HETEROCYCLES, Vol. 77, No. 2, 2009, pp. 657 - 678. © The Japan Institute of Heterocyclic Chemistry
Received, 31st July, 2008, Accepted, 24th September, 2008, Published online, 25th September, 2008
DOI: 10.3987/REV-08-SR(F)5

RING TRANSFORMATIONS OF 2*H*-PYRAN-2-ONES AND FUSED PYRAN-2-ONES WITH NUCLEOPHILIC REAGENTS[#]

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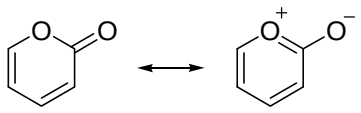
Abstract – In this review we report on several recently described nitrogen- and carbon-nucleophile-induced ring transformations of selected pyran-2-one derivatives. These reactions provide convenient routes for the synthesis of different heterocycles and carbocycles as well as β-heteroaryl-α,β-didehydroamino acid derivatives.

INTRODUCTION

The pyran-2-one ring (**1**), a six-membered, cyclic, unsaturated ester (lactone), can be found in the form of isolated or fused ring systems in bacterial, microbial, plant and animal systems, demonstrating a whole spectrum of bioactivities like antifungal, antibiotic, cytotoxic, neurotoxic, etc.[1] Pyran-2-ones are closely related in structure to pyrylium salts, having five sp^2-hybridized carbon atoms. One of the carbon atoms in the pyran ring is derivatised in the form of a carbonyl group, which can be represented in an alternative canonical form, thus forming the pyrylium betaine structure (**1b**). 2*H*-Pyran-2-one derivatives find a wide variety of synthetic applications:[2] in reactions with electrophiles and nucleophiles, as diene components in Diels-Alder reactions, in photochemical reactions, etc. The question related to the chemistry of pyran-2-ones is "*whether the pyran-2-one ring is aliphatic or aromatic in nature",* as it exhibits the characteristic reactions of both alkenes and arenes. The aromatic nature of 2*H*-pyran-2-ones is demonstrated by their selective substitution patterns in electrophilic reactions, for example, nitration, sulfonation and halogenation, which all occur at the C-3 and C-5 positions. On the other hand, 2*H*-pyran-2-ones have been found to be vulnerable to nucleophilic attack because of the presence of three electrophilic centers, positions C-2, C-4 and C-6. These reactions usually lead to ring opening and rearrangements, and the pyran-2-one ring is difficult to regenerate; a new heterocylic or carbocyclic system tends to be formed instead.

[#] Dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday.

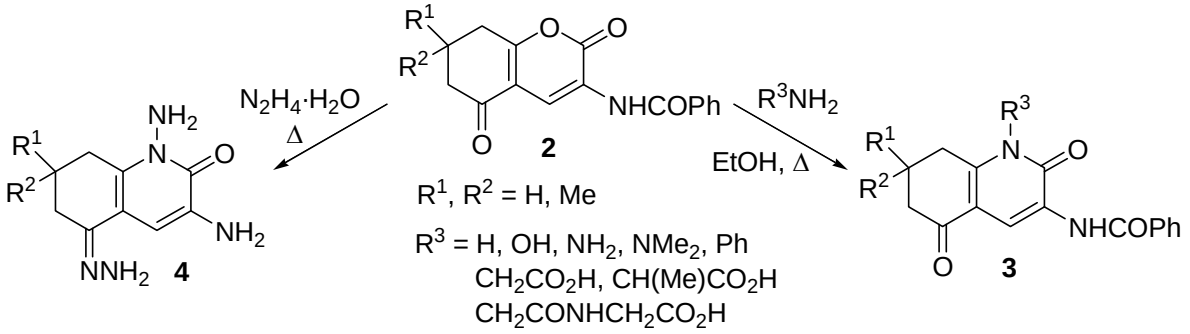
The present review deals with the recently described ring-transformation reactions of selected pyran-2-one derivatives induced with different nitrogen and carbon nucleophiles. These reactions represent a set of fascinating reactions in heterocyclic chemistry, because the 2*H*-pyran-2-one ring can be easily converted into a variety of new heterocycles and carbocycles by using simple procedures.



1a **1b**

NITROGEN-NUCLEOPHILE-INDUCED RING TRANSFORMATIONS OF 2*H*-PYRAN-2-ONES AND FUSED PYRAN-2-ONES

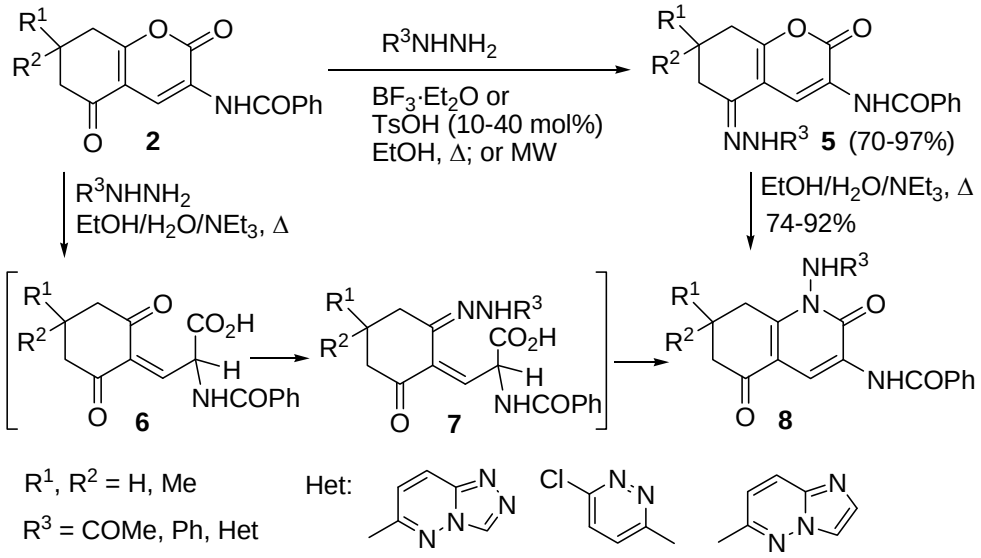
5,6,7,8-Tetrahydro-2*H*-1-benzopyran-2,5-diones (**2**)[3] were converted with ammonia, hydroxylamine, aniline, amino acids, hydrazine and *N*,*N*-dimethylhydrazine in boiling ethanol into 2,5-dioxo-1,2,5,6,7,8-hexahydroquinolines (**3**) (Scheme 1).[4] By heating the benzopyrans (**2**) with an excess of hydrazine hydrate the reaction took place at the pyranone ring and at the 5-oxo group, and even debenzoylation of the benzoylamino group occurred, yielding 3-amino-5-hydrazonoquinolinones (**4**).



Scheme 1

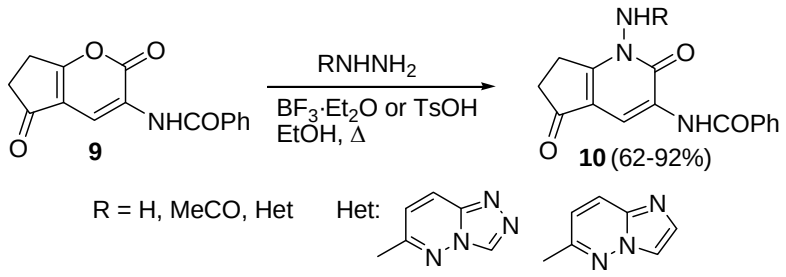
On the other hand, the transformations of benzopyran-2,5-diones (**2**) with hydrazides, phenylhydrazines and heterocyclic hydrazines in the presence of acidic catalysts ($BF_3 \cdot Et_2O$, TsOH) gave selectively 5-hydrazonobenzopyrans (**5**) (Scheme 2).[5] The reaction of benzopyran-2,5-diones (**2**) with aromatic and heteroaromatic hydrazines was remarkably accelerated under microwave conditions in the absence of any catalyst or solvent, thus providing an environmentally friendly route to hydrazones of type **5**.[6] The latter were further converted into quinoline-2,5-diones (**8**) in high yields by heating in a mixture of ethanol, water and triethylamine. The same products were also obtained under basic conditions from **2** *via* the proposed intermediates **6** and **7**.[7] In a particular case the compound **2** ($R^1 = R^2 = Me$) was heated in a mixture of ethanol, water and triethylamine and the compound **6** was isolated (thus confirming the proposed reaction pathway) and further reacted with the corresponding hydrazine derivative yielding the

quinolinone product in a direct conversion.



