



A REVIEW ON THE UTILITY OF CYANO KETENE S,S AND N,S ACETALS IN HETEROCYCLIC SYNTHESIS

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Abstract

This review article describes synthesis and cyclization reactions of cyano ketene *N*, *S* and *S*, *S*-acetals as a building unit for the synthesis of a wide variety of fused and five- to seven-membered heterocycles such as: pyrazoles, thiazole, thiadiazoles, thiophene, triazole, pyridines, pyrimidines, azepines and quinazoline.

Keywords: ketene *N*, *S*, ketene *S*, *S*-acetals, thiadiazoles, thiophene, triazole, pyridines,

Table of Contents

- I. Introduction
- II. Synthesis of cyano ketene *S*, *S* acetals derivatives
- III. Synthesis of cyano ketene *N*, *S* acetals derivatives
- IV. Cyclization reactions of cyano ketene *S*, *S* acetals derivatives
- V. Cyclization reactions of cyano ketene *N*, *S* acetals derivatives
- VI. References

I. Introduction

In recent years, along with increasing reports on the chemistry of ketene *S*, *S* and *N*, *S*-acetals as an active area in push-pull alkenes, which bear electron-donating as mercapto SH, alkylthio (S-Me), or arylamino groups (NH-Ar) and cyano (CN) as accepting group at both termini of a C=C double bond, respectivelyⁱ⁻ⁱⁱⁱ. There has been an increasing wealth of information about the synthesis and applications of ketene *N*, *S*-acetals as the second generation of versatile intermediates derived from ketene *S*, *S*-acetals via replacement of an alkylthio group by aromatic amines^{iv-vii}. The characteristics of ketene *S*, *S* and *N*, *S*-acetals make them versatile and easy to use, especially in cyclization and multicomponent reactions for the synthesis of various heterocyclic systems and related natural products^{viii, ix}. In the present review, we give an overview on the chemistry of ketene *S*, *S* and *N*, *S*-acetals.

II. Synthesis of cyano ketene S, S acetals

The reaction of cyano active methylene compounds **1** with carbon disulfide in the presence of basic medium (Scheme 1 and Table 1) e.g: KOH, NaH and MeONa, alcohol e.g: MeOH, EtOH and methylating agent e.g: MeI and (CH₃)₂SO₄ afforded acyclic cyano ketene S, S acetals derivatives **2(a-n)**^{x-xxii}.

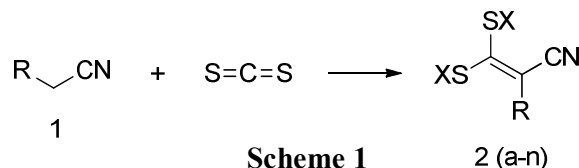
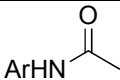
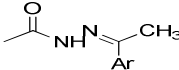
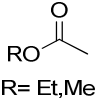
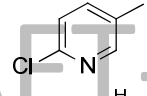
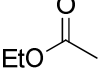
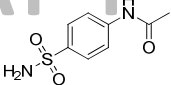
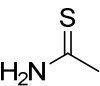
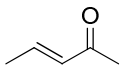
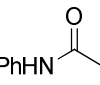
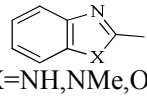
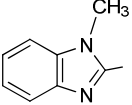
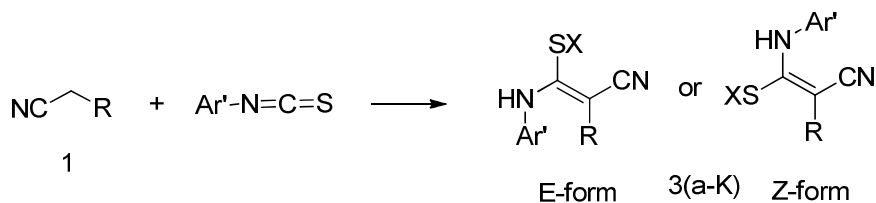


Table 1: Synthesis of cyano ketene S, S acetals derivatives **2(a-n)**.

2	R	X	2	R	Ar	X
a	CN	Me	h		2-MeOC ₆ H ₄	Me
b	CN	K ⁺	i		HOOC-C ₆ H ₄	Me
c		Me	j		<i>p</i> -CH ₃ OPh	Me
d		K ⁺	k		–	Na ⁺
e		Me	l		–	K ⁺
f		Me	m		–	K ⁺
g		Me	n	–	–	Na ⁺

III. Synthesis of Ketene N, S acetal derivatives:

Cyano ketene N,S acetals derivatives **3(a-K)** in (*Z*- form) or (*E*- form) were obtained by the reaction of active methylene compounds **1** with isothiocyanates in the presence of basic medium e.g: KOH (Scheme 2 and Table 2) and solvent e.g: dioxane, DMF and methylating agent e.g: MeI and (CH₃)₂SO₄^{x,xiv,xxiii-xxvii}.

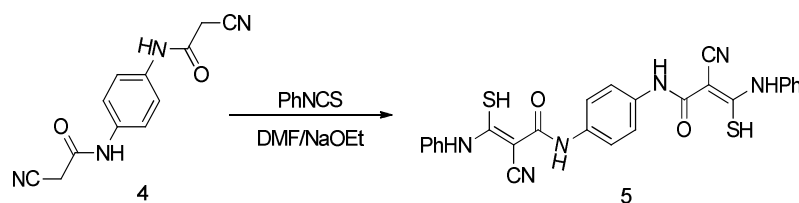


Scheme 2

Table 2: Synthesis of cyano ketene N,S acetals derivatives **3(a-K)**

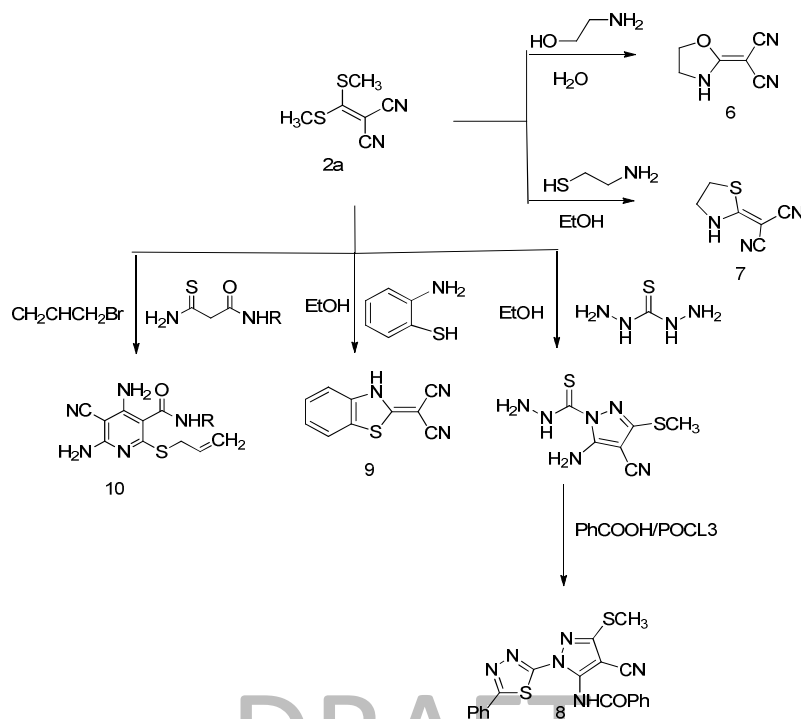
3	R	Ar'	X	3	R	Ar	Ar'	X
a	CN	Ph	Me	g		—	Ph	K ⁺
b		Ph-CO	H	h			Ph	K ⁺
c		Ph	Me	i		<i>p</i> -CH ₃ OPh	Ph	K ⁺
d		Ph	Me or Et	j		—	—	K ⁺
e		Ph	H	k		—	Ph	H
f		Ph	K ⁺	—	—	—	—	—

Hantzsch and Webersynthesized N, N'-(1,4-phenylene) bis(2-cyanoacetamide)**4**^{xxviii} then reacted with phenyl isothiocyanate in dry DMF at room temperature in basic medium to give cyano ketene N,S acetal derivatives**5**^{xxix} as shown in (Scheme3).

**Scheme 3**

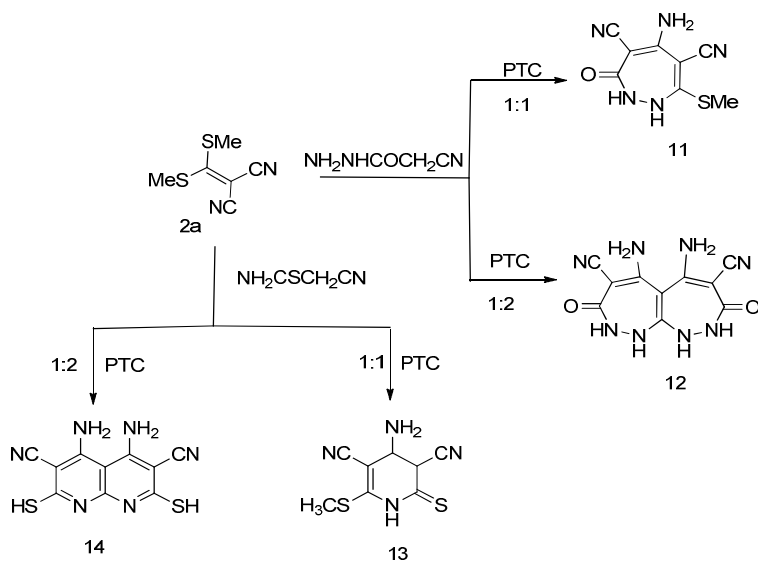
IV. Cyclization of cyano Ketene S,S acetals:

Reaction of ketene S,S acetal **2a** with 2-aminoethanol, 2-aminoethanethiol, thiocarbohydrazide then treated with PhCO₂H/POCl₃, thioxopropanamides derivative then the addition of allyl bromide and 2-aminobenzenethiol afforded 2-(oxazolidin-2-ylidene)malononitrile**6**^{xxx}, 2-(thiazolidin-2-ylidene)malononitrile**7**^{viii}, 5-benzoylamino-3-methylthio-1-(5-phenyl-1,3,4-thiadiazol-2-yl)pyrazole-4-carbonitrile**8**^{xxxi}, 2-(benzo[d]thiazol-2(3H)-ylidene)malononitrile**9**^{ix} and 2-allylsulfanyl-substituted pyridine-3-carboxamides**10**^{xxii} (Scheme 4).



