# Heterocycles as versatile bulding blocks in different synthetic strategies

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**Abstract**
Heterocycle-Heterocycle Synthetic Strategies (HHSS) were based on different types of reactions e.g. cycloaddition, cyclocondensation, molecular rearrangement, ANRORC. Spiro, condensed noncondensed, heterocycles were obtained via HHSS from easy one-pot reactions in moderate to high yields.

**Keywords:** Cyclimides, fused oxazines, fused pyrimidines, fused pyridazines, fused pyrans, fused thiopyrans

## Contents

## Introduction

Heterocycles can offer elegant and efficient routes for building heterocyclic systems in different synthetic strategies including cycloaddition, cyclocondensation, molecular rearrangements, ANRORC, and ANRORC with molecular rearrangement. Imides, 1,3-oxazoles, uracils, 2,3-oxazines, pyridazines, 2,3-benzoxazines, quinazolines, pyridopyridazines, benzopyranes, benzothiopyranes, and spirooxiranes were used as useful building blocks in different synthetic pathways for the synthesis of spiro, condensed, and noncondensed heterocyclic systems.

This lecture will present the context and background to our work in the area of synthetic heterocyclic chemistry. We illustrate the idea of heterocycle-heterocycle synthetic strategies (HHSS) in the following figure 1.

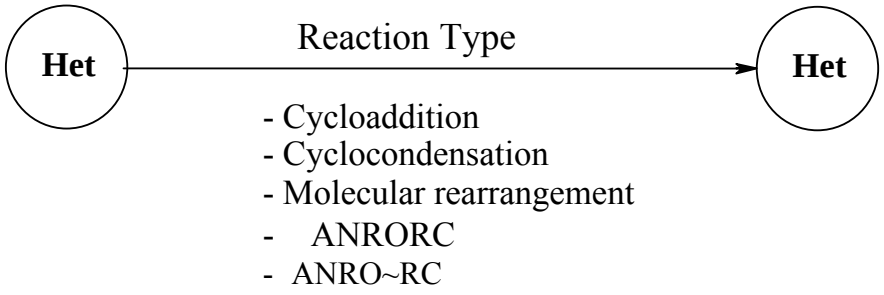


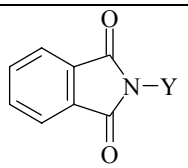

**Figure 1**

## 1. Cyclic imides as building blocks

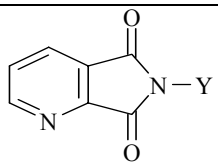
In our studies on the HHSS, cyclic imides **1-2** were used as versatile building blocks in synthesis of different target heterocyclic systems, e.g. benzoxazines, pyridooxazines, quinazolines pyridopyrimidines.

Different building strategies were used based on ANRORC, ANRO~RC, molecular rearrangement, cyclocondensation, and cycloaddation reactions.

**Table 1.** Cyclic imides



| 1 | Y |
|---|---|
| a | - OH |
| b | - $OSO_2$ - $C_6H_5$ |
| c | - $OSO_2$ $C_6H_4$ $CH_3$ (P.) |



| 2 | Y |
|---|---|
| a | OH |
| b | $OSO_2$ - $C_6H_5$ |

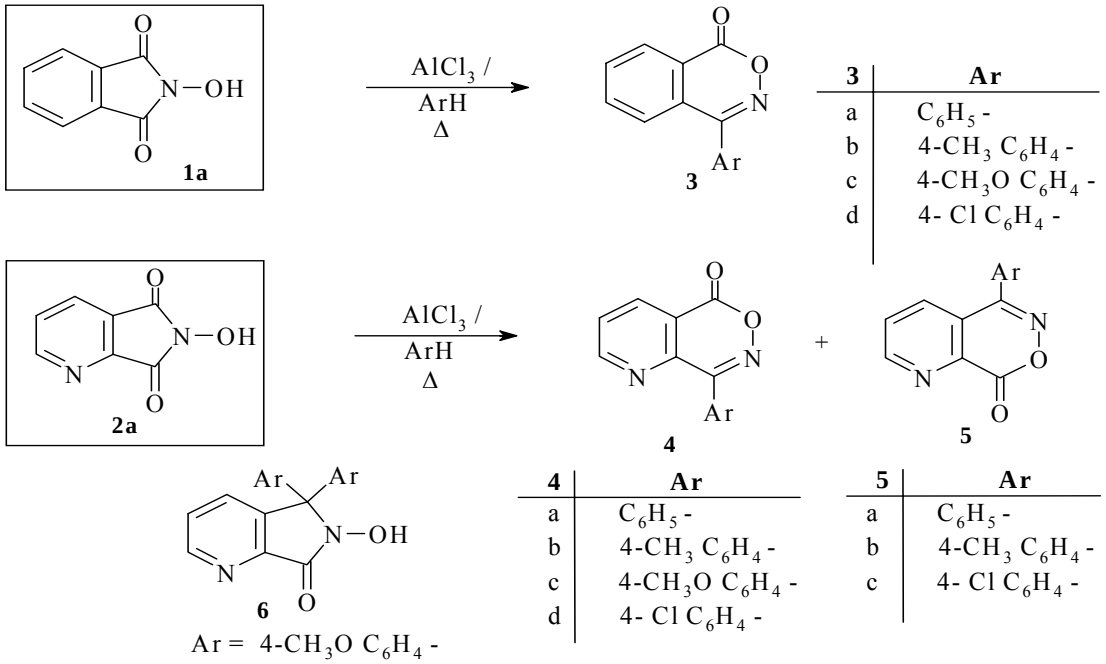
### 1.1. *N*-Hydroxyimides

*N*-Hydroxyimides **1a, 2a** can be used in synthesis of condensed oxazines via one – pot reaction. The reaction takes place via Lewis acid – catalyzed 1,3-acylmigration followed by Beckmann rearrangement.

*N*-Hydroxyphthalimide[1] **1a** reacts with anhydrous $AlCl_3$ in aromatic substrates under reflux to give 4-aryl-*H* [2, 3]-benzoxazin-1-ones[1, 2] **3a-d** in 28 – 35% Yields.

Similarly, *N*-hydroxy-pyridine-2,3-dicarboxylic imides[3] **2a** reacts with anhydrous $AlCl_3$ in aromatic substrates under the same reaction condition to give a mixture of two isomeric pyridooxazines, namely 8-arylpyrido[2,3-*d*][1,2]oxazin-5-ones **4a-d** in 20-24% yields, and 5-arylpyrido-[3,2-*d*] [1,2] oxazin-8-ones **5a-c** in 35 – 45% yields.

In the case of anisole a mixture of 8-[4-anisyl] pyrido[2,3-*d*][1, 2]oxazin-5-one **4c**, in 6% yield, and 5, 5-di-[4.anisyl]6-hydroxypyrrolo[3, 4-*b*]pyridine-7-one **6** was obtained in 49% yield (Scheme 1).




| 3 | Ar |
|---|---|
| a | $C_6H_5$ - |
| b | 4-$CH_3$ $C_6H_4$ - |
| c | 4-$CH_3O$ $C_6H_4$ - |
| d | 4- Cl $C_6H_4$ - |

