Tetrahedron 76 (2020) 131409

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Tetrahedron report 1209

Recent advances towards the synthesis of *4H*-quinolizin-4-one

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ARTICLE INFO

Article history:
Received 6 May 2020
Received in revised form
10 July 2020
Accepted 11 July 2020
Available online 21 July 2020

Keywords:
4H-quinolizin-4-one
Cyclocarbonylation
C–H activation

ABSTRACT

4H-quinolizin-4-one's is an important heterocyclic compound due to its wide range of applications in medicinal chemistry and material science. Despite of the attractive physicochemical properties and interesting biological activities, due to the non-availability of a general method of the synthesis, *4H*-quinolizin-4-one's small molecule library under-represented in medicinal chemistry programs. Therefore, the development of the general methods for the constructions of this core is an area of interest. Which continue to attract from the synthetic organic community and many protocols for the synthesis of functionalized *4H*-quinolizin-4-one were appeared in the literature since 2000. In this review, the results of the synthetic efforts towards the synthesis of the quinolizinone since 2000 are reviewed.

Contents

1. Introduction

4H-quinolizin-4-one is a unique class of heterocyclic bicyclic compound, which contain a nitrogen atom at the ring junction having polar zwitterionic character. It possess attractive physicochemical properties, as well studied for treatment of variety of the biological activities, such as, treatment of spinal muscular atrophy, type-2 diabetes, Alzheimer's disease, HIV integrase inhibitory activity, Mg2+ fluorescent probe for intracellular 3d imaging, anticancer, antibacterial, antimicrobial, anti-allergic, etc. [1–10] Structure of the representative biologically active *4H*-quinolizin-4-one is illustrated in Fig. 1.

Moreover, this scaffold is considered as an important starting material for the synthesis of other heterocycles [11]. Despite of the range of the biological activities and attractive physicochemical properties, the method for the construction of the *4H*-quinolizin-4-one is very limited. Due to the non-availability of the general methods of the synthesis of the functionalized *4H*-quinolizin-4-ones, this scaffold is poorly investigated in medicinal chemistry programs. Hence, the discovery of the new method for the synthesis of the functionalized *4H*-quinolizin-4-one is an area of interest. In this direction, in the recent years, the general method for

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https://doi.org/10.1016/j.tet.2020.131409
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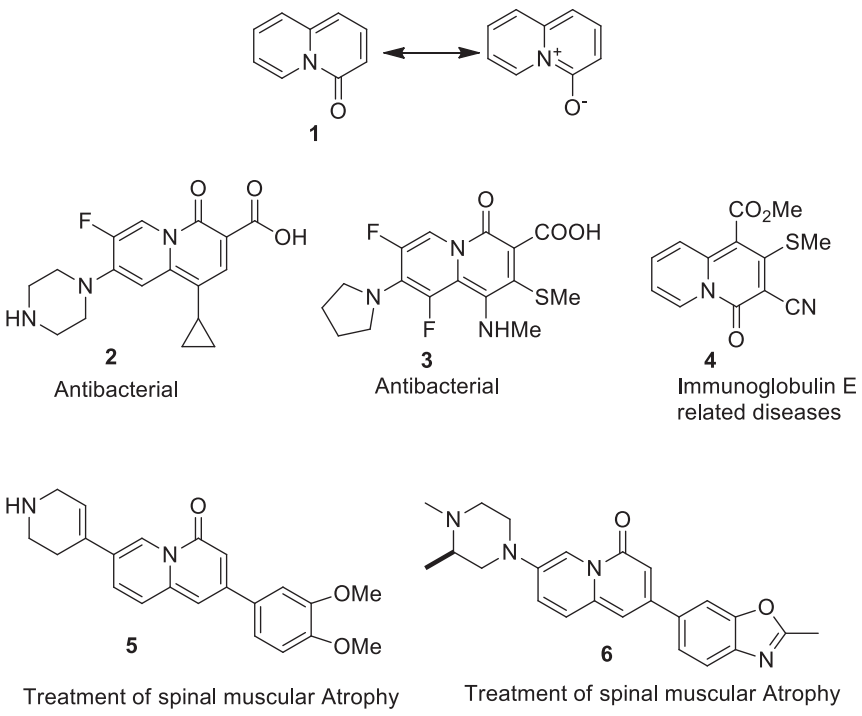


Fig. 1. Molecular structure of *4H*-quinolizin-4-one and representative biologically important *4H*-quinolizin-4-one's.

the synthesis of the functionalized *4H*-quinolizin-4-one reported in literature. Despite of the usefulness of *4H*-quinolizin-4-one in medicinal chemistry and material science no detailed review article in this field with exceptions of a short review by Alnajjar et al. [12] In this review, we have summarized the new methods of synthesis of this *4H*-quinolizin-4-one published since 2000. This helps the researcher to have the literature available methods at a glance and give the direction to discover the new methodology for the synthesis of functionalized *4H*-quinolizin-4-one which could be explored for the development of pharmacological agent.