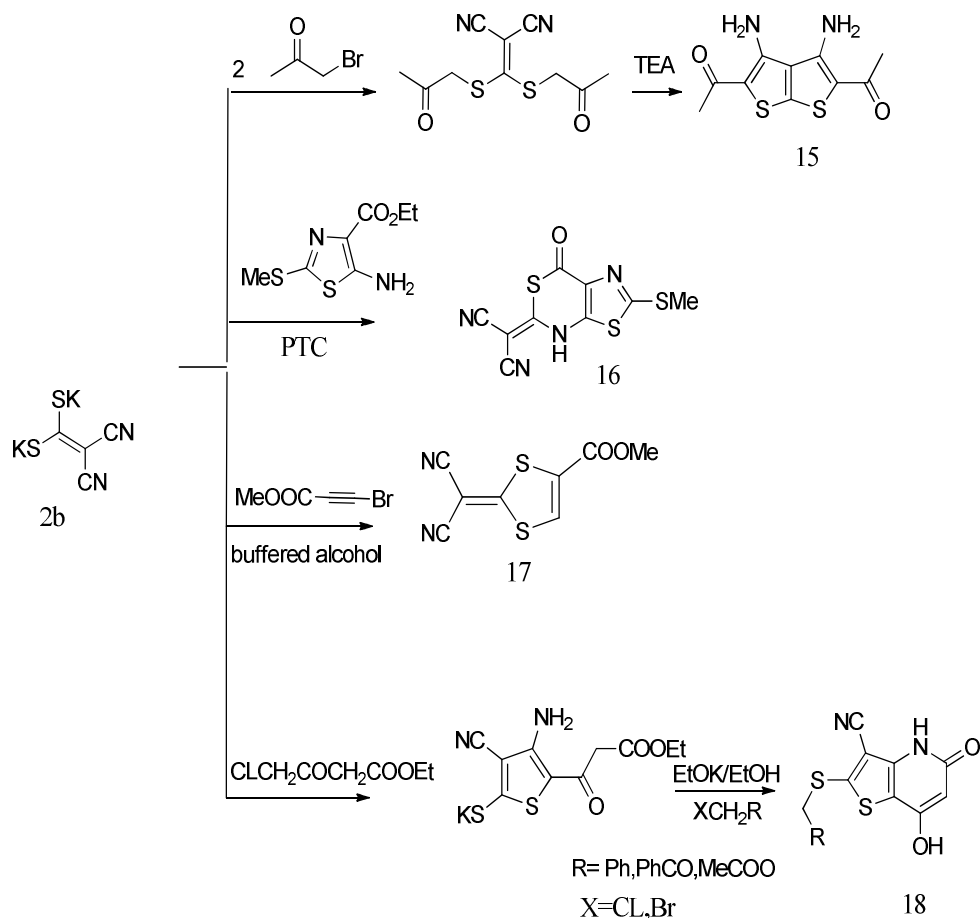
Scheme 4

Compound 2-(bis(methylthio)methylene) malononitrile **2a** was allowed to react with cyanoacetohydrazide in 1:1 or 1:2 molar ratio under phase transfer catalysis (PTC) conditions to get the corresponding azepine **11** or bis 1,2-diazepine derivatives **12**^{xiii} and also, **2a** with cyanothioacetamide in equimolar ratio 1:1 or in 1:2 molar under PTC conditions to give the corresponding pyridines **13** and 1,8-naphthyridines **14**^{xiii} (Scheme 5).



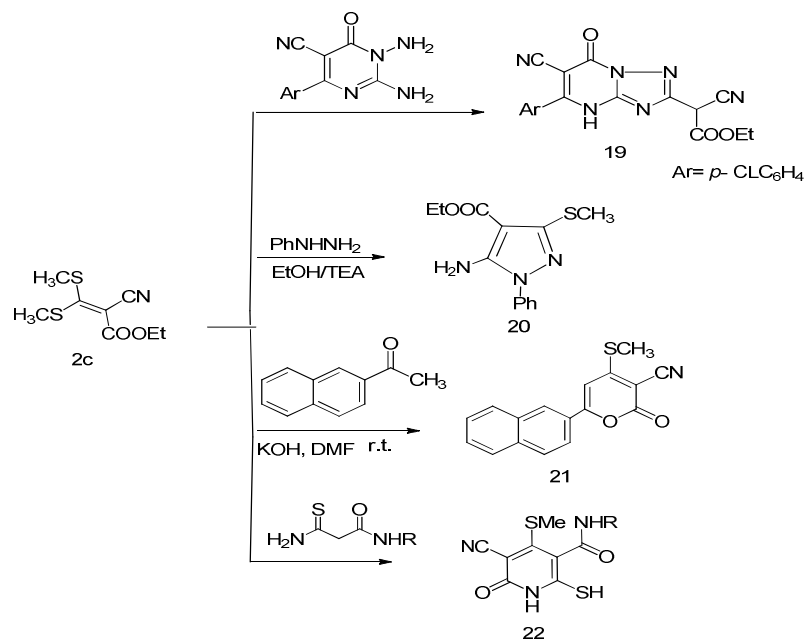
Scheme 5

Reaction of Dithiolate **2b** with 2 equivalent of 1-bromopropan-2-one, ethyl 5-amino-2-(methylthio)thiazole-4-carboxylate, activated haloacetylenes and 4-chloroacetoacetic ester then treated with alkyl halides afforded 3,4-diamino-2,5-S-diacyl thieno[2,3-b]thiophene derivatives **15**^{xxxiii}, 2-(2-methyl sulfanyl-7-oxo-4,7-dihydro thiazolo [5,4-d][1,3] thiazin-5-ylidene)-malononitrile **16**^{xxxiii}, methyl 2-(dicyano methylene) -1,3-dithiole-4-carboxylate **17**^{xxxiv} and 2-(alkylthio)-7-hydroxy-5-oxo-4,5-dihydrothieno[3,2-b]pyridine-3-carbonitrile **18**^{xvii} (Scheme 6).



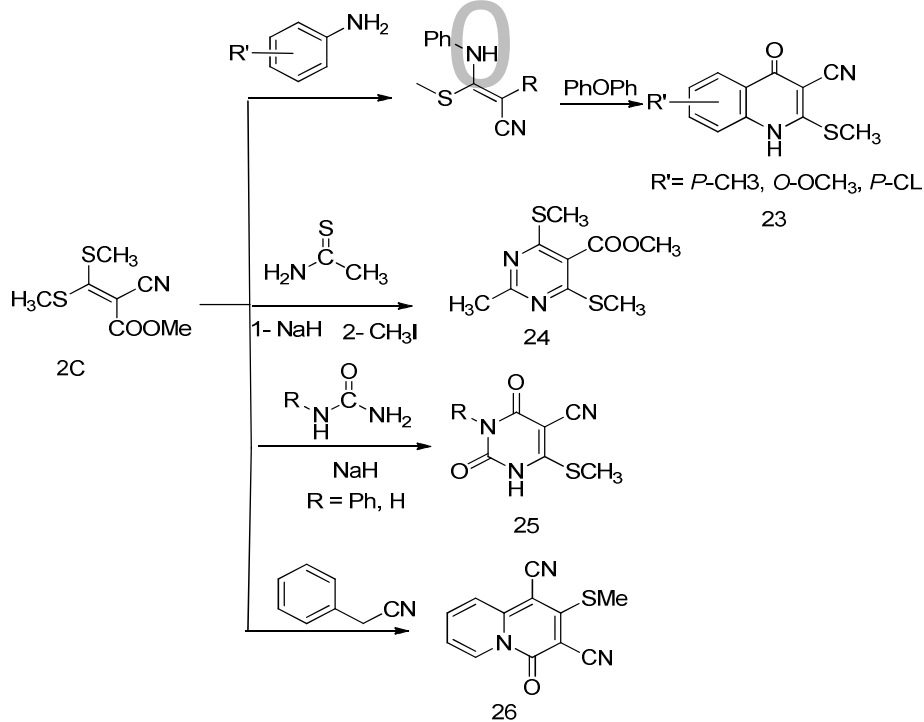
Scheme 6

Triazolopyrimidine derivative **19**^{xxxv}, pyrazole derivative **20**^{xxxvi}, 4-(methylthio)-6-(naphthalen-2-yl)-2-oxo-2H-pyran-3-carbonitrile **21**^{xxxvii} and nicotinic acid amides **22**^{xxii} were synthesized by the reaction of cyano ketene S,S acetal **2c** with diamino pyrimidine derivative, phenyl hydrazine, acetophenone and thioxopropanamide derivative (Scheme 7).



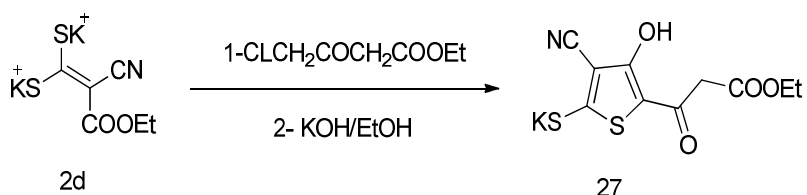
Scheme 7

Ketene dithioacetal **2C** reacted with arylamines then heated with diphenyl ether, thioacetamide, urea or/and N-phenyl urea and 2-pyridine acetonitrile gave 2-(methylthio)-4-oxo-1,4-dihydroquinoline-3-carbonitrile **23**^{xxxviii}, methyl 2-methyl-4,6-bis(methylthio)pyrimidine-5-carboxylate **24**^{xxxix}, uracil derivative **25**^{xxxix} and quinolizinone derivatives **26**^{xl} (Scheme 8).