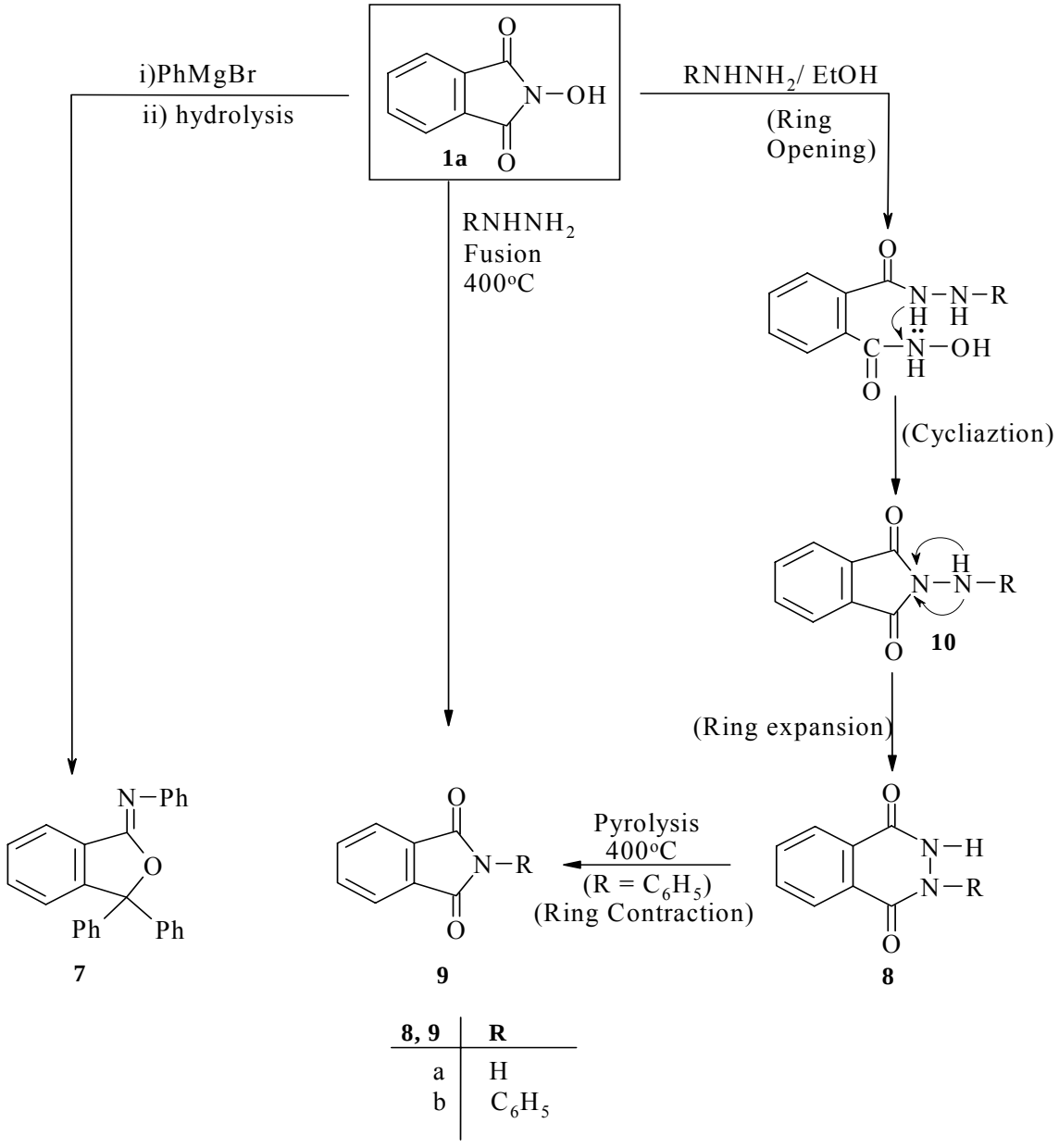
| 4 | Ar |
|---|---|
| a | $C_6H_5$ - |
| b | 4-$CH_3$ $C_6H_4$ - |
| c | 4-$CH_3O$ $C_6H_4$ - |
| d | 4- Cl $C_6H_4$ - |

| 5 | Ar |
|---|---|
| a | $C_6H_5$ - |
| b | 4-$CH_3$ $C_6H_4$ - |
| c | 4- Cl $C_6H_4$ - |

**Scheme 1.** HHSS based on molecular rearrangements.

*N*-Hydroxyphthalimide **1a** reacts with phenyl magnesium bromide to give 1,1-diphenyl-3-(phenylimino)-1,3-dihydrobenzo[*c*]furan **7** in 69% yield.[4] The reaction mechanism might explained in terms of ring opening followed by Beckmann rearrangement, and then cyclization. **1a** was used in synthesis of 1,4-phthalazinediones[4] **8a,b** in 80% yield via the reaction with hydrazines in acetic acid or ethanol. Fusion of **1a** with hydrazines at 400°C gives phthalimides **9a,b** in 62-79% yields.

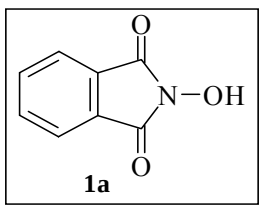
Pyrolysis of 2-phenyl-1,4-phthalazinedione **8b** at 400°C gives *N*-phenylphathalimide **9b** via ring contraction. Fusion of *N*-anilinophthalimide **10** at 200°C gives **8b** via ring expansion. (Scheme 2).

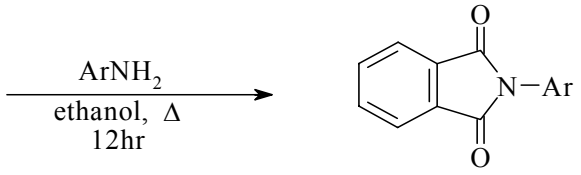



**Scheme 2**

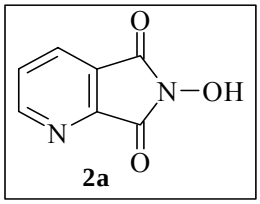
*N*-Hydroxyphthalimide **1a** reacts with ammonia and aromatic amines in ethanol under reflux to give *N*-arylphthalimides **9a-k** in 65-80% yields.[4]

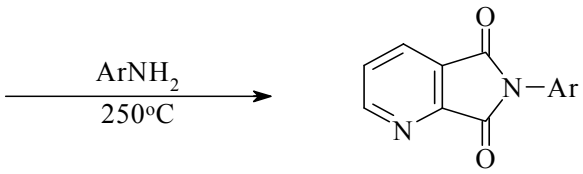
Similarly, *N*-hydroxypyridine dicarboxylic imide **2a** reacts with aromatic amines at 250°C to give *N*-arylpyridine dicarboxylic imides **11a-d** in 80-82% yields [3] (Scheme 3).




| 9 | Ar | 9 | Ar |
|---|---|---|---|
| a | H | f | 4-$CH_3OC_6H_4$ - |
| b | $C_6H_5$ | g | 2-Cl $C_6H_4$ - |
| c | 2-$CH_3$ $C_6H_4$ - | h | 4-Cl $C_6H_4$ - |
| d | 4-$CH_3$ $C_6H_4$ - | i | 4-Br $C_6H_4$ - |
| e | 2-$CH_3O$ $C_6H_4$ - | k | 4-$NO_2$ $C_6H_4$ - |

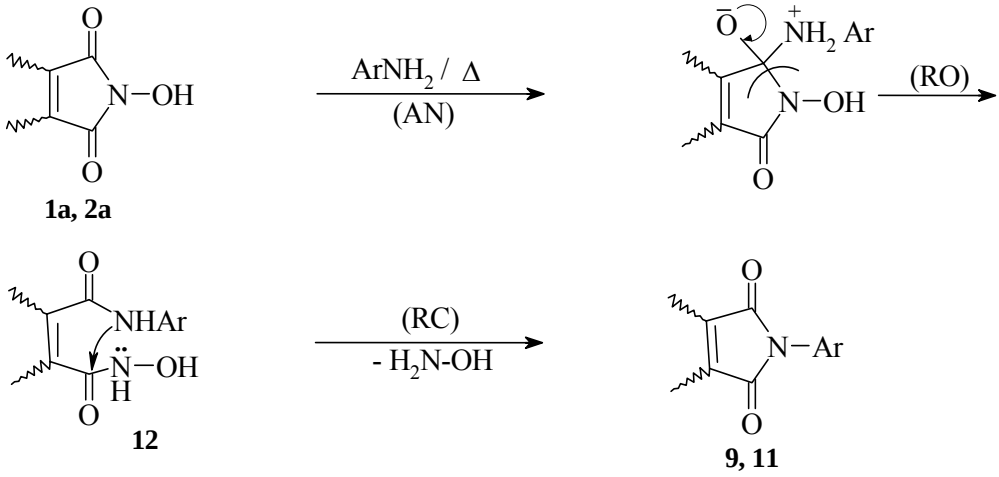



| 11 | Ar |
|---|---|
| a | $C_6H_5$ |
| b | 4-$CH_3$ $C_6H_4$ - |
| c | 4-$CH_3O$ $C_6H_4$ - |
| d | 4-Cl $C_6H_4$ - |

**Scheme 3**

The reaction probably takes place via the following mechanism (Scheme 4).

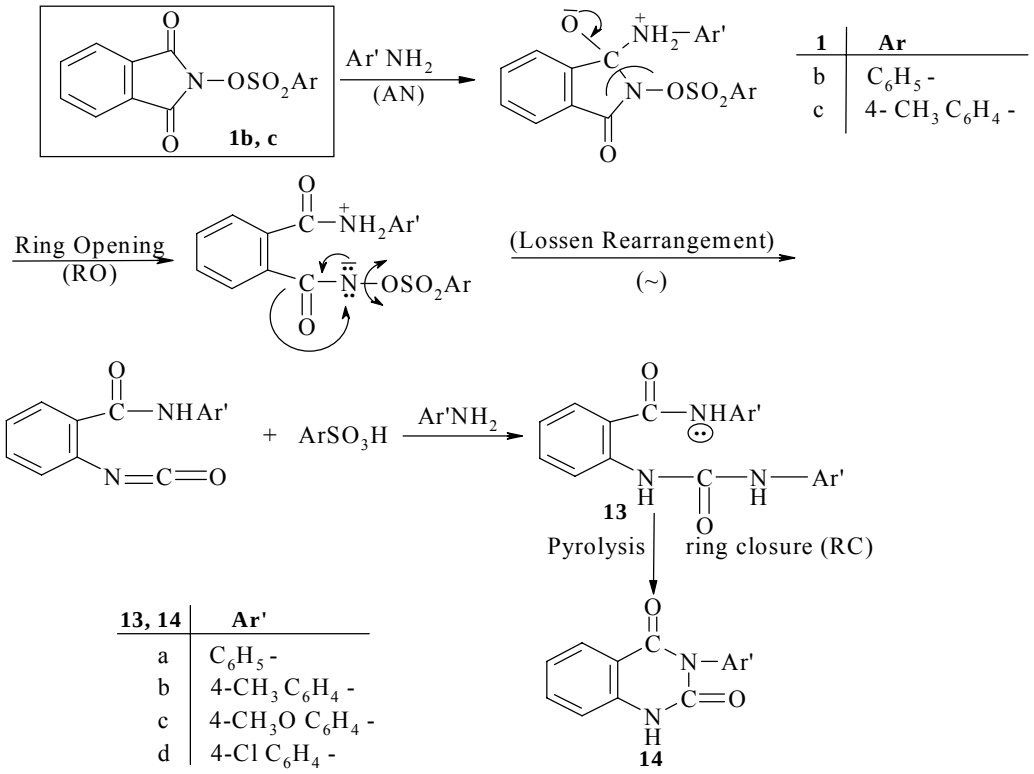



**Scheme 4.** ANRORC mechanism.

### 1.2. *N*-Arylsulphonyloxy cyclic imides

*N*-Arylsulphonyloxy cyclic imides **1b,c** and **2b** were used as building blocks in synthesis of condensed pyrimidines.