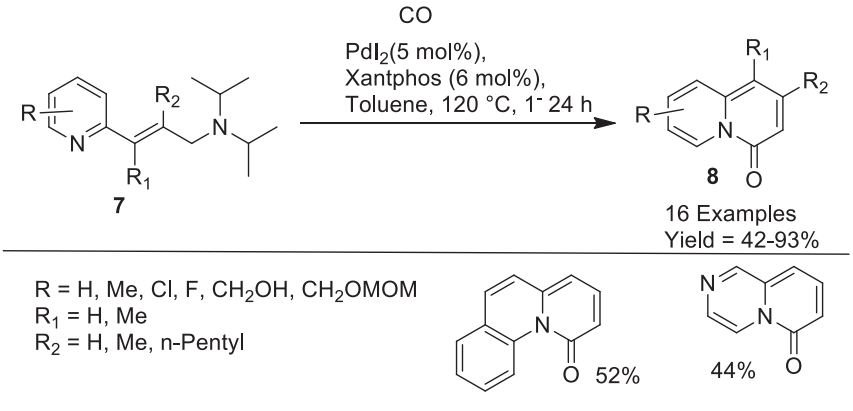
2. Metal catalyzed intramolecular cyclocarbonylation using CO as C1 precursor

Metal catalyzed intramolecular aminocarbonylation is an important method for synthesis of the lactam, Hui Yu et al. used this strategy for the synthesis of the *4H*-quinolizin-4-ones. The palladium catalyzed intramolecular cyclocarbonylation of the azaarene substituted allyl amine **7** gives access to the *4H*-quinolizin-4-ones **8** in good to excellent yield (Scheme 1). This is an example of the dearomative carbonylation and Heck reaction by palladium catalyst [13].

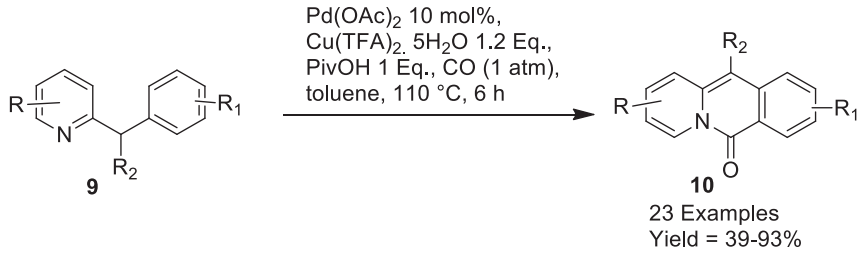
Zeqiang Xie et al. synthesized the pyridoisoquinolinones **10** by Pd-Catalyzed C(sp2)–H carbonylation of 2-benzylpyridines **9**. The pyridyl group in the starting material serves both as a nucleophile as well the directing group in the palladium catalyzed pyridocarbonylation (Scheme 2) [14].

Xibing Zhou et al. synthesized the quinolizinones **12** in 41–98% yield with wide substrate scope. This method involves, palladium catalyzed hydrocabonylative cyclization of the aryl tethered alkene or dienes **11** (Scheme 3). The reaction proceeds via sequential insertion of a C=C, CO, and a C=N bond into palladium–hydride bonds [15].

