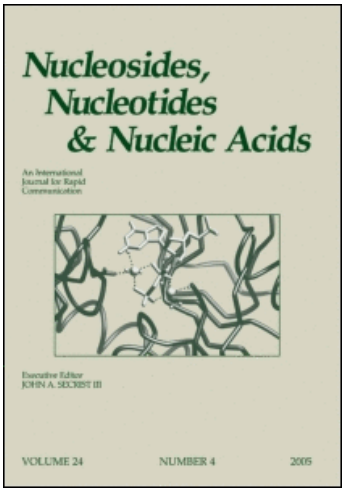

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PYRIMIDINETHIONE NUCLEOSIDES AND THEIR DEAZA ANALOGUES

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NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 21(4&5), 287–325 (2002)

PYRIMIDINETHIONE NUCLEOSIDES AND THEIR DEAZA ANALOGUES

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Helwan University, Ain-Helwan, Cairo, Egypt

ABSTRACT

The methods of preparation, structure, chemical properties and synthetic potentiality of pyrimidinethione nucleosides and their deaza analogues are reported.

INTRODUCTION

There is an increasing interest in the synthesis of nucleoside analogues and their incorporation into DNA sequences for the study of ligand DNA and protein-DNA interactions.[1,2] A variety of nucleoside derivatives has been prepared through the deletion or change in the nature of the functional group present on the heterocyclic bases or their sugar moieties. Such analogues permit the synthesis of oligonucleotides in which a single functional group at a preselected position have been deleted or other wise altered.[3] In this study we are concerning with pyrimidinethione nucleosides as we were involved in synthesizing its deaza analogue known as pyridinethione nucleosides. To our knowledge, no attempt to survey their methods of preparation or their wide range of biological applications has been made. The present article fill this gap and involves an up to date survey in the synthesis, chemistry and biological activities of pyrimidinethione nucleosides either modified or non-modified. The preparation of oligoribonucleotides containing pyrimidinethione nucleosides which have recently reviewed[4,5] is not our aim and will not be discussed here.

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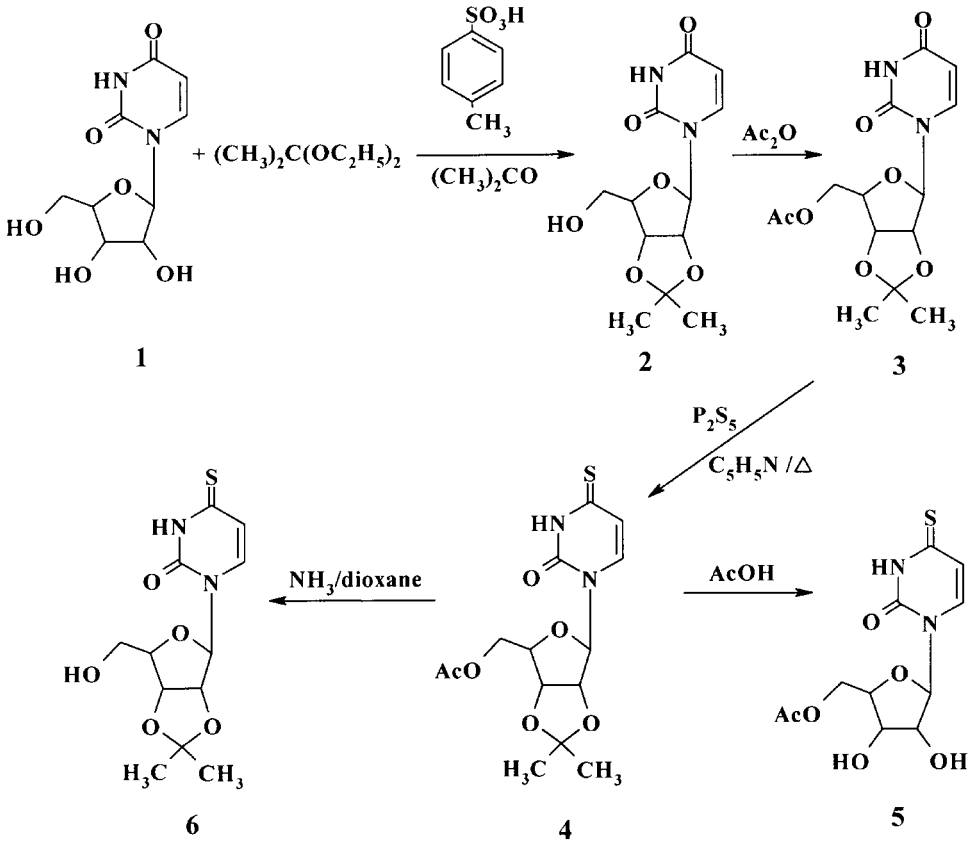
I. SYNTHESIS

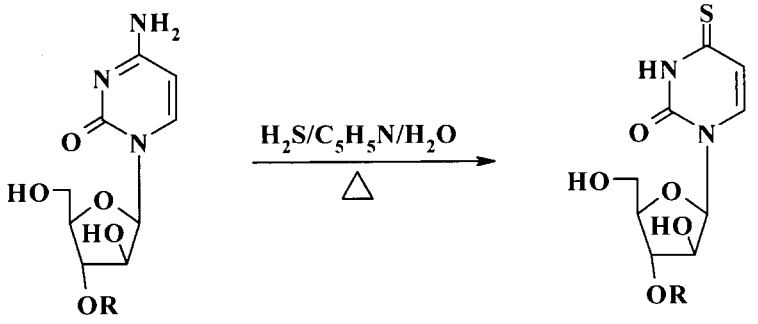
A) Synthesis of Non-modified Pyrimidinethione Nucleosides

The carbonyl group either in sites 2 or 4 and also NH_2 at position 4 are not considered to be a modification hence they are present in natural pyrimidine bases. Reaction of uridine **1** with 2,2-diethoxypropane in acetone in the presence of acid catalyst (p-toluenesulfonic acid) gave 2′,3′-O-isopropylidine-uridine **2**. The latter was acetylated with acetic anhydride in a refluxing pyridine to give 5′-O-acetyl-2′,3′-O-isopropylidene-uridine **3**. Compound **3** was thionated by refluxing with P_2S_5[6–10] in pyridine to give 5′-O-acetyl-2′,3′-O-isopropylidene-4-thiouridine **4**. The acetyl group of compound **4** was removed with aqueous ammonia in dioxane, while the isopropylidene group was eliminated by refluxing in 50% acetic acid, giving compounds **5** and **6**, respectively.[11] Other protecting groups were used as complete acetylation or benzoylation.[11–17]



The amino group in any cytidine derivative is readily replaced by a thione group under the action of hydrogen sulfide in aqueous pyridine.[18–20] Thus

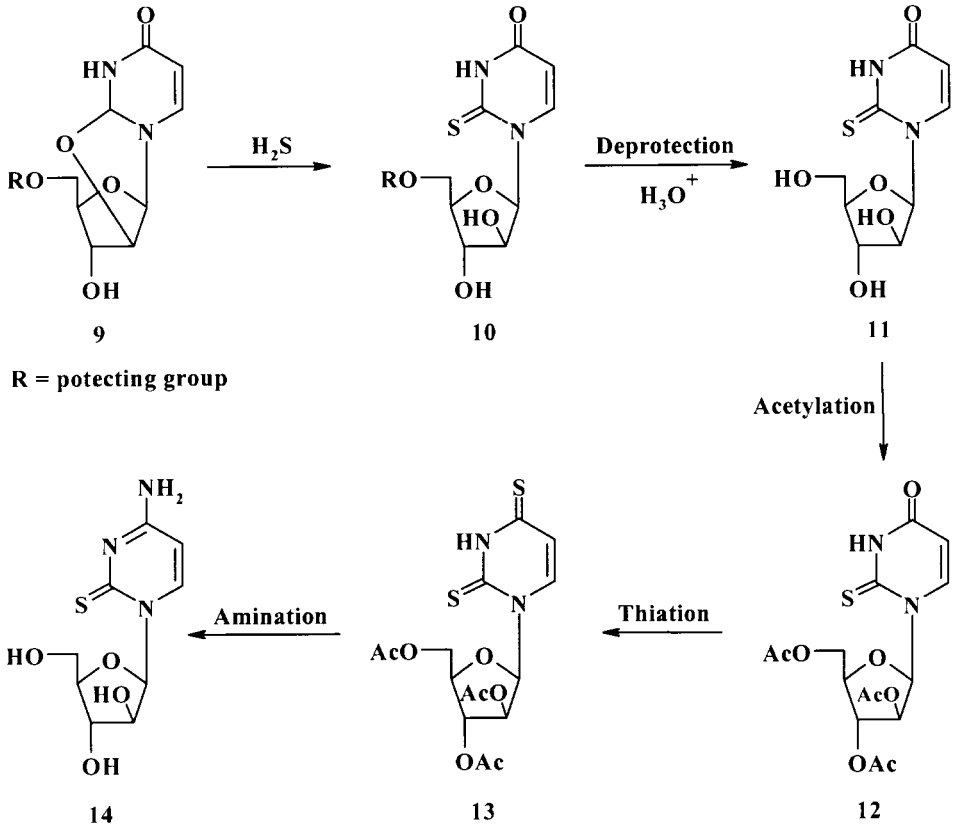
treatment of aracytidine, analogously aracytidine-3′-phosphate **7**,[21,22] with liquid H_2S in pyridine and heating in an autoclave at 80°C for 48 h resulted in the formation of 4-thiouridine and its 3′-phosphate derivative **8**.[23]



7 **8**

R = H, phosphate residue

Treatment of 2,2′-Anhydro-1-[5′-(OR-substituted)-β-D-arabinofuranosyl]-uracil derivatives **9** with H_2S yielded D-arabinofuranosyl-2-thiouracil

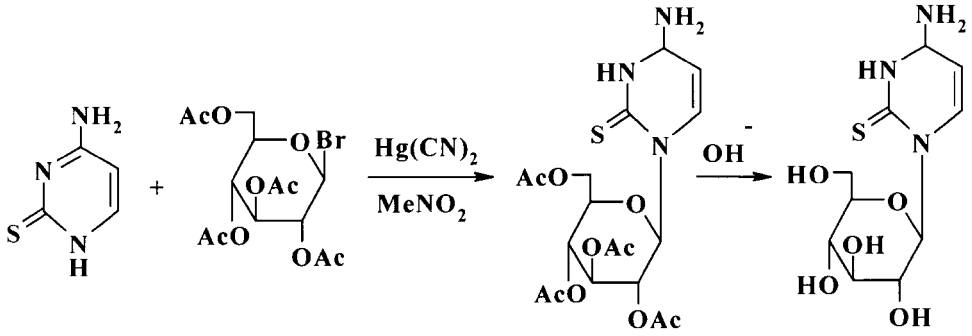


9 **10** **11**

R = potecting group

14 **13** **12**

compounds **10**, the latter were hydrolysed to give the free 2-thiouracil nucleoside **11** which underwent acetylation and thionation to afford the 2,4-dithiouracil analogue **13**. Amination of compound **13** gave the corresponding D-arabinosyl-2-thiocytosine **14**.[24] Treatment of 2-thiocytosine **15** with acetobromoglucose **16** in nitromethane containing a catalytic amount of mercury (II) cyanide gave N(3)-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiocytosine **17**, the structure of the latter was confirmed by subsequent methylation and alkali hydrolysis[25] which give 2-thiocytosine nucleoside **18**.[26,27] Similar reaction of 2-thiocytosine **15** with 2,3,5-triacetylribofuranosyl bromide[28] afforded 2′, 3′, 5′-tri-O-acetyl-β-D-ribofuranosyl-2-thiocytidine.[27]



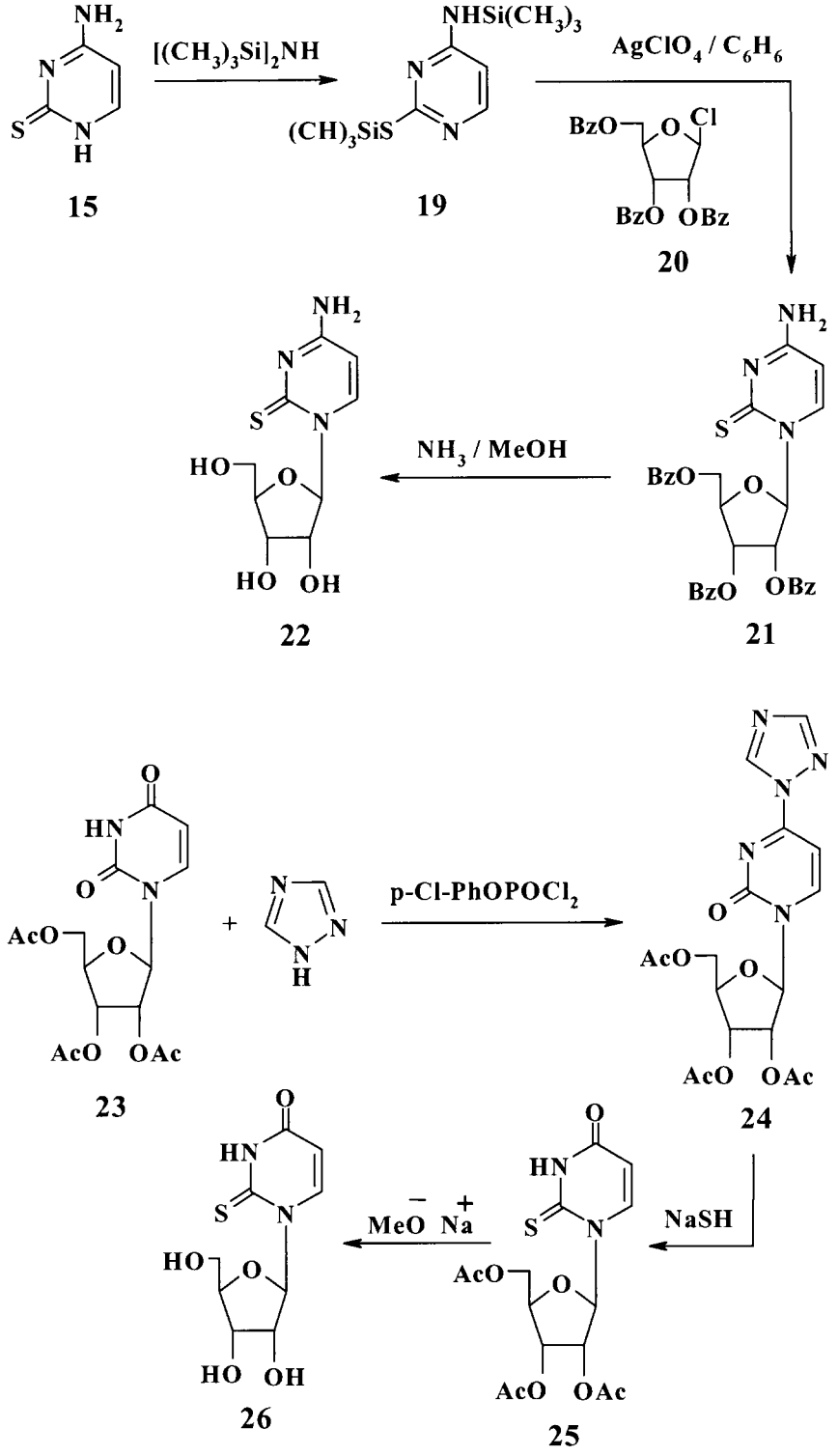
15 **16** **17** **18**

Silylation of 2-thiocytosine **15** gave 4-(trimethylsilylamino)-2-(trimethylsilylthio)pyrimidine **19**, which reacted with 1-chloro-2,3,5-*O*-benzoyl-D-ribofuranose **20** in the presence of silver perchlorate in benzene to the benzoylated 2-thiocytidine nucleoside **21**. Treatment of compound **22** with NH_3/MeOH gave the free nucleoside **22**. A similar reaction but using 2-thiouracil and 2-thiothymine gave the corresponding free nucleosides.[29] 2′,3′,5′-Tri-O-acetyluridine **23** was treated with 1,2,4-triazole and p-chlorophenyl phosphodichloridate in pyridine for 48 h to give the triazolyl derivative **24**.[30,31] Treatment of the latter with sodium hydrogen sulfide in acetone-water for 15 min yielded the acetylated 4-thiouridine derivative **25**. Deacetylation of compound **25** gave the free glycoside **26**.[32]