Scheme 2

In contrast to its six-membered analogues (**2**), the cyclopenta[*b*]pyran-2-one (**9**) gave, with hydrazine, acetohydrazide and heterocyclic hydrazines in ethanol under acidic conditions, directly cyclopenta[*b*]-pyridine-2(1*H*)-ones (**10**) in 62−92% yields without the formation of the corresponding 5-hydrazono derivatives (Scheme 3).[5c]

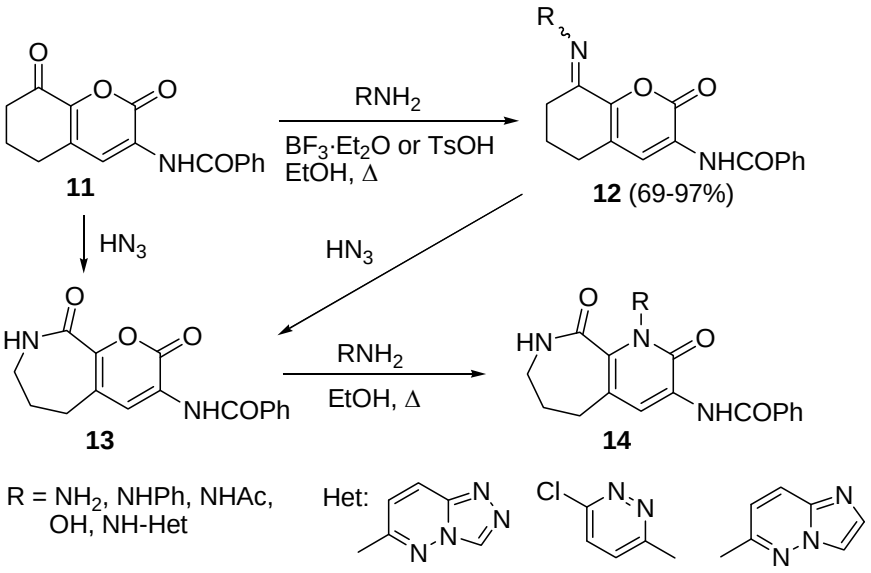


Scheme 3

To explain the difference between the preferential formation of hydrazones of type **5** in the benzopyran-2-one series and compounds of type **10** from cyclopenta[*b*]pyran-2-one (**9**), semi-empirical calculations on these systems were performed, which revealed that for the cyclopenta[*b*]pyran-2-one system cyclopenta[*b*]pyridine derivatives (**10**) are thermodynamically favored over the 5-hydrazone derivatives, whereas for benzopyrans the 5-hydrazono isomers are preferred.[5a,c,d] It is also important to mention that there is no evidence that thermodynamic parameters are controlling these reactions as the sole factors.

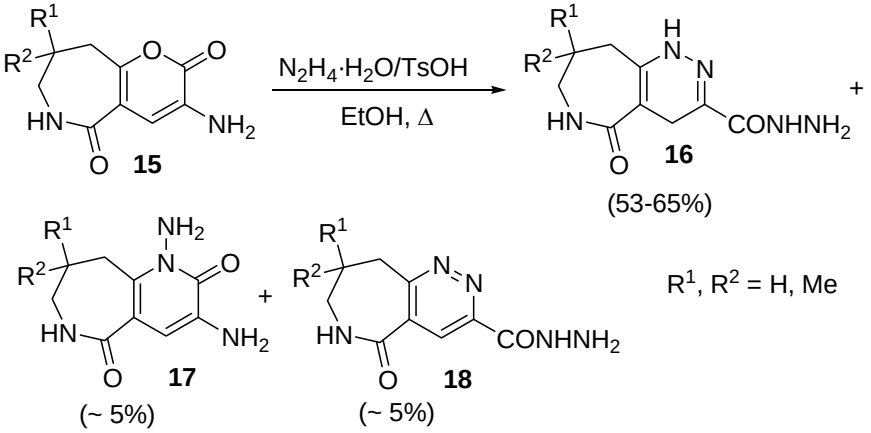
Similarly, the 8-oxobenzopyran derivative (**11**) in the reaction with nitrogen-containing nucleophiles (hydrazine hydrate, heterocyclic hydrazines, acetyl hydrazine and hydroxylamine) in the presence of an acidic catalyst gave the corresponding 8-hydrazono derivatives (**12**).[8] The ring enlargement *via* the

Schmidt reaction employed on some compounds **12** resulted in the formation of pyrano[2,3-*c*]azepine (**13**), which can be further transformed with hydrazine hydrate and phenylhydrazine into pyrido[2,3-*c*]azepines (**14**) (Scheme 4).



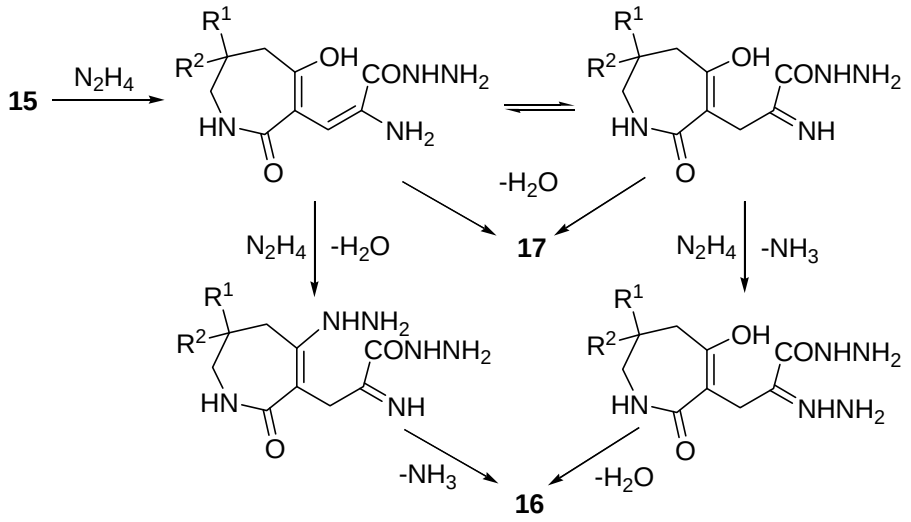
Scheme 4

A totally different chemistry towards hydrazine hydrate is exhibited by pyrano[3,2-*c*]azepines (**15**), bearing a free amino group at position 3. Namely, they were shown to give the 1,4-dihydropyridazino[4,3-*c*]azepines (**16**) in 53-65% yields as the main products (Scheme 5).[9] In addition to the compounds **16**, the formation of small quantities of 1,3-diaminopyridin-2-ones (**17**) and pyridazines (**18**) was also observed. It was shown that for a successful reaction toward pyridazine derivatives (**16**), two equivalents of hydrazine hydrate under acidic conditions (TsOH) have to be employed, while with triethylamine as a solvent the pyridine derivative (**17**) (R^1 = R^2 = Me) was the major product. The aromatized, fused pyridazines (**18**) are obviously the oxidation products of **16**, caused by the air.



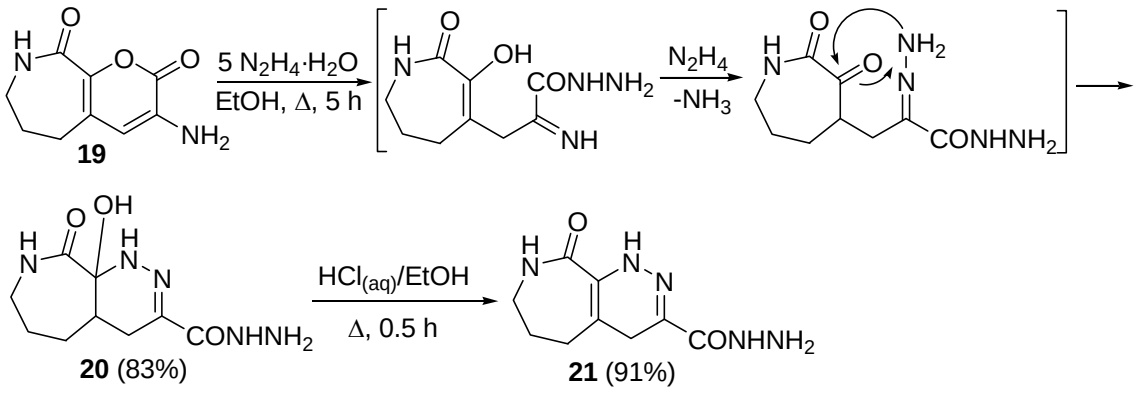
Scheme 5

The above reaction enabled the first synthesis of pyridazino[4,3-*c*]azepine derivatives, and their formation can be explained as outlined in Scheme 6.[9] The nucleophilic attack of a hydrazine molecule onto **15** yields an open-ring intermediate, which is then cyclised by the action of the second molecule of hydrazine and the elimination of water and ammonia to give the products **16**. The products **17** could be formed by cyclisation with the elimination of water from the first tautomeric intermediate.



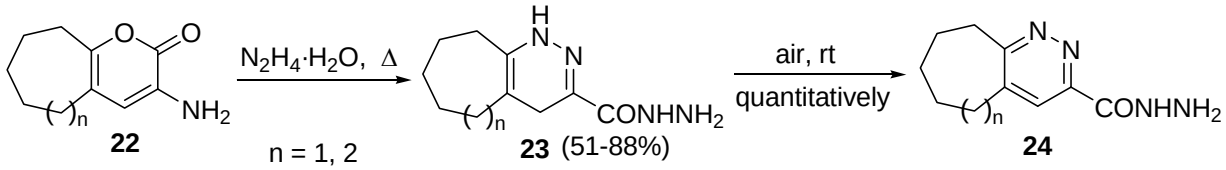
Scheme 6

In contrast to the behavior of pyrano[3,2-*c*]azepines (**15**) in the reaction with hydrazine hydrate, the transformation of the isomeric pyrano[2,3-*c*]azepine derivative (**19**) with 5 equivalents of hydrazine hydrate in boiling ethanol led to the 9a-hydroxypyridazino[3,4-*c*]azepine derivative (**20**) with an 83% yield (Scheme 7).[10] This compound has been found to readily eliminate a water molecule when treated with aqueous HCl in absolute ethanol, thus giving 4,5,6,7,8,9-hexahydro-1*H*-pyridazino[3,4-*c*]azepine derivative (**21**).