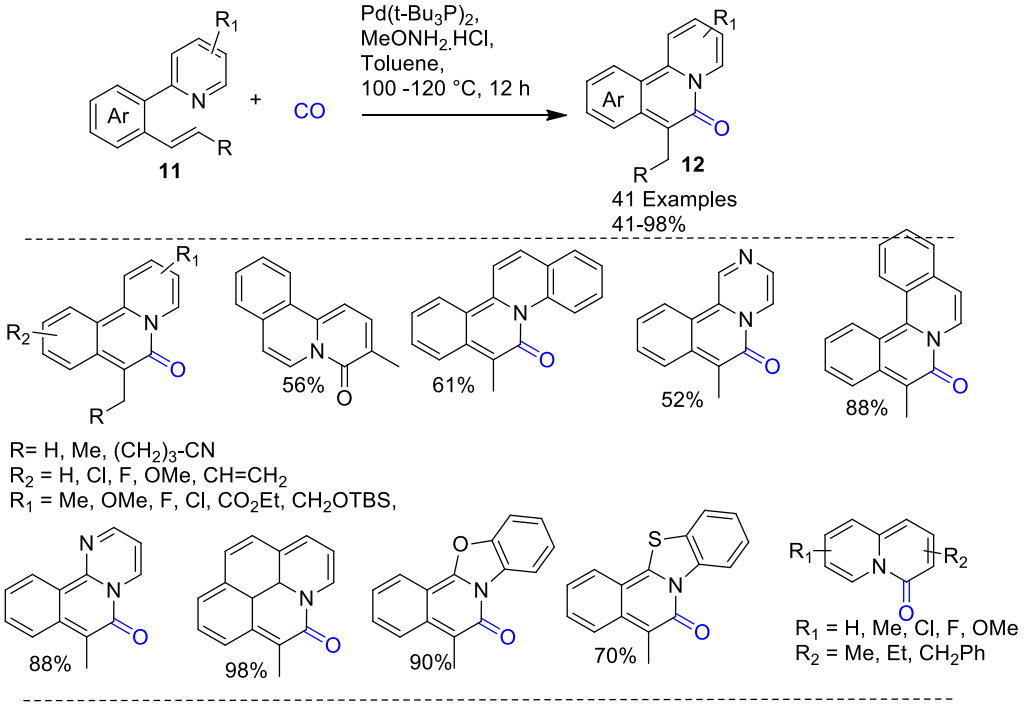
Like to palladium, the dicobalt octacarbonyl serves as the



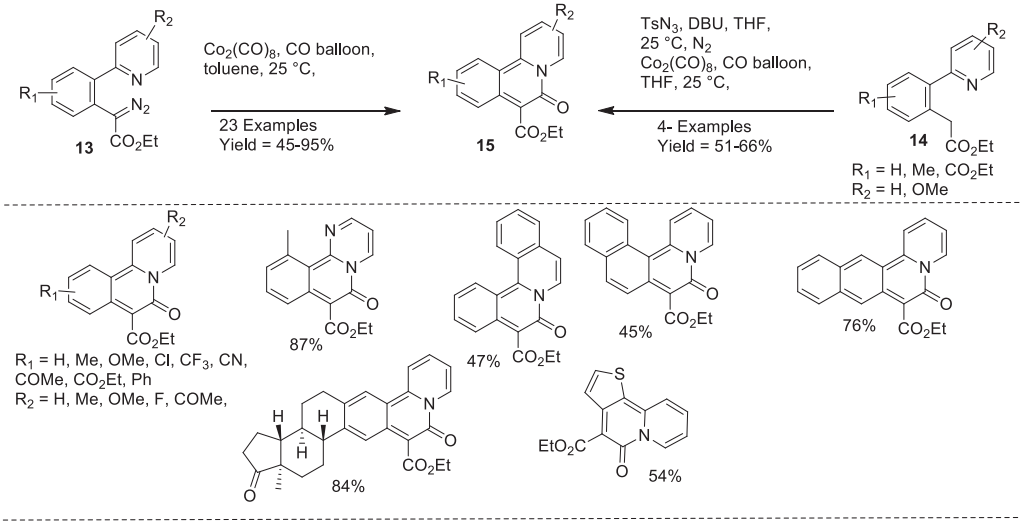
Scheme 1. Cyclocarbonylation of the aza-arene substituted allyl amine to *4H*-quinolizin-4-ones.



Scheme 2. Pd-Catalyzed C(sp2)–H carbonylation of 2-benzylpyridines.



Scheme 3. Palladium catalyzed hydrocabonylative cyclization.



Scheme 4. Dicobalt octacarbonyl catalyzed hydrocabonylative cyclization.

efficient catalyst for the carbonylative cyclization of pyridinyl diazoacetate **13** to pyridoisoquinolinone **15** (Scheme 4). The reaction proceeds at room temperature under balloon pressure of the carbon monoxide with a wide variety of the substituent tolerated under the optimized reaction conditions. Moreover, Yonghyeon Baek et al. demonstrated diazotization and cyclocarbonylation to pyridoisoquinolinone **15** in one pot procedure (Scheme 4) [16].