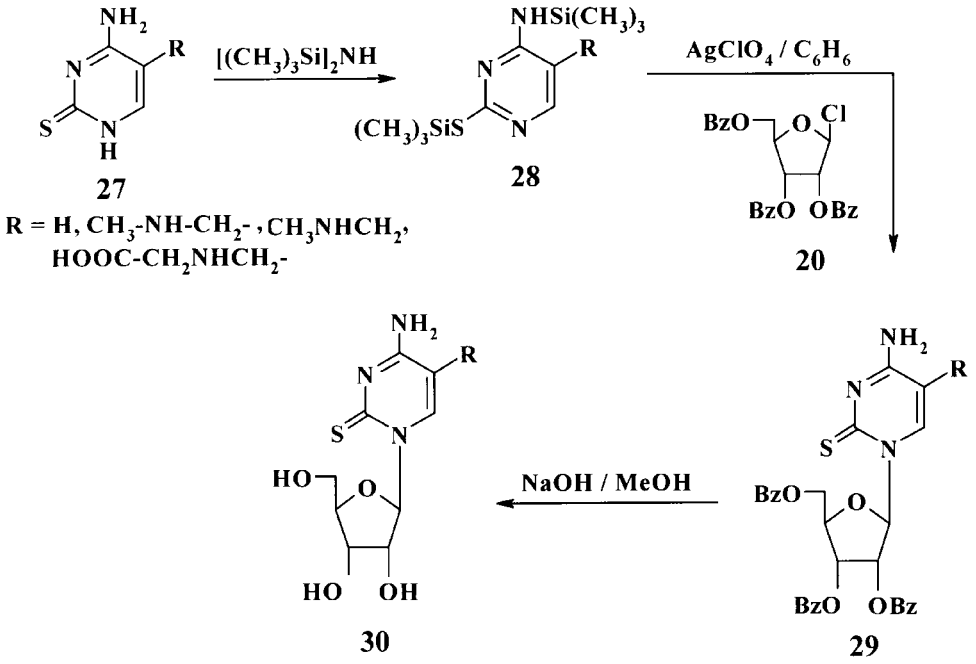
B) Synthesis of Modified Pyrimidinethione Nucleosides

1) Via Alteration of Their Heterocyclic Base

This modification is through substitution at C-5 and/or C-6 of pyrimidinethione ring, via alkylation, halogenation or even hydrogenation. The

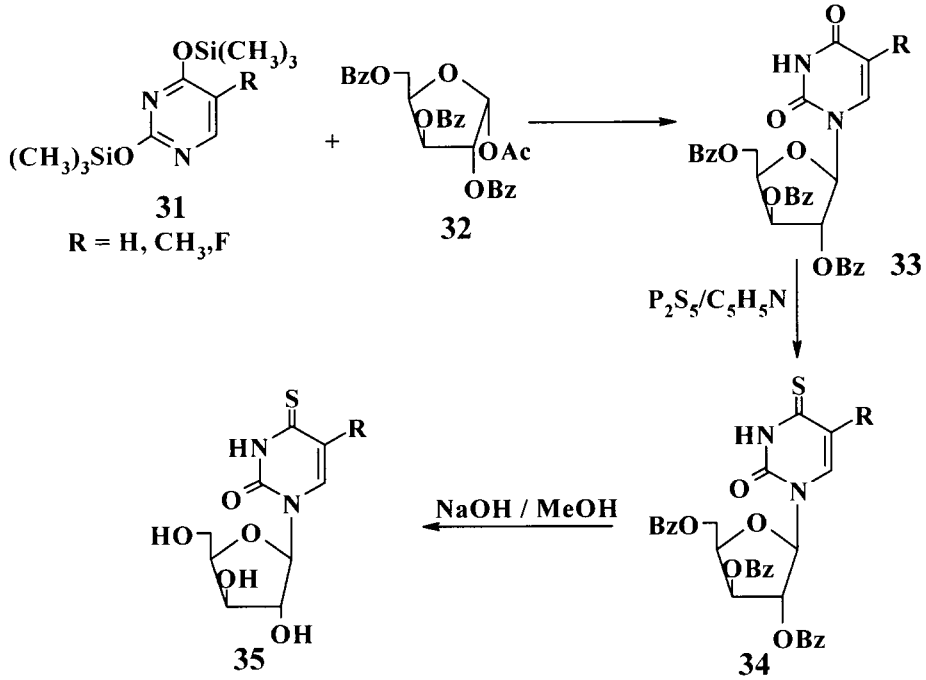


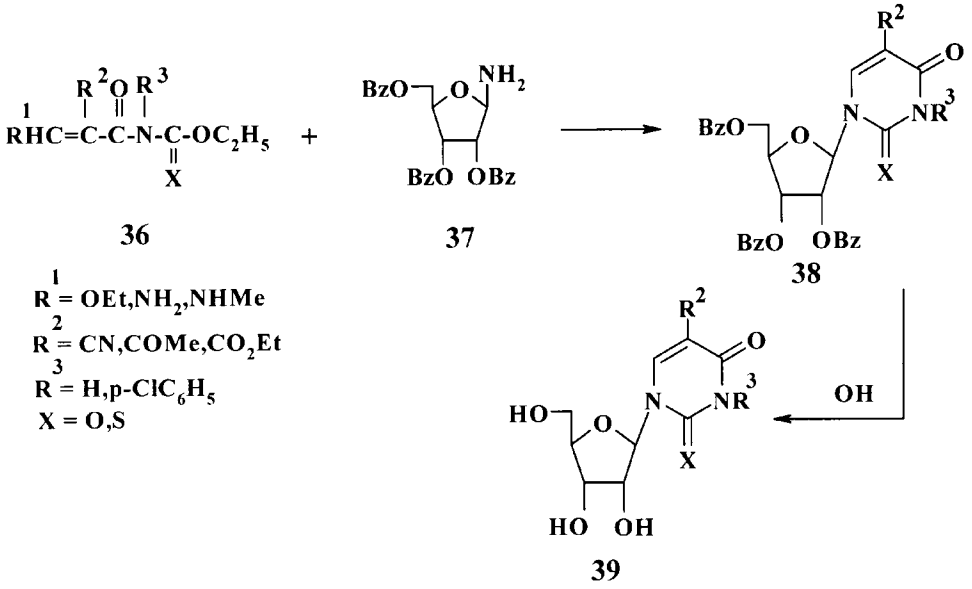
modified bases **27** were usually prepared and silylated to give compounds **28** which were coupled with 1-chloro-2,3,5-tri-O-benzoyl-β-D-ribofuranose **20** and also with protected ribose derivatives in the presence of a Lewis acid to give the protected glycosides **29**. Furthermore, the protective group was removed by alkaline hydrolysis yielding the free nucleosides **30**.[29,33–39] Similarly several pyrimidine and purine nucleosides were synthesized by conjugation of silylated bases with a peracetylated sugar in the presence of a Friedel Craft's catalyst.[40–44]

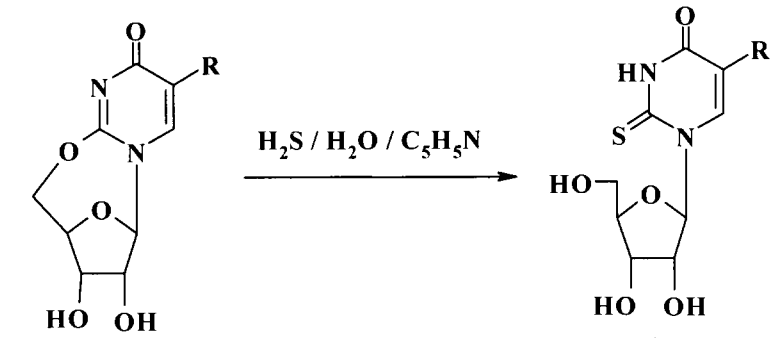


Treatment of bis(trimethylsilyl)-5-(substituted)-2,4-pyrimidindione derivatives **31** with 1-acetyl-2,3,5-O-benzoyl-xylofuranose **32** in vic. dichloroethane containing $SnCl_4$ gave the benzoylated xylofuranosyl nucleosides **33**. Upon thionation of **33**, the corresponding thionucleosides **34** were formed. Hydrolysis of compounds **34** gave the free nucleosides **35**.[45]The Benzoylated β-D-ribofuranosylamine **37** was coupled with different carbamates **36** as heterocylic ring precursors, to form different protected pyrimidine nucleosides **38**. The hydrolysis of compounds **38** gave the free pyrimidine nucleosides substituted at (C-5) **39**.[46]

The reaction of 2,5′-anhydrouridines **40** with aqueous H_2S in pyridine at room temperature for 4-days afforded 5-substituted-2-thiouridines **41**.[47,48]





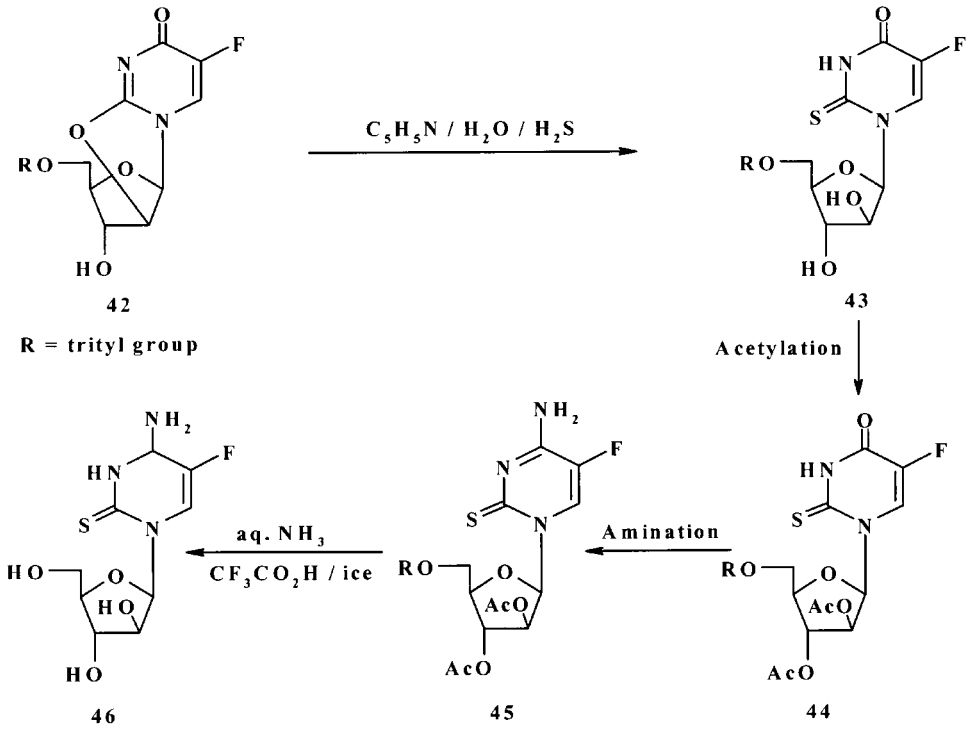


40

R = H, X, alkyl, hydroxyalkyl

41

Similarly, 2,2′-anhydro(β-D-arabinofuranosyl)-5-fluorouridine **42** underwent the same reaction to form 2-thiouridine **43**. Acetylation of compound **43** gave compound **44**, which aminated to give the protected nucleoside **45**. The latter was hydrolyzed to give the free nucleoside **46**.[49]



42

R = trityl group

43

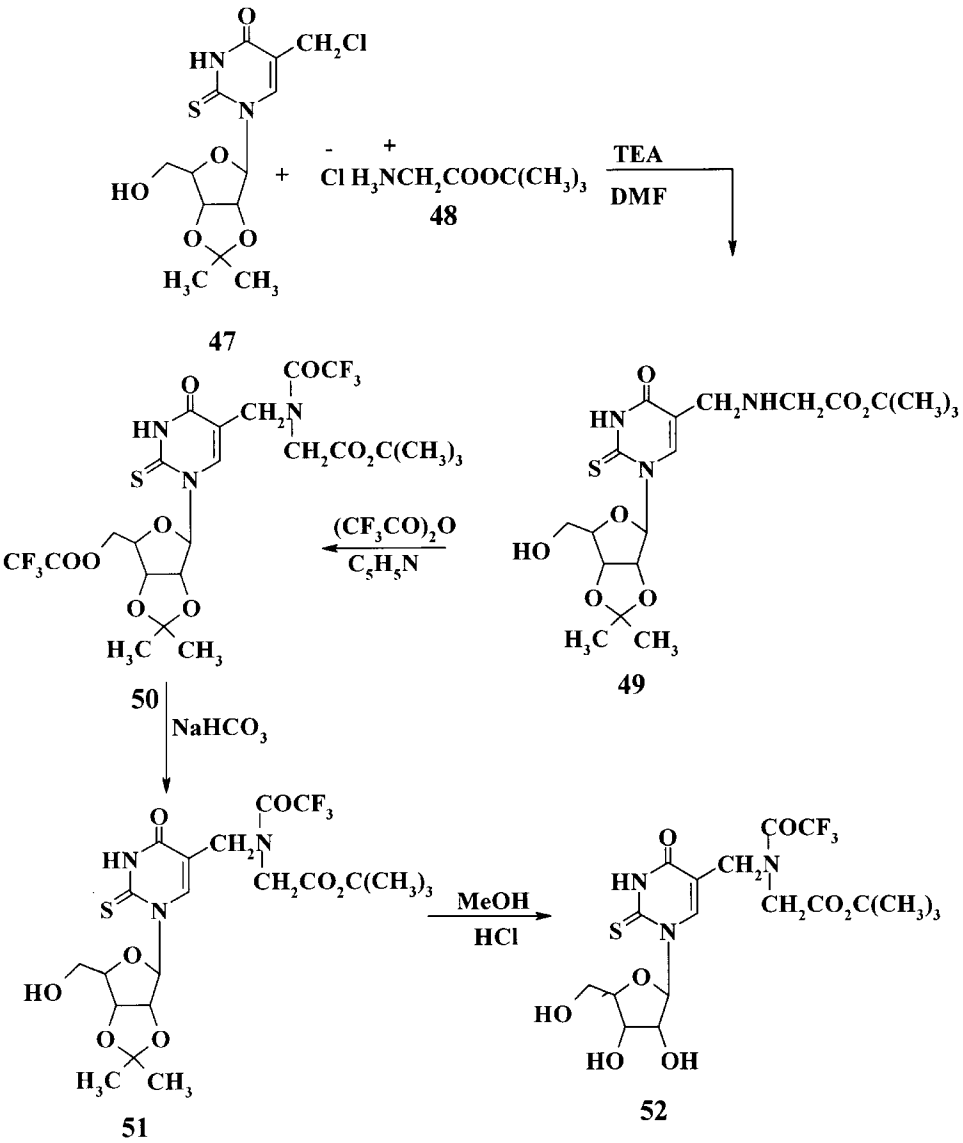
44

45

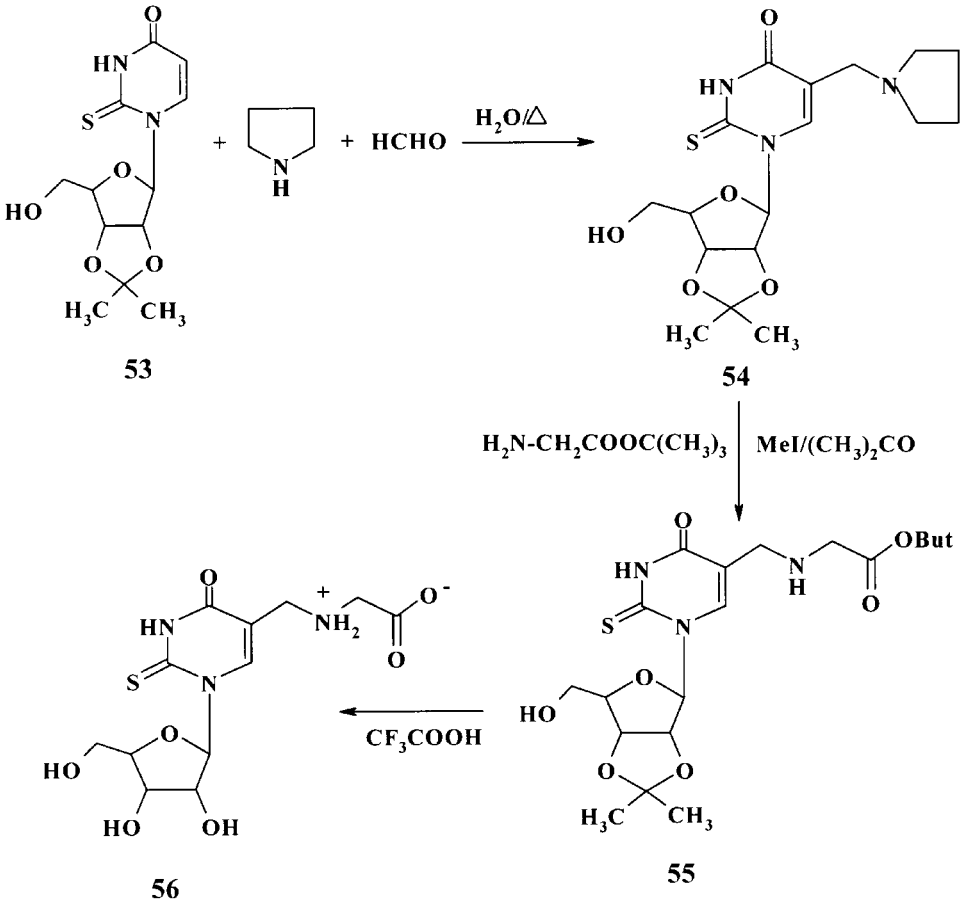
46

Treatment of 2′,3′-O-isopropylidine-5-chloromethyl-2-thiouridine **47** with glycine tert-butyl ester hydrochloride **48** in DMF gave compound **49**, which