*N*-Arylsulphonyloxyphthalimides **1b,c** react with aromatic amines to give diarylurea derivatives **13a-d**, which upon pyrolysis yield, 3-aryl-1,2,3,4-tetrahydroquinazoline-2,4-diones **14a-d** in 40-60% yields (Scheme 5).



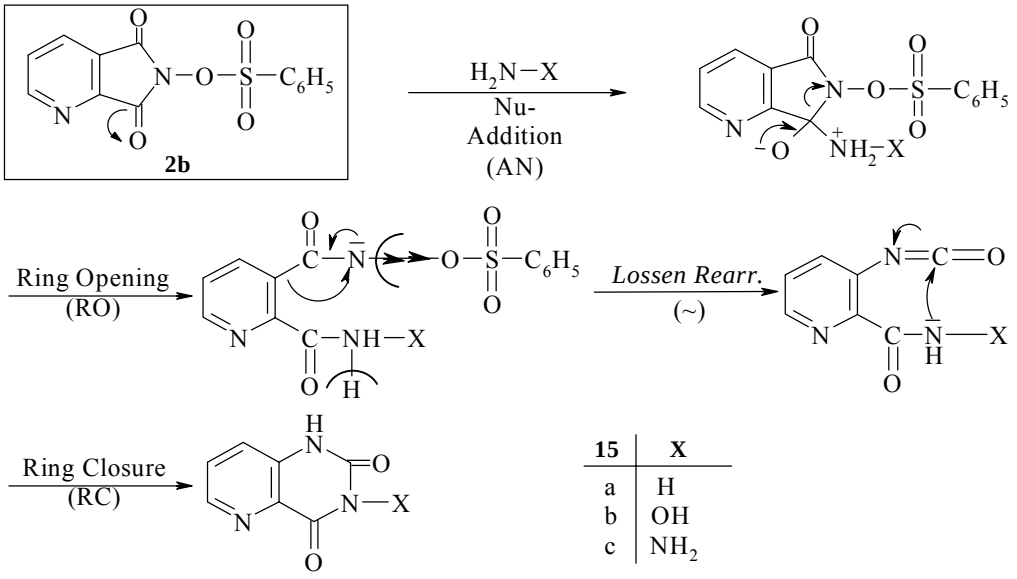

| 1 | Ar |
|---|---|
| b | $C_6H_5$ - |
| c | 4- $CH_3C_6H_4$ - |

| 13, 14 | Ar' |
|---|---|
| a | $C_6H_5$ - |
| b | 4-$CH_3C_6H_4$ - |
| c | 4-$CH_3O C_6H_4$ - |
| d | 4-Cl $C_6H_4$ - |

**Scheme 5**

The reaction of *N*-benzenesulphonyloxy-pyridine2,3-dicarboxylic imide **2b** with ammonia, hydroxylamine and hydrazine now constitutes a facile one- pot synthesis of pyrido[3,2-*d*]pyrimidine-2,4-dione derivatives **15a-c** in 63–74% yields.[5]

Our synthetic strategy depends on nucleophilic addition (AN) of amines followed by ring opening (RO), then Lossen rearrangement (~) followed by ring closure (RC) i.e. (ANRO ~ RC) ring transformation (Scheme 6).




**Scheme 6.** ANRO ~ RC type ring transformation.

Recently pyrido[2,3-*d*]pyrimidines have been prepared from pyrimidinones via regioselective cyclocondensation reaction.[6]

## 2. Spirooxiranes as building blocks

Spirooxiranes **16,** and **17** offer new synthetic routes to target spiro, and condensed heterocycles via one-pot cycloaddition reaction.

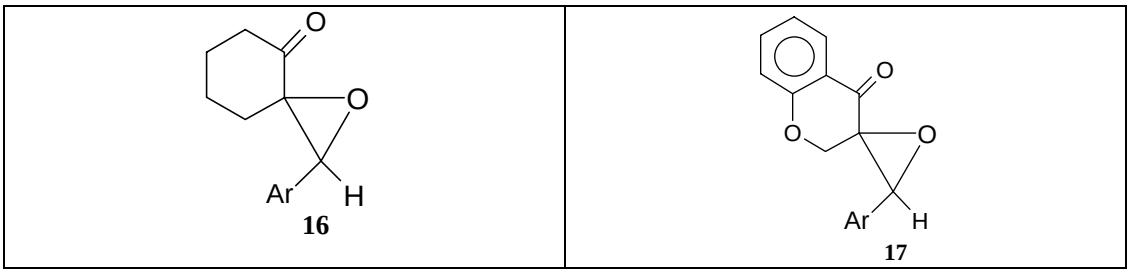
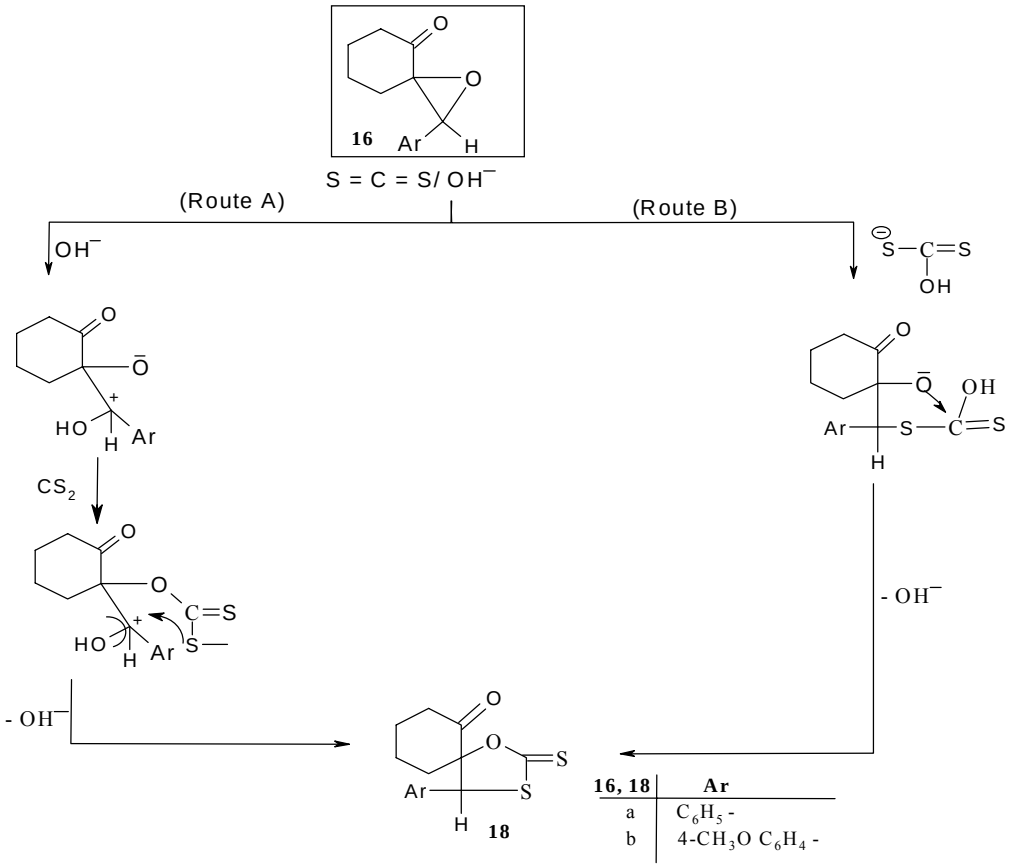