3. CO free cyclocarbonylation

Most commonly CO gas is used as the CO source for carbonylation reaction. Rui Yang et al. developed the CO free palladium catalyzed carbonative cyclization of benzylpyridine **16** to the pyridoiso-quinolinones **17**(Scheme 5).

This procedure makes the use of the formic acid and acetic anhydride as CO source instead of the CO gas. The reaction involves CH-activation of the **16** followed by dearomative cyclization. Benzylpyridine **16** first from palladocyles which underwent dearomative cyclocarbonylation to pyridoiso-quinolinones **17** in 35–91% yield [17].

4. Tandem catalysis approach for CO_2 fixation as C1 precursor

Tandem catalysis involve use of the more than one catalyst in one pot and is one of the most important approach in organic synthesis. Moreover, the use of the CO_2 in for the construction of the complex molecular skeleton is an emerging area. In view of the these facts the Chao-Chen Dong et al. developed the new method for the synthesis of the *4H*-quinolizin-4-ones **19** using the CO_2 as a carbon precursor via multicomponent reaction. The Ag_2O and Cs_2CO_3 serves as the effective orthogonal tandem catalyst for the construction of the 2 C–C and one C–N bond under mild reaction conditions in one pot to give access to *4H*-quinolizin-4-ones **19** (Scheme 6) [18].

5. Metal catalyzed/(double) *C–H* activation protocol

The metal catalyzed *C–H* activation by directing groups is an attractive strategy for the synthesis of many heterocyclic compounds. The primary benzamide **20** on reaction with the two molecules of the alkynes **21** gives access to the *4H*-quinolizin-4-ones derivatives **22**. This reaction proceeds by double C–H activation by Rh(III) catalyst followed by oxidative coupling to give *4H*-quinolizin-4-ones. Ag_2CO_3 serves as internal oxidant and $[Cp^*RhCl_2]_2$ as an efficient catalyst for C–H activation and the reaction proceeds smoothly in acetonitrile. The benzamide bearing both electron withdrawing and electron donating substituents at various positions gave access to corresponding product in good yields. On using 1-phenyl-1-propyne as the alkyne instead of the 1,2-diphenylethyne, only the exclusive product **22C** over the four possible regioisomers (Scheme 7) [19].

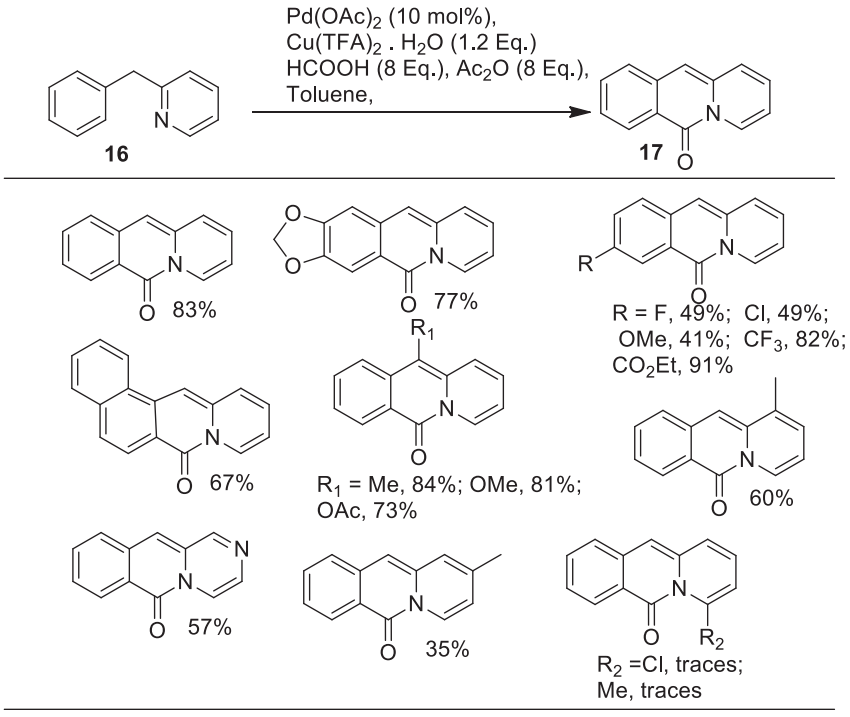
The rhodium catalyzed reaction of the primary benzamide **20** (Scheme 8) with 2 molecules of alkyne **23** to give quinolizinone **24**. The reaction proceeds with the double *C–H* activation and annulation with alkyne, the $Cu(OAc)_2.H_2O$ serves as internal oxidant [20].

