WHAT CAN BE DONE WITH THE ACETYL GROUP OF ARYL-1-ETHANONES?

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Dedicated to academician Vlad Pavel on his 70th birthday

Abstract: Literature data on utilization of acetyl group of aryl-1-ethanones (acetophenones) for the synthesis of organic compounds is generalized. Different approaches of preparation of aromatic compounds by chemical transformations of methyl as well as keto- group of titled compounds are systematized. Examples of the synthesis of organic compounds based on products of primary transformations of aryl-1-ethanones are considered.

Keyword: organic synthesis, aryl-1-ethanones, acetyl group

Content

1. Introduction

Aryl-1-ethanones (acetophenones) **1** are convenient starting substances for the synthesis of various classes of organic compounds. Their acetyl group can be subjected to various transformations leading to formation of a number of substances, including heterocyclic compounds with various dimensions of cycles, number and nature of heteroatoms. Moreover, different substituents in the aromatic ring of **1** can significantly increase the diversification of synthesized products.

Acetophenones are useful models for the development of different synthetic methods. The syntheses of heterocyclic compounds, based on products of primary transformation of aryl-1-ethanones, are considered in a number of monographs [1,2] and reviews [3,4].

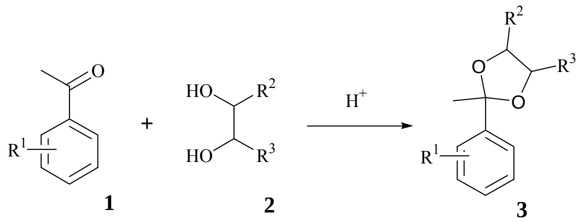
Current review is concentrated mostly on data, published in last 15 years, and investigations, which are not included in the earlier articles [1-4].

Based on the structure of aryl-1-ethanones, usually, reagents interact with methyl or carbonyl group. Further transformation of obtained substances leads to products with a larger or smaller amount of carbon atoms than starting compounds, and this overview will be presented as four main parts: a) syntheses with retention of methyl group; b) syntheses where keto group is retained; c) syntheses where both groups of acetyl fragment are transformed; d) synthetic schemes based on the products of primary transformation of acetyl group.

2. Syntheses with retention of methyl group

Among the large number of products of transformations of **1** with retention of methyl group, the first to be mentioned are 1,3-dioxolanes **3**, which are stable under neutral and basic condition. The most convenient and practical method for their synthesis is the reaction of ketones **1** with 1,2-diols **2** in presence of an appropriate catalyst.

Scheme 1

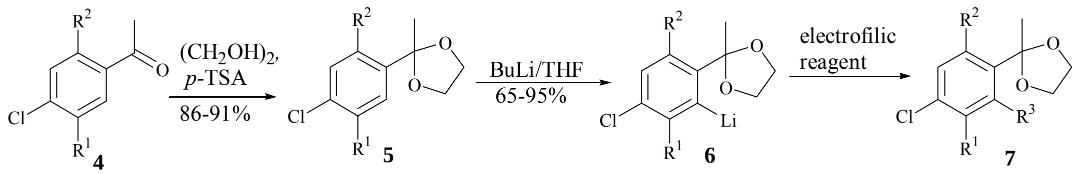


1 **2** **3**

It should be mentioned that the reaction is reversible and proceeds at the presence of acid catalysts [5]. Good yields of 1,3-dioxolanes have been obtained in the presence of an oxalic acid, benzene or toluene sulfonic acids, $HClO_4$, $ZnCl_2$, BF_3-etherate, $SnCl_4$ etc. For example, the synthesis of **3** in the presence of the Ti^{4+}-exchanged montmorillonite as a strong solid acid catalyst is described [6]. Other different heterogeneous catalytic systems are used also: natural kaolinic clay, zeolite HSZ-360, sulfated polystyrene clays, polymers corporate with different metals, triphenylphosphine iodide

[7-10]. Such catalysts have been separated by simple filtration and the possibility for the recycling process was indicated.
The cyclization of substituted benzene derivatives is an important strategy for the synthesis of benzanellated heterocyclic compounds [11]. The synthetic introduction of electrophilic substituents into position 2 (R^2=H) or 6 (R^2=Me) of **4** have led to compounds **7**, and carried out via preliminary prepared of ketals **5,6**.

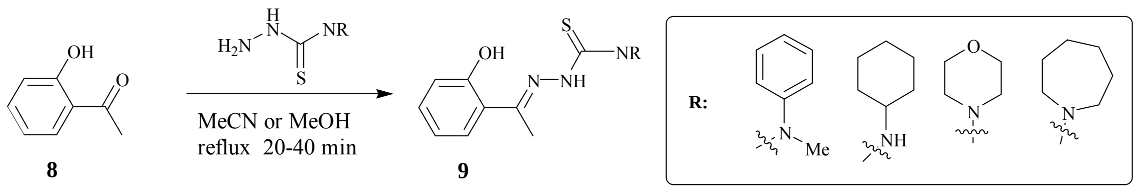
Scheme 2



R^1= H, Cl, Me; **R^2**= H, Me; **R^3**=CO_2H, SO_2Cl

Thiosemicarbazones of aryl-1-ethanones are well known to form stable complexes with transition elements and heavy metal ions. Synthesis and applications of these chelating ligands were also reported [12-14]. The similar strategy was employed for the preparation of thio-derivatives **9** from 1-(2-hydroxyphenyl)-1-ethanone **8** [15].

Scheme 3

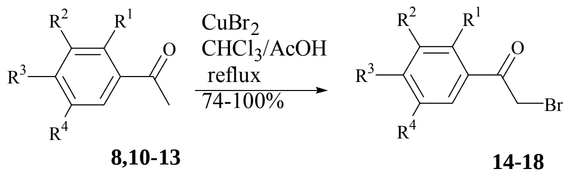


The aryl-1-ethanol chemistry has proved a powerful tool for obtaining C-C, C-N, C-Hal bonds in organic synthesis. Tremendous progresses have been made in the area of asymmetric reduction of discussed ketones to aryl-1-ethanols**.** Due to extensive body of work carried out in the area of transformation of **1**, emphasis here is focused on data that were not overviewed in the past and will be presented in the fourth part of the review.