**Figure 2.** Spirooxiranes

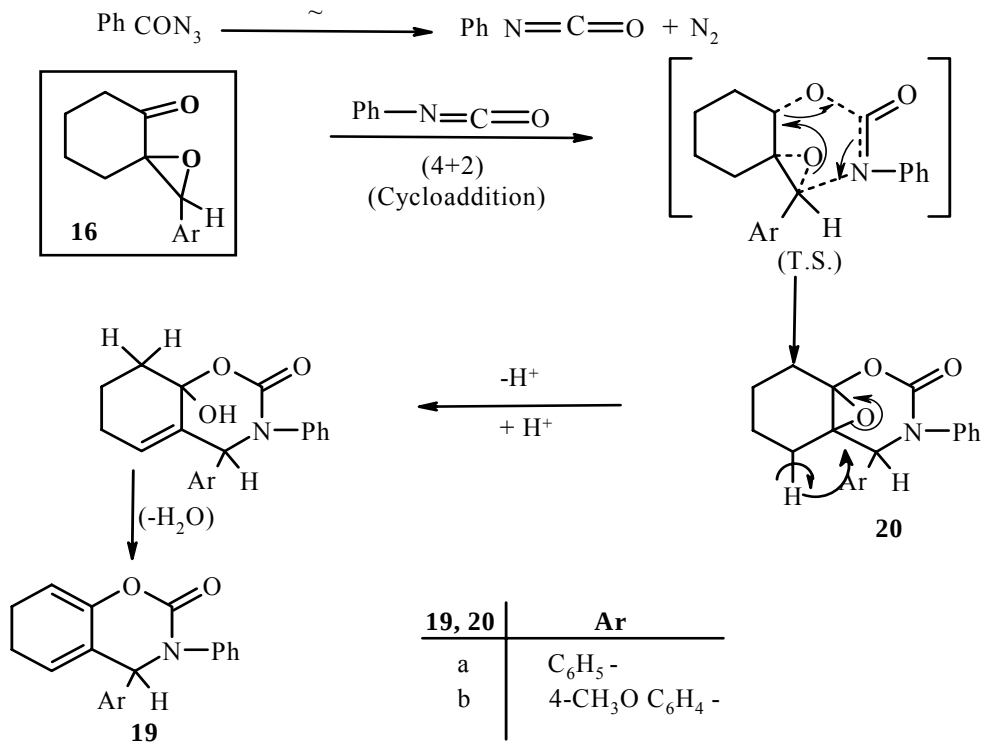
### 2.1. 2-Aryl-1-oxaspiro (2,5) octa-4-ones

2-Aryl-1-oxaspiro(2,5)octa-4-ones **16a,b** our favorite building blocks, were prepared in the usual way.[7] Compounds **16a,b** were reacted with $CS_2$ in alkaline medium to produce 4-aryl-1-oxa-3-thiospiro(4,5)deca-2-thione-6-ones **18a,b** in 50-60% yields. The reaction takes place via cycloaddition reaction (Scheme 7).



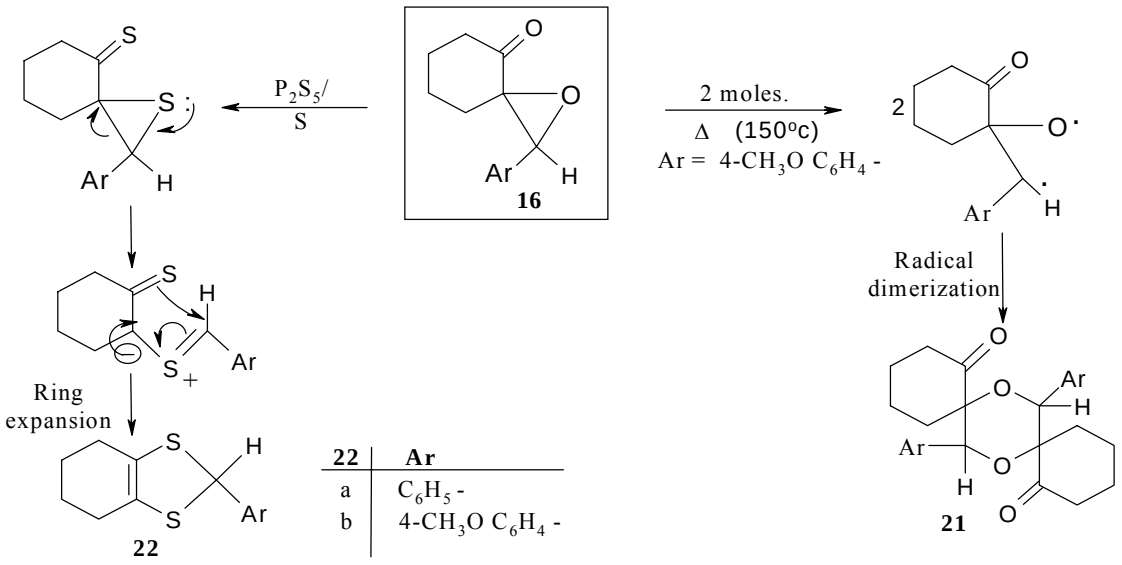

**Scheme 7.** HHSS based on cycloaddition reaction.

Compounds **16a,b** reacted with benzoyl azide in benzene under reflux to give 6,7-dihydro-3,4-diarylbenz-1,3-oxazin-2-ones **19a,b** via a novel (4+2) cycloaddition reaction in which spirooctanone acts as 1,4-dipole to give intermediate adduct **20** followed by opening of the oxirane ring with elimination of a molecule of water to give the final product **19a,b**[8] (Scheme 8).




**Scheme 8.** HHSS based on (4+2) cycloaddition reaction.

When 2-(*p*-anisyl)-1-oxaspiro(2,5)octa-4-one **16b** was heated at 150°C for one hr, bis-spirodioxane **21** was obtained in 30% yield,[8] via radical dimerization reaction (Scheme 9).



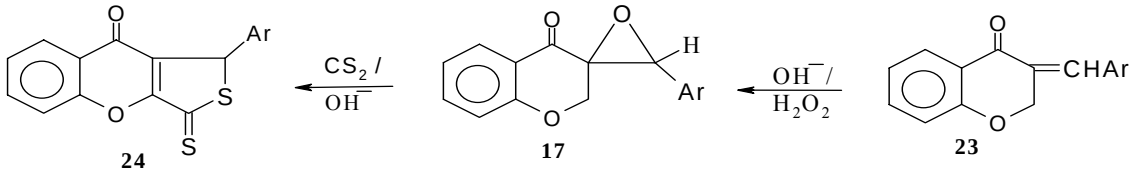

**Scheme 9.** HHSS based on Ring expansion and radical dimerization reactions.

Thiation of **16a,b** with $P_2S_5$ in the presence of sulfur powder yielded 2-aryl-1,2,3,4-tetrahydrobenzo (5,6-*d*)-1, 2,-dithiols **22a, b** in 45-50% yields.[8]

### 2.2. 3`-Aryl-(3`*H*)(2*H*)-spirooxirane (2',3)-benzopyran-4-ones

3'-Aryl-(3'*H*)(2*H*)-Spirooxirane(2',3)benzopyran-4-ones **17a-c** were prepared in (70-75%) yields via the reaction of the corresponding arylmethylene benzopyran-4-ones **23a-c** with ($H_2O_2/OH^-$).[9]

Spirooxiranes **17a-c** reacted with carbon disulfide in the presence of ethanolic sodium hydroxide to give-4-aryl-2-thioxo-(4*H*)-thieno [3,4-*b*]-benzopyran-4-ones **24a-c** in 50 - 60% yields. (Scheme 10).




| 17, 23, 24 | Ar |
|---|---|
| a | 4-$CH_3$ $C_6H_4$ - |
| b | 4-$CH_3O$ $C_6H_4$ - |
| c | 4- Cl $C_6H_4$ - |

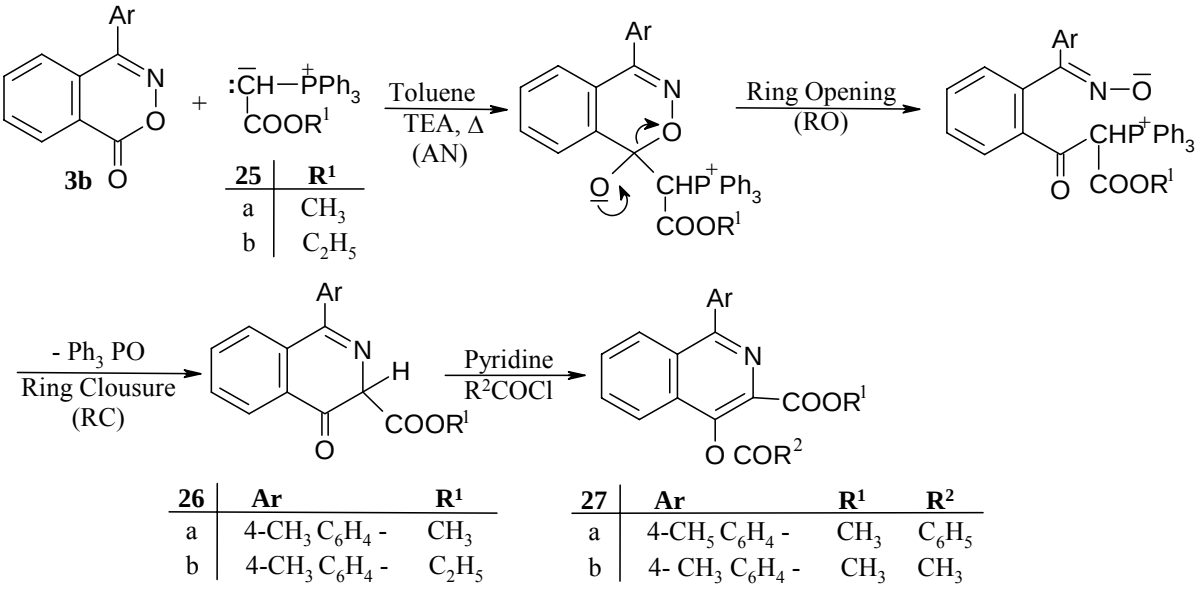
**Scheme 10.** HHSS based on cycloaddition reaction.