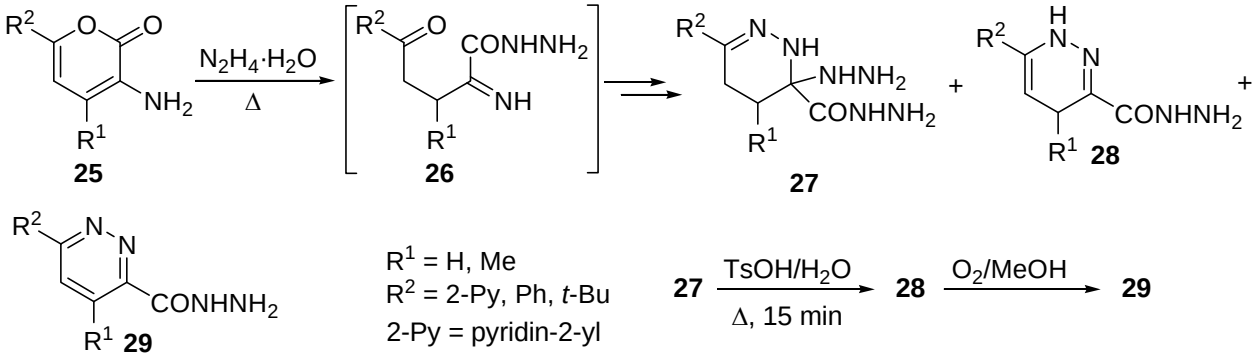
Scheme 7

Interestingly, pyran-2-ones (**22**) containing fused polymethylene chains were shown to be more resistant to the nucleophilic attack of hydrazine. Thus, for the successful preparation of 1,4-dihydropyridazines (**23**) the reaction had to be carried out in boiling hydrazine hydrate, which served as the reagent and as the solvent. Under these conditions, the reaction was finished within 20 minutes and provided the products **23** in good yields (Scheme 8).[10] These products are sensible to oxidation in the air, thus giving quantitatively aromatized analogues (**24**).



Scheme 8

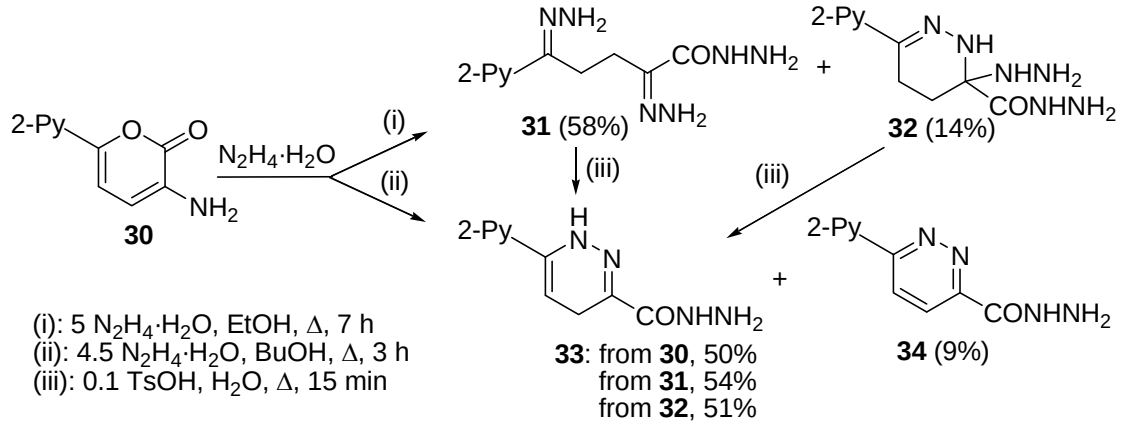
The reaction of non-fused 2*H*-pyran-2-ones (**25**) with hydrazine hydrate provided a deeper insight into the transformations of pyran-2-ones with hydrazine. Due to the absence of a fused ring in the compounds **25**, after the opening of the lactone ring with hydrazine hydrate the formation of a more flexible intermediate **26** (Scheme 9) is expected, which would not be prone to cyclization, thus allowing the attack of additional hydrazine molecules. When the compounds **25** were allowed to react with boiling hydrazine hydrate, 3-hydrazino-2,3,4,5-tetrahydropyridazine derivatives (**27**) were isolated as the main products.[10] In the case of R^1 = H and R^2 = *tert*-Bu a small amount of 1,4-dihydropyridazine derivative (**28**) was also isolated. After refluxing the 2*H*-pyran-2-one (**25**) (R^1 = Me, R^2 = pyridin-2-yl) with 5 equivalents of hydrazine hydrate in ethanol or butanol as a solvent, compound **28** was isolated, which in ethanol was accompanied by the aromatic pyridazine (**29**).



Scheme 9

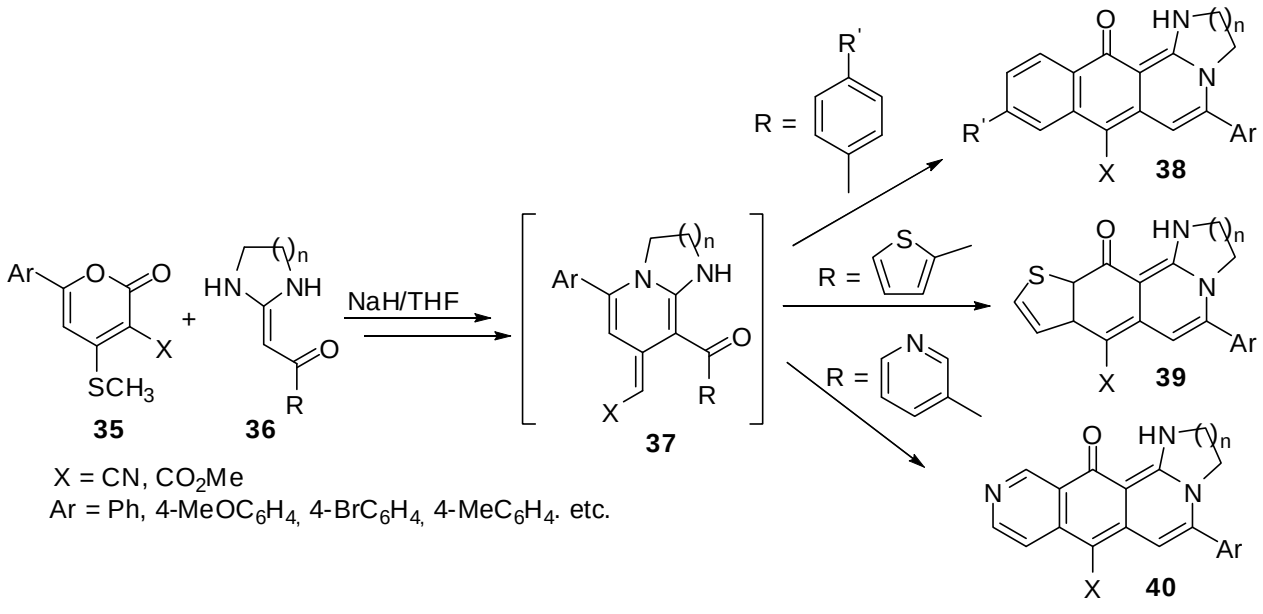
The compounds **27** can easily eliminate a hydrazine molecule when applying acidic conditions (TsOH) to give the products **28**. Here again, 1,4-dihydropyridazines (**28**) are transformed by oxygen to aromatized analogues (**29**).

Interestingly, 2-pyridyl-2*H*-pyran-2-one (**30**) in the reaction with 5 equivalents of hydrazine hydrate in boiling ethanol led to the isolation of an open-ring intermediate α,δ-dihydrazonohydrazide derivative (**31**) accompanied by a small quantity of 2,3,4,5-tetrahydropyridazine derivative (**32**) (Scheme 10).[11] On the other hand, when using butanol as a solvent, dihydropyridazine (**33**) and a small amount of its aromatic analogue (**34**) were obtained.



Scheme 10

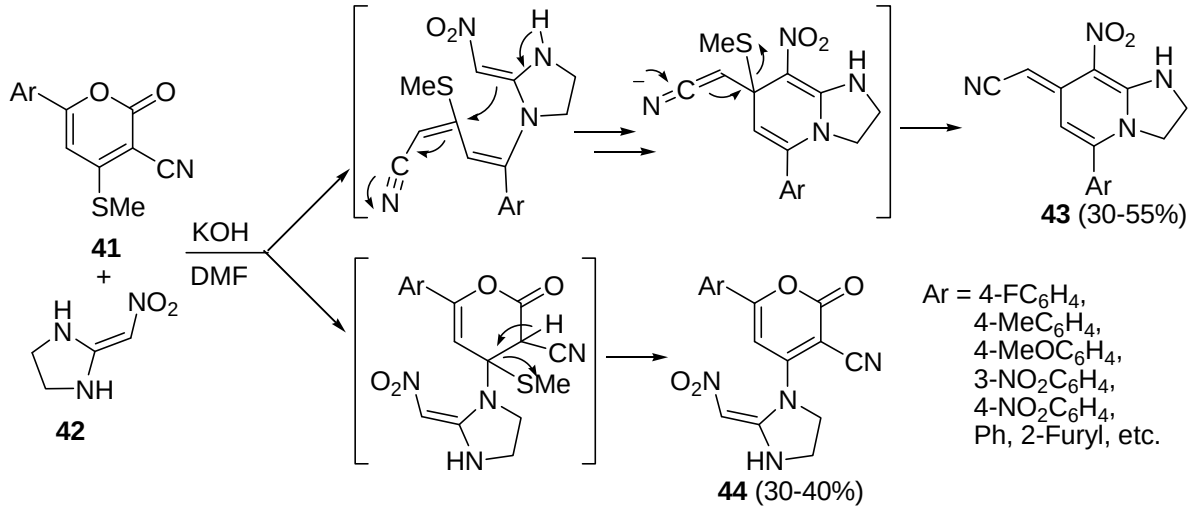
A. Sharon *et al*. reported on a concise synthesis of annulated [*a*]azaanthracenones (**38**), thieno[3,2-*g*]azanaphtalenones (**39**) and triazacyclopenta[*a*]anthracenones (**40**) through a several-step ring transformation of suitably functionalized 2*H*-pyran-2-ones (**35**) with α-oxoketene cyclic aminals (**36**) in the presence of NaH, followed by the photocyclization of the key intermediates (**37**) and a subsequent oxidation with the air (Scheme 11).[12]