The double cascade reaction of the benzoylhydrazine **25** with the 2 molecules of the alkyne produces the quinolizinone **26** in good yield. The reaction proceeds via *C–H* activation by the Rh(III) catalyst directed by the hydrazide functionality. If one equivalent of the alkyne is used, then isoquinolones is the major product under these reaction conditions (Scheme 9) [21].

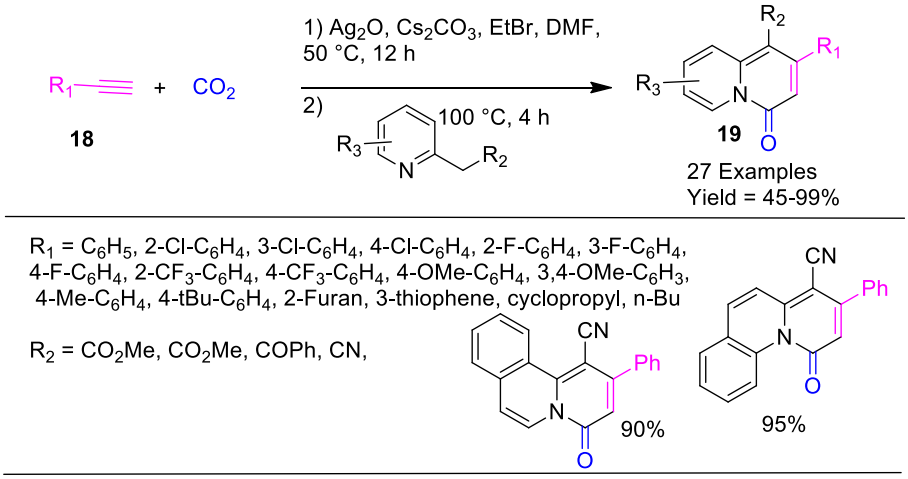
Juan Li et al. used the Rh(III)-catalyzed oxidative annulation of pyridin-2(1*H*)-ones **27** with alkynes via double *C–H* activation with alkyne to construct the highly functionalized *4H*-quinolizin-4-ones (Scheme 10) [22].

Furthermore, this method extended successfully for the annulation of *N*-arylpyridin-2(1*H*)-ones **29** with alkynes which gave access to the library of the 1*H*-pyrido[1,2-*a*]quinolin-1-one **30** (Scheme 11).

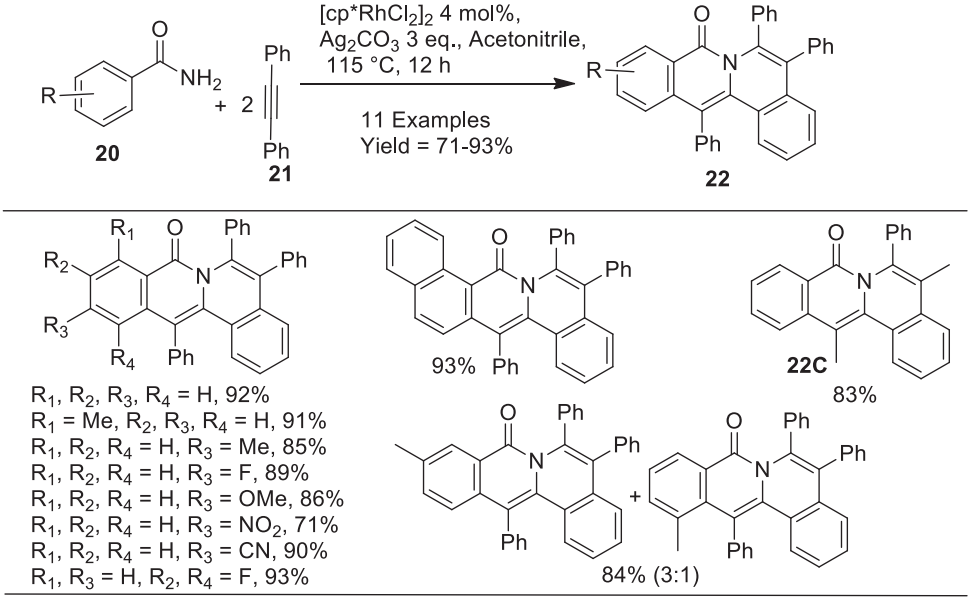
Ju Hyun Kim et al. constructed the isoquinolinone by the Rh(III)