3. Syntheses where keto group is retained

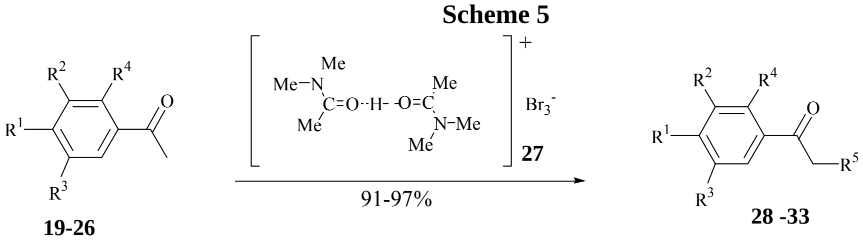
The transformations of methyl group of acetophenones provides an obvious entry to further synthesis of practically important heteroatomic compounds [3,4].

Scheme 4



8,14: R^1=OH, R^2=R^3=R^4=H; **10,15**: R^2=OH, R^1=R^3=R^4=H; **11,16**: R^3=OH, R^1=R^2=R^4=H
12,17: R^1=R^3=OH, R^2=R^4=H; **13,18**: R^1=R^4=OH, R^2=R^3=H

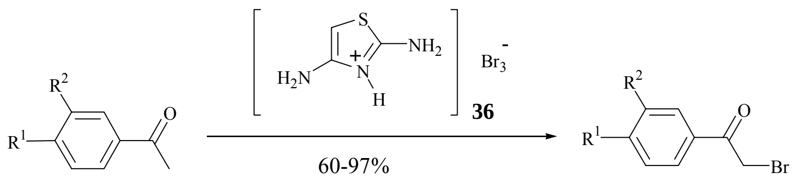
Scheme 5



19, 28: R^1=Cl, R^2=R^3=R^4=H**; 20, 29**: R^1=Br, R^2=R^3=R^4=H**; 21, 30**: R^1=OMe, R^2=R^3=R^4=H;
22, 31: R^1=R^2=Cl, R^3=R^4=H**; 23, 32**: R^1=R^2=OMe, R^3=H, R^4=Me**; 24** R^1=OMe, R^2=NO_2, R^3=R^4=H;
25 R^1=NH_2, R^2=R^3=R^4=H**; 26** R^1=NO_2, R^2=R^3=R^4=H**; 33** R^1=NH_2, R^2=R^3=Br, R^4=R^5=H

α-Bromoketones art as important intermediates in many synthetic schemes. They can be prepared by direct bromination of acetophenones in various solvents (H_2O, $CHCl_3$, CCl_4, AcOH, EtOH, MeOH, DMF) or on free solvent conditions [16]. Chemoselective bromination of 1-(hydroxyphenyl)-1-ethanones **8,10-13** into bromides **14-18** is achieved by treatment with $CuBr_2$ (scheme 4) [17]. According to another report [18], the system: Br_2-$CO(NH_2)_2$-CH_3COOH has been used as a bromination's reagent, but **27** was more effective [19].
High-yielding protocol for exclusive formation **28-32** from **19-23** using complex **27** was reported. It should be mentioned, that 1-(4-aminophenyl)-1-ethanone **25** has produced 1-(3,5-dibromo-4-aminophenyl)-1-ethanone **33** (yield not indicated) as well as the bromination of **24,26** doesn't place. This problem was solved by use of tribromine of 2,4-diamino-1,3-thiazole **36** [20].

Scheme 6

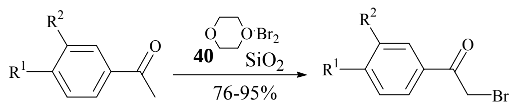


26,34,35 **37-39**

26,38: R^1=NO_2, R^2=H; **34,39**: R^1=H, R^2=NO_2; **35,37**: R^1=R^2=H;

The target products **37-39** from **26, 34** and **35** have been prepared according scheme 6.
It is well known that treatment of methylketones with bromine covalent bonding reagents leads to α-bromoketo derivatives. For example, hexabromocyclopentadiene has shown good properties as reagent for selective bromination of **35** to **37** (yield 80%) [21]. A different approach to **37** using the polymer supported bromine Amberlyst-A26 Br_3^- was described [22], but the yield in this reaction did not exceed 55%.
Chemists still carries out their reactions in solution, even when a special reason for the use of solvent cannot be found. During the last two decades it was found out that many reactions proceed efficiently in solid state. Indeed, in many cases, solid-state organic reaction occurs more efficiently and more selectively than its solution counterpart does, since the molecules in a crystal are arranged tightly and regularly [16]. The investigation of the solvent-free microwave-induced bromination of **19-21, 26, 34, 35** to **28-30, 37-39** with dioxane-dibromide **40** on the surface of SiO_2 was performed. Acidic silica gel has play twofold roles: promoting enol formation from ketone and inducing electrophilic assistance to Br-Br bond breaking.

Scheme 7

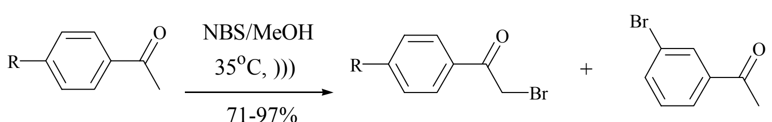


19-21, 26, 34, 35 **28-30, 37-39**

19, 28: R^1=Cl, R^2=H; **20, 29**: R^1=Br, R^2=H; **21, 30**: R^1=OMe, R^2=H
26, 38: R^1=NO_2, R^2=H; **34, 39**: R^1=H, R^2=NO_2; **35, 37**: R^1=R^2=H

Under photochemical conditions, the bromination of compounds **19, 21, 35, 41** with N-bromosuccinimide was performed, and the α-bromoketones **28, 30, 37, 42** were obtained [23]. A mixture **37**, **43** was synthesized by treatment of acetophenone **35** with NBS in the presence of *p*-toluenesulfonic acid.

Scheme 8

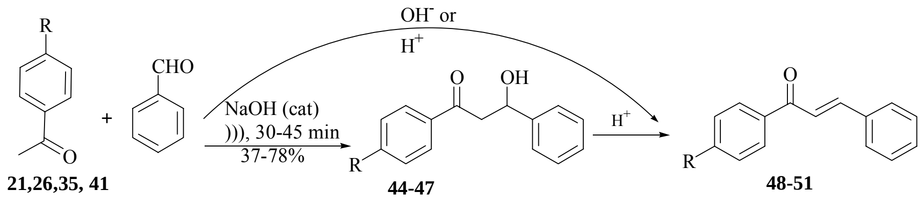


19, 21, 35, 41 **28, 30, 37, 42** **43** (29%)

19, 28: R=Cl; **21, 30**: R=OMe; **35, 37**: R=H; **41, 42**: R=Me

Benzylideneacetophenones present a class of naturally and synthetic occurring pigments, which are often referred to as "chalcones" [1, 2, 24-28]. The simplest method of synthesis of chalkones is involving the Claisen-Schmidt reaction. This is a two step reaction of acetophenones **21, 26, 35, 41** with benzaldehyde in the presence of base and result the aldols **44-47** followed by formation α,β-unsaturated ketones **48-51** (scheme 9). The water formed in this reaction is azeotropically distilled off with xylene.