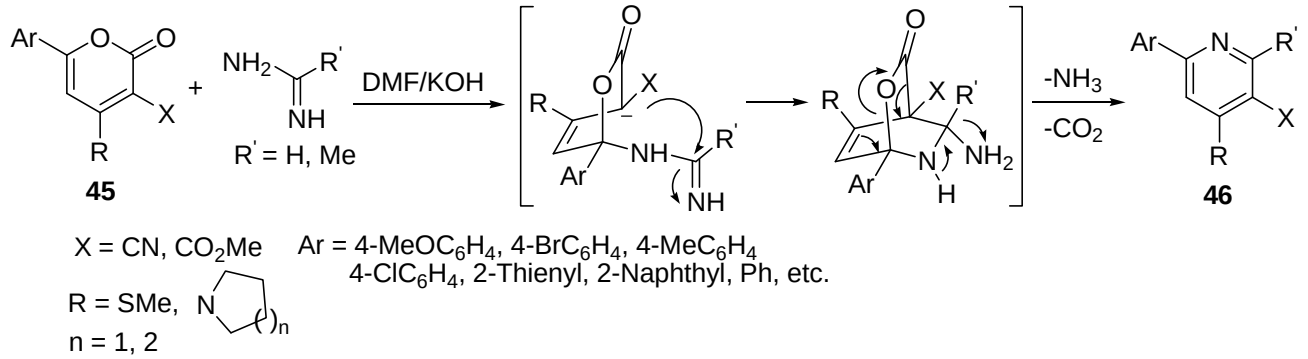
Scheme 11

Similarly, the reaction of 6-aryl-3-cyano-4-methylsulfanyl-2*H*-pyran-2-one (**41**) with imidazoliden-2-ylidene nitromethane (**42**) as the source of an *in situ* generated anion afforded imidazo[1,2-*a*]pyridines (**43**), resulting from the nucleophilic attack of an NH group at position C-6 of the 2*H*-pyran-2-one ring.[13] The competitive reaction of the nucleophile at position C-4 resulted in the 2*H*-pyran-2-one derivatives (**44**) (Scheme 12).

2*H*-Pyran-2-ones (**45**) were used as synthons for the ring-ring transformation reactions induced with amidines, as reported by Pratap *et al.*[14] Thus, the reaction with formamidine and acetamidine in DMF/KOH yielded 6-aryl substituted pyridines (**46**) (Scheme 13). The initial step in these reactions is an attack of the nitrogen nucleophile at position C-6 of the 2*H*-pyran-2-one ring, with ring closure followed by the elimination of carbon dioxide and ammonia to form the products **46**.



Scheme 12

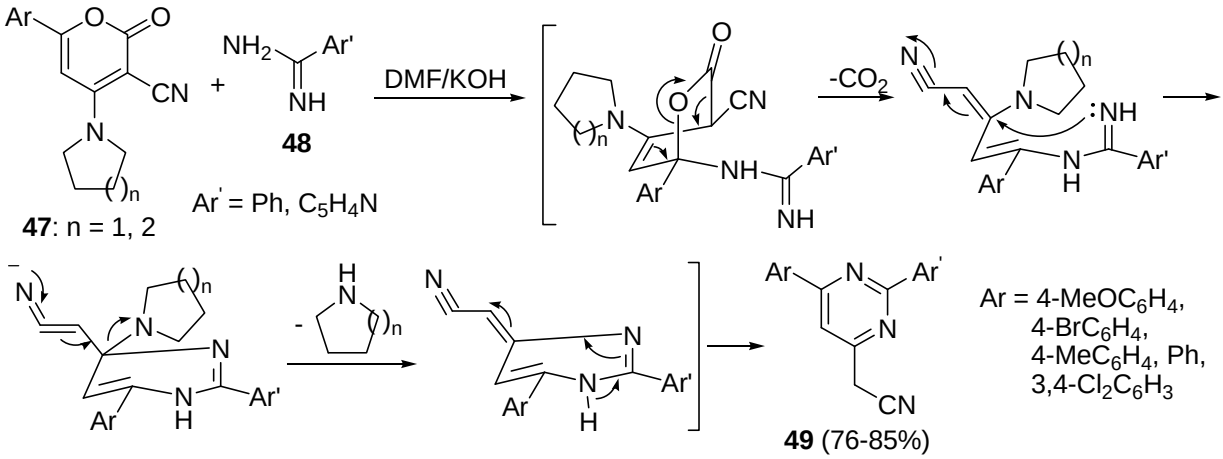


Scheme 13

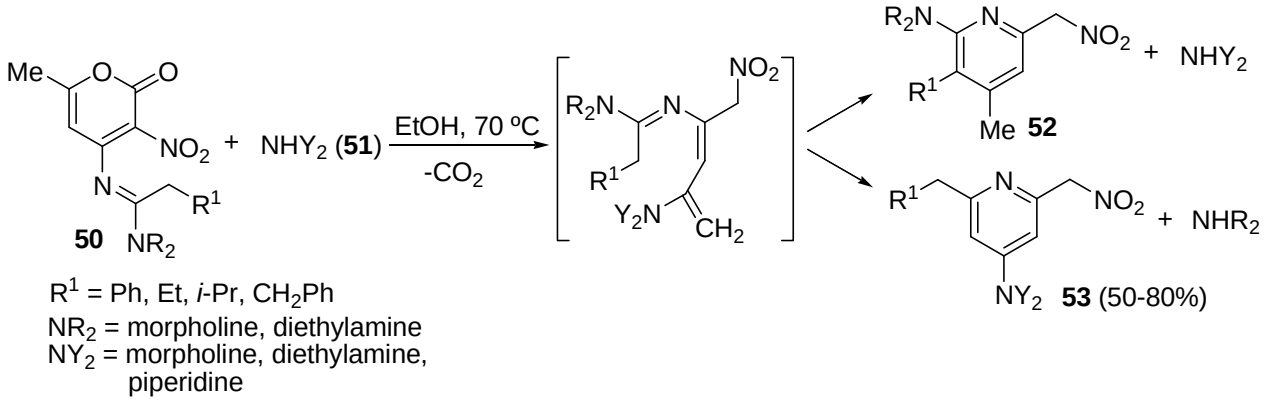
On the other hand, the same group reported an interesting reaction of 4-secondary-amino-substituted 2*H*-pyran-2-ones (**47**) with different salts of arylamidines (**48**) providing (2,6-diarylpyrimidin-4-yl)acetonitriles (**49**) (Scheme 14).[15] In contrast to the above-mentioned mechanism,

the ring closure is accompanied here by the loss of carbon dioxide and a secondary amine (pyrrolidine or piperidine).

4-Methylpyridines (**52**) and 4-dialkylaminopyridines (**53**) were synthesized starting from 3-nitro-2*H*-pyran-2-one acetamidines (**50**) and secondary amines (**51**) as the nucleophilic sources (Scheme 15).[16] The reaction again starts with a nucleophilic attack at position 6 of the 2*H*-pyran-2-one ring. Although two competing routes giving two different pyridines, (**52**) and (**53**), were observed, the reaction pathways could be controlled toward the prevailing 4-dialkylaminopyridine derivatives (**53**). Namely, the yield of the pyridine derivative (**53**) was enhanced when the reaction was performed in ethanol in the presence of TsOH.



Scheme 14

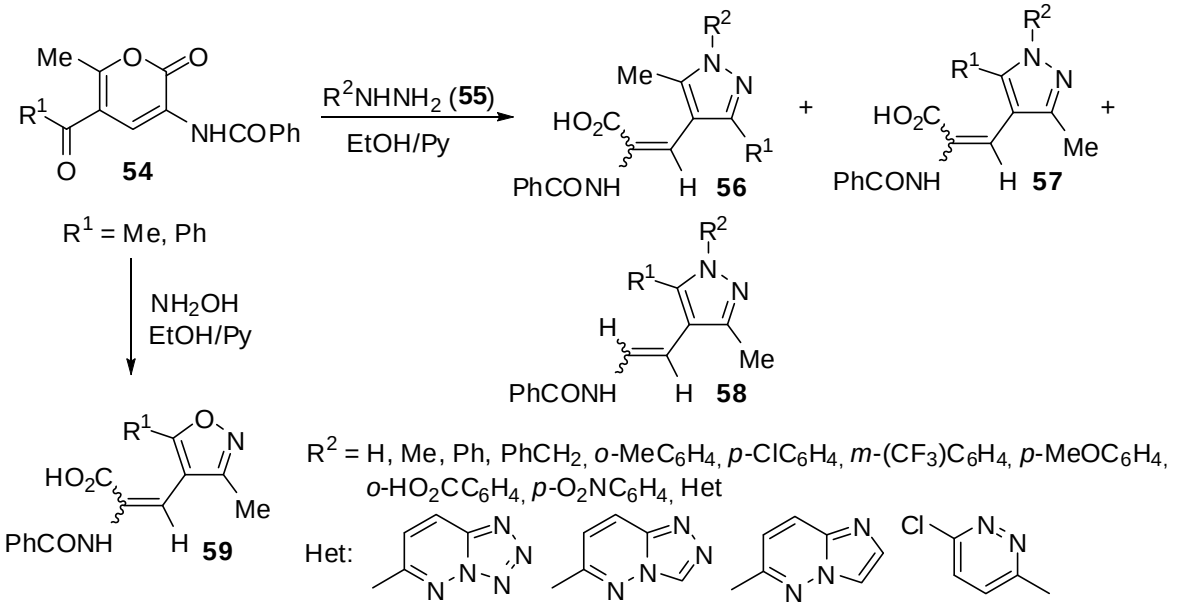


Scheme 15

SYNTHESIS OF α,β-DIDEHYDRO-α-AMINO ACID (α,β-DDAA) DERIVATIVES THROUGH RING TRANSFORMATIONS OF 2*H*-PYRAN-2-ONES

Dehydroamino acids and their derivatives play an important role as the constituents of various natural products and biologically active compounds, as well as representing versatile intermediates in organic