## 3. Oxazines as Building Blocks

We have developed a new approach to the synthesis of condensed nitrogen heterocycles e.g., (quinazolines, pyridopyrimidines, isoquinolines), based on using condensed oxazines **3-5** in the (ANRORC) ring transformation.

### 3.1. 2, 3-Benzoxazin-1-one

4-(4-Methylphenyl)-2,3-benzoxazin-1-one **3b** was used as a precursor in a facile one-pot new synthetic route to isoquinolines. When **3b** reacted with (methoxycarbonyl) methylenetriphenyl phosphorane **25a** in boiling toluene in the presence of triethylamine, methyl 1-(4-methylphenyl)4-oxo-3*H*-isoquinoline-3-carboxylate **26a** was obtained in 74% yield [10]. Similarly, treatment of **3b** with **25b** afforded **26b** in 68% yield. Treatment of **26a** with benzoyl chloride or acetic anhydride in pyridine gave the expected O-benzoyl, and O-acetyl derivatives **27a,b** in 72% and 75% yields, respectively. The reaction takes place via the (ANRORC) mechanism ( Scheme 11).




**Scheme 11.** HHSS based on ANRORC-ring transformation.

Treatment of oxazinone **3b** with an equimolar amount of keto ylide **28a**, for 3 days gave in addition to isoquinolone derivative **29a** (38%), a new ylide **30a** in 22% yield.

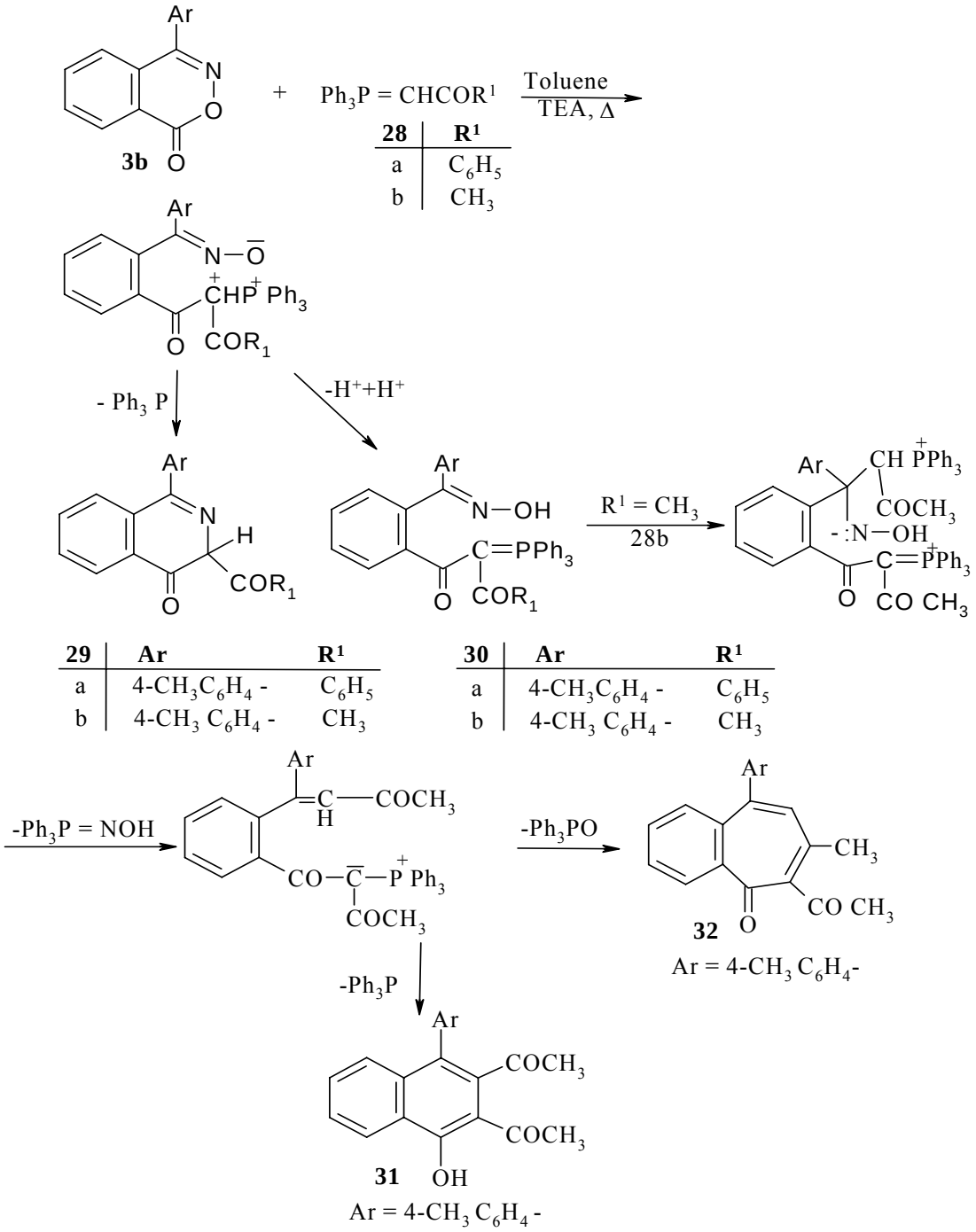
Reaction of **3b** with **28b** only takes place in a molar ratio 1:2. Isoquinoline derivative **29b** was obtained in only 12% yield; beside,2,3-diacetyl-4-(4-methylphenyl)-α-naphthol **31** (33%) and 2-acetyl-3-methyl-5-(4-methylphenyl)-benzocylcohepten-1-one **32** (22%) [10] (Scheme 12).

### 3.2. Benzoxazines and pyrido-oxazines

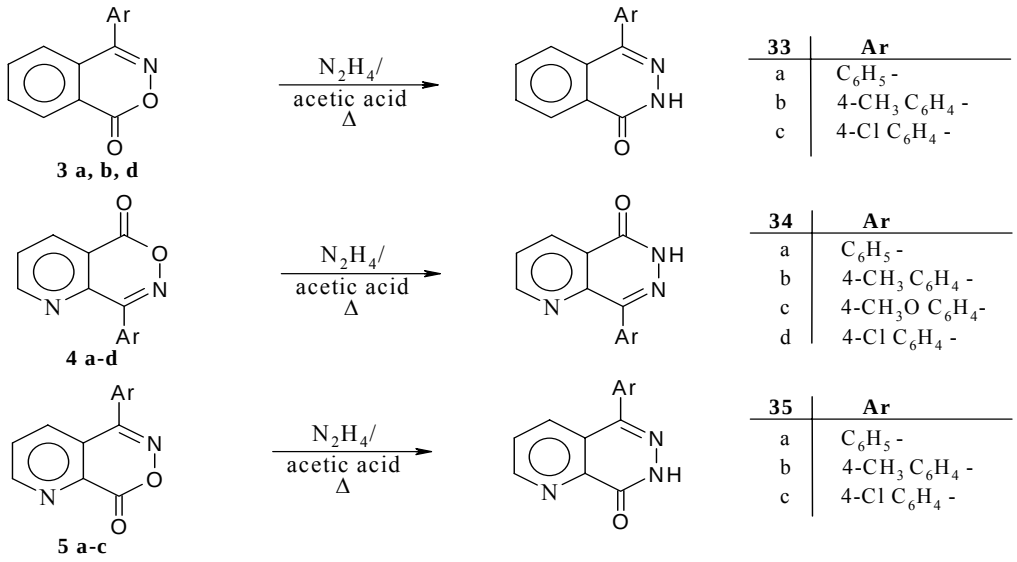
4-Arylphthalazine-1-ones **33a-c** were obtained from the reaction of 4-aryl-2,3-benzoxazin-1-ones **3a,b,d** with hydrazine hydrate in glacial acetic acid in (80 – 90%) yields[11] (Scheme 13).

8-Arylpyrido[2,3-*d*][1,2]oxazin-5-ones **4a-d**, reacted with hydrazine in acetic acid to give 8-arylpyrido[2,3-d]pyridazin-5(6*H*)-ones[11] **34a-d** in 81-89% yields.

The isomeric 5-arylpyrido[3,2-*d*][1,2]oxazin-8-ones **5a-c**, under the same reaction conditions, gave 5-arylpyrido[2,3-*d*] pyridazine[11] 8(7*H*) ones **35a-c** in 62 - 75% yields. (Scheme 13).