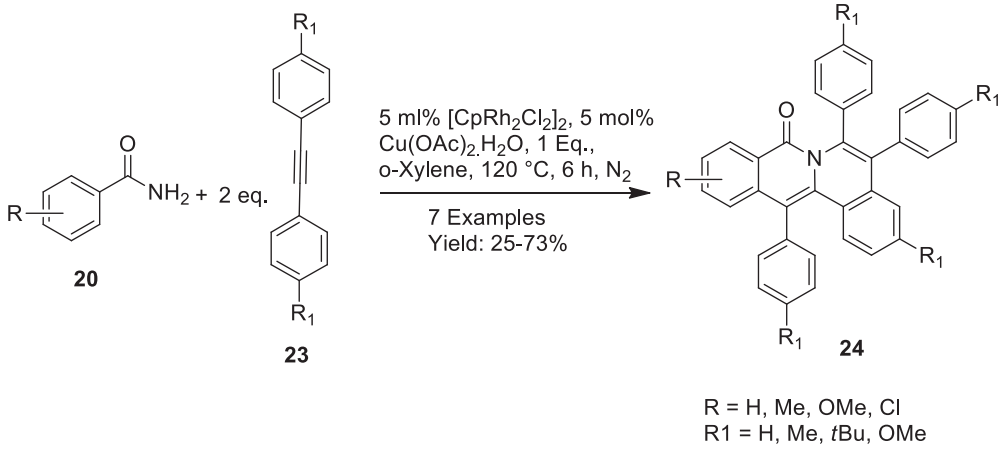
Scheme 5. CO free Cyclocarbonylation.



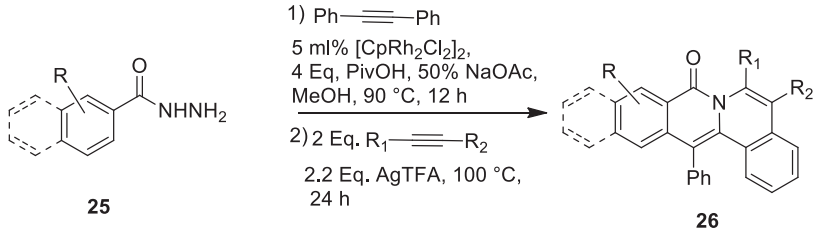
Scheme 6. One-Pot multicomponent synthesis of *4H*-quinolizin-4-ones using the Ag_2O/Cs_2CO_3 Orthogonal Tandem Catalysis and CO_2 as C1 precursor.



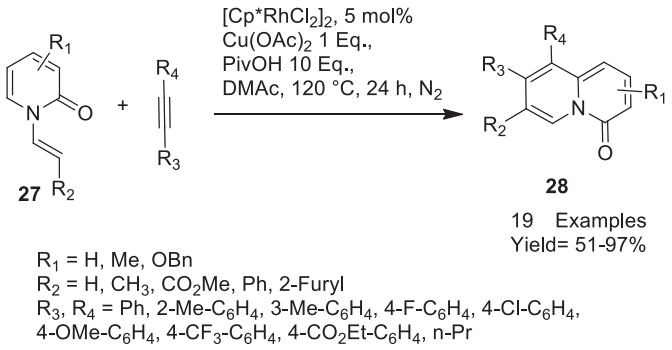
Scheme 7. Synthesis of the polycyclic *4H*-quinolizin-4-ones by Rh(III)-Catalyzed double oxidative coupling of primary benzamides and alkynes.



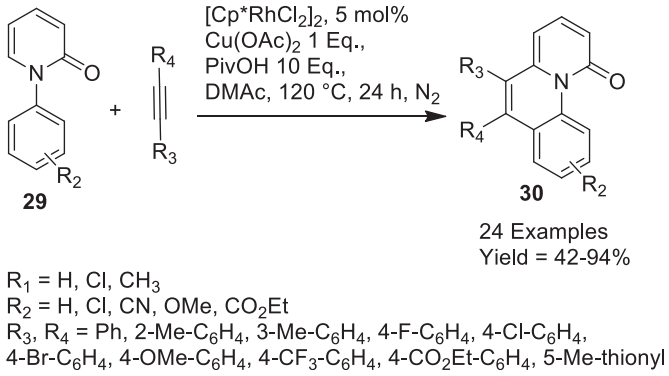
Scheme 8. Synthesis of the polycyclic *4H*-quinolizin-4-ones by Rh(III)-Catalyzed double C–H activation of benzamide.



Scheme 9. Synthesis of the *4H*-quinolizin-4-ones by Rh(III)-Catalyzed double cascade reaction of the benzoylhydrazine with alkyne.