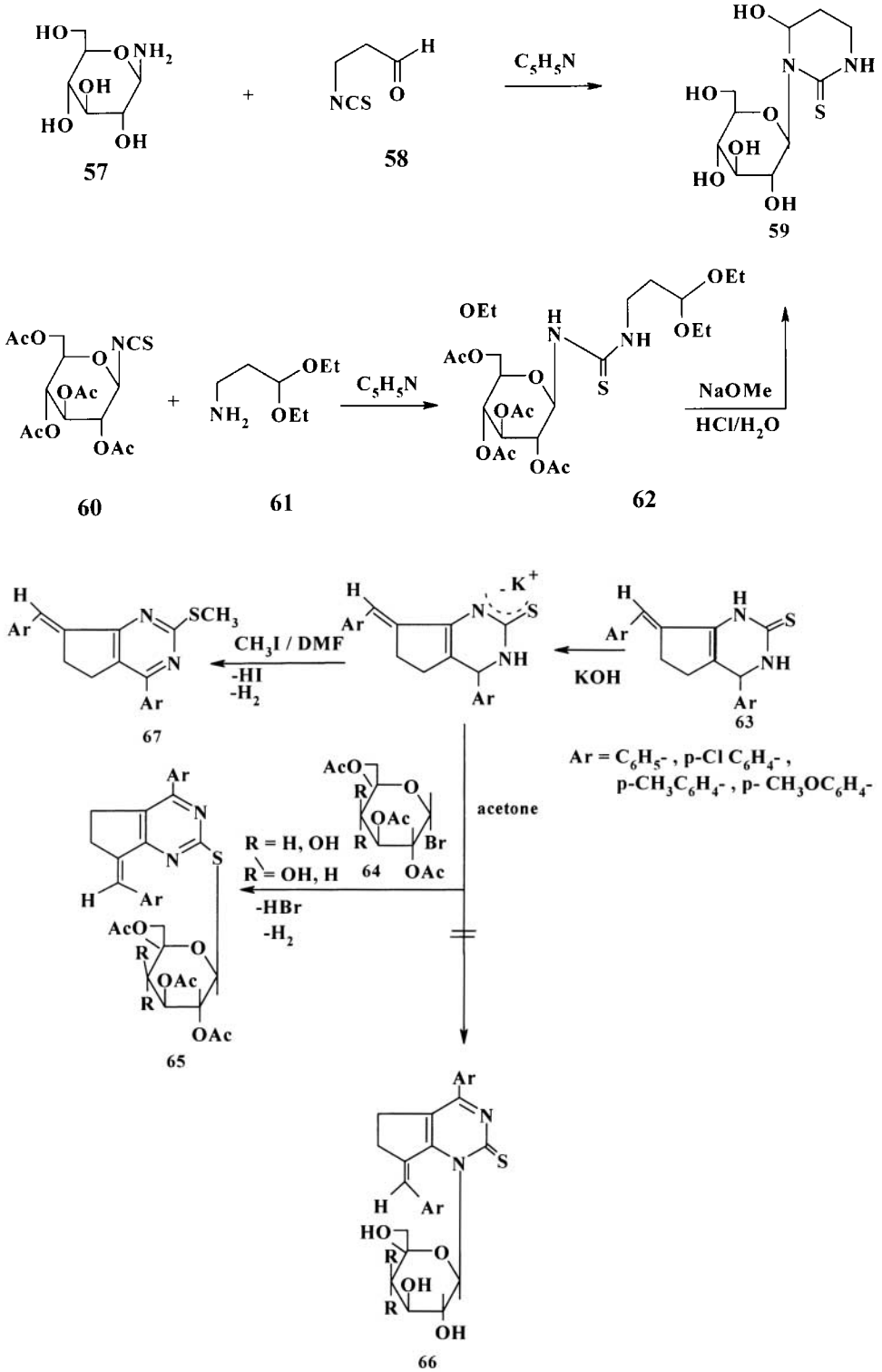
was trifluoroacetylated with an excess trifluoroacetic anhydride in pyridine to give the acylated compound **50**. Hydrolysis of the 5′-O-trifluoroacetyl group of compound **50** with 5% $NaHCO_3$ gave compound **51**, which after refluxing with 0.5 N HCl in methanol afforded the free nucleoside **52**.[50]



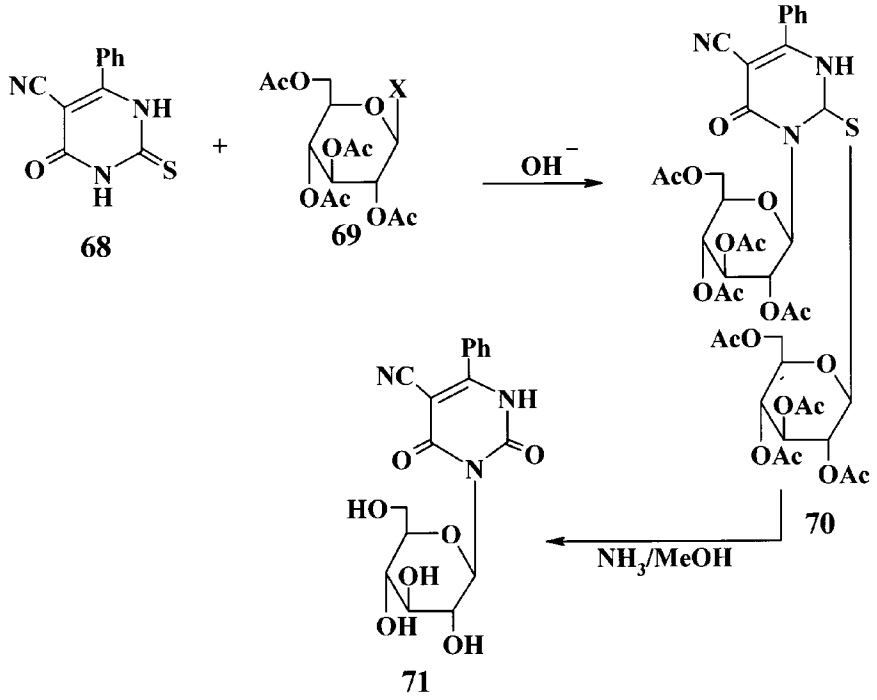
Heating of 2′,3′-O-isopropylidin-2-thiouridine **53**[51,52] in an aqueous Solution of formaldehyde and pyrrolidine gave the Mannich base **54**. Treating of the latter with methyl iodide in acetone and glycine tertbutyl ester[53] gave compound **55**. The free nucleoside **56** was obtained via hydrolysis with trifluoroacetic acid.[54]



The reaction of the glycosyl amine **57** with β-isothiocyanato aldehyde **58** gave the 4-hydroxyhexahydropyrimidine-2-thione nucleoside **59**. Compound **59** could be also prepared by reaction of peracetylated glycoside isothiocyanate **60** with β-aminoaldehydes, ketones as well as their derivatives as 3,3-diethoxypropane-1-amine **61**. Reaction with the latter gave compound **62**, which after deprotection was transformed into the target nucleoside **59**.[55–59] Recently, with the aim of obtaining non classical valuable nucleosides, Elgemeie et al. synthesized the novel condensed bicyclic thiopyrimidine nucleosides **65**, utilizing the cyclopentapyrimidinethiones **63** and α-halosugars **64** as starting components. The formation of the S-glycosides **65** and not the corresponding N-glycosides was proven using ^{13}C NMR which revealed the absence of the thione carbon C-2 at δ 178 ppm. Instead a signal was found at 161 ppm which was the same value found in the corresponding S-alkyl derivatives **67**. Moreover an attempt to remove the protecting groups of **65** with methanolic ammonia failed to give the corresponding free glycosides.[60]

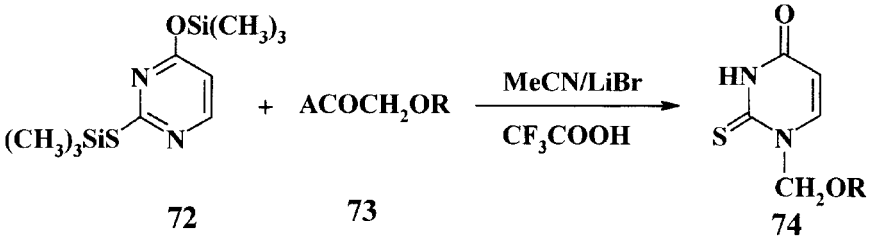


The bi-glyconde **70** was formed when 4-phenyl-5-cyano-2-thiouracil **68** reacted with glycosylhalide **69** however, deacetylation of compound **70** caused a cleavage of the S-glycosyl residue to give the N-3-glycosylated analogue **71**.[61]



2) Via Alteration of Their Sugar Moieties

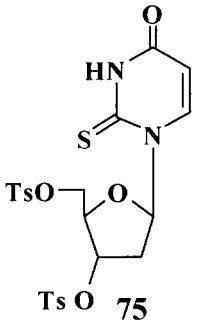
Acyclic nucleosides **74** were prepared by coupling the trimethylsilylated pyrimidine **72** with $ACOCH_2OR$ **73** in actonitrile using lithium bromide as a coupling agent in presence of trifluoroacetic acid.[62]



R = $AcOCH_2CH_2$-, $(phCHOCH_2)_2CH$-

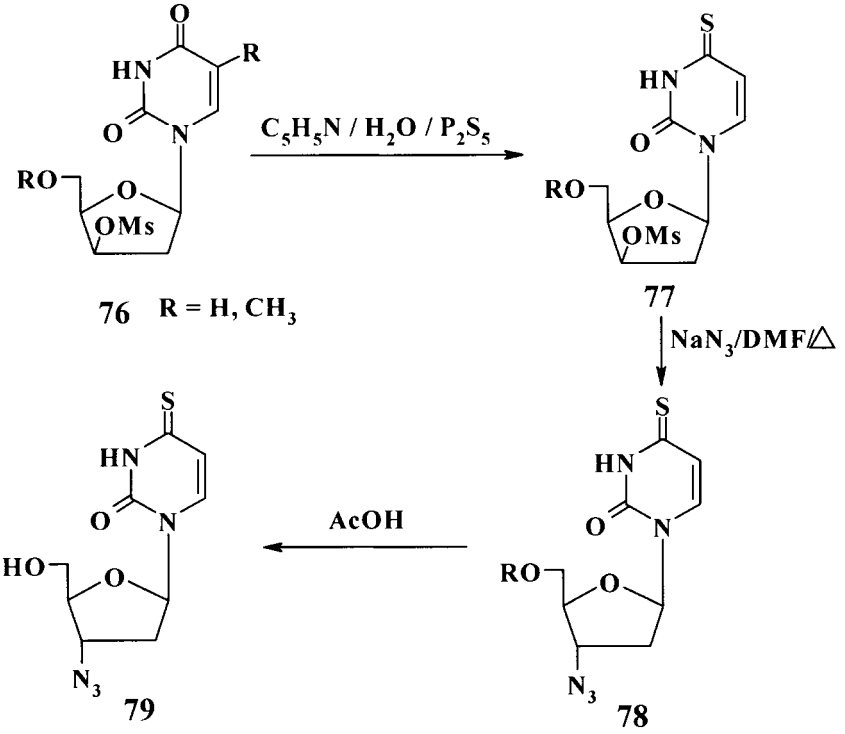
A stereoselective glycosylation was described for synthesis of α- and β-2′-deoxy-2-thiouridine. The reaction passed a silylated glycoside intermediate,

which underwent a S^2-N^1 rearrangement in the presence of $SnCl_4$ to give compound **75**.[63]



75

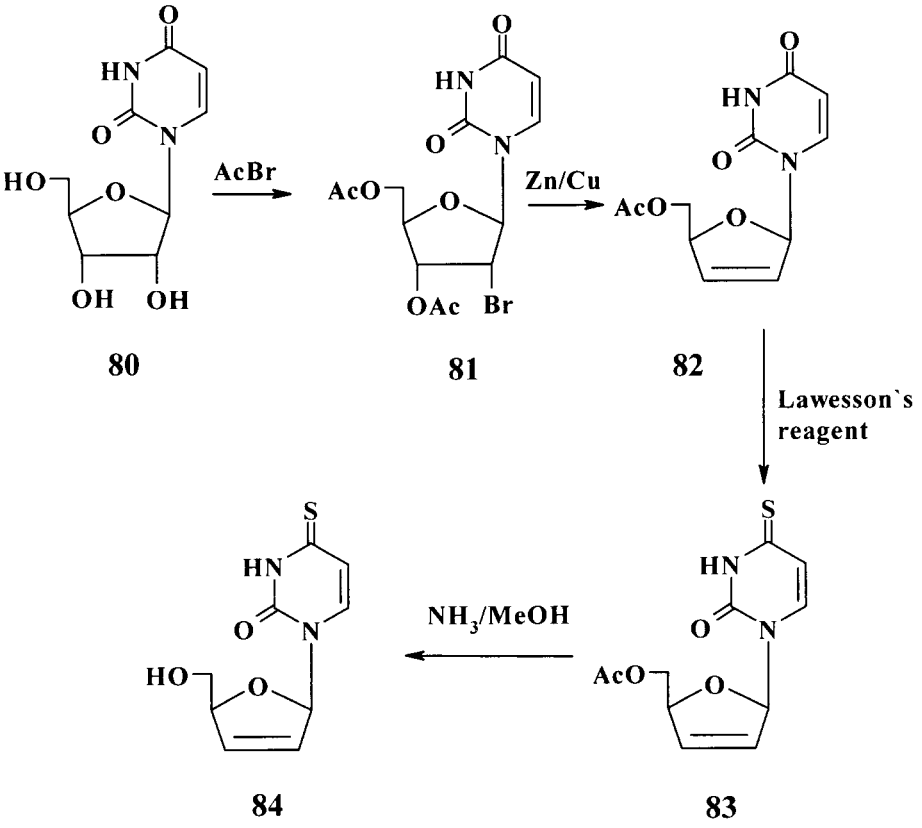
Refluxing of 2′-deoxy-3′-O-mesyl-protected-uridines **76** with P_2S_5 in pyridine gave compounds **77** which reacted with sodium azide in DMF to compounds **78**. Deprotection of the latter was induced by 80% acetic acid to give the azido-deoxy nucleosides **79**.[17,64–66]