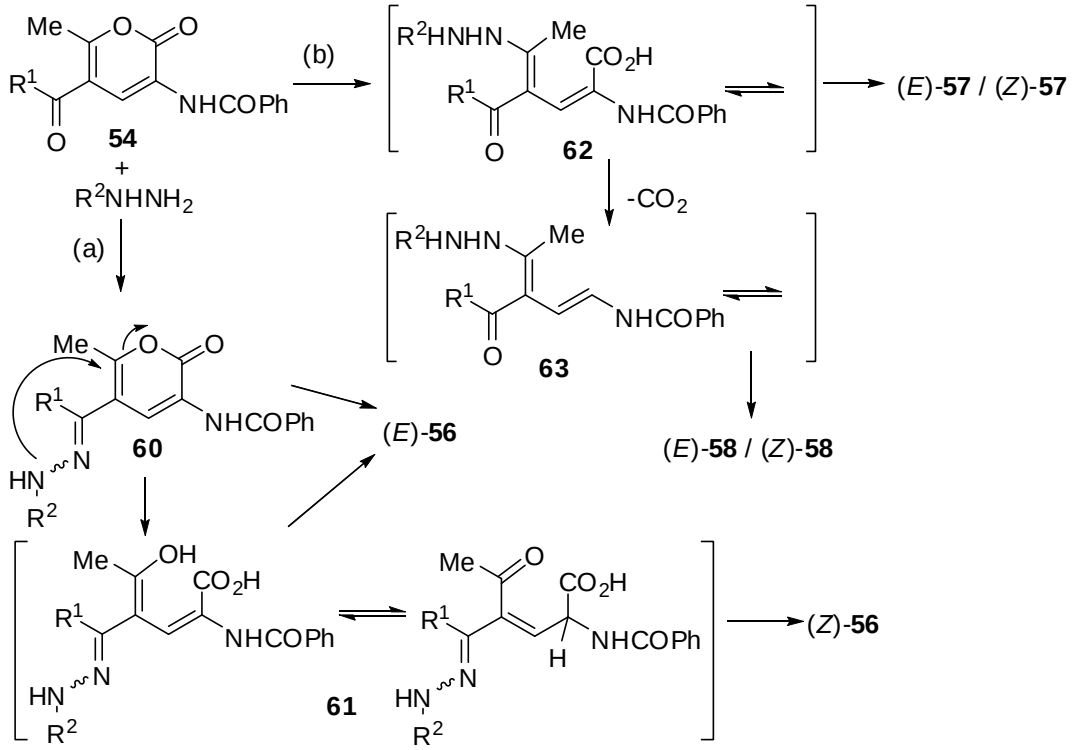
syntheses.[17] Among them, β-heteroaryl-α,β-didehydro-α-amino acid derivatives and compounds containing an amino acid moiety, partly or completely incorporated in the heterocyclic ring, are of current interest.[3,18] An important methodology for the preparation of β-heteroaryl-a,β-DDAA derivatives starts from 2*H*-pyran-2-one derivatives. In contrast to their fused analogues (benzopyran-2,5-diones (**2**)), 5-acyl-2*H*-pyran-2-ones (**54**) do not give the corresponding pyridine derivatives in the reaction with hydrazines and hydroxylamine (Scheme 16). Instead, they react with various hydrazines (**55**) and hydroxylamine as binucleophiles at the C=O moiety of the 5-acyl group and at the carbon 6 yielding very efficiently (*E*)- and/or (*Z*)-α,β-didehydro-α-amino acid derivatives (**56**), (**57**) and (**59**) containing the pyrazolyl or isoxazolyl moiety at the β-position.[19] In some cases decarboxylated products **58** were also observed. Under the applied conditions the hydroxylamine yields predominantly (*Z*)-products **59**. The formation of the regioisomeric products **56** and **57** becomes important when R^1 = Ph. In this particular case the reaction with hydrazine, methylhydrazine and benzylhydrazine led either to pure products **56** or to mixtures of products **56** and **57**. The reaction with phenylhydrazines containing electron-donating groups or weak to moderate electron-withdrawing groups (Me, Cl, CF_3, CO_2H, etc.) on the phenyl moiety gives almost exclusively (*E*)-products **57**, while phenylhydrazines having strong electron-withdrawing groups as well as heterocyclic hydrazines also yield (*Z*)-**57** and/or decarboxylated products **58**.



Scheme 16

On the basis of the isolated products two possible attacks of hydrazines to pyran-2-one were proposed, as depicted in Scheme 17.[19] Attack (a) at the C=O part of the 5-acyl group would result in the formation of a hydrazone derivative, which would give exclusively (*E*)-**56** in a direct conversion. If the 2*H*-pyran-2-one ring of the intermediate **60** was opened toward the tautomeric intermediate **61**, the expected (*E*)-**56** would also be accompanied by (*Z*)-**56**. On the other hand, the attack (b) at position 6-C of the pyran-2-one ring

gives the intermediate **62**, which can lead to the formation of the products (*E*)-**57** and, *via* the tautomeric form of the same intermediate, to the formation of (*Z*)-**57**. The formation of enamines (**58**) can be explained by the decarboxylation of the intermediate **62**, giving a new tautomeric intermediate **63**, which then cyclised into the final products **58**.



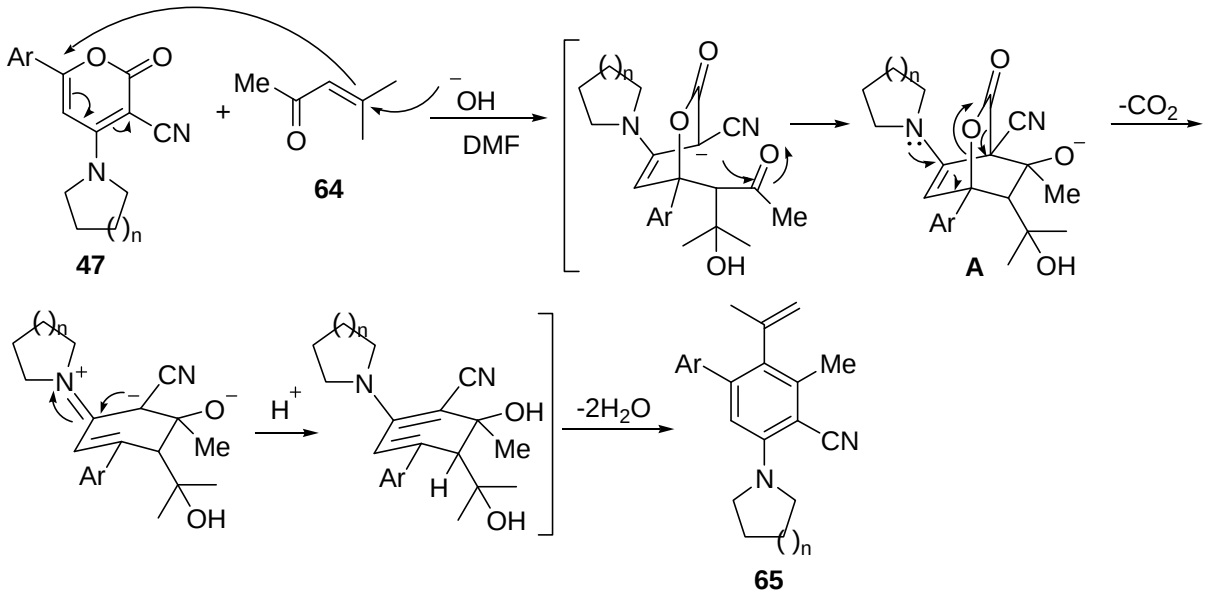
Scheme 17

CARBANION-INDUCED RING TRANSFORMATIONS OF 2*H*-PYRAN-2-ONES

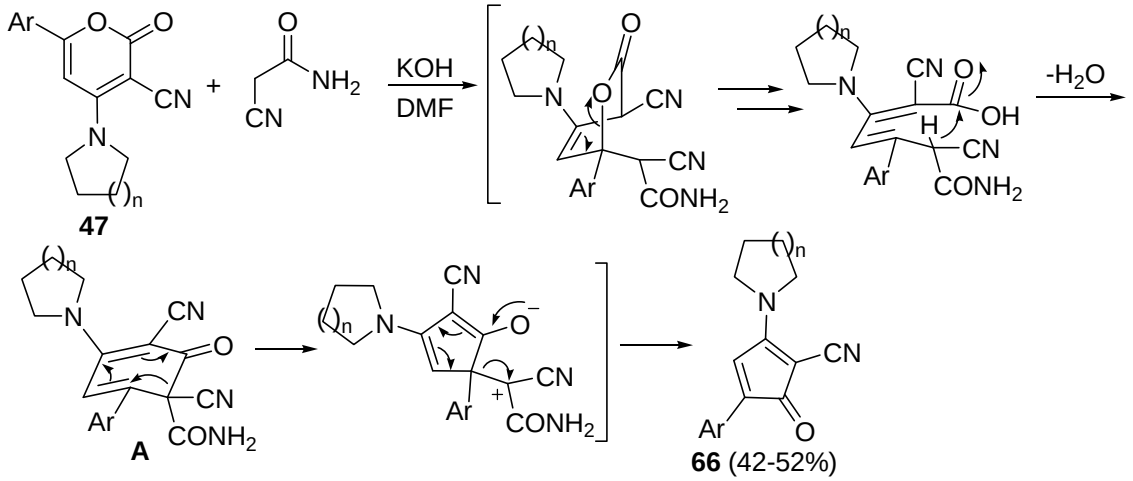
Carbanions can be easily obtained from Grignard reagents or by the reaction of compounds containing an activated methylene or methyl group with a base; they are strong nucleophiles. As such, they mostly react with the C-6 position of the 2*H*-pyran-2-one ring, causing a ring opening with possible decarboxylation followed by recyclization, giving different arenes or, depending on the substituents at the carbanion, heteroarenes.