Scheme 9

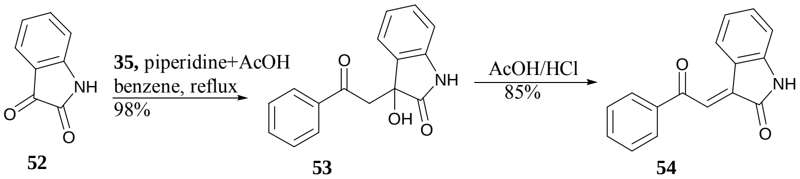


21, 44, 48 : R= 4-OMe; **26, 45, 49** : R=4-NO_2; **35, 46, 50**: R=H; **41, 47, 51**: R= 4-Me

The concentration of alkali used for this reaction usually ranges between 10-60%, but in case of fluoro acetophenones it should not be higher than 1,5% [29]. The use of an acid catalyst has been recommended for prepation of hydroxychalcones [30]. Synthesis of chalcones on the surface of SiO_2 was also reported [31]. Selective synthesis of aldols should be performed by use of ultrasound irradiation [32,33].

Another strategy was employed for the preparation of chiral aldol **53** from acetophenone **35** and 1*H*-indole-2,3-dione **52.** The condition of Knoevenagel reaction was recommended [34].

Scheme 10

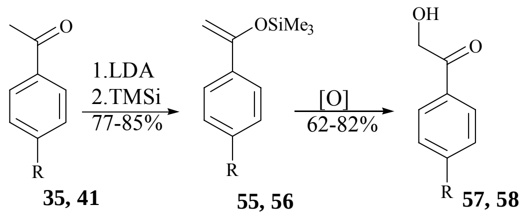


Dehydration of **53** leads to **54** – homolog of inhibitor of *Plasmodium falciparum* [35].

4. Syntheses where both groups of acetyl fragment are transformed

The α-hydroxylation of methyl group of **35, 41** is based on the initial oxidation of enol ethers **55, 56** with 3-chlorobenzenecarboperoxoic acid, chromyl chloride or iodosylbenzene [36-38].

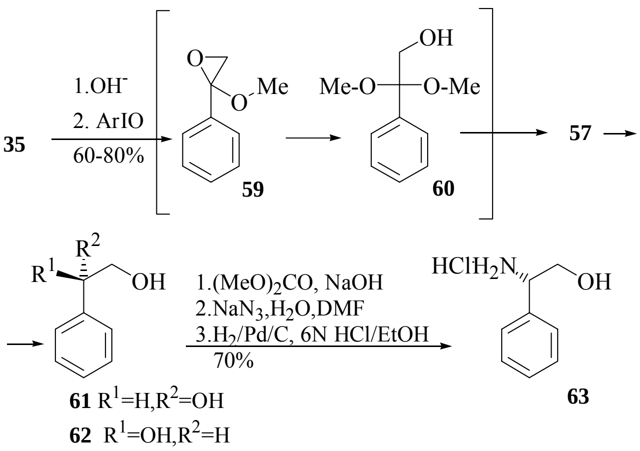
Scheme 11



35, 55, 57: R=H; **41, 56, 58**: R=Me

Yields of products **57, 58** are moderate (from 48 up to 70 %).

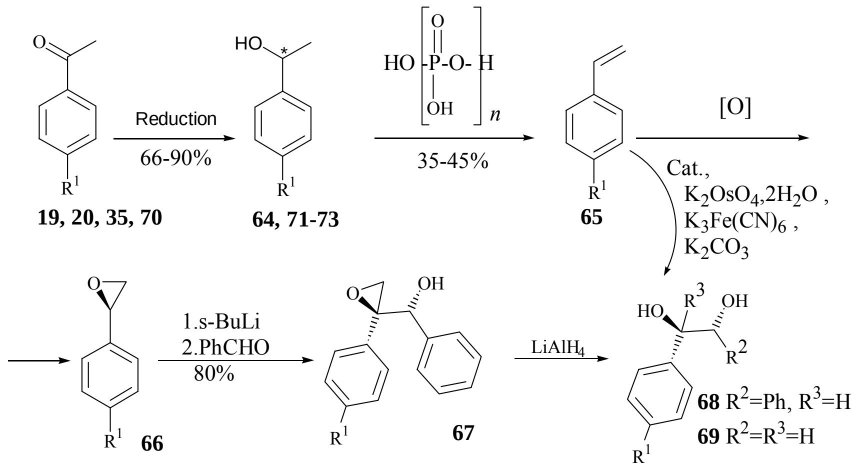
Scheme 12



The direct hydroxylation of acetophenone **35** to **57** is illustrated on the scheme 12 and includes the preliminary formation of enolate anion [39-41]. The elimination of phenyl iodide or - iodo-benzoic acid has accompanied by

addition of anion MeO- to carbonyl group with formation of epoxide **59**, hydroximethylacetal **60**, and ketol **57**, respectively. The reduction of **57** led to a mixture of epimeric 1,2-diols **61, 62** separated by the use of lipases [42].
The synthesis of the enantiomeric pure amino alcohol **63** from **61** was also reported [43].
Conversion of ketone **35** to the alcohol **64**, styrene **65**, epoxides **66, 67** and 1,2-diols **68, 69** is presented on the scheme 13 [43-47].