76 R = H, CH_3

Treatment of uridine **80** with acetylbromide gave 2′-bromo-3′,4′ diacetyluridine **81** which was reduced by Zn/Cu to the unsaturated uridine **82**. Subsequent treatment of compound **82** with 2,4-bis(4-methoxy-phenyl)-1,

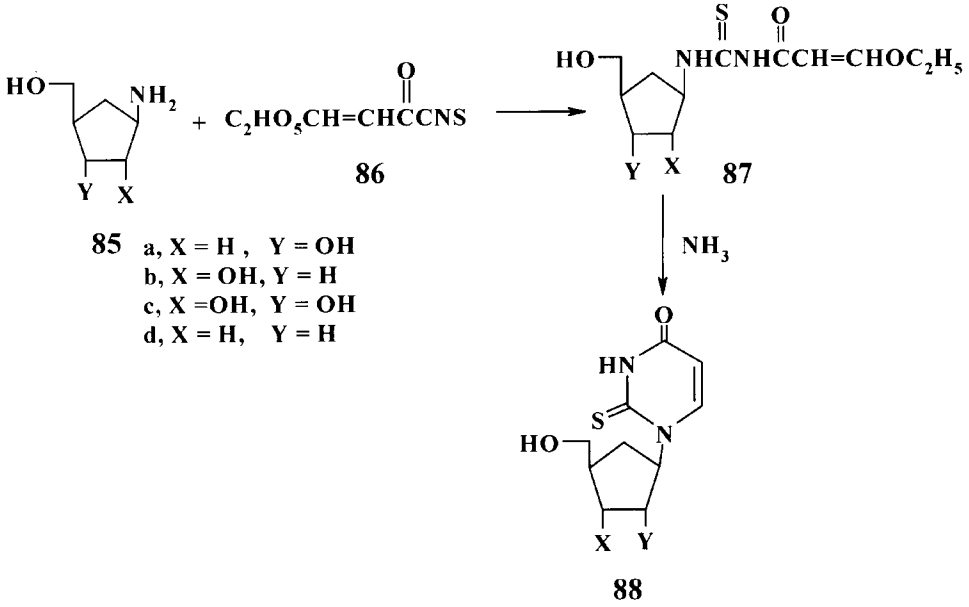
3-dithia-2,4-diphosphetane-2,4-disulfide (Lawesson's reagent)[67] afforded the thioamide **83** which was deprotected to **84**.[68]



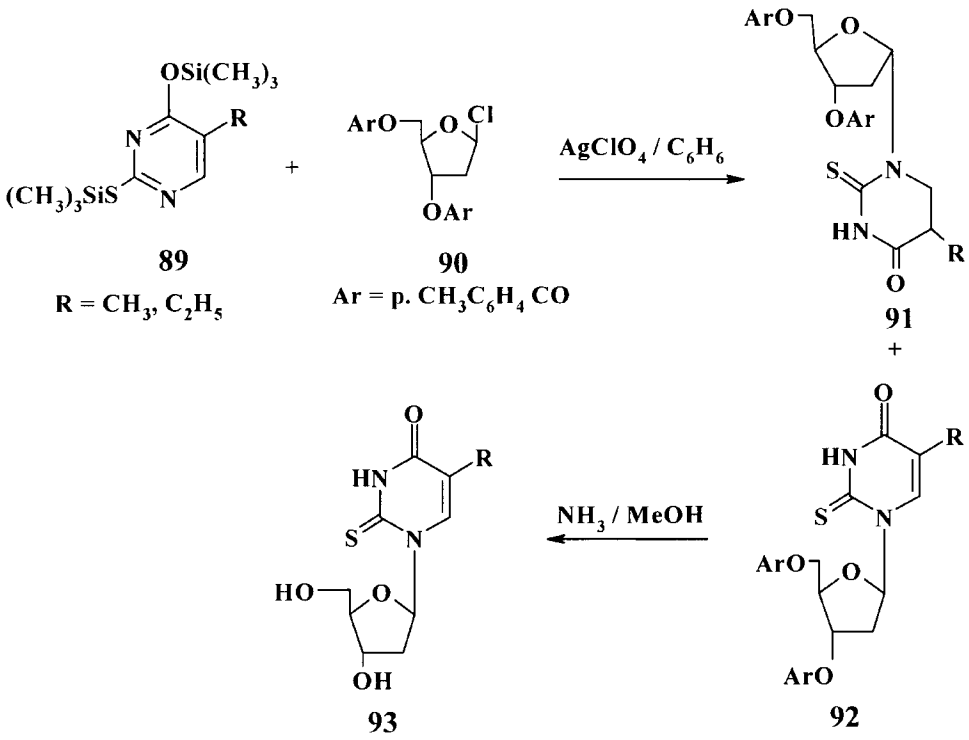
Deoxynucleosides were prepared by coupling of the cyclopentane derivative **85** with 3-ethoxypropenoylisothiocynate **86**[69] to give the acyclic intermediate **87**. This compound cyclized in aqueous ammonia to give the nucleoside analogue **88**.[70,71]

3) Via Alteration of Both Their Heterocyclic Base and Sugar Moieties

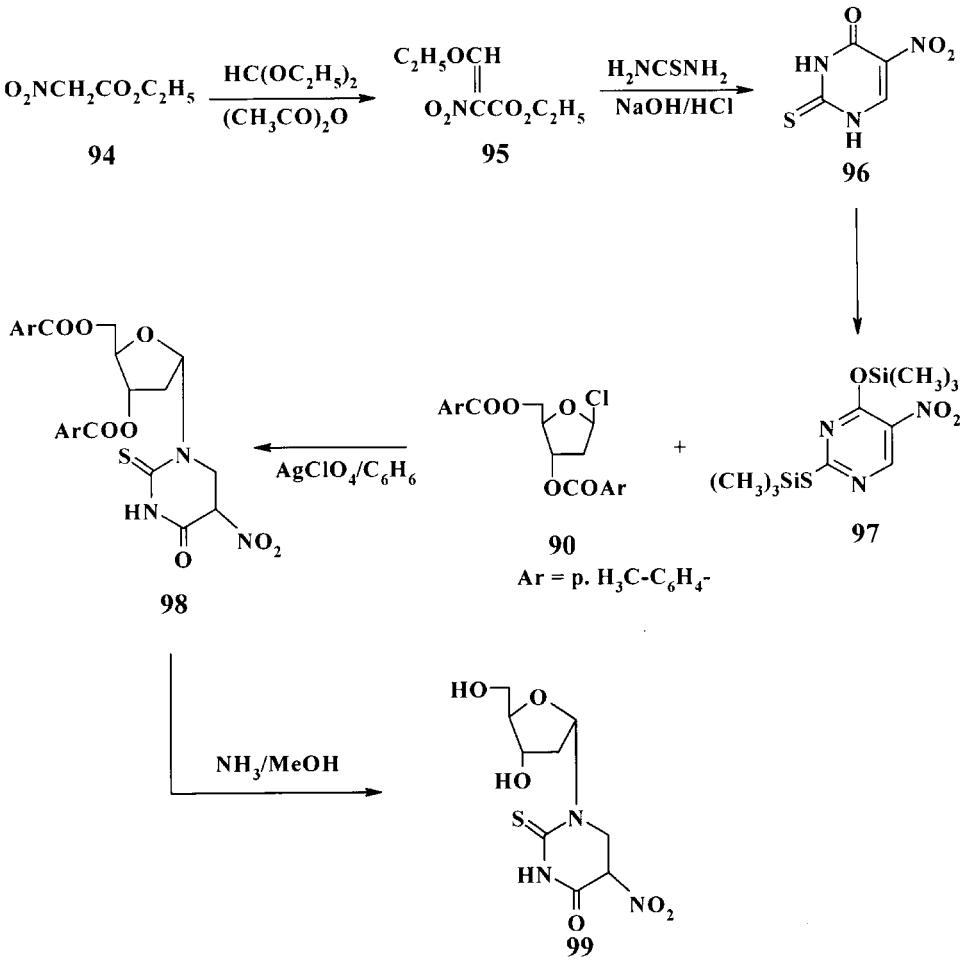
2-Thiothymine derivatives were silylated to form the bis(trimethylsilyl)-5-(subst)-2-thiothymine derivatives **89**. These reacted with 3,5-di-p-tolyl-2-deoxy-D-ribofuranosylchloride **90** in presence of $AgClO_4$ in benzene to both α- and β-anomers **91** and **92** respectively. The β-anomer was hydrolyzed to give compounds **93**.[29] By a similar procedure many other modified nucleosides were prepared.[72–76]



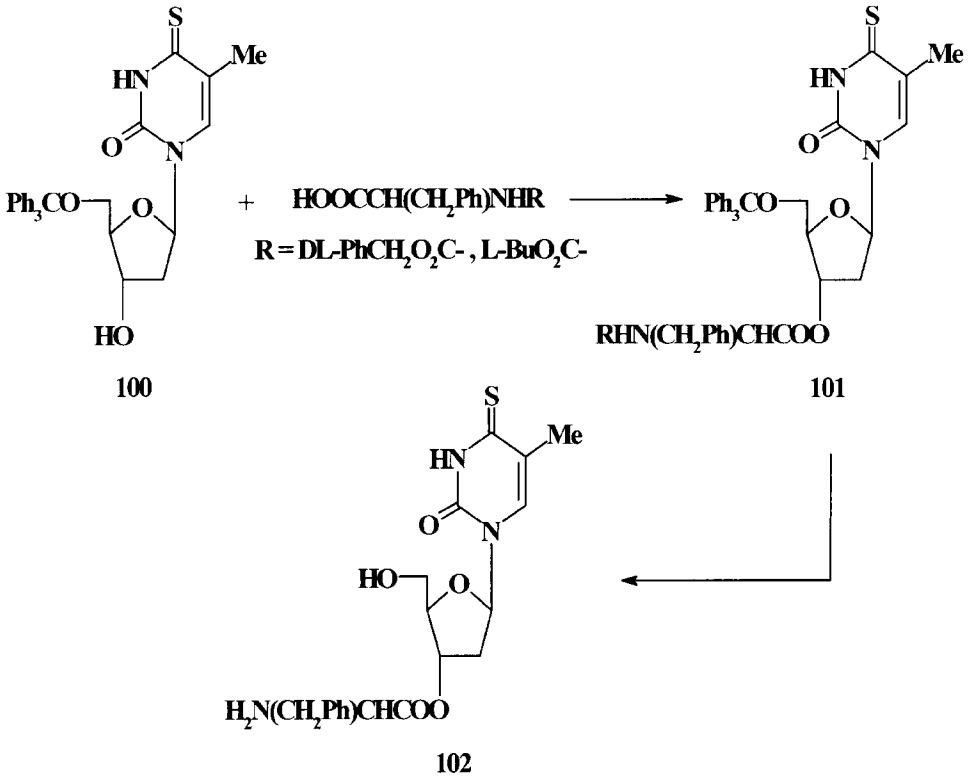
85 a, X = H, Y = OH
b, X = OH, Y = H
c, X = OH, Y = OH
d, X = H, Y = H



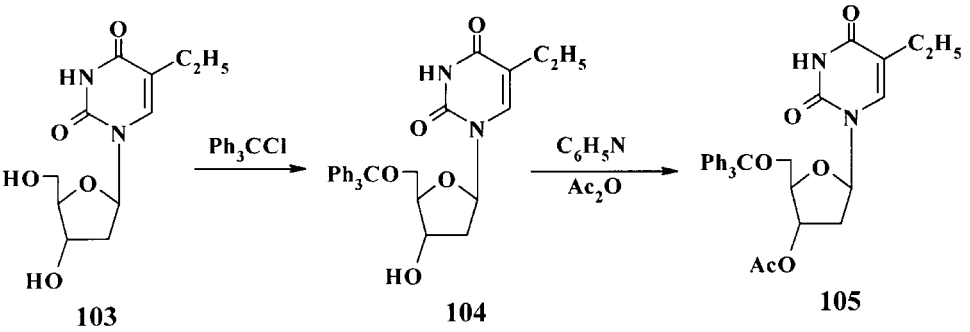
Refluxing ethylnitroacetate **94** with triethylorthoformate in acetic anhydride gave compound **95**, which condensed with thiourea in presence of NaOH. 5-Nitro-2-thiouracil **96** was formed after treatment with HCl. Upon silylation of the latter, compound **97** was formed, which was treated with 1-chloro-2-deoxybenzoylated ribose **90** in presence of $AgClO_4$ in benzene to give the α-anomer of the protected nucleoside **98**. Hydrolysis of compound **98** afforded the free nucleoside **99**.[29]



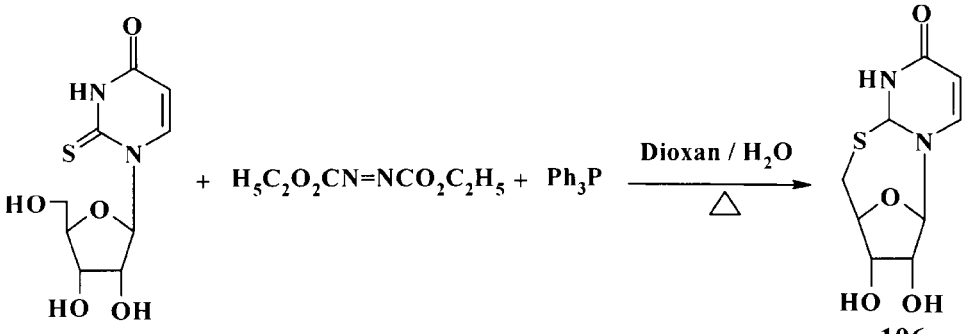
Coupling of 5′-O-triphenylmethyl-4-thiothymine **100** with N-benzyloxy carbonyl-DL-alanine or N-tert-butoxyoxycarbonyl-L-phenylalanine by dicyclohexylcarbodiimide method to form 3′-nucleoside esters **101** which were hydrolysed to give 3′-O-(L-phenylalanyl)-4-thiothymidine **102**.[77]



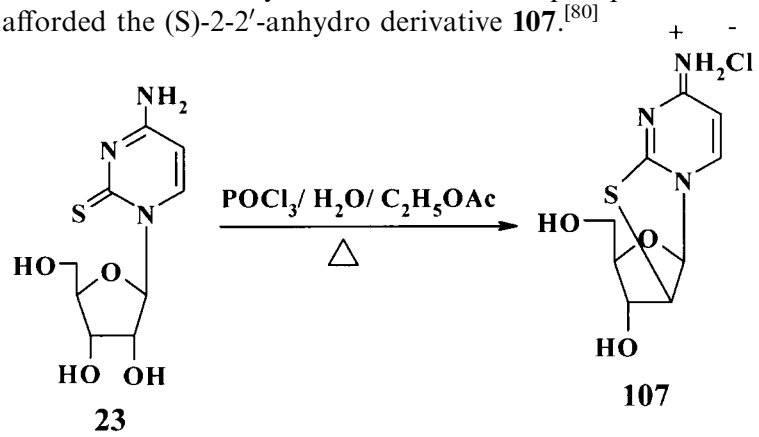
Reaction of 5-ethyl-2′-deoxyuridine **103**, similarly the 2′-deoxy-thiouridine with triphenyl chloromethane gave compound **104**. Acetylation gave the actylated nucleoside **105**.[78]



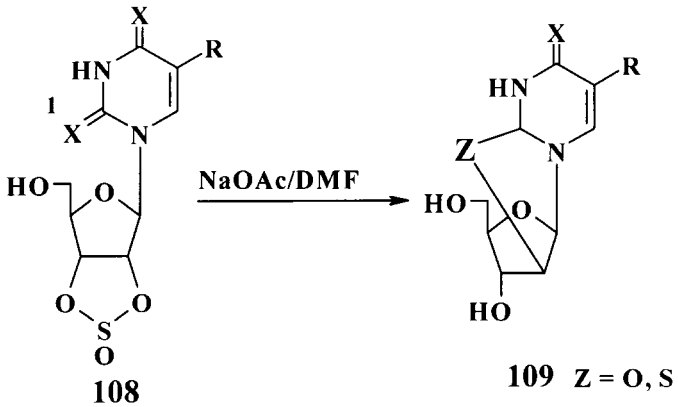
Treatment of 2-thiouridine **27** with triphenylphosphine and the diazoester followed by addition of water afforded the anhydro derivative **106**.[79]