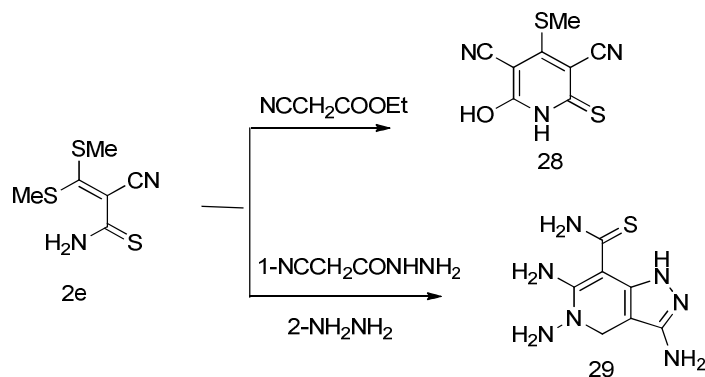


Scheme 8

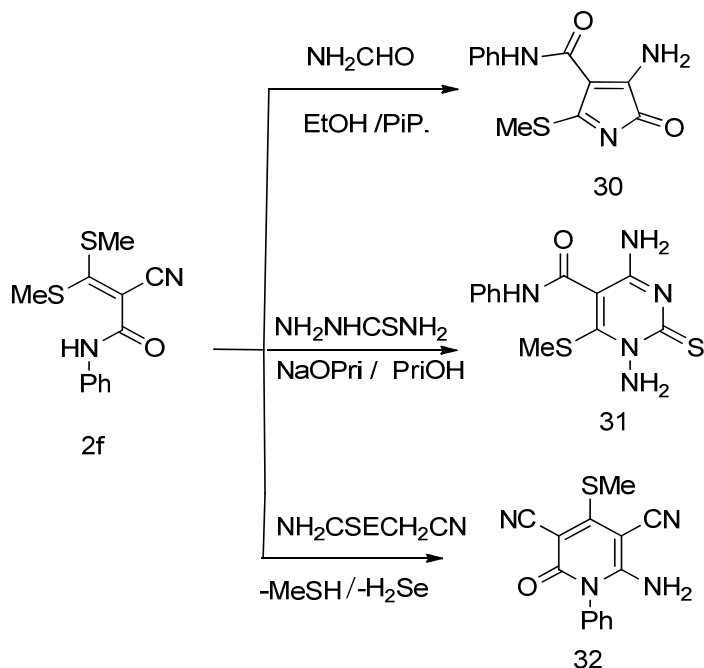
Reaction of dipotassium salt of ketene S,S acetal **2d** with ethyl 4-chloroacetoacetate, then KOH led to formation 3-hydroxythiophenes derivative **27^{xi}** (Scheme 9).



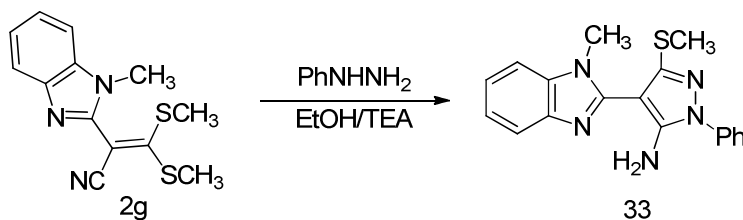
Compound ketene dithioacetal **2e** reacted with ethylcyanoacetate and also, with cyanoacetohydrazide then hydrazine in ethanol gave methyl thiopyridine-2(1H)-thiones **28^{xi}** and pyrazolo [4,3-c]pyridin-2-one derivatives **29^{xi}** (Scheme 10).



Elgemeiet al reacted ketene dithioacetals **2f** with formamide in ethanol, thiosemicarbazide in sodium isopropoxide containing catalytic amounts of piperidine and cyanoselenoacetamide afforded the corresponding 5-methylthiopyrrol-2-one derivative **30^{xi}**, 6-methylthio-1-amino pyrimidine-2-thione derivatives **31^{xi}** and dihydropyridine derivatives **32^{xi}** (Scheme 11).

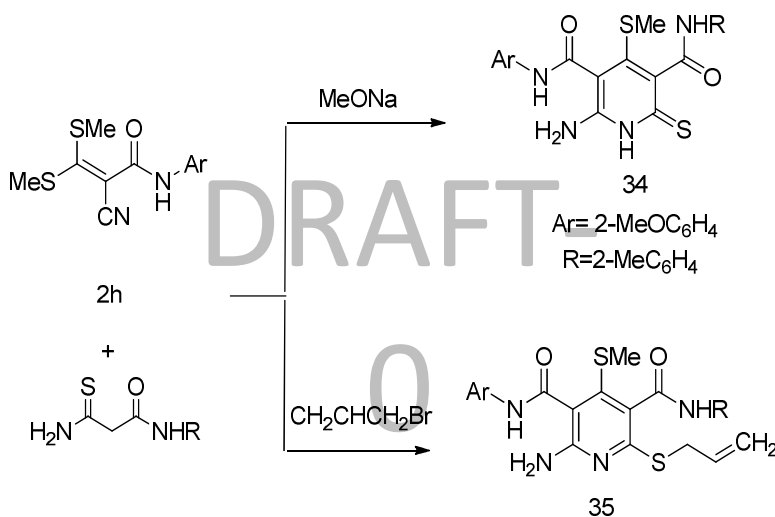


Benzoimidazole ketene S,S acetal derivatives **2g** with phenylhydrazine gave 4-(1-methyl-1*H*-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1*H*-pyrazol-5-amine **33**^{xvi} (Scheme 12).



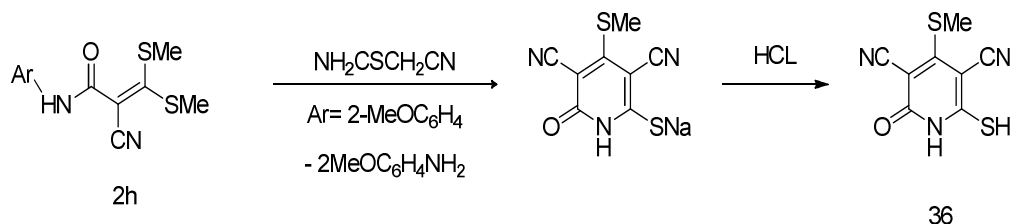
Scheme 12

Dyachenko *et al* showed that the reaction of ketene S,S-acetal **2h** with thioxopropanamide derivative in the presence of sodium methoxide and in the presence of allyl bromide in anhydrous methanol afforded 2-allylsulfanyl-substituted pyridine **34**^{xxii} and substituted 6-amino-4-methylsulfanyl-2-thioxo-*N*3,*N*5-diaryl-1,2-dihydropyridine-3,5-dicarboxamides **35**^{xxii} (Scheme 13).



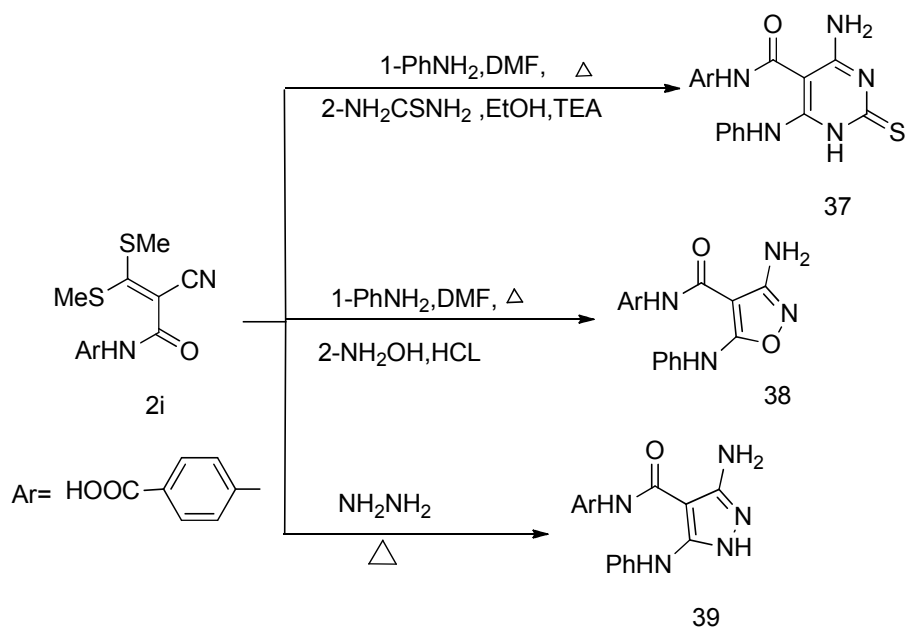
Scheme 13

Reaction of compound ketene S,S-acetal **2h** with cyanothioacetamide then treated with hydrochloric acid afforded dihydropyridine derivatives **36**^{xi, xxii, xlii} (Scheme 14).



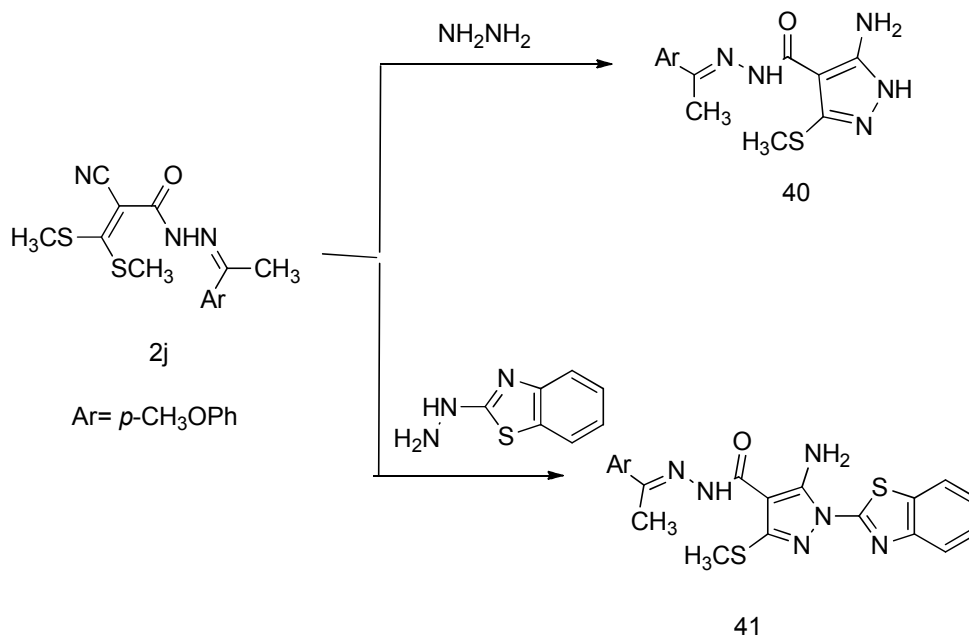
Scheme 14

Reaction of ketene *S,S*-acetal **2i** with aniline then with thiourea in DMF, hydroxyl amine hydrochloride and sodium carbonate in ethanol and hydrazine hydrate afforded pyrimidine **37**, isoxazole **38** and pyrazole derivatives **39**^{xix} (Scheme 15).