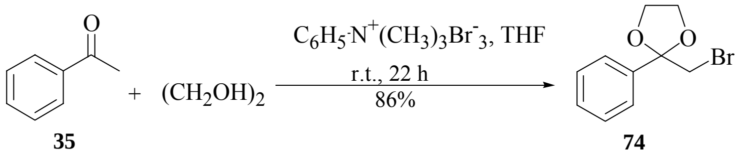
Scheme 13



35, 64-69: R^1=H; **70, 71** : R^1=F; **72** : R^1=Cl; **73** : R^1=Br

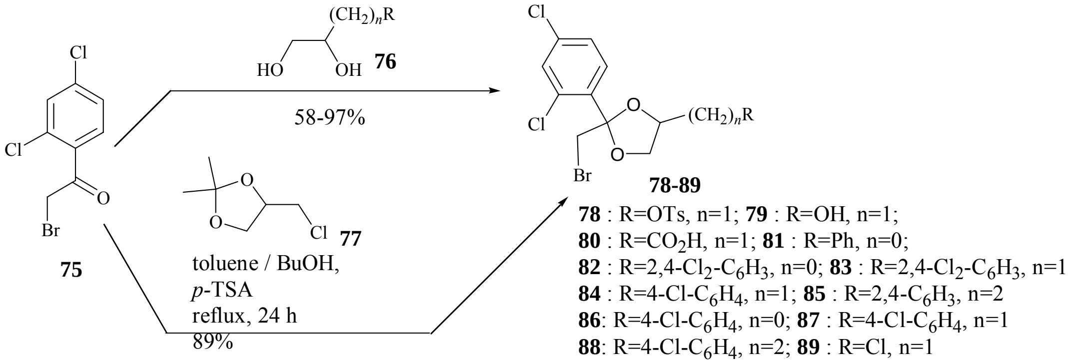
The reduction of unsymmetrical ketone to alcohols is one of the most common reactions in organic synthesis. During the reduction, nucleophile can approach both the faces of a carbonyl group of aryl-1-ethanones with an angle close to 109^o giving rise to a mixture of two isomers. The asymmetric metal complex catalysis is one of the fast developing fields of modern chemistry [48]. Not only academic but also ever growing practical and industrial interest prompts researchers to make more efforts to develop the catalytic synthesis of various enantiomerically pure **64, 71-73** [49]. It is mentioned that many research groups put most their efforts onto catalytic testings of ligands, for example for the separation of **64** via specific palladium catalysed oxidation [50]. On the other hand, the reduction of aryl-1-ethanones **19, 20, 35, 70** with complex sodium borohydride- β-cyclodextrin leads to enantio-enriched alcohols [51]. The epoxide **66** serves as a starting point in the synthesis of alcohols **67**, **68** and **69** [47]. The last compound can be synthesized (yield 94 %, 93 ee) directly from **65** by hydroxylation using optically active catalyst [52].

Scheme 14



α-Bromoketals are useful precursors in the synthesis of different organic compounds, including agrochemicals [53-56]. They can be readily prepared by a number of methods: 1) bromination of methylketones followed by protection of carbonyl group; 2) ketalization with 1,2-diols and then bromination; 3) when bromination and ketalisation going together. The synthesis of phenacylbromides as well as 1,3-dioxolanes has already been overviewed by us, and so just the one pot reaction for formation of α-bromoketals will be discussed.

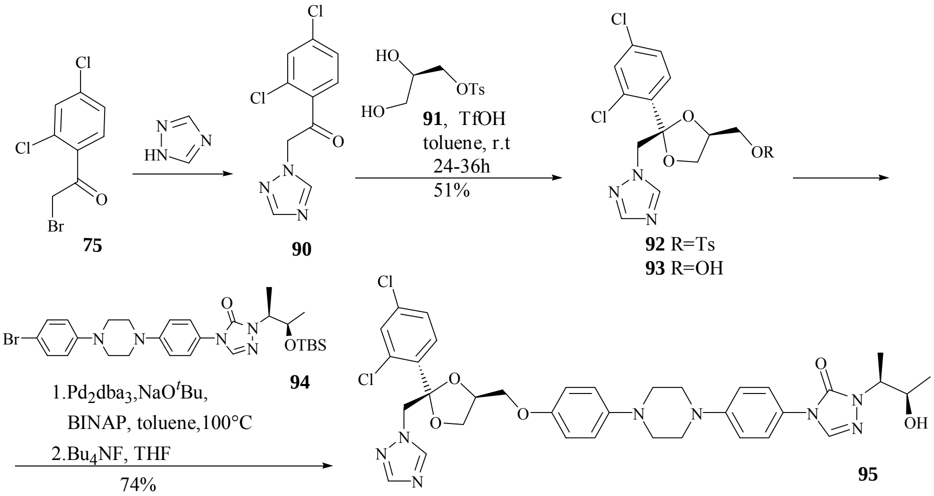
Scheme 15



78 : R=OTs, n=1; **79** : R=OH, n=1;
80 : R=CO_2H, n=1; **81** : R=Ph, n=0;
82 : R=2,4-Cl_2-C_6H_3, n=0; **83** : R=2,4-Cl_2-C_6H_3, n=1
84 : R=4-Cl-C_6H_4, n=1; **85** : R=2,4-C_6H_3, n=2
86: R=4-Cl-C_6H_4, n=0; **87** : R=4-Cl-C_6H_4, n=1
88: R=4-Cl-C_6H_4, n=2; **89** : R=Cl, n=1

Environmental and economical considerations prompt an urgent need to redesign there important processes. In this context, an example of preparation of 2-bromomethyl-2-phenyl-1,3-dioxolane **74** is presented on scheme 14 [57].
The related bromides **78-89** could be prepared in one step from 2-bromo-1-(2,4-dichlorophenyl)-1-ethanone **75** and 1,2-dioles **76** [58]. It was established that the acetalization performs in the presence of *p*-toluenesulfonic acid in a mixture of 1-butanol - benzene. Notably, in absence of 1-butanol the reaction doesn't take place or the yields are usually low [59].
The separation of diastereomeric products **79** as well as **80** can be done by use of lipase [60].
The synthesis of optically active compounds **89** from R- and S-isomers of **77** was also carried out [55]. All the attempts of ketalization **75** with enantiomerically pure epichlohydrines by method [61] have been burst.
The convergent of total synthesis of (2*R*,4*S*,2'*S*,3'*R*)-hydroxyitraconazole **95** was previously reported [62]. The described process includes the conversion of ketone **90** and 1,2-diol **91** to the corresponding acetonide **92**. Palladium-catalyzed coupling of **93** with **94** followed by deprotection was burnished **95**.

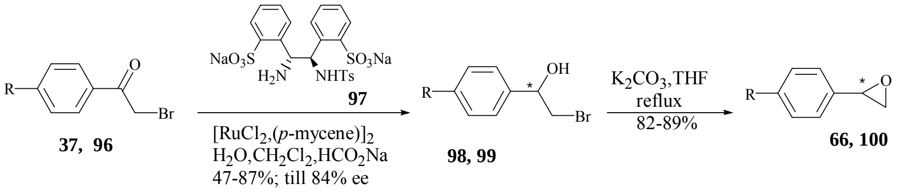
Scheme 16



5. Synthetic schemes based on the products of primary transformation of acetyl group

Heterocyclic compounds are the basis of many pharmaceutical, agrochemical and veterinary products. A large amount of references on synthetic methods of elaboration of heterocycle ring structures based on the products of primary transformation of the acetyl group of acetophenones were early summarized [1-3], however, time passes and new results have been published.
The selective transformation of bromohydrines **98, 99** obtained from 2-bromoacetophenones **37, 96** by chiral catalyst **97** reduction, to enantiomerically-pure epoxides **66** and **100** can be achieved by using K_2CO_3 as a base [63].