Similar treatment of 2-thiocytidine **23** with chlorophosphoric acid in ethyl acetate afforded the (S)-2-2′-anhydro derivative **107**.[80]



Heating of the pyrimidine derivative **108** with alkali metal salts of weak acid, alkali earth metal salts, ammonium salts in polar organic solvents or tertiary cyclic amines to give the nucleosides **109**.[81,82]

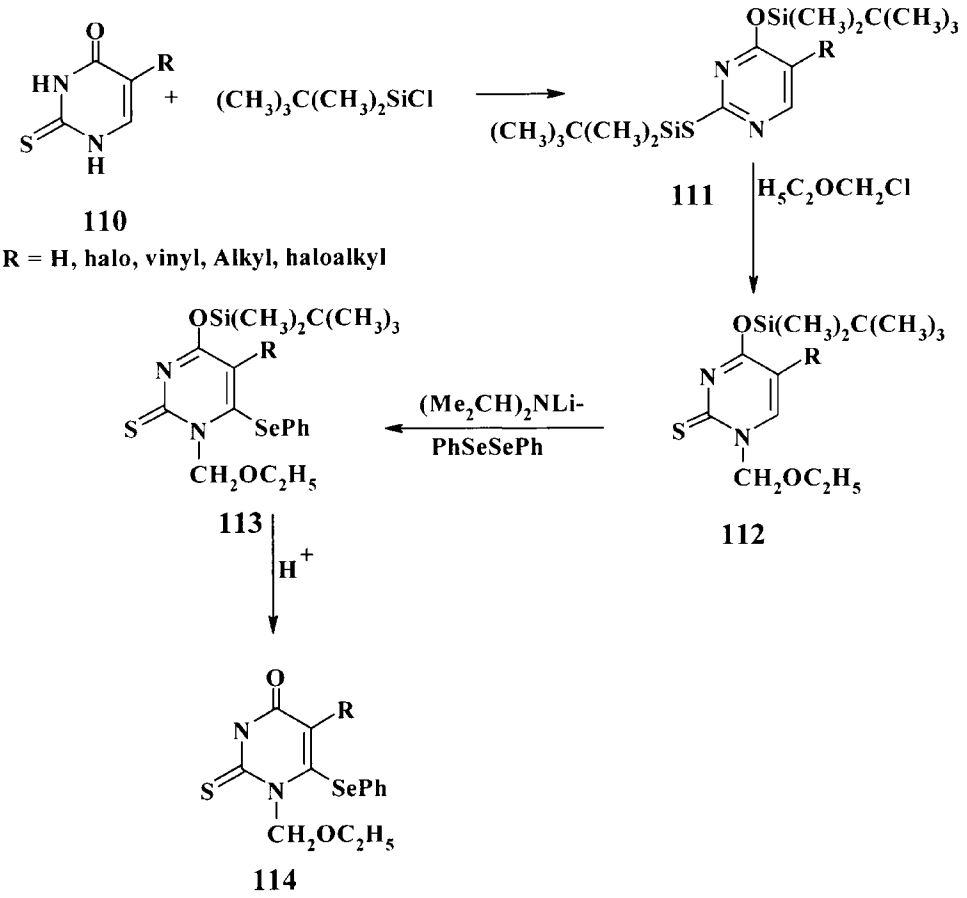


X = O, S, NH, NHR

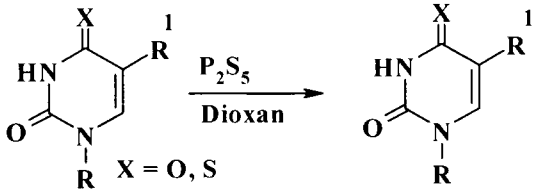
X = O, S

R = H, Halo

Silylation of 2-thiothymine dervatives **110** gave the silylated dervatives **111**, which condensed with ethoxychloromethane to give the derivatives **112**. Upon selenation of the latter with dibutyllithium azide-diphenyldisilane compounds **113** were obtained which were then desilylated to afford the free nucleosides **114**.[83]

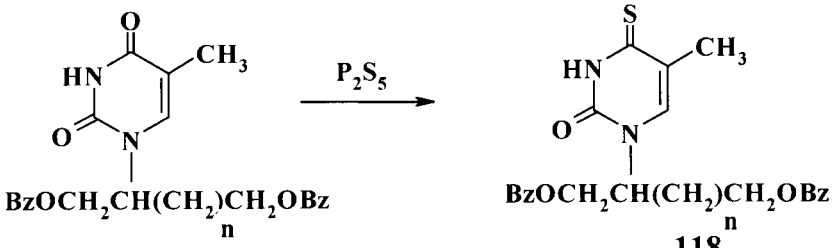


Direct thionation of 5-substituted-4-thiouracil compounds **115** with phosphorous pentaoxide in absolute dioxane[84,85] led to the formation of the 4-thiouracil derivatives **116** with a variety of oxygen containing groups attached to N-1.[86] Thionation of the benzoyl derivatives of 1-(α-ω-dihydroxyalkyl) uracil **117** with P_2S_5 in dioxane gave the benzoylated nucleosides **118**, which were deprotected to give the free diol nucleosides **119**.[86,87]



115 116

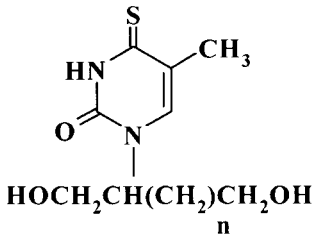
R	R^1
	H
	CH_3
$H_5C_2OOCCHCOOC_2H_5$	F
	Cl
	F



117

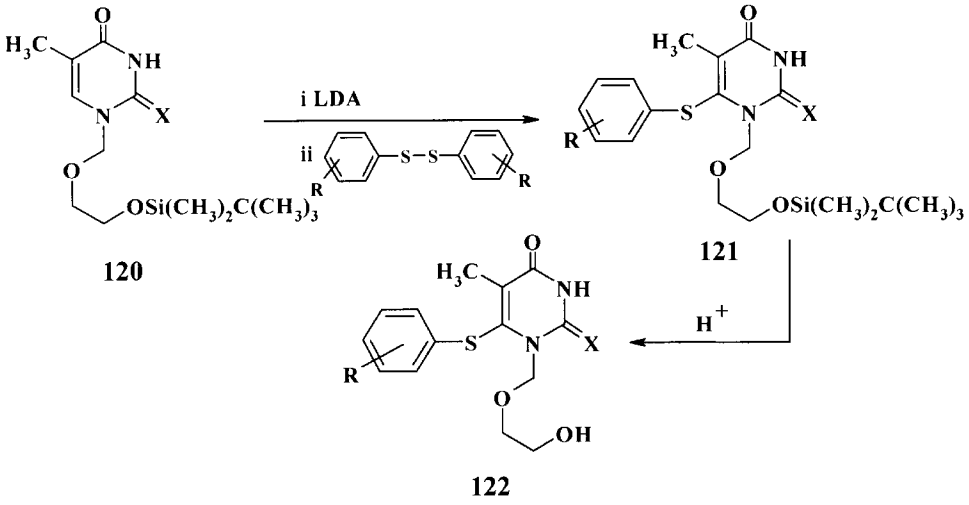
n = 0, 1

118

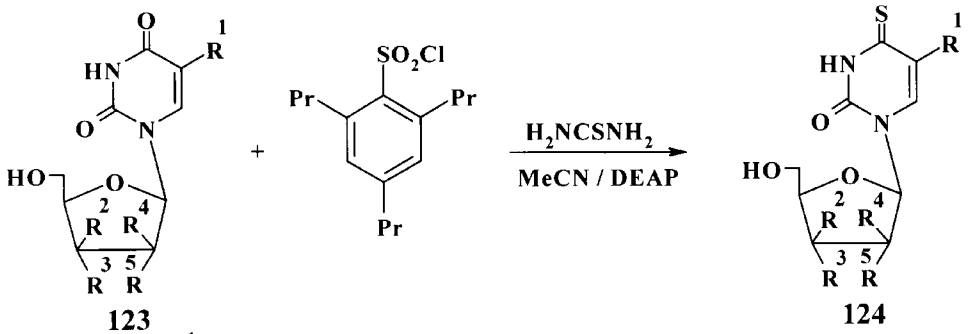


119

Treatment of a tert-butyldimethylsilyl protected 2-thiothymine **120** with lithium diisopropyl amide in THF resulted in the formation of the intermediate lithium compound (lithiation approach originally developed for C-6 modification of uridine) which reacted with a variety of diarylsulphide compounds to form the desired analogues **121**. Deprotection of the latter gave the free nucleosides **122**.[88–92]

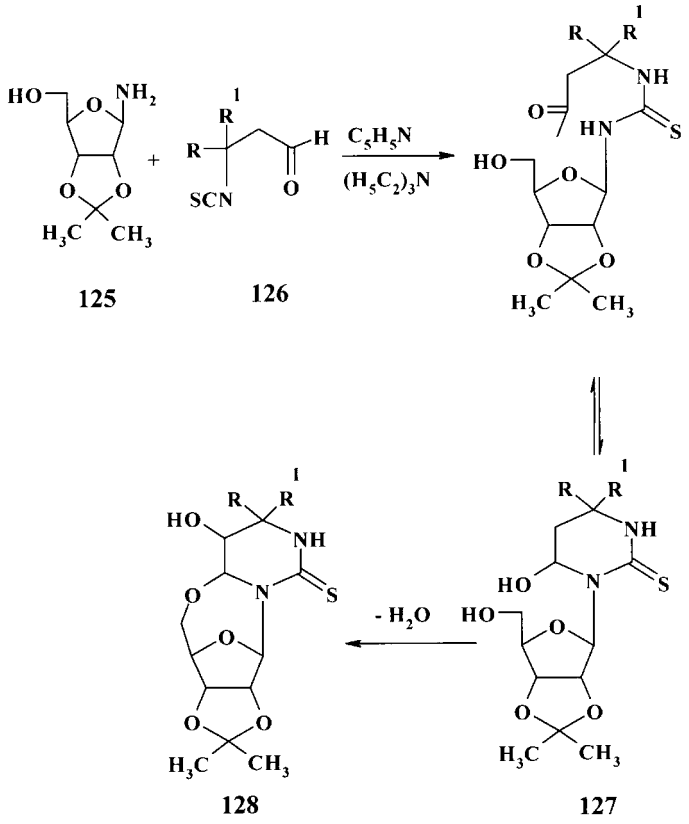


Treatment of different substituted nucleosides **123** with tripropylbenzensulphonylchloride at room temperature followed by reaction with thiourea gave the corresponding thio nucleosides **124**.[93]



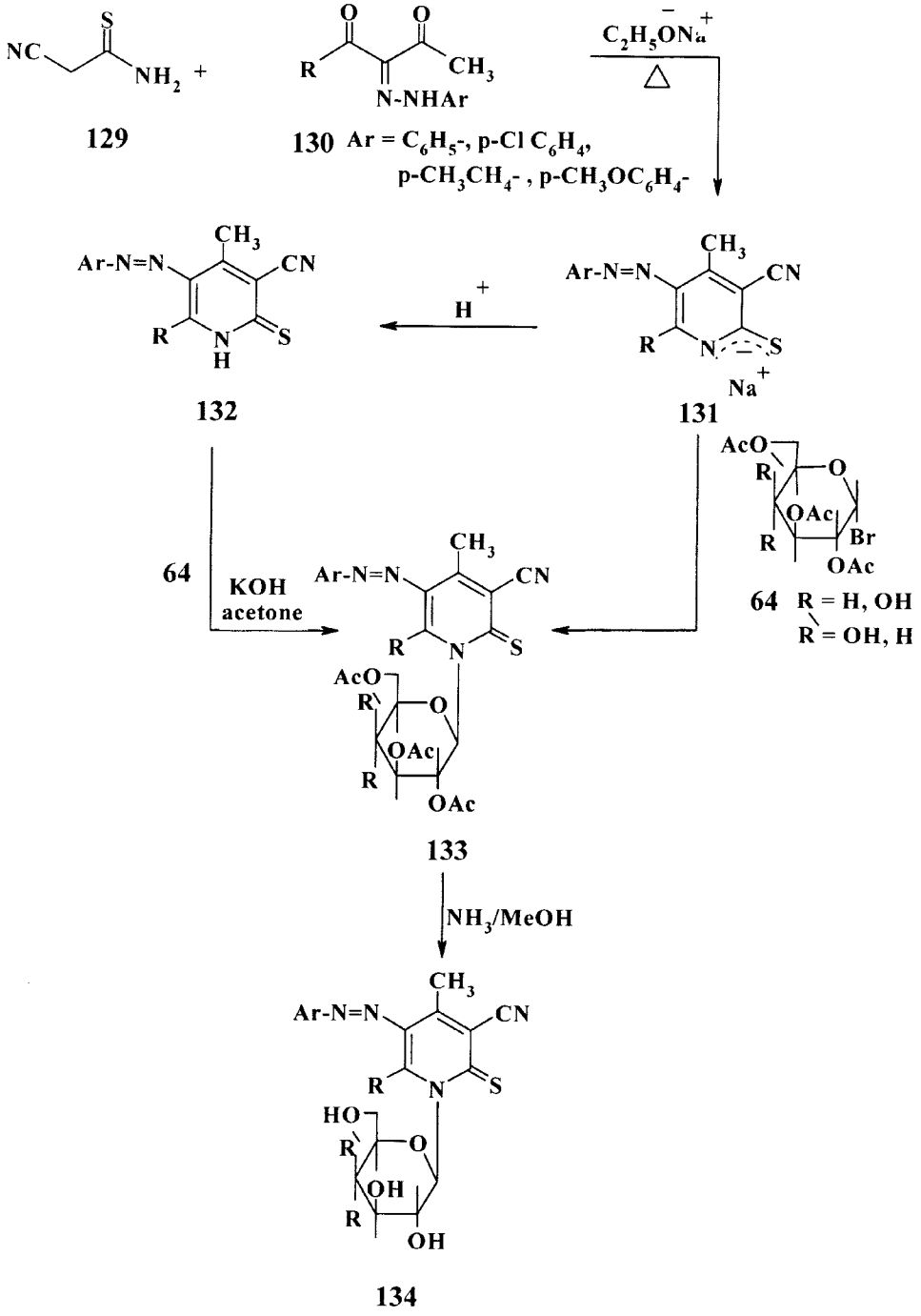
Reacting of the amino sugar **125** with β-isothiocyantocarbonyl compounds **126** in the presence of a base afforded compounds **128** instead of compounds

127 as the result of an intramolecular dehydration.[94–96] Similarly the 4,2′-anhydro derivative was synthesized.[97,98] Furthermore these nucleosides easily reacted with nucleophiles (alcohols, amines) which substituted the hydroxyl group.[99–104]