The carbanion-induced ring transformation of 4-amino-substituted 2*H*-pyran-2-ones (**47**) with 4-methylpent-3-en-2-one (**64**) yielded functionally hindered styrene biaryls (**65**) (Scheme 18).[20] This transformation is possibly initiated by the Michael addition of the anion generated from 4-methylpent-3-en-2-one at the C-6 position of the 2*H*-pyran-2-one ring, followed by intramolecular cyclization involving the carbonyl functionality of **64** and the C-3 position of the pyranone ring to form the intermediate **A**, which on the elimination of carbon dioxide, followed by protonation and dehydration, furnished the final products **65**. On the other side, 2,3,5-trisubstituted cyclopentadienones (**66**) were prepared through the base-induced ring contraction of 6-aryl-4-amino-2*H*-pyran-3-carbonitriles (**47**) using

cyanoacetamide, as reported by Sil *et al*. (Scheme 19).[21] A plausible reaction pathway involves the nucleophilic attack of carbanion generated from cyanoacetamide at position C-6 of the 2*H*-pyran-2-one moiety, followed by the ring opening and by recyclization involving the carboxy group and the active methylene group of the cyanoacetamide with the elimination of water. Though the authors did not succeed to isolate any of the potential intermediates, they proposed a formation and a ring contraction of the cyclic intermediate **A,** followed by the elimination of the cyanoacetamide affording the cyclopentadienones (**66**) as the final products.



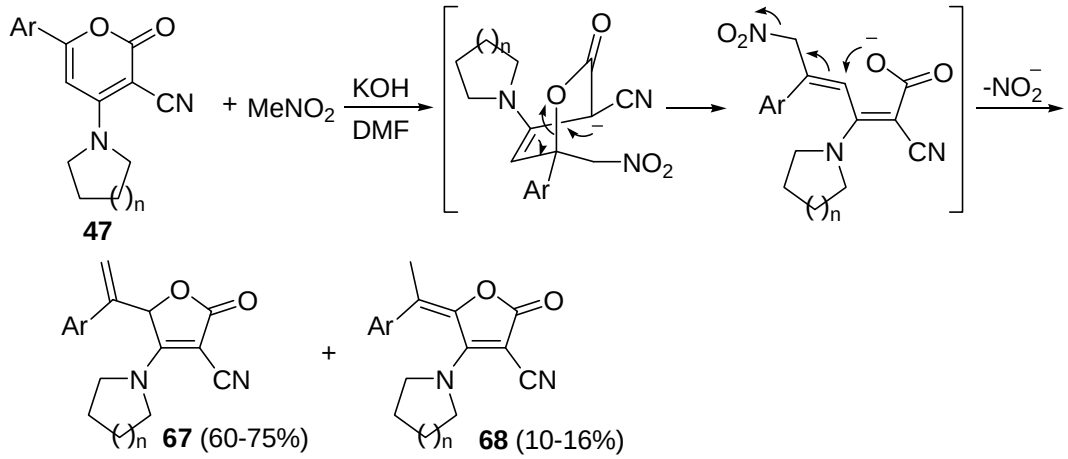
Scheme 18



Scheme 19

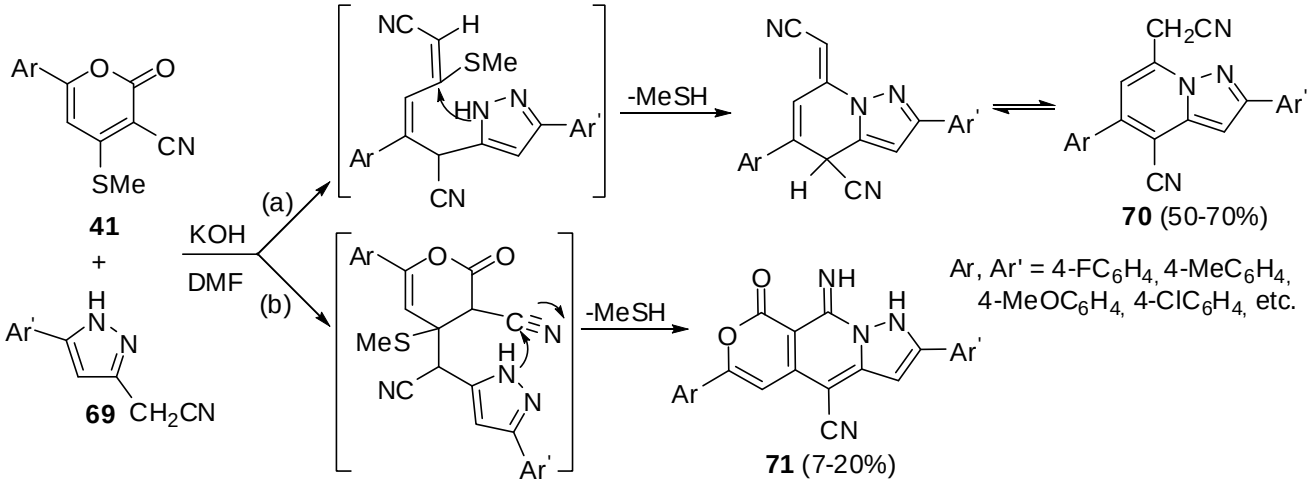
A different ring contraction was observed in the transformation of 2*H*-pyran-2-ones (**47**) by a carbanion generated *in situ* from nitromethane yielding 2-oxo-2,5-dihydrofuran-3-carbonitriles (**67**) and (**68**)

(Scheme 20).[22] The initial step in the formation of **67** is the attack of the carbanion at position C-6 of the pyran ring, followed by ring opening and relactonization, involving the carboxy group and the C-5 position of the pyran ring with the elimination of the nitro group, as depicted in Scheme 20. In some cases the formation of products **68** was observed, which may have been the result of the partial isomerisation of **67**.



Scheme 20

The reaction of 2*H*-pyran-2-one (**41**) and 5-aryl-3-cyanomethyl-1*H*-pyrazoles (**69**) as 1,3-C,N-ambident nucleophiles led to the formation of highly functionalized pyrazolo[1,5-*a*]pyridines (**70**) as the major products, while pyrano[4,3-*d*]pyrazolo[1,5-*a*]pyridines (**71**) were obtained as the minor products (Scheme 21).[23]

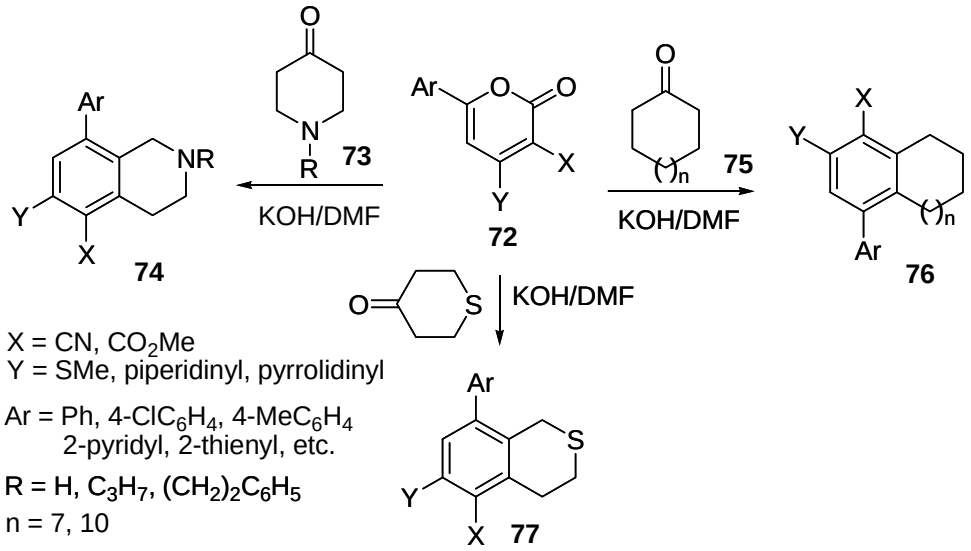


Scheme 21

The difference in the degree of electrophilicity of the positions C-6 and C-4 and their vulnerability to nucleophiles are the two main reasons for the formation of two different products. The attack of carbanion, formed *in situ* from cyanomethylpyrazole (**69**) and KOH as a base, at position C-6 yielded an open-ring

intermediate (path (a)) after decarboxylation. The latter underwent a Michael addition with pyrazole nitrogen and the concomitant elimination of methanethiol to give the products **70**. On the other hand, the competitive nucleophilic attack at position C-4 (path (b)) followed by ring closure *via* the cyano group afforded the products **71**.