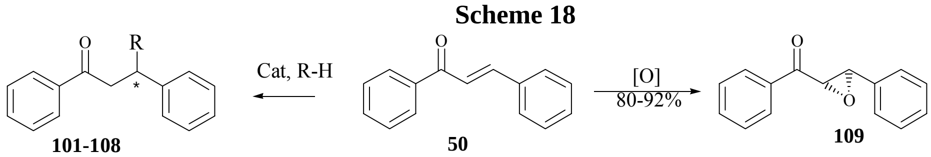
Scheme 17



37, 66, 98 : R=H; **96, 99, 100** : R=OCH_2Ph

Chalcones still remain the subjects for the studing of structure-bioactivity properties [25,64,65], but most efforts involve the generation of functional chiral molecular diversity using their α,β-unsaturated system as illustrated in Scheme 18.

Scheme 18

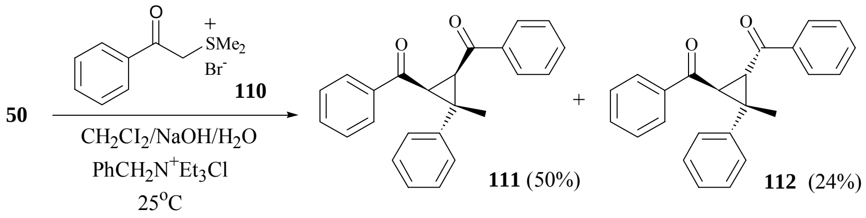


101 : R=-CH_2NO_2; **102** : R=C(O)-CH=CMe_2; **103** : R=C(O)-$(CH_2)_4$Me; **104** : R=C(O)-3-Br-C_6H_4;
105 : R=CH(Me)-C(O)-Ph; **106** : R=CH(CO_2Et)-COMe; **107** : R=CH(CO_2Et)-COMe**;** **108** : R=H

For example, the synthesis of enantio-enriched (3S)-ketone **101** was based on the mediated asymmetric catalyst conjugated 1,4-addition reaction of $MeNO_2$ to **50** [66]. The solvent-free microwave-induced reaction of **50** with wide range of aliphatic and aromatic aldehydes on the surface of SiO_2 gave adducts **102-104** [67]. According to another report, lithium alkoxides was employed as a catalyst for the Michael addition of silyl enol ethers to **50** leading product **105** [68]. The reaction of acetoacetic ester with **50** in the presence of K_2CO_3 produced mixture stereo isomers **106, 107** [69]. Selective reduction of **50** to **108** as well as asymmetric epoxidation to **109** was reviewed recently [70], and published also [71,72].

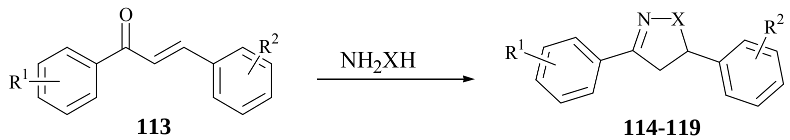
Chalcone **50** was used as a model for the studing of possibility of synthesis of 1,2-dibenzoyl-3-methyl-3-phenylcyclopropanes. It was found out that cyclopropanation by sulfur ilide, generated from salt **110**, leads to a mixture of isomers **111, 112**, although the selectivity in this reaction was not good [73].

Scheme 19



Dihydroisoxazoles **114** and dihydropyrazoles **115-119** can be prepared by the reaction of chalcones **113** with hydroxylamine, hydrazine hydrate, monosubstituted hydrazines, and thiosemicarbazide according scheme 20 [74-80].

Scheme 20

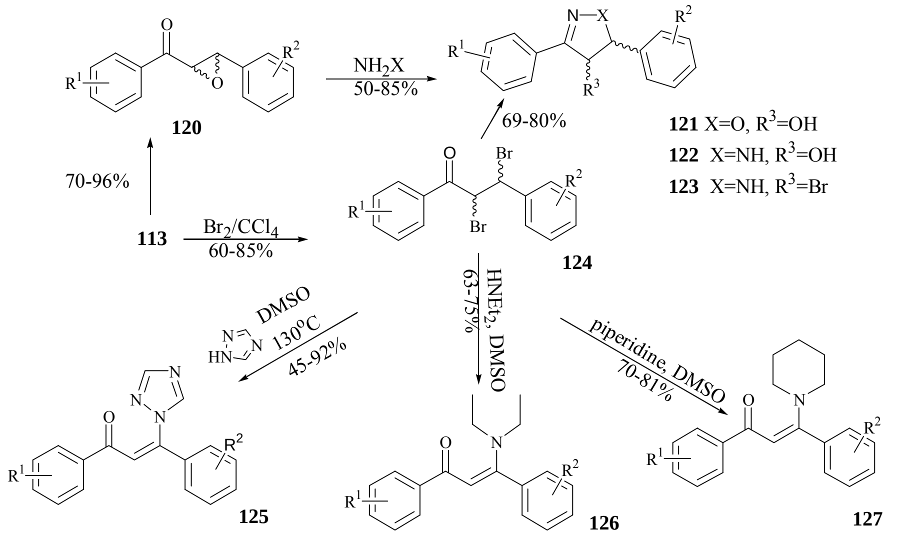


114 : X=O; **115** : X=NH; **116** : X=NAr; **117** : X=NC(S)NH_2; **118** : X=Nalkyl; **119** : X=NAc

One pot synthesis of N-acetyl-substituted dihydropyrazoles **119** was carried out in AcOH [81,82]. 1,3,5-Triphenyl-4,5-dihydro-1*H*-pyrazoles **116** can be prepared it two steps from chalcones **113** and phenyl hydrazine via hydrazone followed by the heterocyclization in boiling acetic acid. The influence of nature of the substituent in chalcone's ring on isolation of intermediate hydrazone is discussed [83]. Formation of N-carbamoyl, N-carbonyl as well as N-sulfanyl dihydropyrazoles by reaction with polymer-bound reagents was also described [84]. Synthesis of 3,5-diaryl-N-alkyldihydropyrazoles **118** from 3,5-diaryldihydropyrazoles **115** can be done by use of the phase transfer catalysis reaction [85]. Some derivatives of 3,5-diaryl-2- dihydropyrazoles **114** and 1,3,5-triphenyl-2- dihydropyrazoles **116** were found to exhibit the antidepressant activity [78,79].