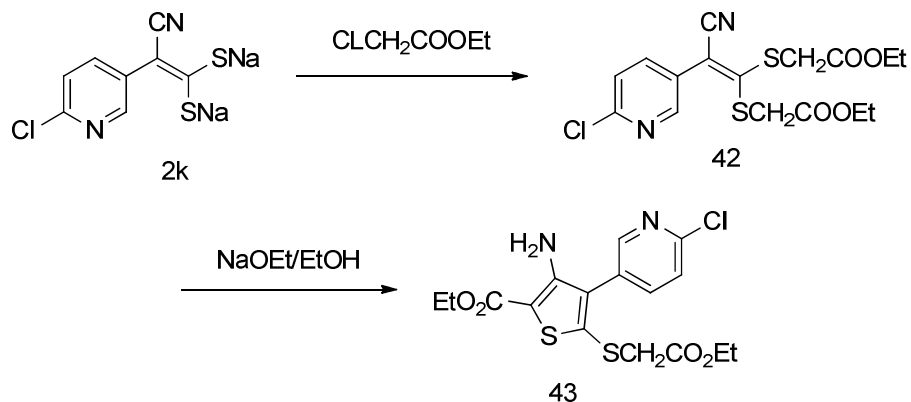
Scheme 15

Cyclocondensation of Ketene *S,S*-dithio-acetals **2j** derivatives with hydrazine derivatives such as: hydrazine hydrate and 2-hydrazino-1,3-benzothiazole afforded the corresponding 5-(methylthio)1H-pyrazole-4-carbohydrazide **40**^{xx} and **41**^{xx}, respectively (Scheme 16).



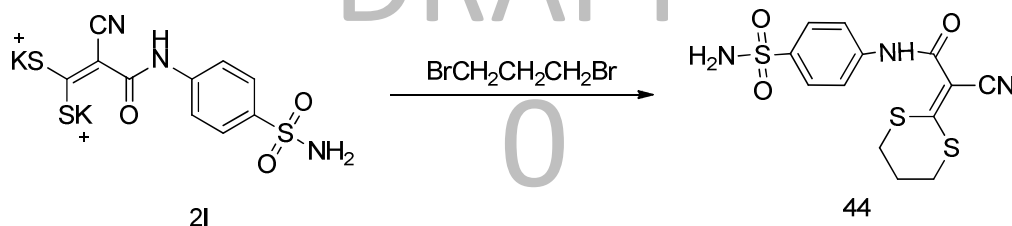
Scheme 16

Reaction of 2-chloropyridine ketene S,S-acetal **2k** with ethyl chloroacetate gave diethyl 2,2'-((2-(6-chloropyridin-3-yl)-2-cyanoethene-1,1-diyl)bis(sulfaneyl))diacetate **42** then treated with sodium ethoxide furnished ethyl 3-amino-4-(6-chloropyridin-3-yl)-5-((2-ethoxy-2-oxoethyl)thio)thiophene-2-carboxylate **43**^{xliii} (Scheme 17).



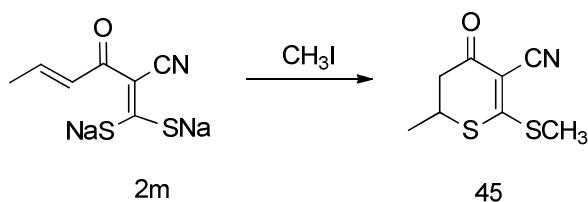
Scheme 17

Potassium 2-cyano-3-oxo-3-((4-sulfamoyl-phenyl) amino) prop-1-ene-1,1-bis(thiolate) **2l** with 1,3-dibromopropane afforded the *N*-[4-(aminosulfonyl)phenyl]-2-cyano-2-(1,3-dithian-2-ylidene)acetamide **44**^x (Scheme 18).



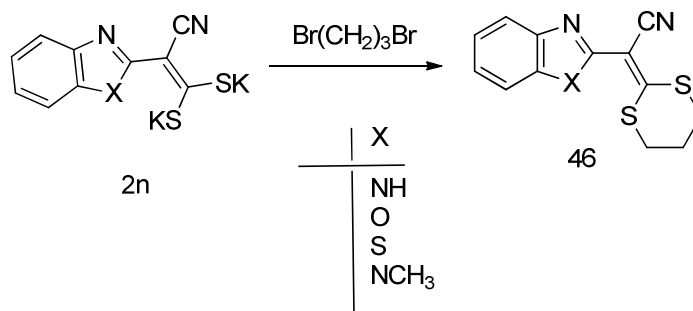
Scheme 18

Treatment of sodium (E)-2-cyano-3-oxohexa-1,4-diene-1,1-bis(thiolate) **2m** with methyl iodide afforded 2-methyl-6-(methylthio)-4-oxo-3,4-dihydro-2H-thiopyran-5-carbonitrile **45**^{xii} (Scheme 19).



Scheme 19

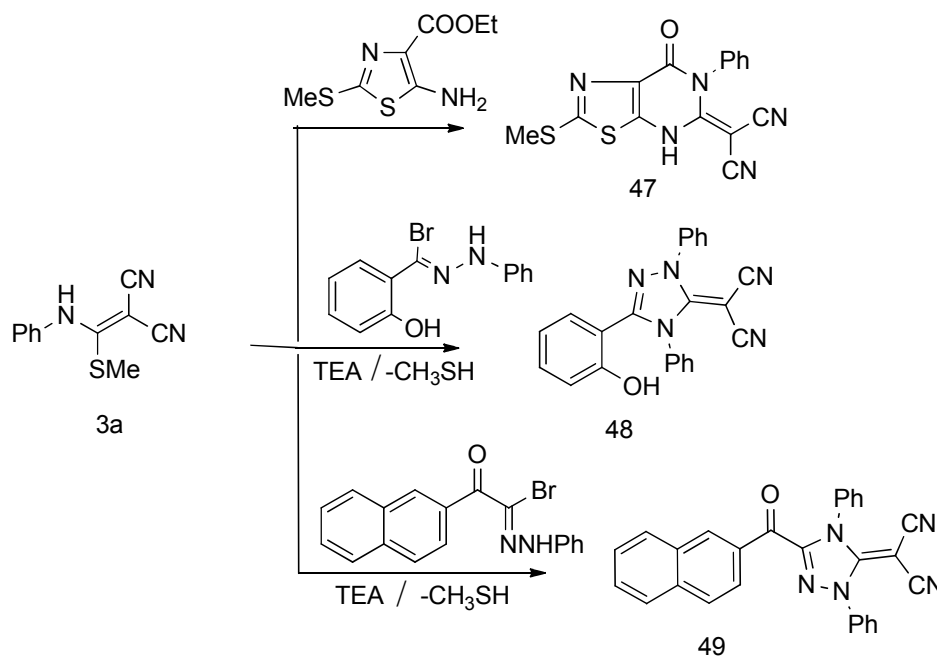
Reaction of 2-[benzazolyl-(2)]-3, 3-bis-(alkylthio)-acrylonitriles **2n** with dibromopropane afforded 1,3-dithiane derivatives **46** in a good yield^{xxi} (Scheme 20).



Scheme 20

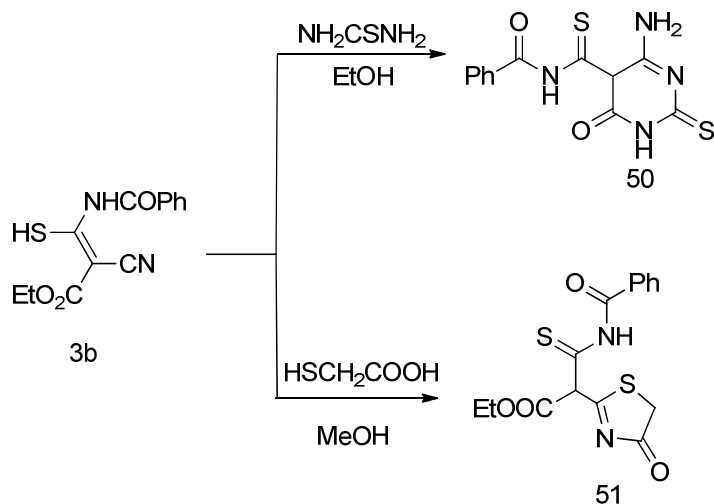
V. Cyclization acyclic cyano Ketene N,S- acetals:

Reaction of cyano ketene N,S acetal **3a** (Z-form) derivatives with 5-amino-2-methylsulfanyl-thiazole-4-carboxylic acid ester ethyl, hydrazonoyl bromide and 2-(2-phenylhydrazono)-2-bromo-1-(naphthalene-2-yl) ethanone gave the corresponding 2-(2-methylsulfanyl-7-oxo-6-phenyl-6,7-dihydro-4H-thiazolo[5,4-d]pyrimidin-5-yl-idene) malononitrile **47**^{xxxiii}, 1,2,4-triazole derivatives **48**^{xliv} and **49**^{xliv}, respectively (Scheme 21).