3b
Ph3P = CHCOR1
Toluene
TEA, Δ
28 | R1
a | C6H5
b | CH3
- Ph3 P
-H+ +H+
R1 = CH3
28b
29 | Ar | R1
a | 4-CH3C6H4 - | C6H5
b | 4-CH3 C6H4 - | CH3
30 | Ar | R1
a | 4-CH3C6H4 - | C6H5
b | 4-CH3 C6H4 - | CH3
-Ph3P = NOH
-Ph3PO
-Ph3P
32
Ar = 4-CH3 C6H4-
31
Ar = 4-CH3 C6H4 -

**Scheme 12**



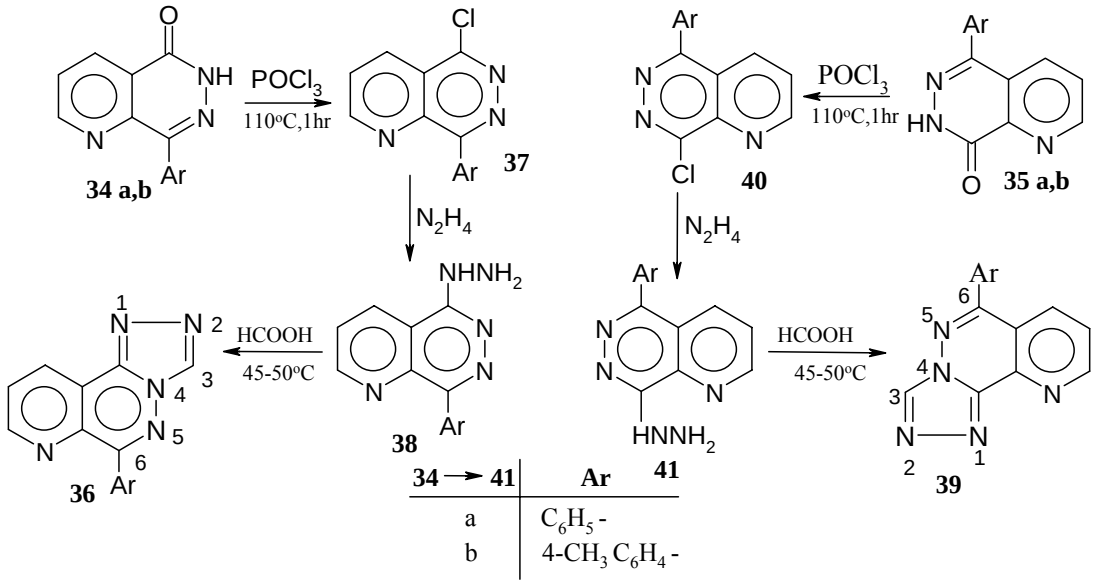

**Scheme 13.** HHSS based on ANRORC ring transformation.

## 4. Pyridopyridazines as building blocks

8-Arylpyrido[2,3-*d*]pyridazin-5(6*H*)-ones **34a,b** were used as building blocks in synthesis of 6-aryl-1,2,4-triazolo[3,4-*b*]pyrido[2,3-*d*]pyridazines **36a,b** in 68-71% yields via the intermediate compounds **37a,b** and **38a,b** in a three-step synthesis.[11]

Similarly, 5-arylpyrido[2,3-*d*]pyridazine-8(7*H*)-ones **35a,b** were used in synthesis of 6-aryl-1,2,4-triazolo[4,3-*d*]pyrido[2,3-*d*]pyridazines **39a,b** in 82–86% yields via intermediate compounds **40a,b** and **41a,b.**

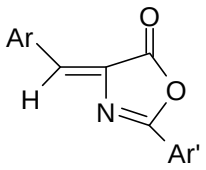
Our work towards the synthesis of **36a,b** and **39a,b** is shown (Scheme 14) in which the key step involves cyclocondensation of the hydrazine derivatives **38** and **41** with formic acid at 40-45°C.[11]




**Scheme 14.** Three-step synthesis.

## 5. Oxazolones as building blocks

Oxazoles are well known building blocks[12-15]. We have been interested in developing efficient synthetic routes to imidazoles, tetrazoles,1,3,5-oxadiazines, and 1,2,4-tetrazines based on 1,3-oxazolones **42a-l** as building blocks (Figure 3).



| 42 | Ar | Ar' | 42 | Ar | Ar' |
|---|---|---|---|---|---|
| a | $C_6H_5$ - | $C_6H_5CH$ = CH- | g | $C_6H_5$ - | $CH_3$ |
| b | 4-$CH_3O$ $C_6H_4$- | $C_6H_5$ CH = CH- | h | 4-$CH_3O$ $C_6H_4$ - | $CH_3$ |
| c | $C_6H_5$ - | $C_6H_5$ | i | 4-Cl $C_6H_4$ - | $CH_3$ |
| d | 4-$CH_3O$ $C_6H_4$- | $C_6H_5$ | j | 4-Cl $C_6H_4$ - | 4-$CH_3O$ $C_6H_4$- |
| e | 4-Cl $C_6H_4$ - | $C_6H_5$ | k | $C_6H_5CH$ = CH- | $C_6H_5$ |
| f | 4-$NO_2$ $C_6H_4$ - | $C_6H_5$ | l |  | $C_6H_5$ |

**Figure 3**

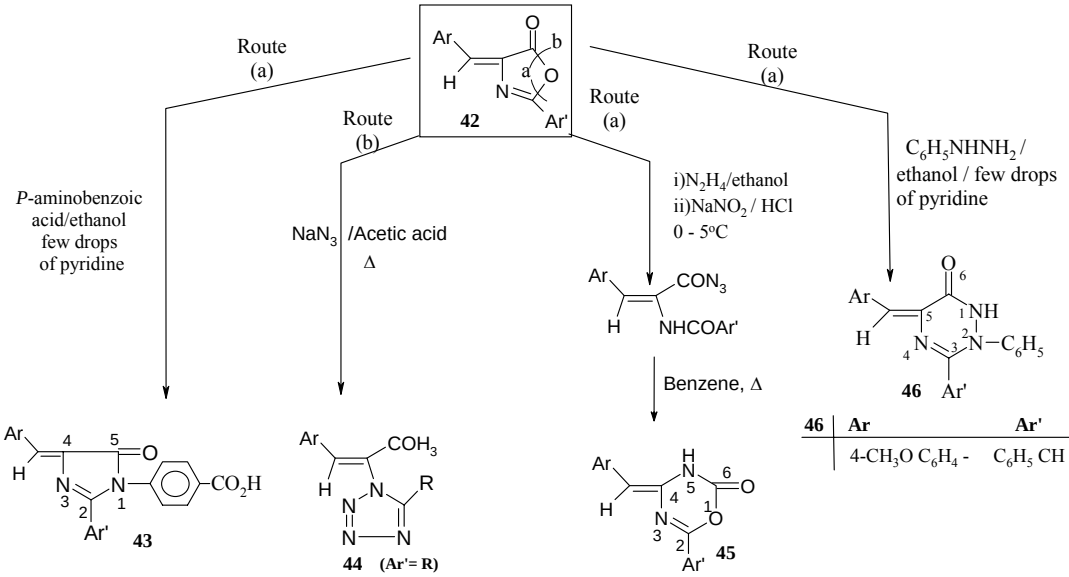
4-Arylidene-2-styryl-5(4) oxazolones **42a,b** reacted with *p*-aminobenzoic acid in refluxing ethanol to give 4-arylidene-1-[4'-carboxypheny]-2-styryl-5-oxo-imidazoles **43a,b** in 85-95% yields.[16]

The reaction takes place via nucleophilic addition (AN) followed by ring opening RO ($C_5$-O- fission) then ring closure (RC) i.e. ANRORC ring transformation.

Oxazolone derivatives **42c-i** were used in synthesis of α-tetrazolycinnamic acid derivatives[17] **44a-g** in 70-75% yields via ($C_2$ – O) fission (Route-b).

2-Arylidene-4-aryl-6-oxo-1,3,5-oxadiazines **45a-d** were obtained in 45-55% yields from oxazolones **42b, j, k, l** via two-step synthesis[18] (Scheme 15).