4-Substituted dihydroizoxazole **121** and dihydropyrazoles **122, 123** were prepared from oxides **120** or dibromides **124** (Scheme 21) [2,86].

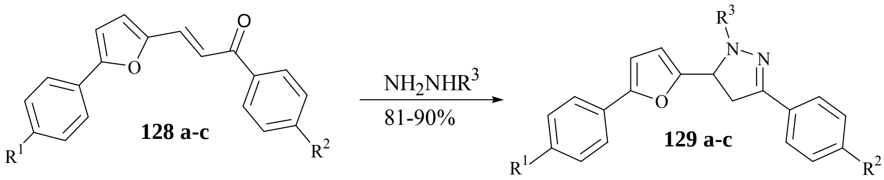
Scheme 21



Compounds **121-123** represent an unstable mixture of isomers resulting diphenylisoxazoles and diphenylpyrazoles. The treatment of the **124** with secondary amines furnished enamines **125-127** [87,88].

Antimicrobial agents **129a-c** have to be synthesized by reaction of 1-aryl-3-(5-aryl-2-furyl)-2-propen-1-ones **128a-c** with hydrazine hydrate or phenyl hydrazine [89].

Scheme 22

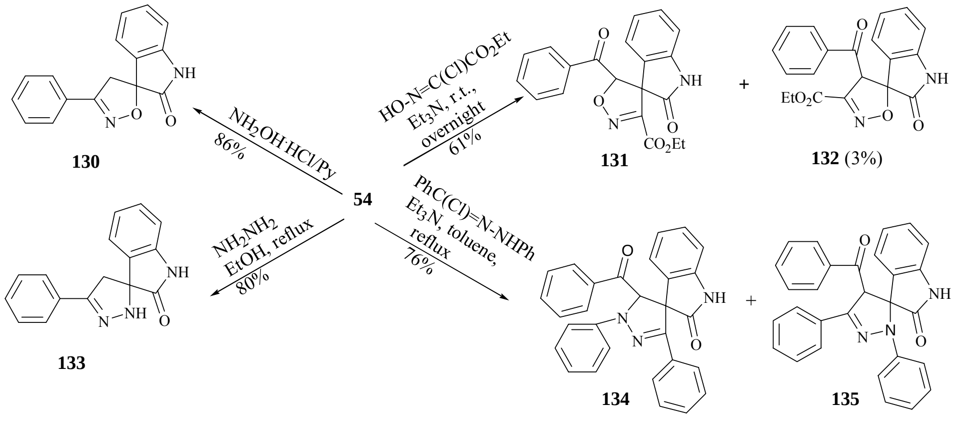


a: R^1=NO_2, R^2=Cl, R^3=H**;** **b**: R^1=Cl, R^2=H, R^3=Ph; **c**: R^1=Br, R^2=Me, R^3=H

The stead of spiran stems among natural and synthetic products arouses a great interest in there. A special position among these compounds is occupied by spiro-indolin-2-ones. There are many methods of synthesis of such type derivatives**,** which are discussed in review [90].

α,β-Unsaturated ketone **54** can be readily transformed into spiro-products **130** and **133** upon treatment with hydroxylamine, hydrazine hydrate [74,91,92].

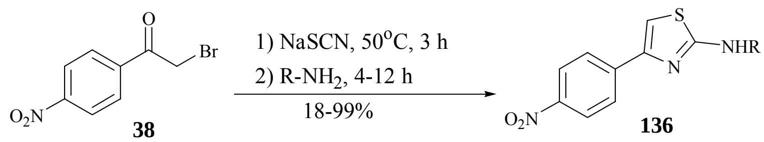
Scheme 23



Regioselective cycloaddition of carboethoxyformonitrile oxide (generated *in situ* from hydroxamoyl chloride) to **54** could be regarded as one of the approaches to spiroproducts **131** [93]. The content of regioisomer **132** is not more than 3%. The same author reported the synthesis of mixture of **134** and **135**.

The syntheses of organic compounds starting from α-halogeno ketones were overviewed [3,94]. Based on this information, new data for the synthesis of heterocyclic systems will be reviewed. For example, N-substituted 2-aminothiazoles **136** are synthesized in one-pot procedure using **38** and amines (Scheme 24) [95].

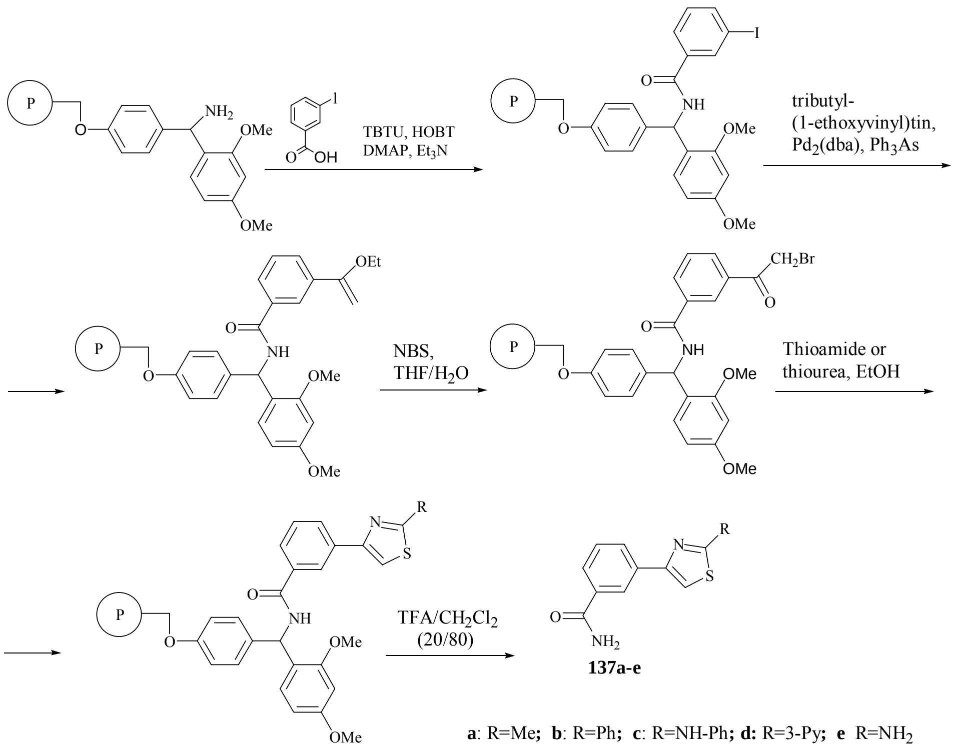
Scheme 24



Selectivity of the reaction decreases for α,α-disubstituted amines, and with α,α,α'-trisubstituted amines no reaction occurs. Only ethanol proved to be a suitable solvent for the described above transformation; the yield of target compound was very poor in DMF or acetonitrile.