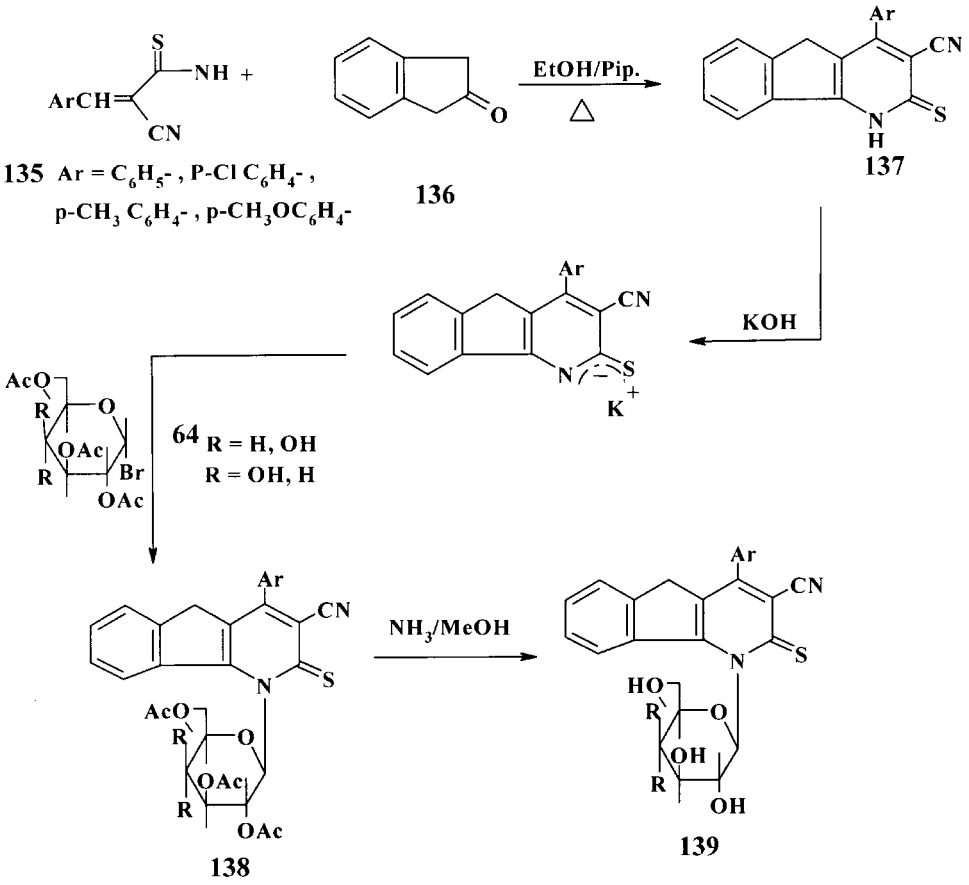


4) Via Deletion of N-3 Nitrogen "Pyridinethione Nucleosides"

The function of various 3-deaza analogues of pyrimidine nucleosides in biological systems has been the subject of considerable comment and speculation.[105] Although a number of N-glycosyl pyridines have been prepared, no pyridinethione nucleosides have been synthesized or biologically evaluated. Recently, Elgemeie and his co-workers reported their one-pot pyridin-2-(1H)thiones synthesis and their corresponding nucleosides.[106–120] Thus, it has been found that the pyridine-2-(1H)-thiones **132** reacted with 2,3,4,6-tetra-O-acetyl-α-D-gluco- and galacto-pyranosyl bromide **64** in an aqueous potassium hydroxide to afford the corresponding glycosides **134**.[121,122]



The following simple and high-yield methodology by Elgemie et al. provided a facile and convenient route for the synthesis of non-classical nucleosides of biological significance, which were not readily accessible.[122]

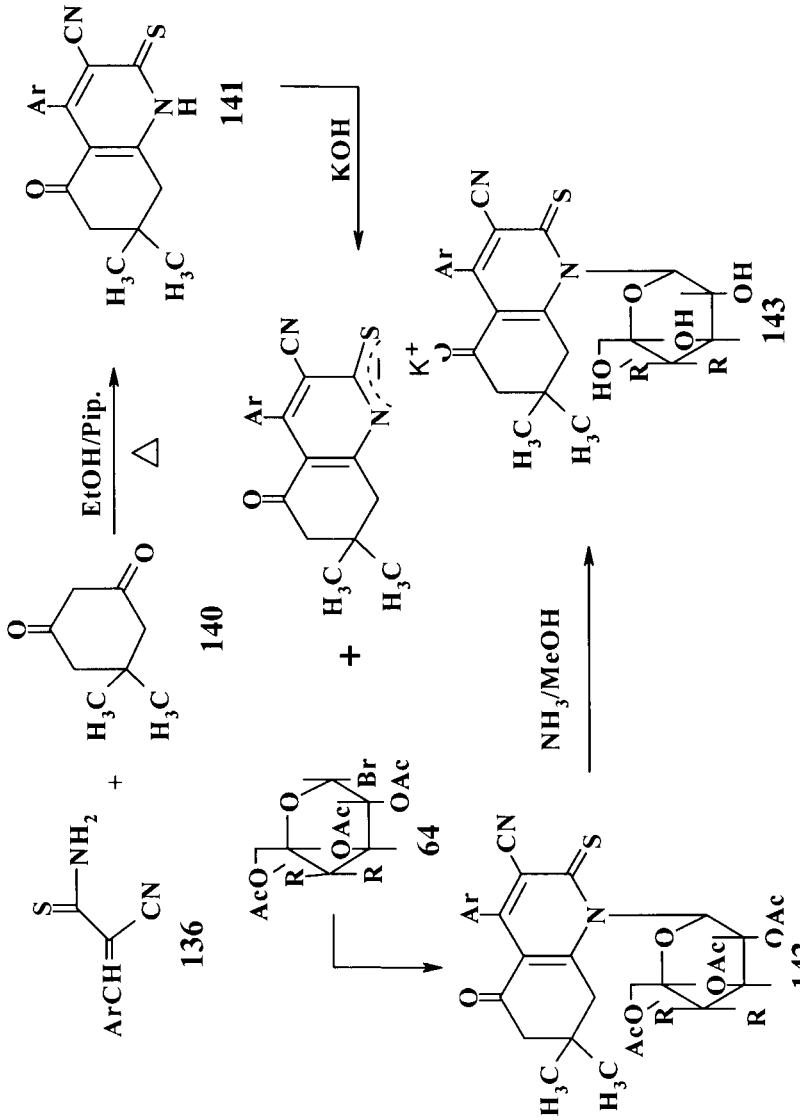


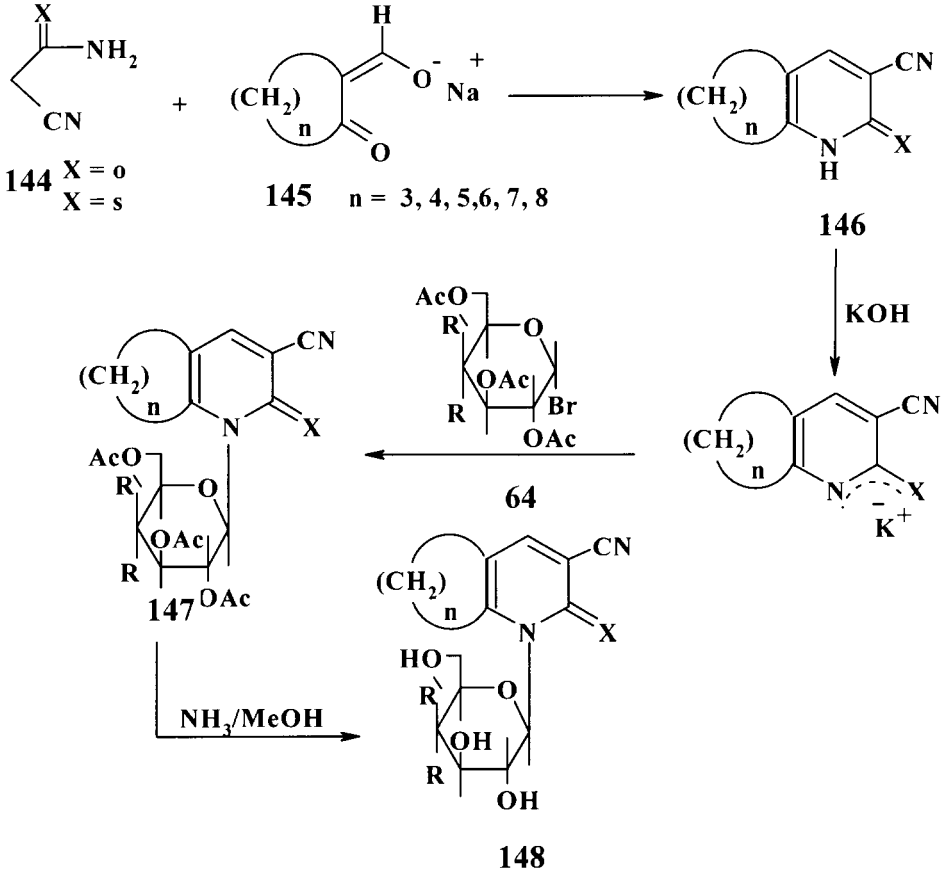
Another example of the metal salt pyridin-2(1H)thione technique by the same authors is the synthesis of the interesting cycloalkane ring fused pyridinthione nucleosides **143** and **148** as illustrated in schemes shown below.[123–127]

II. CHEMICAL REACTIONS

A) Alkylation

Methylation of protected 4-thionucleoside **149** with an excess of diazomethane in methanol (or methyliodide) gave 4-methylthiopyrimidin-2-one **150** and N(3)methyl-4-thiouridine **151**. Compound **150** when heated with NH_3 in a bomb tubes gave the corresponding aminonucleoside **152**. Compound **150** could also be reacted with hydrazine hydrate to form the hydrazino compound **153**, which upon treatment with silver oxide or manganese dioxide in refluxing methanol gave compound **154**.[16,26]



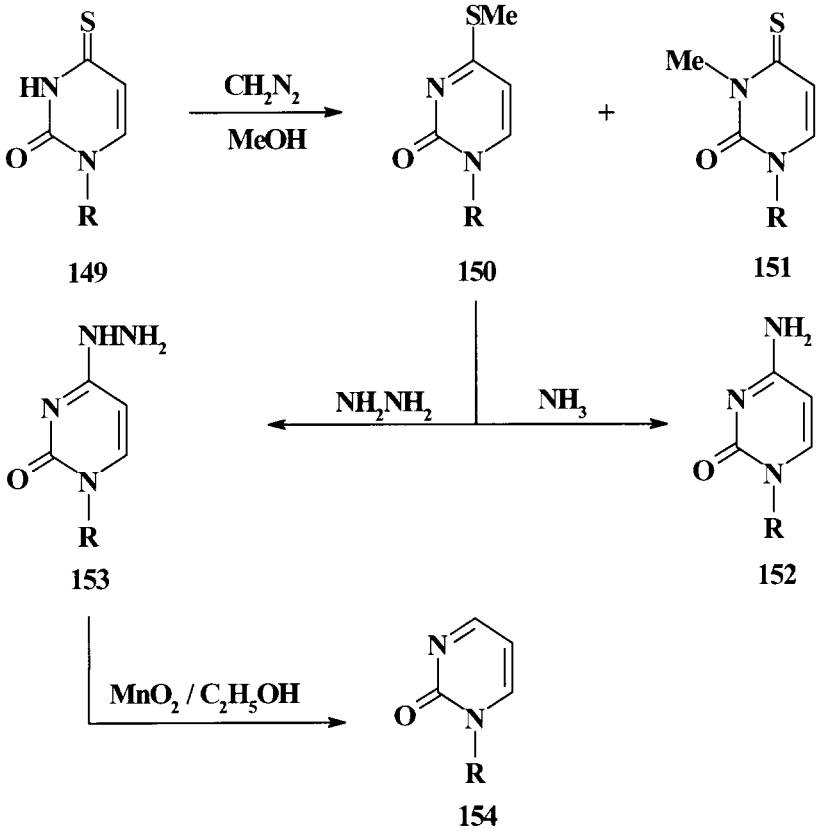


B) Reaction of 4-Thiouridine with Cyanogen Bromide

The reaction of 4-thiouridine **155** with cyanogen bromide in a phosphate buffer at pH = 6.5 gave the disulphide **156**. The 4-thiouridine could be recovered by reaction with mercaptoethanol. The disulfide **156** further reacted to give a mixture of a thiocyanate **157** and 4-thiouridine **155**. The thiocyanate decomposed at pH = 8.5 to give a mixture of uridine **158** and 4-thiouridine **155**. In the presence of an excess BrCN, compound **156** was quantitatively converted into uridine **158** at pH = 8.5.[128]

C) Transformation Reactions

The protected anhydro 2-thiouridine **159** was transformed in methanolic HCl and a ring cleavage at the 3,4 position occurred to give the hydrochloride of thio-oxa-azabicyclononane **160** which structure was verified by reaction with H_2S to give the corresponding thione **161**.[129]



R = 2,3,5-tri-O-benzoyl-*B*-D-ribofuranosyl

R = 2,3,5-tri-O-benzoyl-*B*-D-xylofuranosyl

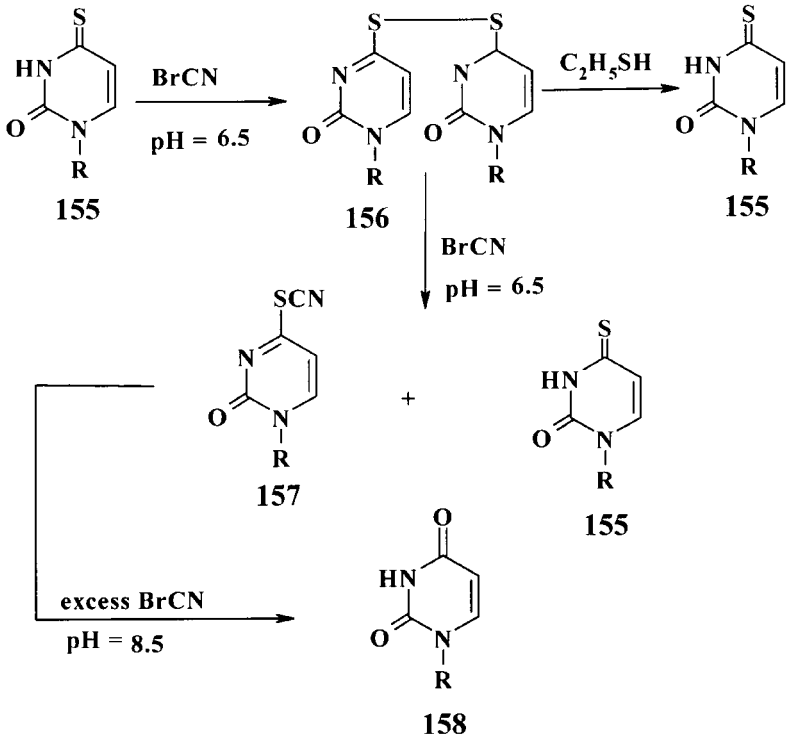
R = 2,3,5-tri-O-benzoyl-*B*-D-arabinofuranosyl

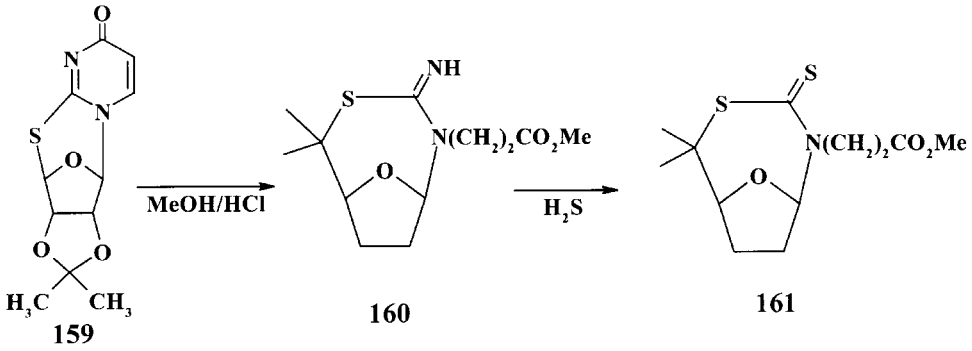
D) Hydroxy Methylation Reaction

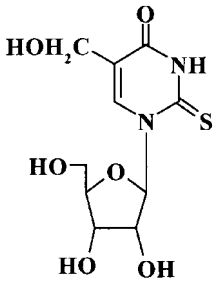
Reaction of 2′,3′-O-etheoxymethylene-2-thiouridine **6** with aqueous formaldehyde in potassium hydroxide gave the corresponding 5-hydroxymethylthiouridine derivative and then acid hydrolysis to afford the free-nucleoside **162**.[130]

