.* **2005,** *15,* 137–140; *Chem. Abstr.* **2006,** *145,* 8088.
(114) Pardasani, R.T.; Pardasani, P.; Sharma, I.; Saxena, A.; Kohli, S. *Indian J. Chem.* **2003,** *42B,* 3075–3080; *Chem. Abstr.* **2004,** *141,* 38562.
(115) El-Shafei, A.K.; El-Sayed, A.M.; Abdel-Ghany, H.; El-Saghier, A.M. *Gazz. Chim. Ital.* **1990,** *120,* 193–195.
(116) Hussain, S.M.; El-Reedy, A.M.; Rezk, A.M.H.; El-Dien, K.A. *J. Heterocycl. Chem.* **1987,** *24,* 1605–1610.
(117) Solov'eva, S.Yu.; Ramsh, S.M.; Ginak, A.I. *Khim. Geterotsikl. Soedin.* **1983,** *10,* 1352–1356; *Chem. Abstr.* **1984,** *100,* 103230.
(118) Solov'eva, S.Yu.; Ramsh, S.M.; Ginak, A.I. *Khim. Geterotsikl. Soedin.* **1983,** *9,* 1204–1209; *Chem. Abstr.* **1984,** *100,* 68262.
(119) Solov'eva-Yavits, S.Yu.; Ramsh, S.M.; Ginak, A.I. *Khim. Geterotsikl. Soedin.* **1981,** *4,* 477–480; *Chem. Abstr.* **1981,** *95,* 80900.
(120) Kassab, R.R. *Al-Azhar Bull. Sci.* **1997,** *8,* 1–6; *Chem. Abstr.* **1998,** *130,* 110187.
(121) Manhi, F.M.; Mahmoud, M.R. *Heteroat. Chem.* **2005,** *16,* 121–131.
(122) Hurst, D.T.; Stacey, A.D.; Nethercleft, M.; Rahim, A.; Harnden, M.R. *Aust. J. Chem.* **1988,** *41,* 1221–1229.
(123) Mehrotra, V.N.; Achari, R.S. *J. Indian Chem. Soc.* **1985,** *62,* 306–307; *Chem. Abstr.* **1986,** *105,* 78866.
(124) Jakse, R.; Svete, J.; Stanovnik, B. Zbornik Referatov s Posvetovanja Slovenski Kemijski Dnevi, Maribor, Slovenia, Sept. 28–29, 2000; Pt. 1, 141–146; *Chem. Abstr.* **2000,** *134,* 163195.
(125) Jakse, R.; Recnik, S.; Svete, J.; Golobic, A.; Golic, L.; Stanovnik, B. *Tetrahedron* **2001,** *57,* 8395–8403.
(126) El-Saghier, A.M.M. *Phosphorus Sulfur Silicon Relat. Elem.* **2002,** *177,* 1213–1221.
(127) Haiza, M.A.A. *Rev. Roum. Chim.* **2000,** *45,* 1019–1020.
(128) Zawisza, T.; Wagner, E. *Polish J. Chem.* **1985,** *59,* 149–158; *Chem. Abstr.* **1986,** *105,* 152978.
(129) Vorob'eva, N.N.; Razvodovskaya, L.V.; Negrebetskii, V.V.; Grapov, A.F.; Mel'nikov, N.N. *Zh. Obshch. Khim.* **1987,** *57,* 781–786; *Chem. Abstr.* **1988,** *108,* 186832.