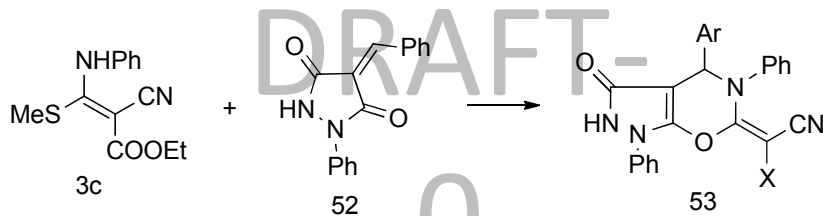
Scheme 21

Reaction of Ketene N,S (Z-form) **3b** reacted with thioglycolic acid and thiourea afforded pyrimidine **50**^{xxv} and thiazole derivatives **51**^{xlv} (Scheme 22).



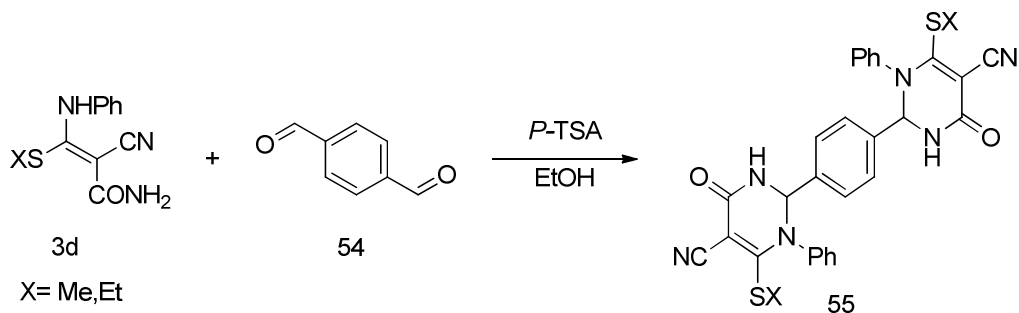
Scheme 22

Activated nitriles N,S-acetals (*Z*-form) **3c** reacted with 4-Arylidene-1-phenyl-3,5-pyrazoline diones **52**^{xlvi} which reacted with to give pyrazolino-1,3-oxazine derivatives **53**^{xlvii} (Scheme 23).



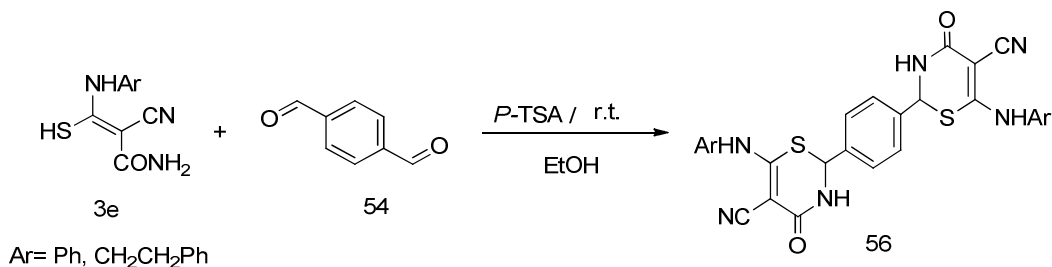
Scheme 23

Reaction of 2 equivalents of Ketene N,S acetal **3d** (*Z*-form) with terephthalaldehyde **54** by reflux gave 2,2'-(1,4-phenylene)-bis(6-(alkylthio)-4-oxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbonitrile) **55**^{xlviii} (Scheme 24).



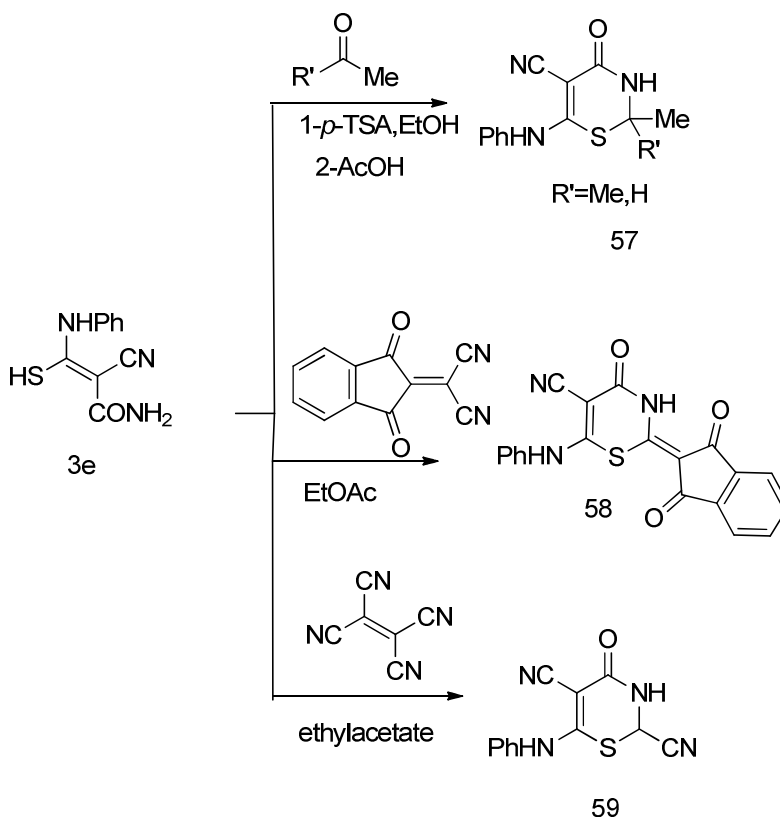
Scheme 24

Reaction of 2 equivalents of Ketene N,S acetal **3e** (Z-form) with terephthalaldehyde **54** at room temperature 2,2'-gave (1,4-phenylene)bis(6-(alkylamino)-4-oxo-3,4-dihydro-2H-1,3-thiazine-5-carbonitrile) **56**^{xlix,1} (Scheme 25).



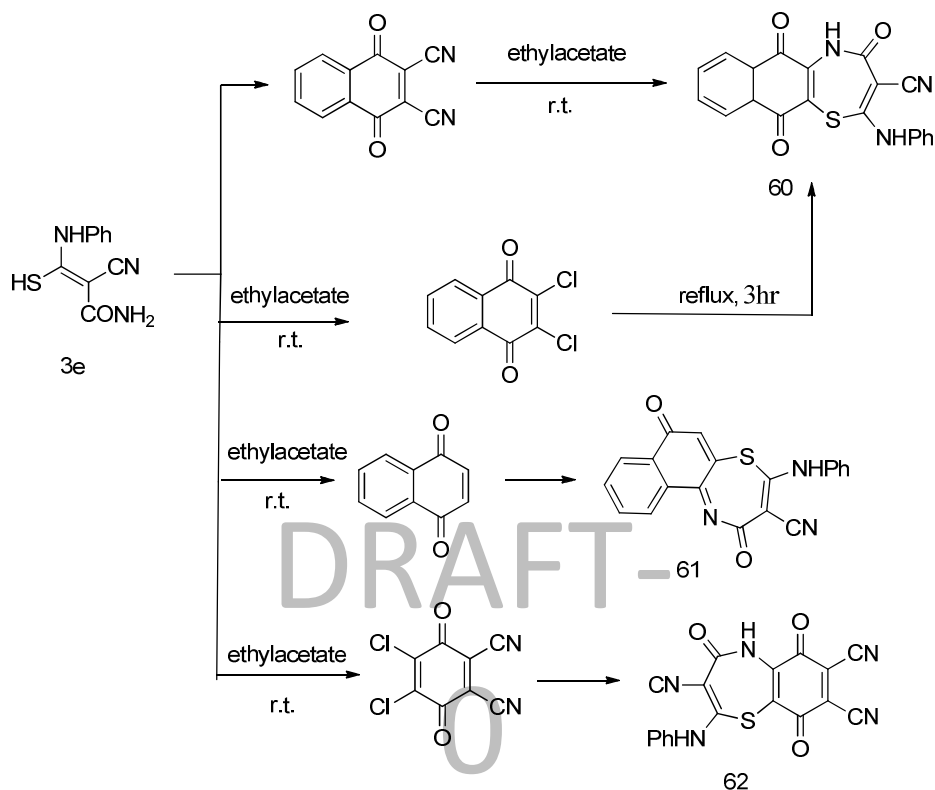
Scheme 25

Thiazine **57**, **58** and **59** derivatives were synthesized by cyclocondensation of 3-alkyl (aryl) amino-2-cyano-3-mercaptoacrylamides **2e** (Z- form) with aldehydes or ketones in boiling ethanol using *p*-TSA or in glacial acetic acid^{li} or with 2-(dicyanomethylidene)-indane-1,3-dione in the presence of ethyl acetate under reflux conditions^{lii-lv} (Scheme 26).



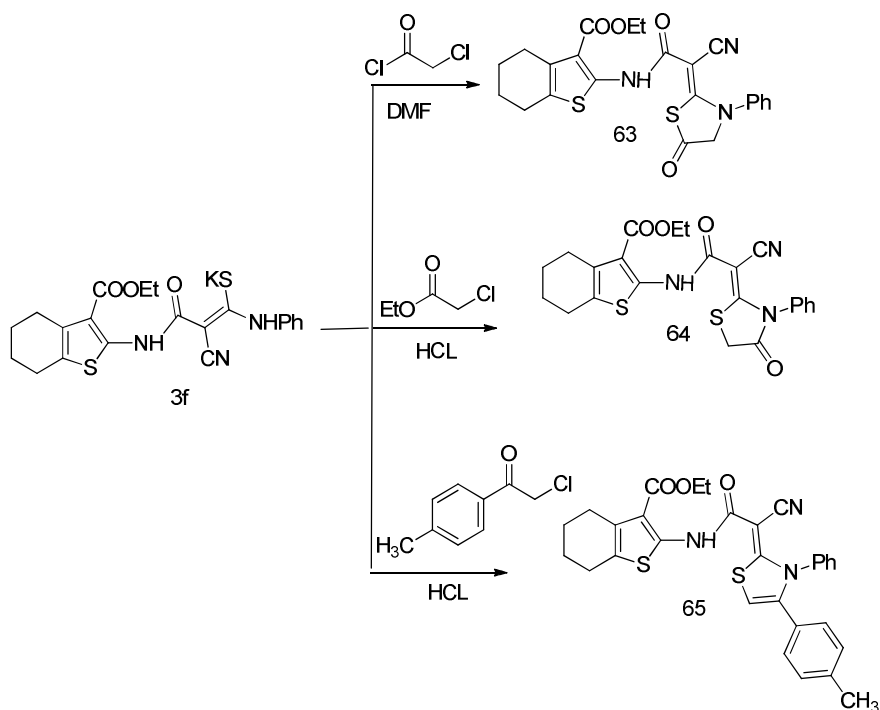
Scheme 26

Reaction of 2,3-dicyano-1,4-naphthoquinone), 2,3-dichloro-1,4-naphthoquinone and 1,4-naphthoquinone in dry ethyl acetate afforded 4,6,11-trioxo-2-(phenyl amino)-4,5,6,11-tetrahydronaphtho [2,3-*b*][1,4]thiazepine-3-carbo nitrile **60**, 2,7-dioxo-4- (phenylamino)-2,7-dihydronaphtho[2,1-*b*][1,4]thiazepine-3-carbonitrile**61**and 4,6,9-trioxo-2-(phenylamino)-4,5,6,9-tetrahydrobenzo[*b*][1,4]thiazepine-3,7,8-tricarbonitrile **62**^{lii}(Scheme 27).