E) Reaction with Thionyl Chloride

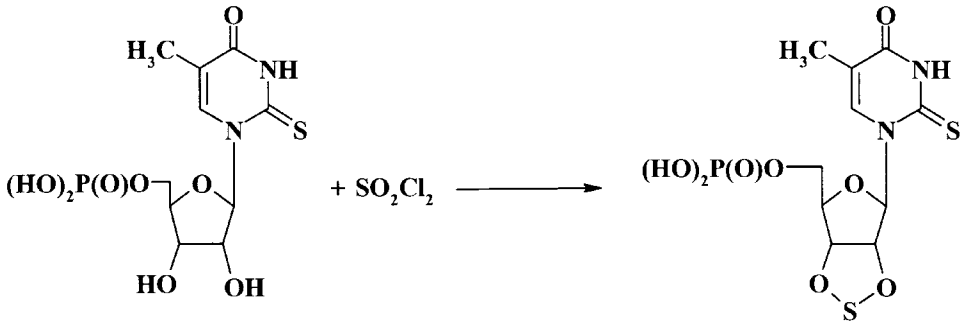
Reaction of pyrimidinthione-5′-phosphate **163** with thionylchloride in a polar organic solvent and a cyclic tertiary amine to give the altered nucleoside **164**.[131]







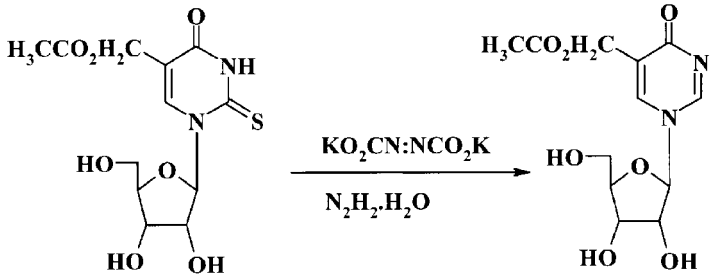
162



163 164

F) Desulfurization Reaction

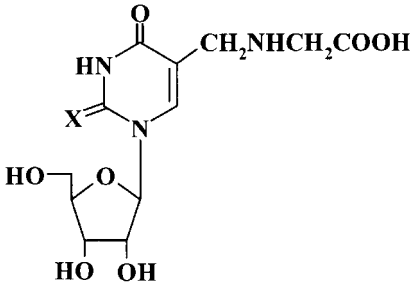
Reaction of 2-thiouridine **165** with KO_2CN: NCO_2K and with hydrazine in H_2O_2 gave compound **166**, suggesting that the reaction involved a diimide. Treatment of the first compound **165** with H_2O_2 gave the same compound **166**.[132]



165 166

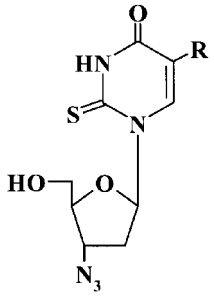
III. BIOLOGICAL ACTIVITIES OF PYRIMIDINETHIONE NUCLEOSIDES

Among the minor components of some t-RNA's have been found nucleotides containing sulfur in a pyrimidine or purine bases, that t-RNA of *Escherichia Coli* has been found to contain 4-thiouridine phosphate among 140 nucleotides present in it.[133–136] The modified bases located in the first position of the anticondon of $t\text{-RNA}^{LYS}$ and $tRNA^{GLY}$ of *B. Subtilis*, were determined as 5-carboxymethylaminouridine **167a**[137] and 5-carboxymethylamino-2-thiouridine **167b**.[138]



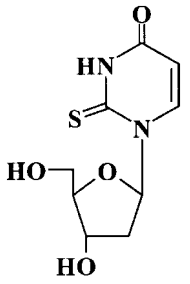
167
a, x = o
b, x = s

Various modified nucleosides when present in the Wobble position of the anticondons of t-RNAs strongly influence the condon anticondon recognition.[139,140]. We conclude that pyrimidinethione nucleosides could interact with DNA synthesis, t-RNA transcriptions and protein synthesis that have antiviral, antibacterial, antitumor and cytotoxic activities.[141–144] 4-thiopyrimidine nucleosides viz, 4-thiouridine, 2-thiouridine, 2-thiocytidine and their derivative have antitumor and antiviral activities.[145–147] In 1991 a group of Japanese workers reported the synthesis of some azidodeoxynucleosides **168** and compound **168b** ($R = CH_3$) showed a virucidal activity against *Rous. Sarcoma* virus.[17] Three years latter Czernecki and and his coworkers recorded the preparation other derivatives, among these compound a ($R = H$) that exhibited an unexpectedly marked anti HIV activity and higher selectivity index.[63,64]



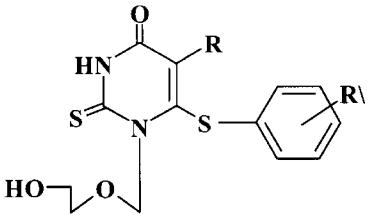
168
a, R = H
b, R = CH_3

2-Thiouracil was found to possess some virucidal and antitumor activities that inhibit the multiplication of infective Turnip yellow and tobacco Mosaic viruses.[148–151] An analogue of thiouracil, 2′-deoxy-2-thiouracil **169** was investigated against melanomas. It proved to have selective inhibition properties.[152]



169

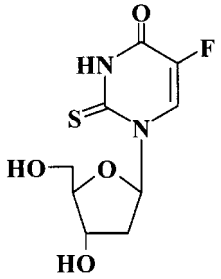
T. Hiromichi et al. registered the synthesis of many acyclic-uridine dervatives **170** and many of them were found to have antiviral activty and an excellent inhibitory effect against HIV-virus.[90–92]



170

R = H, lower alkyl
R\ = H, lower alkyl, X, -CN, -COOH, -NO_2

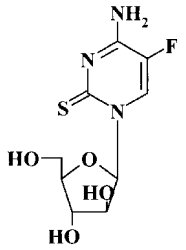
5-Fluoro-2-deoxyuridine-5-monophophate FDUrd **171** was reported to be an antitumor and antifungal chemotherapeutic agent. In 1993 Bertner and co-workers modified this nucleoside by the introduction of a 2-thio group. This compound reaveled to be a good substrate for thymidylate synthase isolated from *Ehrlich carcinoma* and was selective with respect to the tumor cells.[71]



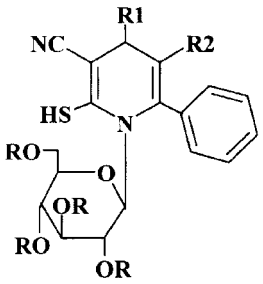
171

Also the 5-chloro derivative of **171** showed a moderate cytotoxic activity in vitro against mouse leukemic cells.[73]

In 1997 M. Saneyoshi and others reported the synthesis of 5-fluoro-2-thiocytosine **46** that inhibited HSV-1 in vitro and which showed low toxicity against the host cells.[49]

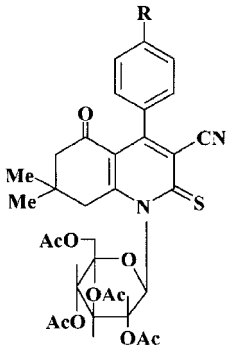


46



172

	R1	R2	R
a,	2-furyl	H	Ac
b,	2-furyl	H	H
c,	phenyl	H	H
d,	phenyl	H	Ac
e,	4-methoxyphenyl	Ac	Ac



173

a, R = Cl
b, R = OCH_3

Beside to their biological activities, nucleosides and nucleotides modified in the base or sugar moiety were convenient probes for the study of various enzymes, proteins and DNA sequences. 4-Thiothymidine was used to investigate the mechanism of DNA photodamage. This corresponds to the second most abundant DNA photolesions produced by the ultraviolet portion of solar spectrum that induce human skin cancer.[153,154] 4-Thiothymidine was also used to obtain structural information within nucleic acid assemblies that were used in labeling models of DNA.[155,156] A number of novel pyridinthiones nucleosides **172** and **173** was recently reported by Elgemeie et al. and were analysed in multidrug resistant human colon carcinoma cells. These compounds were prospectively defined as pgp substrates and antagonists.[157]

REFERENCES

1. Lootiens, F.G.; Mclaughlin, L.W.; Diekmann, S.; Clegg, R.M. Biochemistry. **1991**, *30*, 182.
2. Mazzarelli, J.M.; Rajur, S.B.; Iadarola, S.B.; Mclaughlin, L.W. Biochemistry **1992**, *31*, 5925 and references therein.
3. Rajur, S.B.; Mclaughlin, L.W. Tetrahedron Lett. **1993**, *33*, 6081.
4. McGregor, A.; Rao, M.; Duckworth, G. Nucleic Acids Res. M. A. **1996**, *16*, 3173.
5. Warren, Murray, J.B.; Connolly, B.A. J. Mol. Biol. **1998**, *279*, 89.
6. Saneyoshi, M.; Sawada, F. Chem. Pharm. Bull. (Tokyo) **1969**, *17*, 181.
7. Saneyoshi, M.; Sawada, F. Chem. Pharm. Bull. (Tokyo) **1971**, *19*, 493.
8. Scheit, K.H. Ber. **1968**, *101*, 1141.
9. Shinji, S.F.; Yamasoshoya, K.K. Jpn Kokai Tokyo Koho Jp 0474, 171 (92, 74 171) (CL. C07 D239/56) 09 March 1992. Chem. Abst. **1992**, *117*, 151, 295k.
10. Scheit, K.H. Tetrahedron Lett. **1967**, 113.
11. Kolobushkina, L.I.; Kritsyn, A.M.; Florent'ev, V.L. Khim. Geterotsikl. Soedin **1973**, 996.
12. Tadao, K.; Hisao, N.; Toshio, G. Tetrahedron Lett. **1972**, 1881.
13. Minoru, H.; Takeshi, K.; Nobuo, M. Jpn. Kokai Tokyo koho 78, 108, 982, (Cl. CO7H7/06), 22 Sep. 1978. Chem. Abst. **1975**, *82*, 104,309 g.
14. Brokes, J.; Beranek, J. Collect. Czech. Chem. Commun. **1994**, *39*, 3100; Chem. Abst. **1975**, *82*, 98,319 b.
15. Cech, D.; Holy, A. Collect. Czech. Chem. Commun. **1977**, *42*, 2246; Chem. Abst. **1978**, *88*, 23,297 h.
16. Antonin, H.; Dieter, C. Czech. 185, 447 (Cl. C07D239/36), 15 Sep. 1980. Chem. Abst. **1981**, *95*, 81,429 h.
17. Tokahiro, S.; Eiji, K.; Hisctoshi, Y.; Kunimuta, M. Jpn. Kokai, Tokyo Koho, JP. 02,255,596 [90, 255, 696] (Cl. C07H19/06), 16 Oct. 1990. Chem. Abst. **1991**, *114*, 143,933 q.
18. Ueda, T.; Imawaza, M.; Mirura, K.; Iwanta, T.; Odajima, K. Tetrahedron Lett. **1971**, 2507.

19. Kikugawa, K.; Ichino, M. J. Org. Chem. **1972**, *37*, 284.
20. Toru, U.; Kazunobu, M.; Masatoshi, S. Japan. Kokai, 74 54, 384 (Cl.16E461), 27 May. **1974**, Chem. Abst. **1974**, *81*, 120,951 d.
21. Toru, U.; Kazunobu, M. Japan. Kokai, 74 54, 384 (Cl. 16 E461), 27 May. 1974. Chem. Abst. **1974**, *81*, 120950 d.
22. Nagjvary, J. J. Amer. Chem. Soc. **1969**, *91*, 4509.
23. Kolobushkina, L.I.; Kritsyn, A.M.; Mikhailov, S.N.; Spiridonova, N.I.; Florent'ev, V.L. Khim. Geterotsikl. Soedin **1973**, *8*, 1143; Engl. Trans. Chemistry of Heterocyclic Compound **1972**, 1065.
24. Tsung, Y.S.; William, V.R. U. S. 3, 463, 850 (Cl. 424–180; A 61k, C07d), 26 Aug. 1969. Chem. Abst. **1970**, *72*, 44,075u.
25. Ueda, T.; Ieda, Y.; Ikeda, K.; Mizuno, Y. Chem. and Pharm. Bull. (Japan) **1968**, *16*, 1788.
26. Ruyle, W.V.; Shen, T.Y. J. Med. Chem. **1967**, *10*, 331.
27. Rogers, G.T.; Ulbrict, T.L.V. J. Chem. Soc. (C) **1970**, 1109.
28. Winkley, M.; Robins, R.K. J. Org. Chem. **1968**, *33*, 2822.
29. Vorbrüeggen, H.; Strehlke, P. Chem. Ber. **1973**, *106*, 3039.
30. Sung, W.L. J. Chem. Soc. Chem. Commun. **1981**, 1089.
31. Sung, W.L. Nucleic Acids Res. **1981**, *9*, 6139, throught J. Chem. Soc. Chem. Commun. **1982**, 522.
32. Sung, W.L. J. Chem. Soc., Chem. Commun. **1982**, 522.
33. Vorbrüeggen, H.; Krolikiewicz, K. Angew. Chem. **1975**, *87*, 251.
34. Vorbrüeggen, H.; Krolikiewicz, K. Liebigs Ann. Chem. **1980**, *9*, 1438.
35. Malkiewicz, Sochacka, E. Tetrahedron Lett. **1983**, *24*, 5387.
36. Bretner, M.; Balinska, M.; Krawiec, K.; Kierdaszuk, B.; Shugar, D.; Kulikowski, T. Nucleosids & Nucleotids **1995**, *14*, 657.
37. Malkiewicz, Nawrot, B.; Sochacka, E. Nucleic Acid Sym. Ser. 1987 (18) (Symp. Chem. Nucleic Acid Compon. 17th, 1987), 97; Chem. Abst. **1988**, *108*, 20,500q.
38. Gracz, H.S.; Sochacka, E.; Malkiewicz, A.; Kuo, K.; Charles, W.G.; Paul, F.A. J. Am. Chem. Soc. **1987**, *109*, 7171.
39. Malkiewicz, Nawrot, B. Heteroat. Chem. **1994**, *5*, 375; Chem. Abst. **1995**, *122*, 240,303g.
40. Niedballa, U.; Vorbrüeggen, H. J. Org. Chem. **1974**, *39*, 3654; **1974**, *39*, 3660; **1974**, *39*, 3664; **1974**, *39*, 3668; **1974**, *39*, 3672; **1976**, *41*, 2084.
41. Lichtenthaler, F.W.; Voss, P.; Heerd, A. Tetrahedron Lett. **1974**, 2141.
42. Akhrem, Adarich, E.K.; Kulinlowich, L.N.; Mikhailopulo, I.A.; Posschast;eva, E.B.; Timoshchuk, V.A. Doki. Akad. Nauk. SSSR 219, **1975**, 757; Chem. Abst. **1976**, *85*, 177,846m.
43. Vorbrüeggen, H.; Krolikiewich, K. Angew. Chem. **1975**, *87*, 417; Angew. Chem., Int. Ed. **1975**, *14*, 421.
44. Vorbrüeggen, H.; Bennua, B. Tetrahedron Lett. **1978**, 1339.
45. Kazmina, E.M.; Kenbaev, R.M.; Stepanenko, B.N. Zh. Obshch. Khim. **1978**, *48*, 1892; Chem. Abst. **1978**, *89*, 180,287t.
46. Noel, J.C.; Brian, J.H.; David, H.R.; Peter, W.R.; Gordon, S. J. Chem. Soc. Perkin Trans 1 **1973**, 1720.