Hydrazinolysis of 4-anisylidene-2-styryl-5(4*H*) oxazolone **42b** with phenylhydrazine gave 1, 2, 4-triazine derivative **46** via ANRORC mechanism (Scheme 15).




| 43 | Ar | Ar' |
|---|---|---|
| a | $C_6H_5$ | $C_6H_5$ CH = CH- |
| b | 4-$CH_3O$ $C_6H_4$ - | $C_6H_5$ CH = CH- |

| 44 | Ar | R |
|---|---|---|
| a | $C_6H_5$ - | $C_6H_5$ |
| b | 4-$CH_3O$ $C_6H_4$ - | $C_6H_5$ |
| c | 4-Cl $C_6H_4$ - | $C_6H_5$ |
| d | 4-$NO_2$ $C_6H_4$ - | $C_6H_5$ |
| e | $C_6H_5$ - | $CH_3$ |
| f | 4-$CH_3O$ $C_6H_4$ - | $CH_3$ |
| g | 4-Cl $C_6H_4$ - | $CH_3$ |

| 45 | Ar | Ar' |
|---|---|---|
| a | 4-$CH_3O$ $C_6H_4$ - | $C_6H_4$ CH=CH- |
| b | 4-Cl $C_6H_4$ - | 4-$CH_3O$ $C_6H_4$- |
| c | $C_6H_5$ CH = CH- | $C_6H_5$ |
| d |  | $C_6H_5$ |

| 46 | Ar | Ar' |
|---|---|---|
| | 4-$CH_3O$ $C_6H_4$ - | $C_6H_5$ CH = CH- |

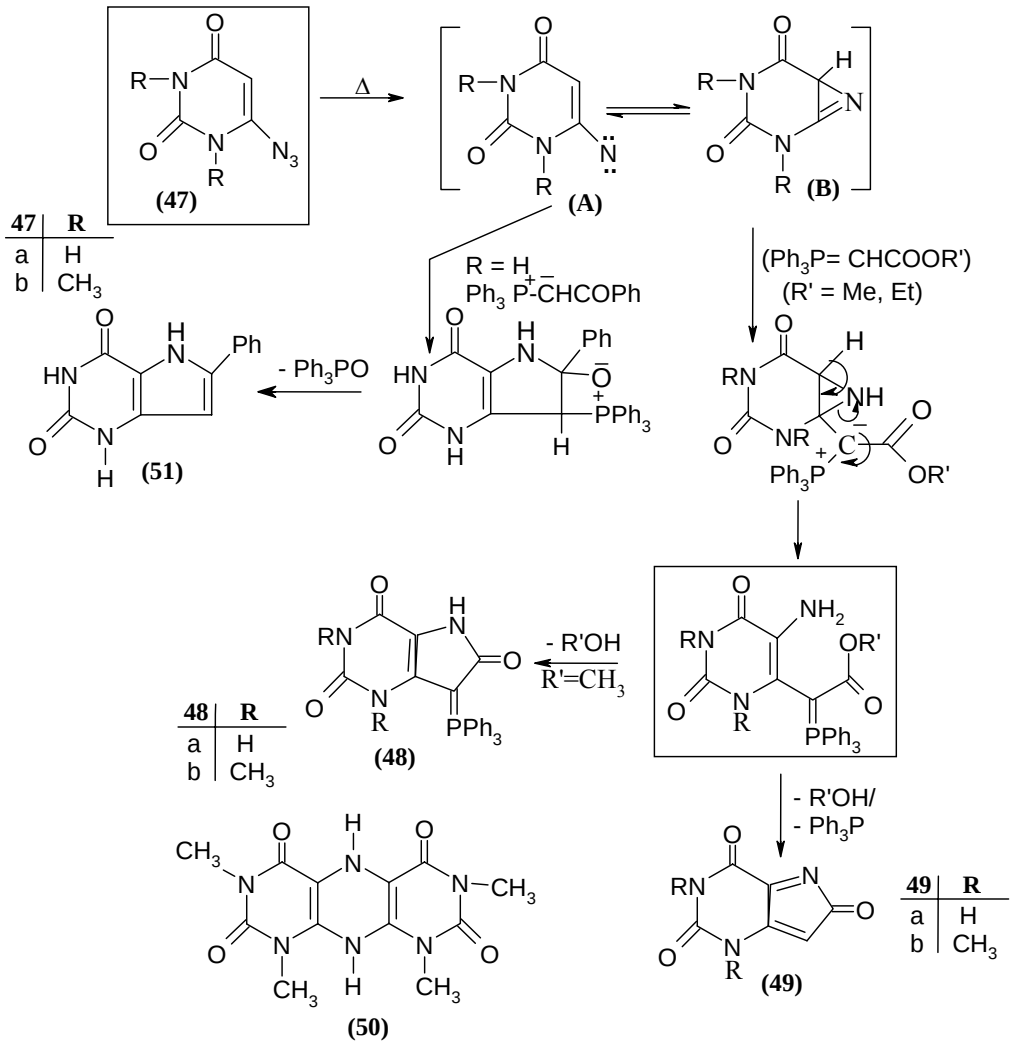
**Scheme 15**

## 6. Uracils as building blocks

6-Azidouracils **47a** reacted with phosphorus ylides **25a,b** in refluxing ethylacetate to give a mixture of (7-triphenylphosphoranylidene) pyrimido[5,4-*d*]-pyrrole-6-(5*H*)-one **48a** in 48% yield, and pyrimido[5,4-*d*]pyrrole-6-one **49a** in 24% yield (Scheme 16). When 6-azido-1,3-

dimethyluracil **47b** was treated with an equimolar amount of **25a** under the same experimental conditions, products **48b** (28%) and **49b** (13%) and 1,3,6,8-tetramethylpyrimido[5,4-*g*] pteridine-2,4,5,7 tetrone **50** (17%) were obtained.[19]

6-Azidouracil **47a** reacted with benzoylmethylenetriphenylphosphorane to give 6-phenylpyrrolo[3,2-*d*] pyrimidine **51** in 63% yield according to the mechanism shown in Scheme 16.

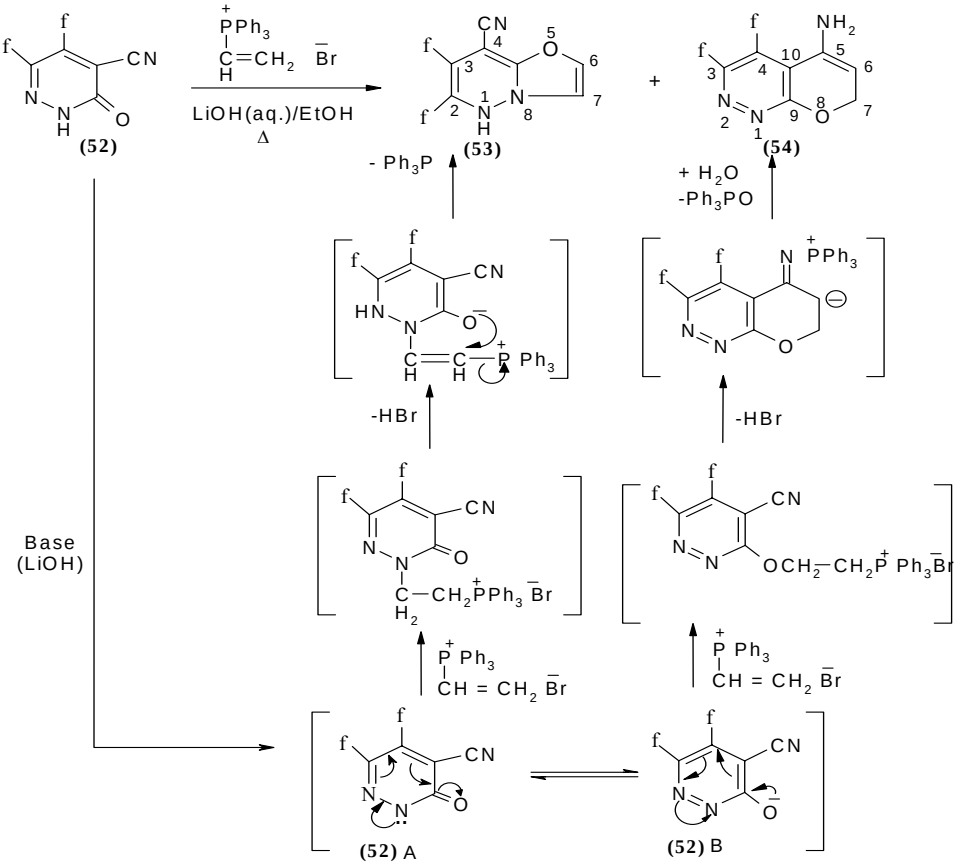



**Scheme 16**

## 7. Pyridazinones as building blocks

Treatment of 4-cyano-5,6-difur-2'-yl-2*H*-pyridazine-3-one **52** with an equimolar amount of vinyltriphenylphosphonium bromide in a mixture of LiOH/$H_2O$/EtOH yielded 2,3-difur-2`yl-4-cyano-5,8-oxazolo[2,3-*b*]1,2-dihydropyridazine **53** (63%), beside 5-amino-3,4-difur-2'-yl-