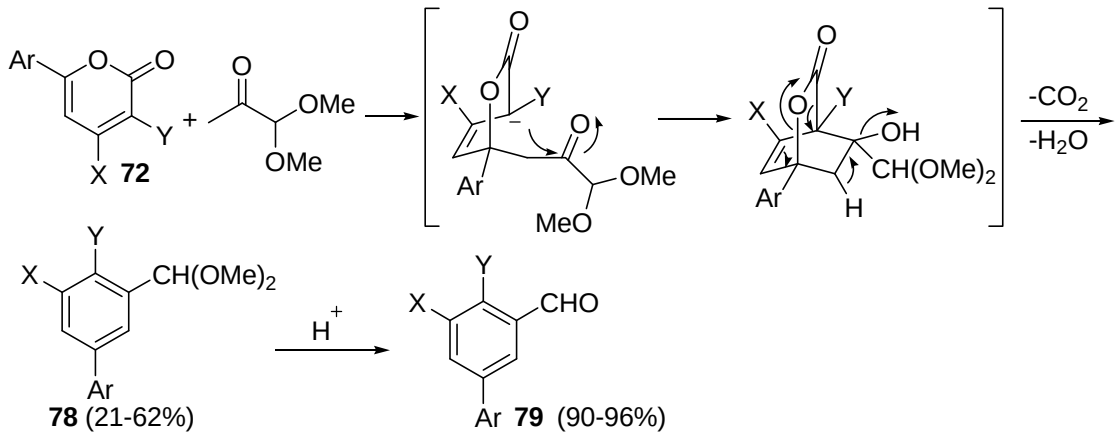
An innovative one-pot synthesis of tetrahydroisoquinolines (**74**), macrocyclic biaryls (**76**) and dihydro-1*H*-isothiochromenes (**77**) was described by Ram *et al*.[24] These compounds were obtained through base-catalyzed ring-transformation reactions of suitably functionalized 2*H*-pyran-2-one (**72**) by a carbanion generated from 4-piperidone (**73**), cycloalkanone (**75**) or tetrahydrothiopyran-4-one (Scheme 22). This procedure is very simple and opens up a new avenue for the convenient synthesis of unsymmetrical biaryls.



Scheme 22

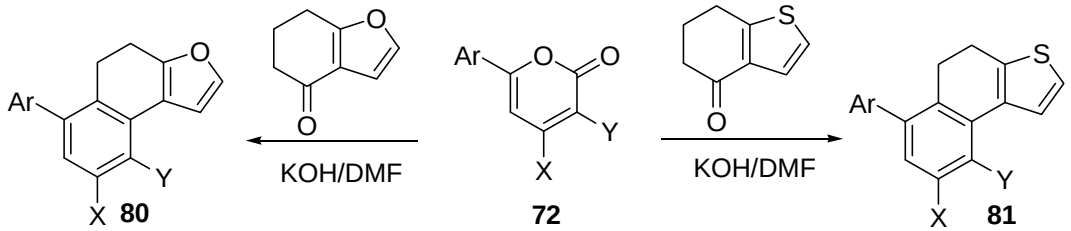
Similarly, reactions of 2*H*-pyran-2-ones (**72**) with benzene-fused cycloalkanone and benzene-fused tetrahydrothiopyran-4-one led to the formation of benzo[*c*]chromenes and benzo[*c*]thiochromenes, respectively.[25]

2*H*-Pyran-2-ones (**72**) were used as the precursors for the ring-ring transformation reaction, using 1,1-dimethoxypropan-2-one as the carbanion source; the carbanion was generated *in situ* by the action of KOH in DMF.[26] The reaction is possibly initiated by the attack of the carbanion at position C-6 followed by the concomitant ring closure. In the next step, after decarboxylation and dehydration-substituted benzaldehyde dimethyl acetal (**78**) is obtained, which on acetal hydrolysis by Amberlyst 15 or ethanolic HCl led to the substituted benzaldehydes (**79**) (Scheme 23).



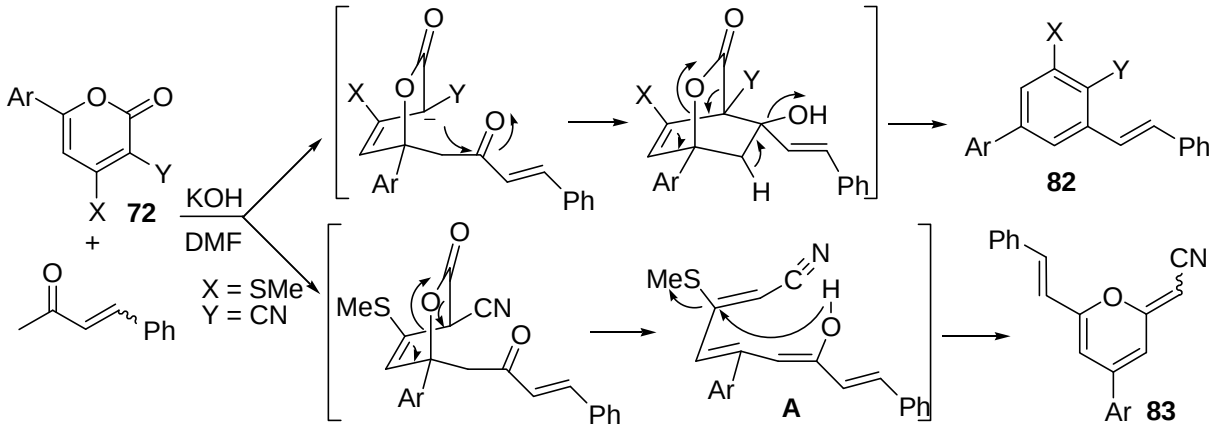
Scheme 23

On the other hand, the reaction of 2*H*-pyran-2-one (**72**) with 6,7-dihydro-5*H*-benzofuran-4-one and 6,7-dihydro-5*H*-benzothiophene-4-one provided a one-pot synthesis of diversely functionalized naphtho[2,1-*b*]furans (**80**)[27] and naphtho[*b*]thiophenes (**81**),[28] respectively, as reported by Goel and Dixit (Scheme 24).



Scheme 24

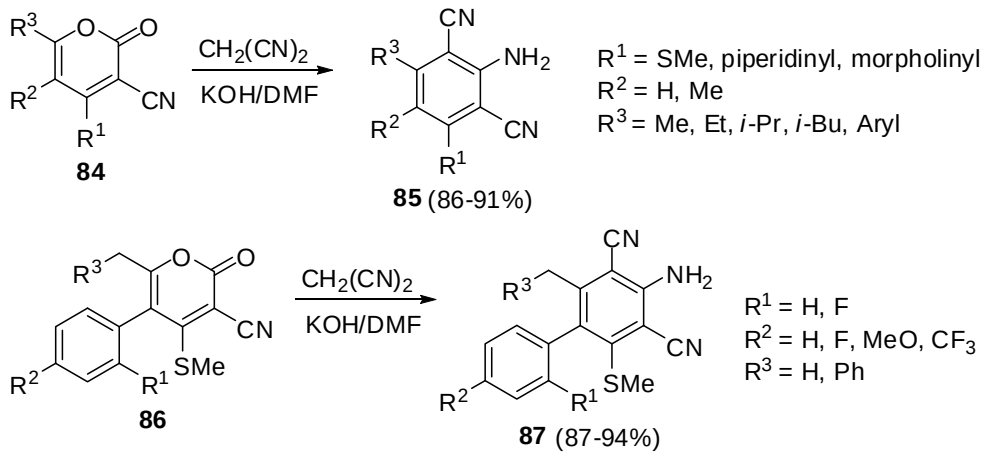
Moreover, the 2*H*-pyran-2-one (**72**) was converted with (*E*/*Z*)-4-phenylbut-3-en-2-one through a ring-ring transformation into highly functionalized (*E*)-stilbenes (**82**) (Scheme 25).[29] In some cases (X = SMe, Y = CN), the formation of the compounds **82** was accompanied by 4-aryl-6-styrylpyran-2-ylidineacetonitriles (**83**). The products **82** are formed by the attack of the carbanion at position C-6 of the 2*H*-pyran-2-one ring of **72** followed by the ring closure and by the liberation of carbon dioxide and water. On the other hand, the products **83** are generated through the attack of a nucleophile at position C-6 followed by decarboxylation and recyclization involving position C-4 of the previous pyran ring and the enolic OH of the intermediate **A**.



Scheme 25

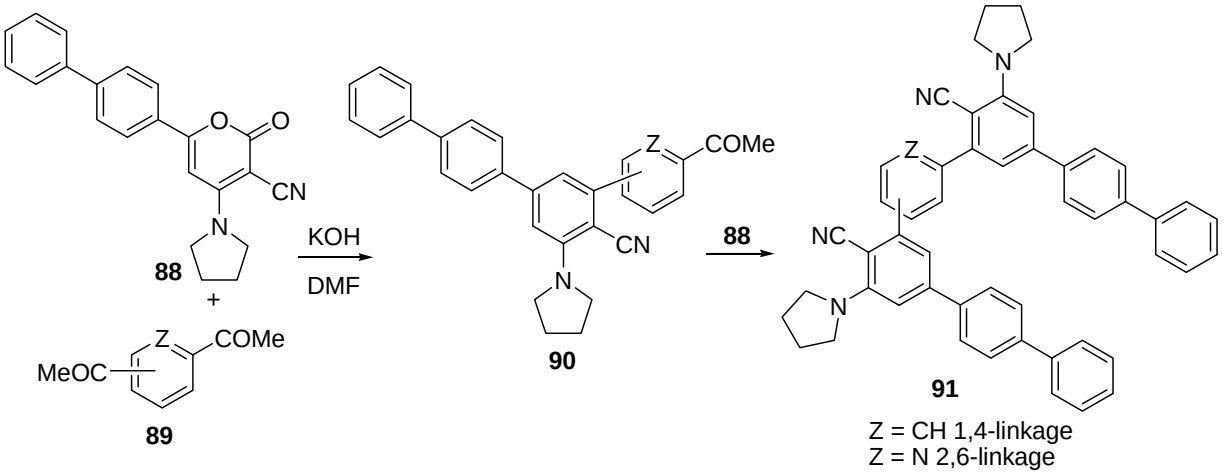
A convenient synthesis of highly functionalized isophthalonitriles (**85**) and (**87**) was achieved through a base-catalyzed ring-ring transformation of 6-alkyl/arylpyran-2-ones (**84**) and 5-arylpyran-2-ones (**86**) with malononitrile (Scheme 26).[30] The strength of the reaction lies in the creation of an aromatic ring from six-membered lactones under mild reaction conditions. This approach is an alternative to the Diels-Alder reactions of 2*H*-pyran-2-ones with dienophiles, which require forcing thermal conditions to obtain benzene derivatives and offers the flexibility of introducing the electron donating or accepting groups in the benzene scaffold.