Authors [96] have reported the solid support synthesis of 2,4-disubstituted aminothiazoles. Rink amide resin with loaded 3-iodobenzoic acid was involved in Pd(0) coupling reaction with tributyl(1-ethoxyvinyl)tin followed by bromination leads to bromoketones. Last were condensed with thiourea and thioamide, followed by trifluoroacetic acid cleavage from resin, to give targets **137 a-e** (total yields 61-90%).

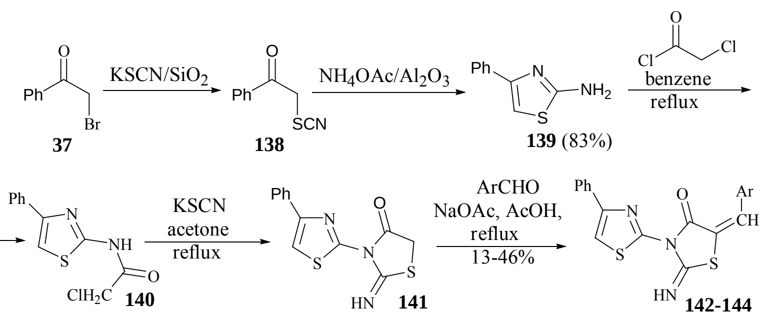
Scheme 25



a: R=Me; **b**: R=Ph; **c**: R=NH-Ph; **d:** R=3-Py; **e** R=NH_2

2-Aminothiazole **139** was obtained from the **37** in one-pot reaction, using supported reagents systems KSCN/SiO_2-NH_4Oac/Al_2O_3 (Scheme 26) [97].

Scheme 26

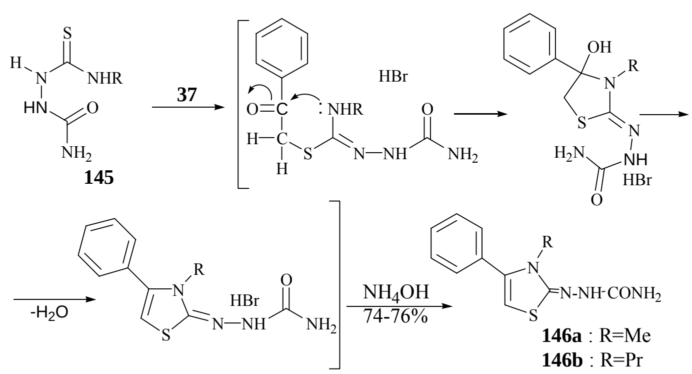


142 : Ar=2-NO_2-C_6H_4; **143** : Ar=3-NO_2-C_6H_4; **144** : Ar=2-Cl-C_6H_4

First, 2’-bromoacetophenone **37** reacts with KSCN/SiO_2, and then the obtained α-thiocyanatoketone **138** reacts with NH_4Oac/Al_2O_3 to afford final product **139**. Fungicides **142-144** could be prepared via aminothiazoles **140**, **141** [98].

As a new variant of Hantzsch thiazole synthesis, the reactions of 1-alkyl-2-thiobiureas **145** with 2-bromo-1-phenyl-1-ethanone **37** yielded 3-alkyl-4-aryl-2-semicarbazono-Δ^4-dihydrothiazoles **146a,b** was presented [99].

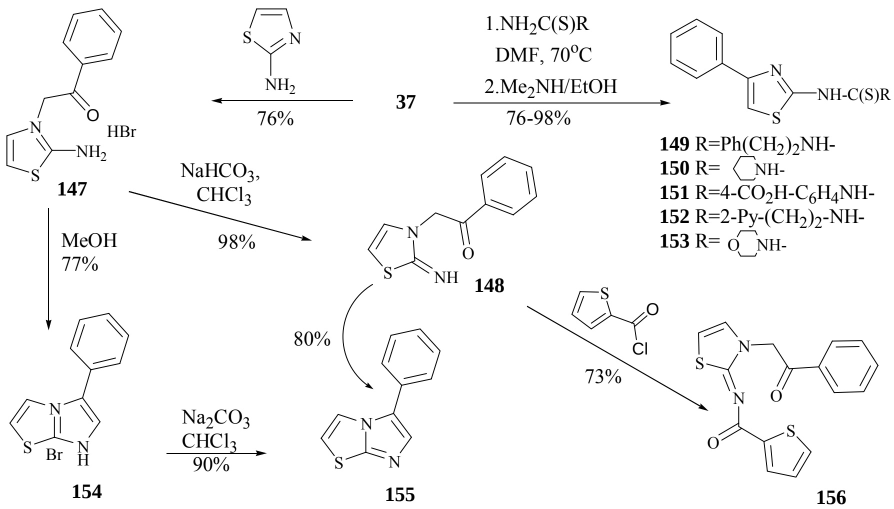
Scheme 27



146a : R=Me
146b : R=Pr

The combinatoric method for synthesis the molecular libraries of 2-aminothiazoles **149-153** is based on use of DMF as a solvent and dimethylamine as acceptor of HBr [100].

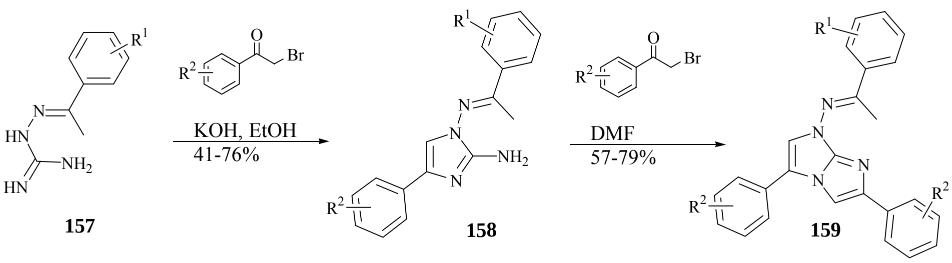
Scheme 28



The imidazo[2,1-*b*]thiazoles **154,155** were prepared from 2-aminothiazole and **37** [101]. The adduct **147** was used for the synthesis of ketones **148, 156**.