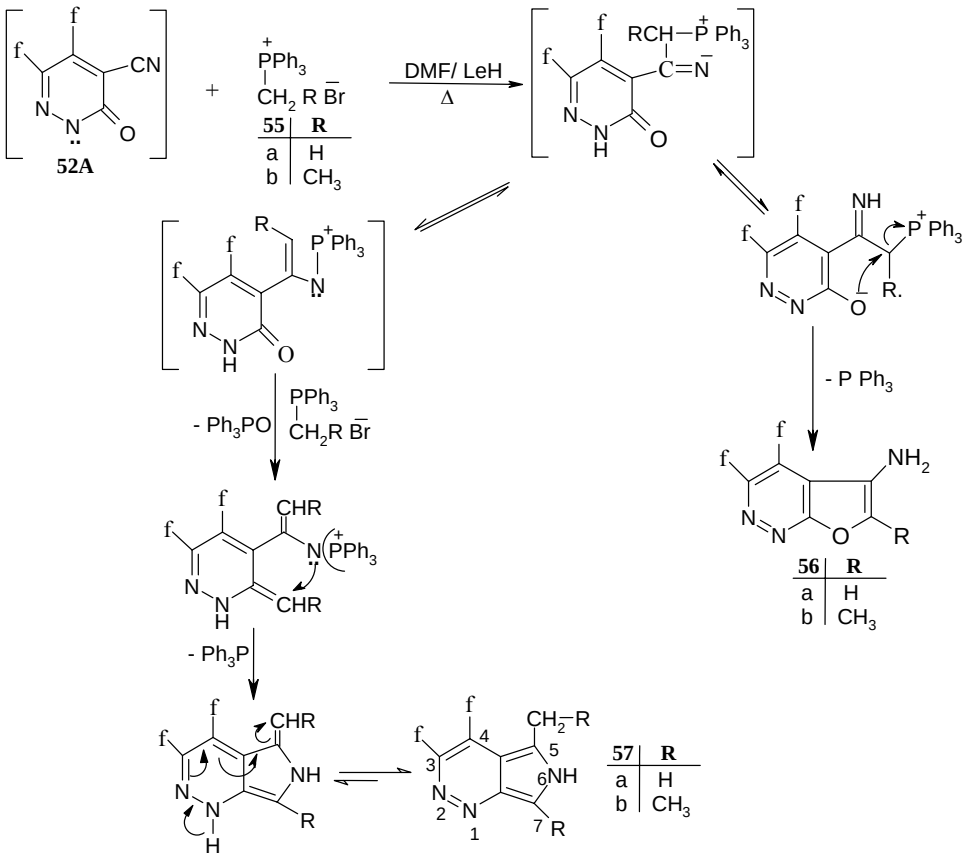
pyrano[2,3-*c*]1,2-dihydropyridazine **54** (23%).[20,21] The reaction takes place according to the mechanism shown (Scheme 17).




**Scheme 17**

Reaction of **52a** with an excess of methylidinetriphenylphosphorane **55a** in the presence of lithium hydride in refluxing DMF, for 30 hr afforded, 5-amino-3,4-difur-2'yl-furano[2,3-*c*]1,2-dihydro-pyridazine **56a** (22%) and 5-methyl-3,4-difur-2'yl-6*H*-isopyrrolo[2,3-*c*]1,2dihydropyridazine **57a** (43%) [20,21] (Scheme 18).

Similarly, **52a** reacts with **55b** under the same reaction conditions to give a mixture of **56b** (22%), and **57b** (47%). The reaction takes place according to the following mechanism (Scheme 18).




**Scheme 18**

## 8. Benzopyran and benzothiopyran derivatives as building blocks

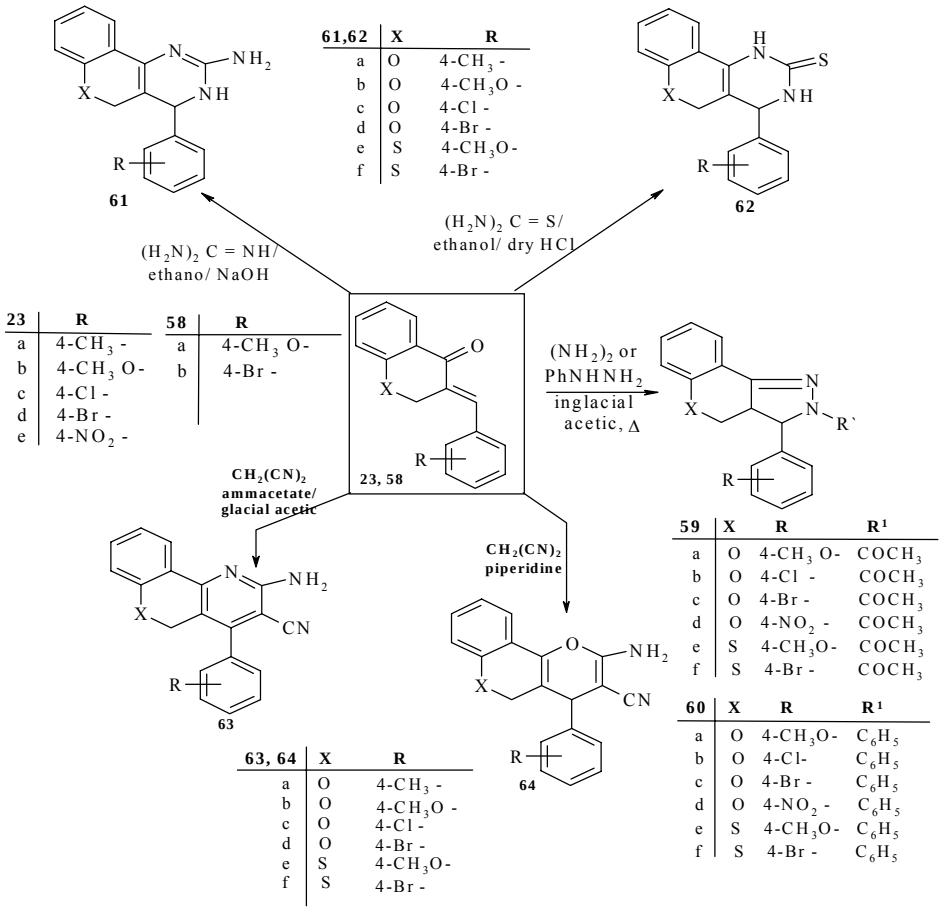
Arylmethylenebenzopyrans and arylmethylenebenzothiopyrans were used as versatile building blocks in one-pot reactions for new synthesis of target heterocyclic systems in reasonable yields e.g. Benzopyranopyrazoles, benzothiopyranopyrazoles, benzopyranopyrimidines, benzothiopyranopyrimidines, benzopyranopyridines, benzothiopyranopyridines, benzopyranopyran, benzothiopyranopyran.

This building strategy depends on cyclocondensation reactions with different reagents. Reaction of 3-arylmethylene-3,4-dihydro[1]benzopyran-4-ones **23b-e** with hydrazine or phenylhydrazine in refluxing glacial acetic acid gave 2-acetyl-3-aryl-2,3,3a,4-tetrahydro(4*H*)[1]benzopyrano[4,3-*c*]pyrazoles **59a-d** (71-88%), and 2-phenyl-3-aryl-2,3,3a,4-tetrahydro-(4*H*)[1]benzopyrano[4,3-*c*]pyrazoles **60a-d** (65–73%), respectively.

Similarly, 3-arylmethylene-3,4-dihydro[1]benzothiopyran-4-ones **58a,b** reacted with hydrazine or phenylhydrazine under the same experimental conditions to give 2-acetyl-3-aryl-2,3,3a,4-tetrahydro-(4*H*)[1]benzothiopyrano[4,3-*c*]pyrazoles **59e,f** (80-82%) and 2-phenyl-3-

aryl-2,3,3a,4-tetrahydro-(4*H*)[1]benzothiopyrano[4,3-*c*]pyrazoles **60e,f** (65-82%), respectively (Scheme 19).

Reaction of **23a-d** and **58a,b** with guanidine hydrochloride in ethanol and NaOH yielded 2-amino-4-aryl-3,4-dihydro-(5*H*)[1]benzopyrano[4,3-*d*]-pyrimidines **61a-d**(65-75%), and 2-amino-4-aryl-3,4-dihydro-(5*H*)[1]benzothiopyrano[4,3-*d*] pyrimidines **61e,f** (60%), respectively (Scheme 19).




**Scheme 19.** HHSS based on cyclocondensation.

Also, compounds **23a-d** and **58a,b** react with thiourea in ethanol and dry HCl gas to give 4-aryl-1,2,3,4-tetrahydro-(5*H)*[1]benzopyrano[4,3-*d*]pyrimidine-2-thioxo **62a-d** 70-85%, and 4-aryl-1,2,3,4-tetrahydro-(5*H)*[1]benzothiopyrano[4,3-*d*]pyrimidine-2-thioxo **62e,f** 61-65%, respectively.

2-Amino-4-aryl-(5H)[1]benzopyrano[4,3-*b*]pyridine-3-carbonitriles **63a-d** 60-71%, and 2-amino-4-aryl-(5*H)*[1]benzothiopyrano[4,3-*b*]pyridine-3-carbonitriles **63e,f** 67-75% were obtained from the reaction of **23a-d** and **58a,b** with malononitrile, ammonium acetate in refluxing glacial acetic acid (Scheme 19).

Compounds **23a-d** and **58a,b** reacted with malononitrile in a mixture of ethanol and piperidine to give 2-amino-4-aryl-(4*H*),(5*H*)[1]benzopyrano[4,3-*b*]pyrano carbonitriles **64a-d**, 67-81% and 2-amino-4-aryl-(4*H*),(5*H*)[1]benzothiopyrano[4,3-*b*]pyrano carbonitriles **64e,f** 65-72% respectively,[9] (Scheme 19).

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