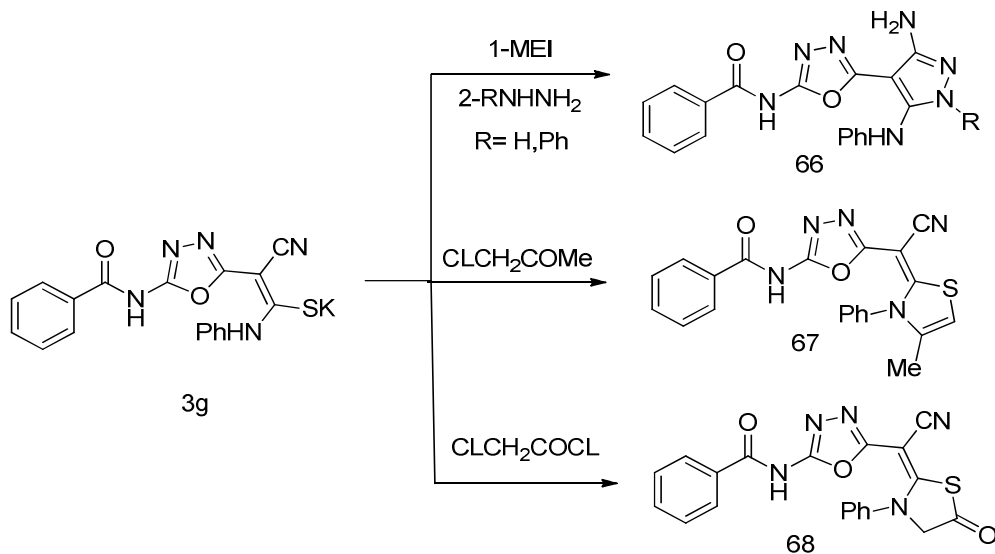
Scheme 27

Compound ketene N, S acetal (Z-form) **3f** reacted with chloroacetyl chloride, *p*-methylphenacyl chloride and ethyl chloroacetate to afford 2-(5-oxothiazolidin-2-ylidene) cyanoacetamide derivative **63**, thiazol-2-ylidene **64** and **65** derivatives^{xxvii}(Scheme 28).



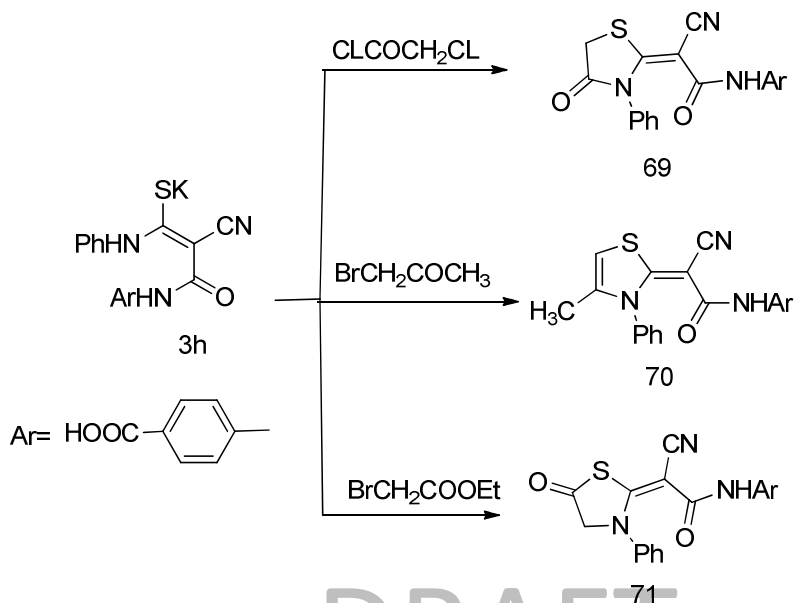
Scheme 28

Treatment of 1, 3, 4-Oxadiazol-2-yl Ketene N, S acetals **3g** (*E*-form) with methyl iodide then hydrazine hydrate or phenyl hydrazine afforded 3-aminopyrazole **66** and also, compound **3g** with chloroacetyl chloride or chloroacetone respectively, under mild reaction conditions afforded thiazol-2-ylidene derivatives **67** and **68**^{1vi} (Scheme 29).

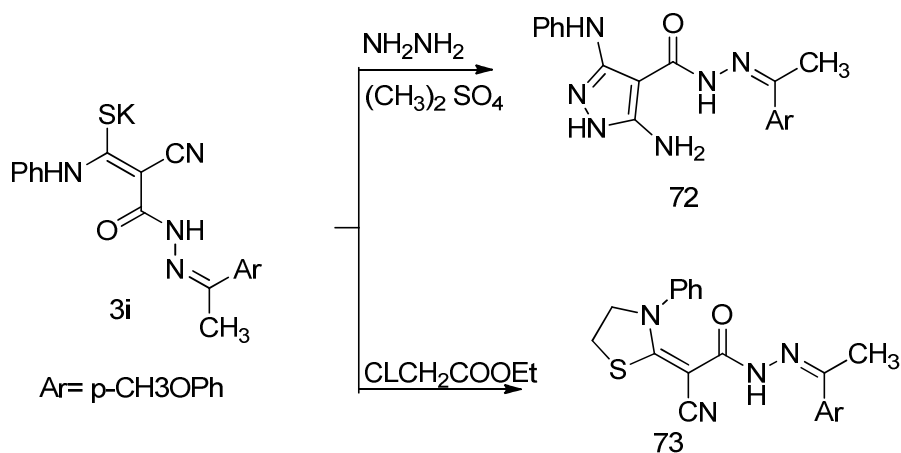


Scheme 29

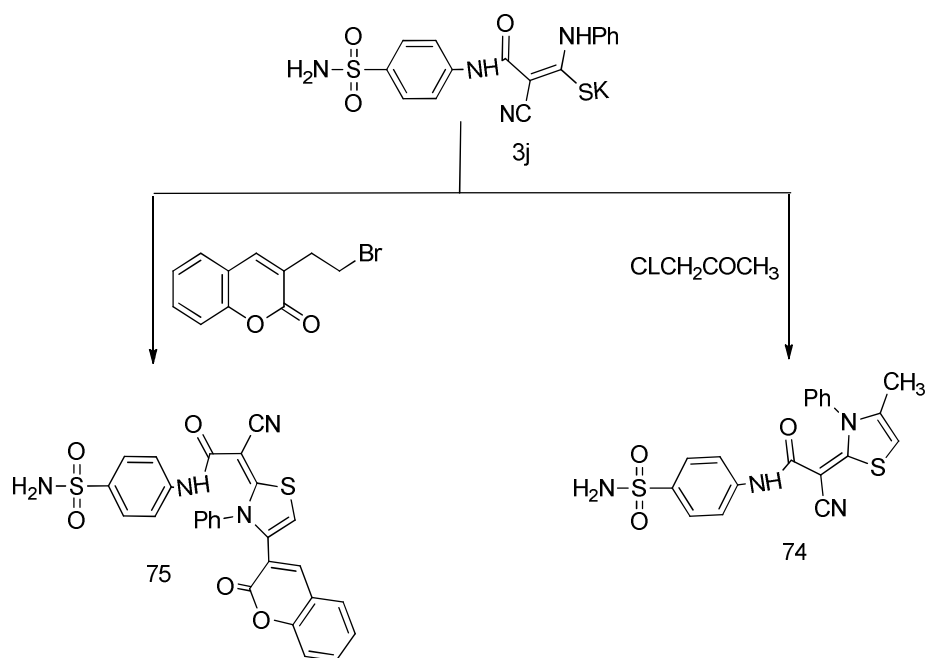
Heterocyclization of cyano ketene N,S acetal (*E*-form) **3h** with α -halocarbonyl compounds such as: chloroacetyl chloride, bromoacetone and ethyl bromoacetate afforded the corresponding thiazole derivatives **69**, **70** and **71**^{xi} (Scheme 30).



Cyclocondensation of the cyano ketene N, S acetal (*E*-form) **3i** with hydrazine hydrate or ethylchloroacetate in boiling ethanol afforded aminopyrazole derivative **72** and 1, 3-thiazolidinone derivative **73**^{xx} (Scheme 31).