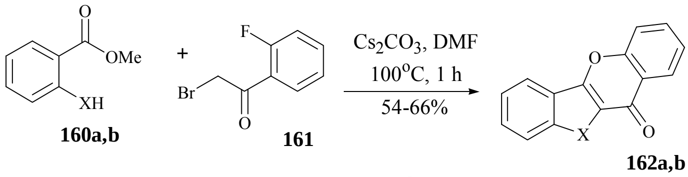
We established that 2-amino-1-arylideneaminoimidazoles **158** and 1-arylideneaminoimidazo[1,2-*a*]imidazoles **159** can be synthesized through combination of hydrazones **157** as well as 2-bromo-1-aryl-1-ethanones [102].

Scheme 29



One-pot procedure for the rapid synthesis of 5,11-dioxa- and 5-oxa-11-thiabenzo[*b*]fluoren-10-ones **162a,b** via condensation of esters of salicylic and thio-salicylic acids **160a,b** with α-bromoketone **161** was discovered [103].

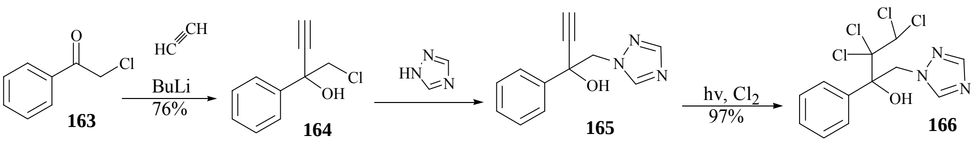
Scheme 30



a : X=O**;** **b** : X=S

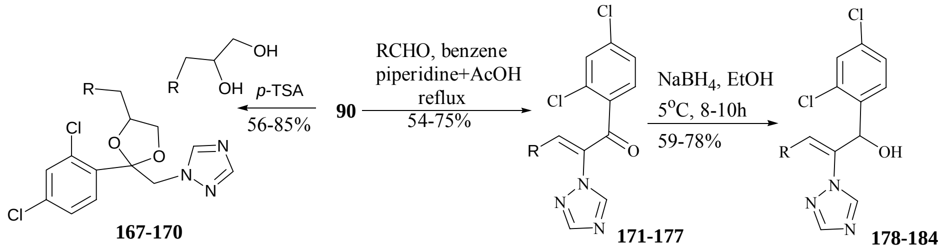
The preparation of 1,2,4-triazolechlorohydrine **166** has involved three step process transformation of chloroketone **163** via alkynes **164, 165** as illustrated in Scheme 31 [103].

Scheme 31



We reported our efforts to find the relationship of the bioactivity from the nature of substituents in 1,2,4-triazoles **167-178** [104,105]. Condensation of ketone **90** and aldehydes (Knoevenagel reaction) gives the specific formation of *Z*-isomer of N-vinyl-1,2,4-triazoles **171-177**. Synthesized allylic alcohols **178-184** and its precursors exhibit anti-fungal and anti-bacterial activity. The selective synthesis of 2,4-bis(azolylmethyl)-2-(2,4-dichlorophenyl)-1,3-dioxolanes **169, 170** has to be carried out via preliminary preparation of alcohols **167** and corresponding mesylates **168** [59].

Scheme 32

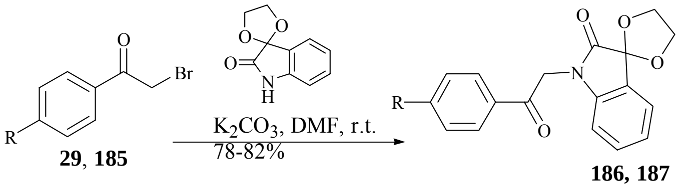


167 : R=OH; **168** : R=OMs; **169** : R=-1,2,4-Tr; **170** : R=Im; **171, 178** : R=-n-C_3H_7; **172**, **179** : R=-i-C_3H_7; **173, 180** : R=-n-C_4H_9; **174, 181** : R=-i-C_4H_9; **175, 182** : R=-3-Py; **176, 183** : R=-Ph; **177, 184** : R=-4-Cl-C_6H_4

The computer-aided study "structure-activity" of synthesized compounds was also reported [106].

Recently, we have select 2-bromo-1-(4-halogenophenyl)-1-ethanones **29**, **185** as an intermediates for the synthesis of new anxiolytics **186, 187** (Scheme 33) [107].

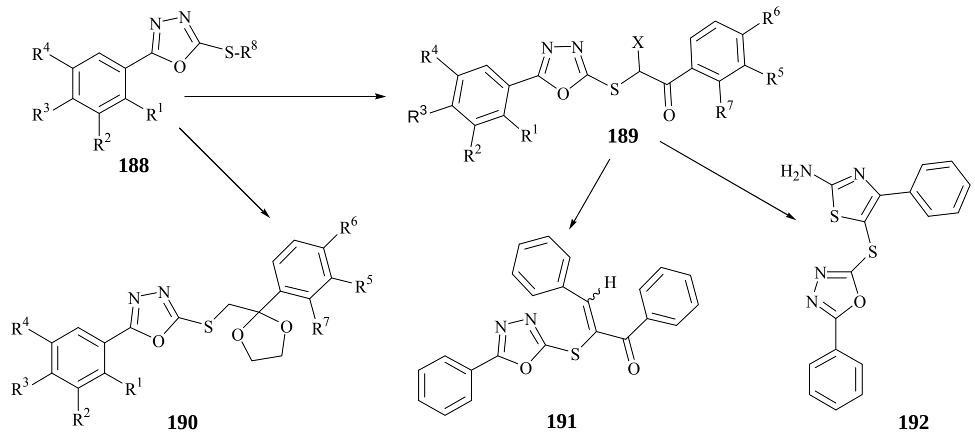
Scheme 33



29, 186 : R=Br; **185, 187** : R=F

Also, a series of 2,5-disubstituted-1,3,4-thiadiazoles **188-192** aws designed and synthesized, and these compounds were screened for anti-tuberculosis activity against *Mycobacterium tuberculosis* H37Rv [108].

Scheme 34



It was found that 1,3-dioxolane derivatives **190** are less active than the corresponding keto-precursor compounds **189**. Compound **190** (R^1=R^2=R^3=R^4=R^5=R^6=R^7=H) is a notable exception. The last compound showed the highest target activity (82%) among all the 5-aryl-2-thio-1,3,4-oxadiazoles.

6. Conclusions

The present compilation showed clearly the diversity in the field of synthetic organic chemistry by use of the acetyl group of aryl-1-ethanones. In the future, more complex target compounds, new methodology will be required for rapid construction of molecules bearing unusual substitution patterns. Thus, work is being continued in an effort to elucidate innovative new regio-, stereo- and enantio-selectively processes using the acetophenones to obtain products with target properties.

7. Acknowledgments

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