Scheme 10. Rh (III) Catalyzed synthesis of quinolizinones via *C—N* activation or *C—H* Activation.



Scheme 11. Rh (III) Catalyzed Synthesis of quinolizinones.

catalyzed *C—H* activation of 2-arylpyridine **31** and the pyridotriazole **32** was used as a carbene source to give access to isoquinolinone **33** in 50—99% yield (Scheme 12). The synthesized derivative are fluorescent in nature and studied for the application in metal detection [23].

Ruthenium catalyzed reaction of the benzamide **20** and diphenyl acetylene **21** gives access to isoquinolinone **22** in moderate yield (18—56%) (Scheme 13). The Cu(OAc).H_2O serves as internal oxidant. Frist C—H activated by ortho amide group undergoes ruthenocycle formation which further coordinated with alkyne followed by reductive elimination to give corresponding isoquinoline [24,25].

Bin Li et al. have optimized the ruthenium catalyzed method for the coupling of isoquinoline **34** and alkyne to quinolizinone derivatives **35**. The reaction proceeds smoothly with wide substrate scope and proceeds via *C—H*, *N—H* activation. In this first step formation of the cyclometalated compound assisted by the acetate which undergoes mono alkyne insertion to Ru—C bond of the metalocycle then oxidative coupling of *C—N* bond insertion (Scheme 14) [26].

The Amitava Rakshit et al. developed one pot protocol for the synthesis of isoquinolinone **37** from the α-ketomalonitrile derivative **36** (Scheme 15). First one of the nitrile undergoes the selective hydrolysis by copper acetate monohydrate give corresponding amide which underwent dehydrative cyclization and annulation with alkyne in the presence of the ruthenium catalyst in one pot. This transformation involves one *C—C*, two *C— N*, two *C═C* and a *C═O* bonds in one pot [27].

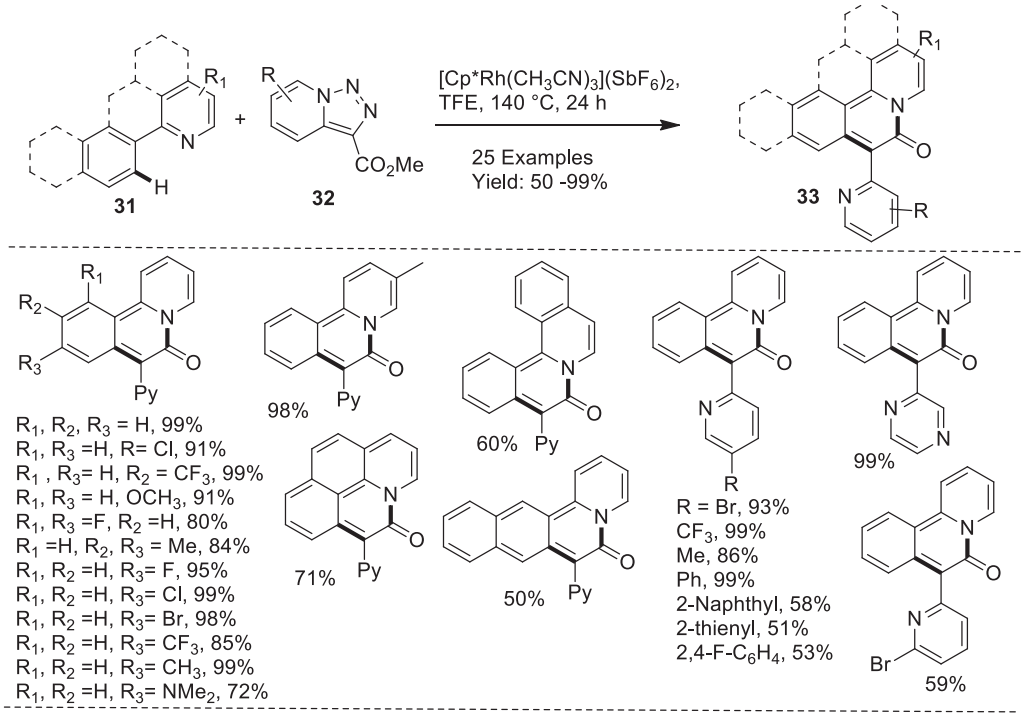
Cobalt catalyzed *C—H* functionalization with diazo compound **39** gives access to the quinolizinone **40** in good to excellent yield. The diazo compound **39** is generates the carbene which undergoes annulation to yield polycyclic compound **40** (Scheme 16) [28].