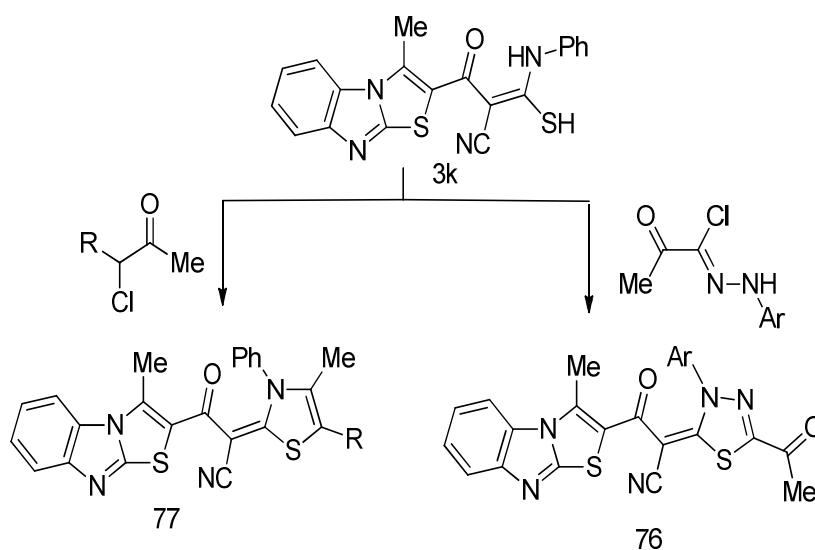


Heterocyclization of ketene *N,S*-acetal (*E*-form) **3j** with chloroacetone or 3-(2-bromoacetyl)-2*H*-chromen-2-one furnished thiazole derivatives **74** and **75**^{x,xiv} (Scheme 32).



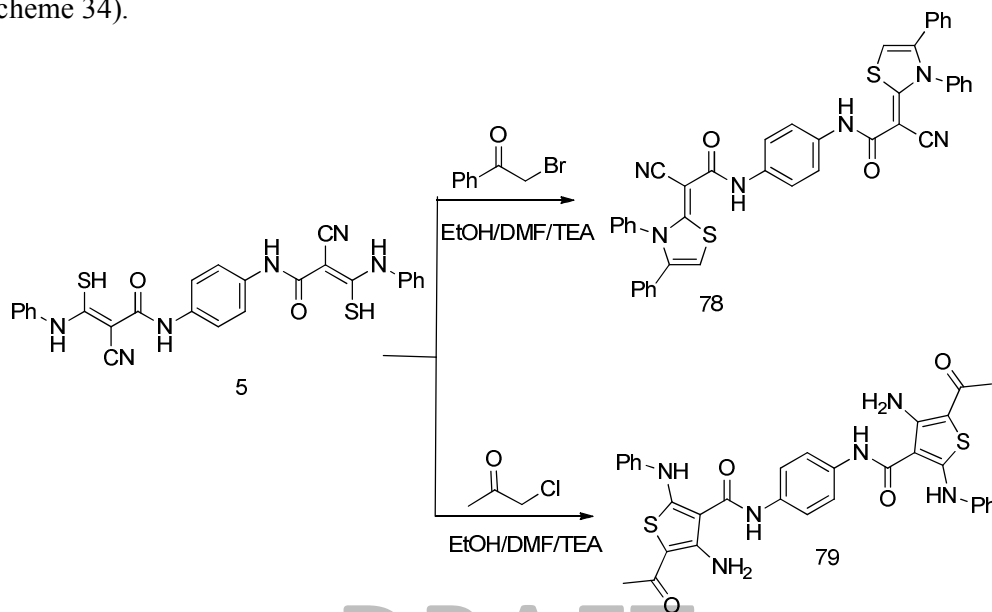
Scheme 32

(*E*)-3-mercapto-2-(3-methylbenzo[4,5]imidazo[2,1-*b*]thiazole-2-carbonyl)-3-phenylamino)acrylonitrile (*E*-form) **3k** reacted with α -chloro acetylacetone or ethyl α -chloroacetoacetate in ethanol resulted in formation of 1,3-thiazole derivatives **76**. Furthermore, the reaction of cyano ketene *N,S* acetal derivative **3k** with hydrazonyl chlorides under the same reaction conditions afforded 1,3,4-thiadiazole derivatives **77**^{x,xiii} (Scheme 33).



Scheme 33

Cyano ketene N,S acetal derivative (Z-Form) **5** underwent cyclization upon the reaction with phenacyl bromide in a mixture of ethanol and in presence of triethylamine yielded di (2-cyano-2-(3,4-diphenylthiazol-2(3H)-ylidene)acetamide) **78** and also, by refluxing with chloroacetone in ethanol in presence of triethylamine afforded the thiophene derivative **79**^{xxix} (Scheme 34).



Scheme 34

VI. References

- i. Dieter, R. K., α -Oxo ketene dithioacetals and related compounds: versatile three-carbon synthons. *Tetrahedron* **1986**,*42* (12), 3029-3096.
- ii. Junjappa, H.; Ila, H.; Asokan, C., α -Oxoketene-S, S-, N, S-and N, N-acetals: versatile intermediates in organic synthesis. *Tetrahedron* **1990**,*46* (16), 5423-5506.
- iii. Kolb, M., Ketene dithioacetals in organic synthesis: recent developments. *Synthesis* **1990**,*1990* (03), 171-190.
- iv. Pan, L.; Bi, X.; Liu, Q., Recent developments of ketene dithioacetal chemistry. *Chemical Society Reviews* **2013**,*42* (3), 1251-1286.
- v. Pan, L.; Liu, Q., [5+ 1]-Annulation Strategy Based on Alkenoyl Ketene Dithioacetals and Analogues. *Synlett* **2011**,*2011* (08), 1073-1080.
- vi. Liu, Q., 1, 1-Bis (organosulfanyl) alk-1-enes (Ketene S, S-Acetals). Georg Thieme: Stuttgart, Germany: **2014**; pp 245-286.
- vii. Wang, L.; He, W.; Yu, Z., Transition-metal mediated carbon-sulfur bond activation and transformations. *Chemical Society Reviews* **2013**,*42* (2), 599-621.
- viii. Huang, Z.-T.; Shi, X., Synthesis of heterocyclic ketene n, s-acetals and their reactions with esters of α , β -unsaturated acids. *Synthesis* **1990**,*1990* (02), 162-167.
- ix. Huang, Z. T.; Shi, X., Synthesis, Reactions, and Tautomerism of Ketene N, S-Acetals with Benzothiazoline Ring. *Chemische Berichte* **1990**,*123* (3), 541-547.
- x. Darwish, E. S.; Fattah, A. M. A.; Attaby, F. A.; Al-Shayea, O. N., Synthesis and antimicrobial evaluation of some novel thiazole, pyridone, pyrazole, chromene, hydrazone derivatives bearing a biologically active sulfonamide moiety. *International journal of molecular sciences* **2014**,*15* (1), 1237-1254.

- xi. **Elgemeie, G. H. E., A.H; Elzanate, A.M. ;Ahmed, S.A.,** *J. Chem. Soc., Perkin Trans.*, **1997**,1 3285- 3289.
- xii. **Elnagdi, M. H.; Elmoghayar, M. R. H.; Elgemeie, G. E. H.,** The chemistry of 3-oxoalkanenitriles. *Synthesis* **1984**,1984 (01), 1-26.
- xiii. **El-Sayed, A.,** One—pot synthesis of pyridines, thienopyridines, pyrrolothienopyridines and (1, 8) naphthyridines under phase-transfer catalysis conditions. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2000**,163 (1), 29-40.
- xiv. **Gorobets, N. Y.; Yousefi, B. H.; Belaj, F.; Kappe, C. O.,** Rapid microwave-assisted solution phase synthesis of substituted 2-pyridone libraries. *Tetrahedron* **2004**,60 (39), 8633-8644.
- xv. **Jensen, L.; Dalgaard, L.; Lawesson, S.-O.,** Reactions of β -ketoesters and nitriles with carbon disulphide: Tautomerism of dithioesters and thio-Claisen rearrangement of ketene mercaptals. *Tetrahedron* **1974**,30 (15), 2413-2423.
- xvi. **Khalil, M. A.; Sayed, S. M.; Raslan, M. A.,** Reactivity of 2-Cyano-N-(4-(1-methyl-1H-benzo [d] imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl) acetamide: A Facile Synthesis of Pyrazole, Thiazole, 1, 3, 4-Thiadiazole and Polysubstituted Thiophene Derivatives. *American Journal of Organic Chemistry* **2012**,2 (6), 161-170.
- xvii. **Shestopalov, A. M.; Rodinovskaya, L. A.; Shestopalov, A. A.,** Combinatorial Synthesis of Substituted Thieno[3,2-b]pyridines and Other Annulated Heterocycles via New SN2 \rightarrow Thorpe–Ziegler \rightarrow Thorpe–Guareschi Domino Reactions. *Journal of Combinatorial Chemistry* **2010**,12 (1), 9-12.
- xviii. **Wang, X.; Huang, Z.,** Synthesis and spectral and structural characteristics of cyano substituted heterocyclic ketene amins. *Acta Chimica Sinica* **1989**,47 (9), 890-895.
- xix. **Fadda, A.; Mukhtar, M.; Refat, H. M.,** Utility of activated nitriles in the synthesis of some new heterocyclic compounds. *Am. J. Org. Chem* **2012**,2 (2), 32-40.
- xx. **Salman, A. S.,** Utility of activated nitriles in the synthesis of novel heterocyclic compounds with antitumor activity. *Organic Chemistry International* **2013**,2013.
- xxi. **Manfreda Augustin, W. D.,** Synthese von 2- [Benzazolyl-(S)] -3,3-bis-(alkylthio)-acrylnitrilen und Umsetzungen mit N-Nucleophilen. *Journal f. prakt. Chemie* **1982**,1, 3-11.
- xxii. **Dyachenko, V.; Bityukova, O.; Dyachenko, A.,** Synthesis of new functionally substituted 2-oxo (thioxo) nicotinic acid amides and nitriles by S N Vin reaction. *Russian Journal of Organic Chemistry* **2011**,47 (9), 1335.
- xxiii. **Hamdy, N. A.; Abdel-Aziz, H. A.; Farag, A. M.; Fakhr, I. M.,** Synthesis of Some 1, 3-Thiazole, 1, 3, 4-Thiadiazole, Pyrazolo [5, 1-c]-1, 2, 4-triazine, and 1, 2, 4-Triazolo [5, 1-c]-1, 2, 4-triazine Derivatives Based on the Thiazolo [3, 2-a] benzimidazole Moiety. *Monatshefte für Chemie-Chemical Monthly* **2007**,138 (10), 1001-1010.
- xxiv. **Sallam, M. M. M. E. n., M.H.; Fleita, D.H.; Hartmann, E. Z.,** *Naturforsch*, **1976**, ,31 ((b):), 989-992.
- xxv. **Mohareb, R.; Habashi, A.; Ibrahim, N.; Sherif, S.,** Reaction of Benzoyl Isothiocyanate With Active Methylene Reagents: A Convenient Synthesis of Pyrazolo [5, 4-c] pyrazole, 1, 3-Oxazine, Thiazole and Pyrimidine Derivatives. *Synthesis* **1987**,1987 (03), 228-231.
- xxvi. **Farhat, M.; El-Saghier, A.; Makhlof, M.; Kredan, K.; Elmezoughi, A.,** Ketene N, S-acetals in heterocyclic synthesis: Part 1: Synthesis of N-phenyl-2-ylidene and 2, 5-diylidene-4-thiazolidinone derivatives. *Journal of Sulfur Chemistry* **2007**,28 (6), 563-572.