47. Susumu, S.; Akira, K.; Hirioshi, Y. Japan Kokai 74 47, 379 (Cl.16 E461), 08 May 1974; Chem. Abst. **1974**, *81*, 120,947h.
48. Malkiewicz, A.J.; Nawrot, B.; Elzbieta, S.Z. Naturforsch B. Chem. Sci. **1987**, *42*, 360.
49. Minero, S.; Toshui, W.; Toshuki, N.; Msao, Y. Jpn. Kokai Tokyo Koho JP 09 31,091[97 31, 091] (Cl. C07 H19/067), 4 Feb 1997. Chem. Abst. **1997**, *126*, 212,374v.
50. Malkiewicz, Sochacka, B.; Ahemed, A.F.S.; Yassin, S. Tetrahedron Lett. **1983**, *24*, 5395.
51. Brown, D.M.; Parihar, D.B.; Todd, A.; Varadarajan, S. J. Chem. Soc. **1958**, 3028.
52. Chambers, R.W.; Kurkov, V. J. Am. Chem. Soc. **1963**, *85*, 2160.
53. Müller, E.; Emden, H.H. Liebigs Ann. Chem. **1962**, *54*, 660.
54. Colin, R.; Sanghvi, S.Y. J. Chem. Soc. Chem. Commun. **1984**, 62.
55. Shutalev, A.D.; Ignatova, L.A.; Unkovsky, B.V. USSR 1392864 (Cl 07 H 19/06), 15 Sept 1987. Chem. Abst., **1987**, *107*, 217,984m.
56. Shutalev, A.D.; Ignatova, L.A.; Unkovsky, B.V.; Sinilova, N.G.; Duplischeva, A.P. Khimikofarmatsevtich. Zhurnal **1985**, 1447, through (related articles/posters: 064 117 062).
57. Shutalev, A.D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1984**, 548.
58. Shutalev, A.D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1982**, 825.
59. Shutalev, A.D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1982**, 269.
60. Elgemeie, G.E.H.; Attia, A.M.; Alkabai, S.S. Nucleosides & Nucleotides **2000**, *19*, 723.
61. Khodier, I.; Ibrahim, E.E.; El Ashry, E.S.H. Nucleosides & Nucleotides **1997**, *16*, 433.
62. Young, J.K.; Hac, Y. Khim, Bull. Korean. Chem. Soc. **1988**, *9*, 295; Chem. Abst. **1989**, *110*, 193,296x.
63. Kwimelias, G.R.; Hope, H.; Nambier, P.K. Nucleosides & Nucleotides **1993**, *12*, 737.
64. Milton, J.; Connlly, A.B.; Nikiforov, T.T.; Cosstick, R. J. Chem. Soc. Chem. Commun. **1993**, 779.
65. Czernecki, S.; Le Diguarher, T.; Valery, J.M. Nucleosides & Nucleotides **1993**, *12*, 369.
66. Czernecki, S.; Valery, J.M.; Le Diguamei, T. Fr. Demande FR 2, 667, 026 (Cl. C07H19/06), 04 Dec 1992. Chem. Abst. **1994**, *120*, 8931.
67. Niu, H. Anal. Biochem. **1984**, *139*, 404.
68. Starrett, E.J.; Trotolani, R.D.; Baker, C.D.; Omar, T.M.; Hebbler, K.A.; Wos, A.J.; Martin, C.J.; Mansuri, M.M. Nucleosides & Nucleotides **1990**, *9*, 885.
69. Shaw, G.; Warrener, R.N. J. Chem. Soc. **1958**, 153.
70. Lucjan, J.J.H.; Walter, A.S. Can. J. Chem. **1986**, *64*, 1620.
71. Lucjan, J.J.H.; Walter, A.S. Can. J. Chem. **1988**, *66*, 61.

72. Bretner, M.; Kulilowski, T.; Dzik, J.M.; Balinska, M.; Rode, W.; Shugar, D. J. Med. Chem. **1993**, *36*, 3611.
73. Bretner, M.; Balinska, M.; Krawiec, K.; Kiebaszuk, B.; Shugar, D.; Kulikowski, T. Nucleosides & Nucleotides **1995**, *14*, 657.
74. Felczak, K.; Bretner, M.; Balinska, M.; Golos, B. Dzik, J.M.; Rode, W.; Kulikowski, T. Nucleosides & Nucleotides **1995**, *14*, 653.
75. Magdy, Z.; Abdel-Megied, A.E.-S.; Abed-Rahman, A.A.-H.; Ali EL-Emam, Pedersen, B.E.; Pielsen, C. Heterocycles **1995**, 41, 2507.
76. Solan, K. Jpn. Kokai Tokyo Koho 80 49, 395 (Cl. C07H19/06), 09 Apr 1980. Chem. Abst. **1980**, *93*, 95,597g.
77. Sharic, V.; Lacan, G.; Skaric, D. Croat. Chem. Acta **1976**, *48*, 351; Chem. Abst. **1977**, *86*, 121,664d.
78. Gebhard, K. Ger. Offen. 2, 658, 672 (Cl. C07 H19/06), 29 Jun 1978. Chem. Abst. **1978**, *89*, 163,903y.
79. Susumu, S.; Akira, K.; Hiroschi,Y. Chem. Pharm. Bull. (Japan) **1974**, *22*, 719; Chem. Abst. **1974**, *81*, 4180d.
80. Tadashi, K.; Takashi, K.; Motonobu, I.; Tokuro, N. Jpn. Kokai 74, 117, 497 (Cl. 16E621), 09 Nov 1974. Chem. Abst. **1975**, *82*, 140,454u.
81. Kozo, T.; Tsuneo, S.; Kiyohide, S.; Nobuyuki, S. Japan. Kokai 76, 108, 099 (Cl. C07H19/06), 25 Sep 1976. Chem. Abst. **1977**, *86*, 73,082p.
82. Kozo, T.; Tsuneo, S.; Kiyohide, S.; Nobuyuki, S. Japan. Kokai 76, 108, 098 (Cl. C07H19/06), 25 Sep 1976. Chem. Abst. **1977**, *86*, 73081n.
83. Raymond, F.S. PCT Int. Appl. Wo 93 02, 044 (Cl. C07C239/06), 04 Feb 1993, US, Chem. Abst. **1993**, *119*, 117, 755s.
84. Hamamura, E.H.; Sato, K.; Moffatt, J.G. J. Med. Chem. **1972**, *15*, 1061.
85. Wepen, I.; Duschinsky, R.; Kaplan, L.; Fox, J.J. J. Am. Chem. Soc. **1961**, *83*, 47,755.
86. Kaulinya, L.T.; Lidak, M.Yu.; Zhuk, R.A. Khim. Geterotsikl. Seodin. **1980**, 1109.
87. Holly, Collect. Czech. Chem. Commun. **1975**, *40*, 187.
88. Tanaka, H.; Hayakawa, H.; Miyasaka, T. Tetrahedron Lett. **1982**, *38*, 2635.
89. Hiromichi, T.; Matsuda, A.; Iijima, S.; Hayakawa, H.; Miyasaka, T. Chem. Pharm. Bull. **1983**, *31*, 2164.
90. Todashi, M.; Hiromichi, T.; Erik, D.C.; Alice, D.; Mansori, B.; Richared, T.W.; Masouri, U. Eur. Patt. Appl. Ep 449,726 (Cl. C07 D239/06), 02 Oct 1991. J. p. Chem. Abst. **1992**, *116*, 41,986h.
91. Hiromichi, T.; Hideaki, T.; Masouri, U.; Kouichi, S.; Issei, N.; Mansori, B.; Shiro, S.; Richared, T.W.; Erik, D.C.; Todashi, M. J. Med. Chem. **1992**, *35*, 337.
92. Hiromichi, T.; Mansori, B.; Masouri, U.; Hideaki, T.; Kouichi, S.; Issei, N.; Shiro, S.; Richared, T.W.; Erik, D.C.; Todashi, M. J. Med. Chem. **1991**, *34*, 1394.
93. Takeya, S. Jpn. Kokai Tokyo Koho Jp 09 77, 788 [97, 77, 788] (Cl. C07H19/067), 25 Mar 1997. Chem. Abst. **1997**, *127*, 17,918u.
94. Unkovsky, V.; Ignatova, L.A.; Zaitseva, M.G. Khim. Geterotsikl. Seodin. **1969**, 889.

95. Unkovsky, V.; Ignatova, L.A.; Donskaya, M.M.; Zaitseva, M.G. in problems of Organic Synthesis, Nauka, Moscow-Leningrad, **1965**, 202.
96. Shutalev, D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1986**, 1652.
97. Shutalev, D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1985**, 852.
98. Shutalev, D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1984**, 244.
99. Shutalev, D.; Ignatova, L.A.; Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1990**, 279; Chem. Abst. **1990**, *113*, 17,261d.
100. Shutalev, D.; Alekseeva, S.G. Khim. Geterotsikl. Seodin. **1995**, 377.
101. Shutalev, D.; Komarova, E.N.; Ignatova, L.A. Chemistry of Heterocyclic Compounds **1993**, 1182; Engl. Transl. from Khim. Geterotsikl. Seodin **1993**, 1378.
102. Shutalev, D.; Komarova, E.N.; Pagaev, T.; Ignatova, L.A. Chemistry of Heterocyclic Compounds **1993**, 1077; Engl. Transl. from Khim. Geterotsikl. Seodin. **1993**, 1259.
103. Shutalev, D.; Ignatova, L.A. Khim. Geterotsikl. Seodin. **1991**, 228.
104. Ignatova, L.A.; Shutalev, A.D.; Shingareeva, A.G.; Dymova, S.F. Unkovsky, B.V. Khim. Geterotsikl. Seodin. **1985**, 260.
105. Copp, R.R.; Marques, V.E. J. Med. Chem. **1991**, *34*, 208.
106. Elgemeie, G.E.H.; Regaila, H.A.; Shehata, N. Sulfur Letters **1989**, *9*, 253.
107. Elgemeie, G.E.H.; Ramiz, M.M. Phosphorus, Sulfur, Silicon **1989**, *46*, 95.
108. Elgemeie, G.E.H.; Elfahham, H.A.; Nabey, H.A. Sulfur Letters **1989**, *9*, 47.
109. Elgemeie, G.E.H.; Zohdi, H.F.; Sherif, S.M. Phosphorus, Sulfur, Silicon **1990**, *54*, 215.
110. Elgemeie, G.E.H. Heterocycles **1990**, *31*, 123.
111. Elgemeie, G.E.H.; El-Ezbawy, S.R.; Ramiz, M.M.; Mansour, O.A. Org. Prep. Proced. International **1991**, *23*, 645.
112. Elgemeie, G.E.H.; Alnaimi, I.S.; Alarab, H.F. Heterocycles **1992**, *34*, 1721.
113. Elgemeie, G.E.H.; Ali, H.A.; Eid, M.M. J. Chem. Research (S), **1993**, 256.
114. Elgemeie, G.E.H.; El-Zanate, A.M.; Mansour, A.K. Bull. Chem. Soc. Japan **1993**, *66*, 555.
115. Elgemeie, G.E.H.; Hussain, B.A. Tetrahedron **1994**, *50*, 199.
116. Elgemeie, G.E.H.; Attia, A.M. Phosphorus, Sulfur, Silicon **1994**, *92*, 95.
117. Elgemeie, G.E.H.; Attia, A.M.; Ali, H.A.; Mansour, A.K. J. Chem. Research (S) **1994**, 78.
118. Elgemeie, G.E.H.; Attia, A.M.; Fathy, N.M. Liebigs Ann. Chem. **1994**, 955.
119. Elgemeie, G.E.H.; Attia, A.M. Carbohydrate Research **1995**, *268*, 295.
120. Elgemeie, G.E.H.; Elghandour, A.H.; Ali, H.A.; Hussain, A.A. J. Chem. Research (S) **1997**, 260.
121. Elgemeie, G.E.H.; Attia, A.M.; Elzanate, A.M.; Mansour, A.K. Bull. Chem. Soc. Japan **1995**, *67*, 1627.
122. Attia, M.; Elgemeie, G.E.H. Nucleosides & Nucleotides **1995**, *14*, 1211.
123. Elgemeie, G.E.H.; Mansour, O.A.; Metwally, N.H. Nucleosides & Nucleotides **1999**, *18*, 113.

124. Elgemeie, G.E.H.; Attia, A.M.; Farag, D.S.; Sherif, S.M. J. Chem. Soc. Perkin Trans. I **1994**, 1285.
125. Elgemeie, G.E.H.; Attia, A.M.; Hussain, B.A. Nucleosides & Nucleotides **1998**, *17*, 855.
126. Elgemeie, G.E.H.; Attia, A.M.; Shehada, L. Tetrahedron **1998**, *53*, 17,441.
127. Elgemeie, G.E.H.; Attia, A.M.; Hussain, B.A. Nucleosides & Nucleotides **1999**, *18*, 2335.
128. Walkar, R.T. Tetrahedron Lett. **1971**, 2145.
129. Vinko, S.; Marijan J. Chem. Soc. Chem. Commun. **1973**, 495.
130. Hans, R.R.; Scheit, K.H.; Carb. J. Nucleosides & Nucleotides **1972**, *2*, 407.
131. Kozo, T.; Tsuneo, S.; Nobbuki, S.; Kiyohide, S. Jpn. Koki 76, 108, 076 (Cl. C07H19/10), 25 Sep 1976, Chem. Abst. **1977**, *86*, 73076q.
132. Takuo, O.; Oyo, M. Chem. Lett. **1982**, 1621.
133. Lipsett, M.N. J. Biol. Chem. **1965**, *240*, 3975.
134. Lipsett, M.N.; Doctor, B.P. J. Biol. Chem. **1967**, *242*, 4072.
135. Lipsett, M.N. J. Biol. Chem. **1967**, *242*, 4067.
136. Carbon, J.; David, H.; Studier, M.H. Science **1968**, *161*, 1146.
137. Nihimura, S. Minor Component in t-RNA: their Characterization, Locations and Functions, Prog. in Nucleic Acid Research and Molecular Biology **1972**, *12*, 49.
138. Murao, K.; Ishikura,H. Nucleic Acid Res. **1978**, (5), 1333.
139. Yamada, Y.; Murao, K.; Ishikura, H. Nucleic Acid Res. **1981**, *9*, 1933.
140. Mccloskey, J.A.; Nihimura, S. Acc. Chem. Res. **1977**, 10,403; Singha, R.; Fallis, P.A.M. Prog. Nucleic Acids Res. Mol. Biol. **1979**, *23*, 225.
141. Kawaguchi, T.; Kusumi, M.; Hasegawa, T.; Nagata, T.; Saneyoshi, M.; Nakano, M.; Hanada, A. Biol. Pharm. Bull. **2000**, *23*, 979.
142. Kawaguchi, T.; Ichikawa, T.; Hesegawa, T.; Saneyoshi, M.; Wakayana, T.; Kato, H.; Yukita, A.; Nagata, T. Chem. Pharm. Bull. **2000**, *48*, 454.
143. Coates, W.J.; Hunter, D.J.; Maclachlan, W.S. Drug Discovary Today **2000**, *5*, 521.
144. Sochacka, E. Nucleosides & Nucleotides **2001**, *20*, 1871.
145. Adamiak, R.; Gornicki, P. Prog. Nucleic Ac. Res. Mol. Biol. **1984**, 3227.
146. Bolch, A.; Robins, R.K.; Winkley, M.W.; Witkowski, J.T. Proc. Am. Assoc. Cancer Research Abstracts **1969**, *10*, 8.
147. Lozzio, Wigler, P.W. J. Cell physiol. **1971**, *78*, 25.
148. Hamamura, H.; Sato, K.; Moffatt, J.G. J. Med. Chem. **1972**, *15*, 1061.
149. Commoner, B.; Mercer, F.L. Nature **1951**, *168*, 113.
150. Commoner, B.; Mercer, F.L. Biochem. Biophys. **1952**, *35*, 278, through chem. Abstract **1952**, *46*, 6205e.
151. Badwen, C.; Kassanis, B. J. Gen. Microbiol **1954**, *10*, 160, through Chem. Abst. **1954**, *48*, 7715c.
152. Amos, H.; Volymayer, E. Virology **1955**, *6*, 337.
153. Watjen, Buchardt, O.; Langvad. J. Med. Chem. **1982**, *25*, 956.
154. Mitchell, L.; Nairn, R.S. Photochem. Photobiol. **1989**, *49*, 805.

155. Clivio, P.; Fourrey, J.L.; Gasche, J. Tetrahedron Lett. **1992**, *33*, 1615.
156. Saintome, Clivio, P.; Fourrey, J.L.; Woisard, A.; Favre, A. Tetrahedron Lett. **1994**, *35*, 873 .
157. Elgemeie, G.E.H.; Stein, W.D.; Bates, S.E. Molecular Pharmacology **1997**, *51*, 1024.

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