Another approach to the synthesis of unsymmetrical biaryls was described in the transformation of 6-aryl-2*H*-pyran-2-ones or 6-isopropyl-2*H*-pyran-2-ones with the carbanion generated from 2-methylpentan-3-one or substituted phenylacetones.[31] By using this simple method *o*,*m*-cymene-cored derivatives were prepared in excellent yields. Biaryls functionalized with electron-withdrawing or electron-donating substituents were prepared from the corresponding pyran-2-ones and acetyltrimethylsilane.[32]



Scheme 26

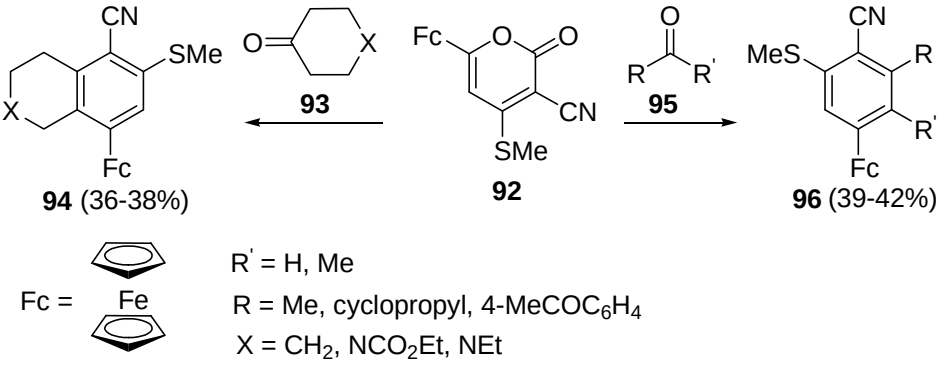
An efficient route for the synthesis of functionalized oligoarenes and heteroarenes starting from suitably substituted 2*H*-pyran-2-one (**88**) and aromatic ketones (**89**) (1,4-diacetylbenzene, 2,6-diacetylpyridine) was described by Sil *et al*.[33] The first step of this conversion is the formation of quaterarene (**90**), which was further exploited as a reagent for the ring transformation of the same starting 2*H*-pyran-2-one (**88**) to obtain septiarene (**91**) (Scheme 27). In this way oligoarenes containing only benzene rings (Z = CH) and oligoarenes with a central pyridine ring (Z = N) were prepared.



Scheme 27

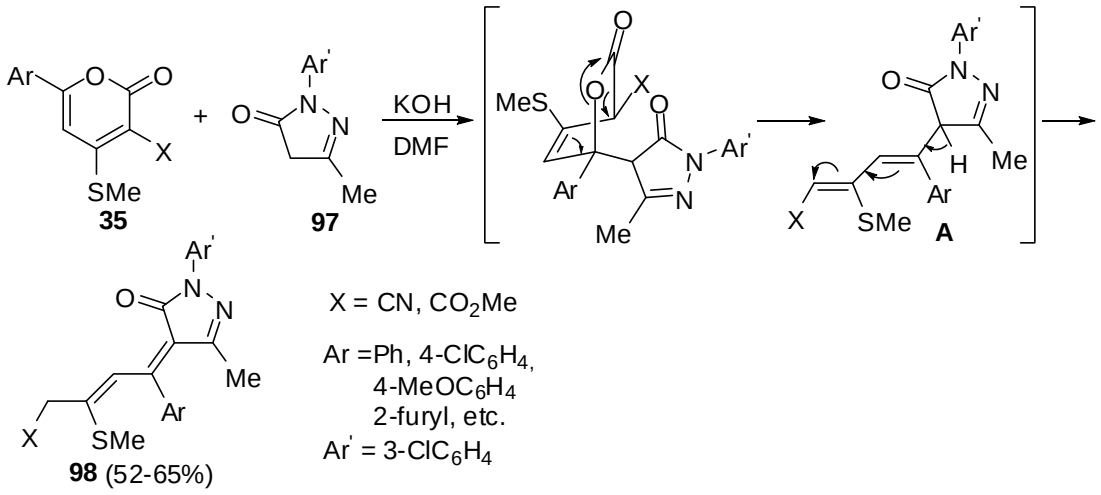
Similarly, a synthetic methodology for preparing unsymmetrical *meta*- and *para*-terphenyls starting from 6-aryl- and 5-aryl-substituted 2*H*-pyran-2-ones and 2-methoxyacetophenone was developed.[34]

3-Cyano-6-ferrocenyl-4-methylsulfanyl-2*H*-pyran-2-one (**92**) was allowed to react with aliphatic, alicyclic and heterocyclic ketones (**93**) and (**95**) under basic conditions to obtain various highly substituted ferrocenylarenes (**94**) and (**96**) (Scheme 28).[35] This methodology might replace an alternative procedure for the preparation of ferrocenylarenes from ferrocenylalkynes and zirconium cyclopentadiene.[36]



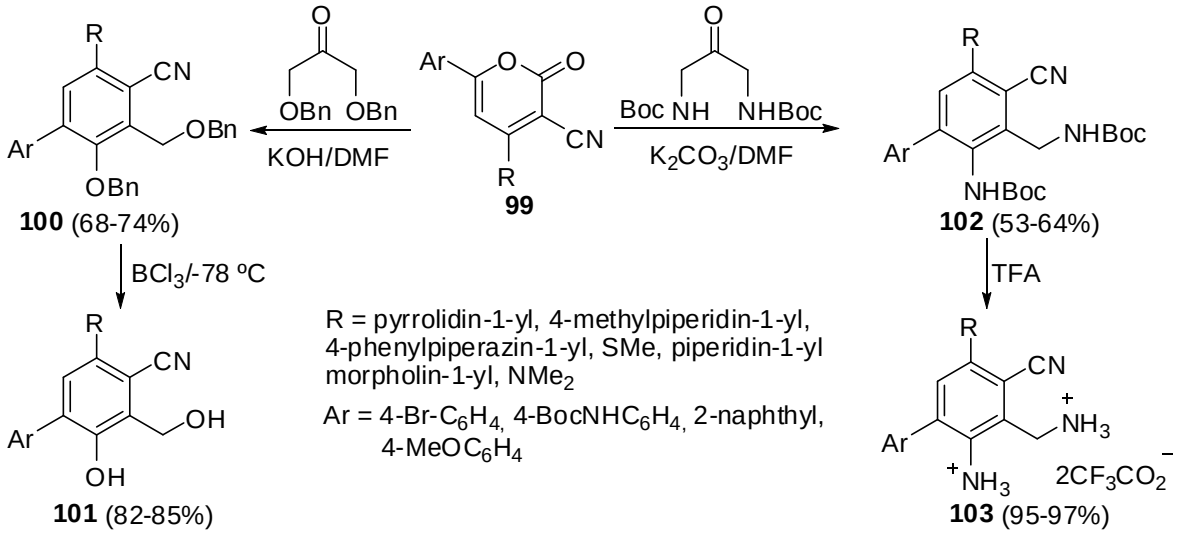
Scheme 28

The carbanion generated *in situ* at position 4 of 1-aryl-3-methyl-1*H*-pyrazol-5(4*H*)-one (**97**) reacts at position 6 of the pyran-2-one (**35**) with ring opening and decarboxylation, as depicted in Scheme 29.[37] Here, no ring closure occurred, but the initially formed intermediate **A** tautomerizes to the pure *E*-isomer of the final product **98**. This method enables the synthesis of substituted pyrazol-5(4*H*)-ones, which may be useful precursors for the construction of various heterocycles.



Scheme 29

A concise protocol for the construction of highly congested aryl-substituted 2-hydroxybenzyl alcohols (**101**) in two steps was developed by Ram's group.[38] The first step is the synthesis of 3-benzyloxy-2-benzyloxymethylbenzonitriles (**100**) through the base-catalyzed ring transformation of suitably functionalized pyran-2-ones (**99**) by 1,3-dibenzyloxypropan-2-one (Scheme 30). In the second step, debenzylation by stirring with BCl_3 afforded the desired products **101**. Similarly, 2-aminobenzylamines (**103**) as TFA salts were prepared from the same pyran-2-ones and Boc-protected 1,3-diaminopropan-2-one, followed by the TFA-catalyzed hydrolysis of the intermediate **102**.[39]



Scheme 30

CONCLUSION

In summary, we have presented some selected ring transformations of suitably functionalized 2*H*-pyran-2-ones and fused analogues with nitrogen- and carbon-nucleophiles. These reactions have provided convenient routes for the synthesis of different heterocycles and carbocycles as well as α,β-DDAA derivatives applying simple and economical procedures.

ACKNOWLEDGEMENTS

We thank the Ministry of Higher Education, Science and Technology of the Republic of Slovenia and the Slovenian Research Agency for their financial support (P1-0230-0103).

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