- xxvii. **Gouda, M. A.; Abu-Hashem, A. A.**, Synthesis, characterization, antioxidant and antitumor evaluation of some new thiazolidine and thiazolidinone derivatives. *Archiv der Pharmazie* **2011**,344 (3), 170-177.
- xxviii. **Hantzsch, A.; Weber, J.**, Ueber verbindungen des thiazols (pyridins der thiophenreihe). *Berichte der deutschen chemischen Gesellschaft* **1887**,20 (2), 3118-3132.
- xxix. **Fadda, A.; Refat, H.; Kamal, S.**, Utility of thiocarbamoyl moiety in synthesis of some new sulphur containing heterocyclic compounds and evaluation of their antimicrobial activity. *European Journal of Chemistry* **2014**,5 (2), 296-304.
- xxx. **Chanu, L. G.; Singh, O. M.; Jang, S.-H.; Lee, S.-G.**, Regioselective synthesis of heterocyclic ketene N, N-, N, O-and N, S-acetals in aqueous medium. *Bulletin of the Korean Chemical Society* **2010**,31 (4), 859-862.
- xxxi. **Hassan, S. M. E., H. A.; Abdelall, M. M.**, *J. Chem. Res., Synopses* **2000**, (12), 544-545, 1301-1315.
- xxxii. **Fuchigami, T.; Kandeel, Z. E. S.; Nonaka, T.; Tien, H. J.**, A Facile Synthesis of 3, 4-Diamino-2, 5-Diacylthieno [2, 3-b] Thiophenes from Disodium (Dimercaptomethylene) Malononitrile and α -Halo Ketones. *Journal of the Chinese Chemical Society* **1986**,33 (3), 241-244.
- xxxiii. **El-Emary, T.I.; Khodairy, A.**, Synthesis of Thiazolo[5,4-d]pyrimidine, Thiazolo[5,4-b]pyridine, Thiazolo[4,5-b]pyrrolizine and Thiazolo[5,4-d]thiazaphosphinine. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2006**,181 (5), 1073-1085.
- xxxiv. **Komarova, E.; Yufit, D.; Struchkov, Y. T.; Drozd, V.**, Sudden Formation Of 5-Membered 1, 3-Dithiols Under The Interaction Of Geminal Dimercaptans With Activated Haloacetylenes. *Zhurnal Organicheskoi Khimii* **1989**,25 (7), 1512-1519.
- xxxv. **Abdelghani, E.; Said, S. A.; Assy, M. G.; Abdel Hamid, A. M.**, Synthesis and antimicrobial evaluation of some new pyrimidines and condensed pyrimidines. *Arabian Journal of Chemistry* **2017**,10, S2926-S2933.
- xxxvi. **Gompper, R.; Töpfl, W.**, Ketenderivate, II. Reaktionen substituierter Ketenmercaptale. *Chemische Berichte* **1962**,95 (12), 2871-2880.
- xxxvii. **Nandre, J.; Patil, S.; Patil, V.; Yu, F.; Chen, L.; Sahoo, S.; Prior, T.; Redshaw, C.; Mahulikar, P.; Patil, U.**, A novel fluorescent “turn-on” chemosensor for nanomolar detection of Fe (III) from aqueous solution and its application in living cells imaging. *Biosensors and Bioelectronics* **2014**,61, 612-617.
- xxxviii. **Tominaga, Y.; Michioka, T.; Moriyama, K.; Hosomi, A.**, Synthesis of quinoline derivatives using ketene dithioacetals. *Journal of Heterocyclic Chemistry* **1990**,27 (5), 1217-1225.
- xxxix. **Kohra, S.; Tominaga, Y.; Hosomi, A.**, Synthesis of pyrimidine derivatives by the reaction of ketene dithioacetals with amides. *Journal of heterocyclic chemistry* **1988**,25 (3), 959-968.
- xl. **Kobayashi, G.; Matsuda, Y.; Natsuki, R.**, Quinolizine Derivatives. VI. Synthesis and Reaction of 1-Cyano-2-methylthio-4H-quinolizin-4-ones. *Chemical and Pharmaceutical Bulletin* **1973**,21 (5), 921-925.
- xli. **Larionova, N.; Zubarev, A.; Rodinovskaya, L.; Shestopalov, A.**, Synthesis of ethyl 3-(3-hydroxy-2-thienyl)-3-oxopropanoates. *Russian Chemical Bulletin* **2013**,62 (5), 1297-1298.
- xlii. **Dyachenko, V.**, Unusual reaction of ethyl 2-cyano-3, 3-bis (methylsulfanyl)-acrylate with cyanothioacetamide. *Russian journal of organic chemistry* **2006**,42 (7), 1085-1086.

- xliii. **Sturrock, K. R.; Bremner, D. H.; Wishart, G.**, The preparation of ketene dithioacetals and thiophenes from chloropyridines containing an active methylene group. *Heterocycles*. **82** (2) **2011**.
- xliv. **Al-Omair, M. A.; Sayed, A. R.; Youssef, M. M.**, Synthesis of novel triazoles, tetrazine, thiadiazoles and their biological activities. *Molecules* **2015**, **20** (2), 2591-2610.
- xlv. **Elnagdi, M. H.; Elmoghayar, M. R. H.; Hammam, A. E. F. G.; Khallaf, S. A.**, The reaction of malononitrile with thioglycolic acid. A novel procedure for the synthesis of thiazolone derivatives. *Journal of Heterocyclic Chemistry* **1979**, **16** (8), 1541-1543.
- xlvi. **Kumar H.A.H. ; Junjappa, H.**, *Synthesis* **1976**, , 324.
- xlvii. **Khodairy, A.**, Synthesis of fused and spiro heterocyclic compounds derived from 3, 5-pyrazolidinedione derivatives. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2000**, **160** (1), 159-180.
- xlviii. **Elgemeie, G. H.; Elghandour, A. H.; Elaziz, G. W. A.**, Novel Cyanoketene N, S-Acetals and Pyrazole Derivatives using Potassium 2-Cyanoethylene-1-thiolates. *Synthetic Communications* **2007**, **37** (17), 2827-2834.
- xlix. **Goerdeler, J.; Keuser, U., Über Isothiazole, VI.** Synthese von 5-Amino-3-hydroxy (alkoxy-, amino-)isothiazolen und von Derivaten der Pyrimidinthione-(4). *Chemische Berichte* **1964**, **97** (11), 3106-3117.
- i. **Shaker, R. M. I., Y. R.; Abdel-Latif, F. F. ; Hamoda, A.** , *Z. Naturforsch.* **2010**, **65** (b), 1148 – 1154.
 - ii. **Vovk, M. V.; Sukach, V. A.; Chernega, A. N.; Pyrozhenko, V. V.; Bol'but, A. V.; M. Pinchuk, A.**, Synthesis of 2, 3-dihydro-1, 3-thiazin-4 (1H)-ones and their remarkably facile recyclization to 2, 3-dihydropyrimidin-4 (1H)-ones. *Heteroatom Chemistry* **2005**, **16** (5), 426-436.
 - iii. **El-Shaieb, K. M.; Abdel-Latif, F. F.; El-Din, A. G.**, Synthesis of thiazine and thiazepine derivatives from (Z)-2-cyano-3-mercapto-3-(phenylamino)acrylamide. *Journal of Chemical Research* **2012**, **36** (5), 308-311.
 - liii. **Shaker, R. M.; Hamoda, A.; Ibrahim, Y. R.; El-Shaieb, K. M.; Abdel-Latif, F. F.**, An Efficient Synthesis of 1-Thia-5-azaspiro [5.5] undec-2-ene and its Recyclization to 1, 5-Diazaspiro [5.5] undec-2-ene and/or Spiro-Thieno [2, 3-d] pyrimidin-4 (1H)-one Derivatives. *Zeitschrift für Naturforschung B* **2011**, **66** (5), 487-492.
 - liv. **Shaker, R. M.; Ibrahim, Y. R.; Abdel-Latif, F. F.; Hamoda, A.**, Synthesis of 2, 2-(1, 4-Phenylene) bis-3, 4-dihydro-2H-1, 3-thiazin-4-ones and their Facile Recyclization to 2, 2-(1, 4-Phenylene) bis (pyrimidin-4-one) and/or 2, 2-(1, 4-Phenylene)-bis-(thieno [2, 3-d] pyrimidin-4 (1H)-one) Derivatives. *Zeitschrift für Naturforschung B* **2010**, **65** (9), 1148-1154.
 - lv. **Shaker, R. M.; Ibrahim, Y. R.; Abdel-Latif, F. F.; Hamoda, A.**, Synthesis of novel 1-thia-5, 9-diaza-spiro [5.5] undec-2-ene and its recyclization to 1, 5, 9-triaza-spiro [5.5] undec-2-ene and/or spiro (piperidine-4, 2'-thieno [2, 3-d] pyrimidine). *Arkivoc* **2011**, **2**, 57-68.
 - lvi. **Bondock, S.; Adel, S.; Etman, H. A.; Badria, F. A.**, Synthesis and antitumor evaluation of some new 1, 3, 4-oxadiazole-based heterocycles. *European journal of medicinal chemistry* **2012**, **48**, 192-199.

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