Zhengwang Chen et al. developed the one pot protocol for the synthesis of the highly functionalized 4*H*-quinolizin-4-ones **44** using the Sonogashira coupling of the variety of the aryliodide **41** with methylpropiolate **42** gave alkyne derivative which undergo the cyclization with the β-pyridyl analogues **43**. The both electrons withdrawing and donating substituent on the aryl iodide **41** as well as the variety of the 2-pyridyl derivatives **43** were tolerated under optimized reaction condition (Scheme 17) [29].

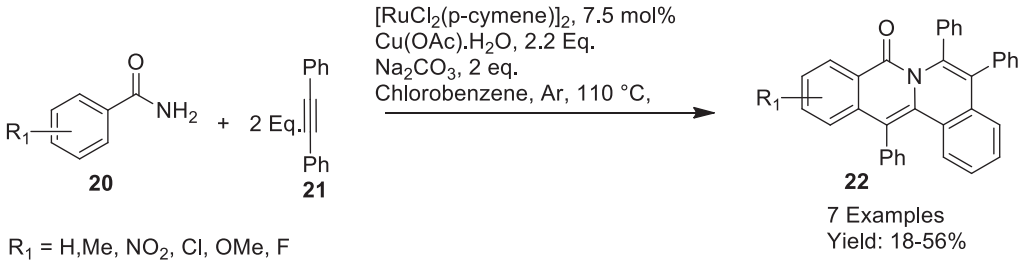
René den Heeten et al. constructed the *4H*-quinolizin-4-ones derivatives by using multicomponent alkylation, Heck reaction procedure. This protocol gives access to highly functionalized *4H*-pyrido[2,1-*a*]isoquinolin-4-one in three steps (Scheme 18) [30].

Popat S. Shinde et al. developed the gold catalyzed amino-alkenylation protocol for the synthesis of the quinolizinone **50**. The gold catalyzed reaction of the 2-pyridylalkyne **49** with 1-[(triisopropylsilyl)-ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX) gives access to the quinolizinone **50** in 48—87% yield. The reaction proceeds smoothly at 50 °C (Scheme 19) [31].

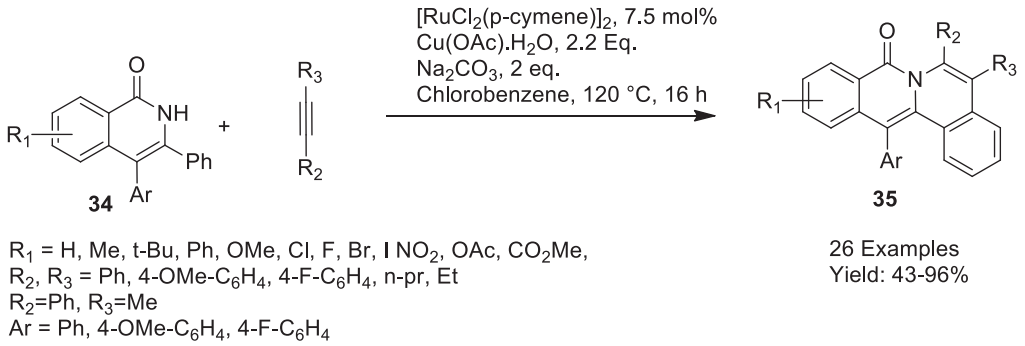
Alfredo Rosas-Sánchez et al. synthesized the 3-substituted 4*H*-quinolizin-4-ones using (η4-vinylketene)-$Fe(CO)_3$ complexes under mild reaction condition in good yield (Scheme 20). The key intermediate (η4-vinylketene)-$Fe(CO)_3$ complex **55** synthesized as per the reaction sequence depicted in Scheme 20 starting from 2-formyl pyridine derivative **52**. 2-formylpyridine's on reaction with ketone **51** gave the chalcone's **53** which on reaction with $Fe_2(CO)_9$ followed by treatment with methyl lithium in the presence of the CO balloon gave (η4-vinylketene)-$Fe(CO)_3$ complex **55** which on refluxing in benzene for 4 h gave 4*H*-quinolizin-4-ones **56** and **57** in 59—93%. These compounds studied for important photo luminescent which could give opportunities to design the novel organic light emitting diodes [32].



Scheme 12. Synthesis of the *4H*-quinolizin-4-ones by Rh(III) catalyzed *C–H* activation of 2-arylpyridine and the pyridotriazole.



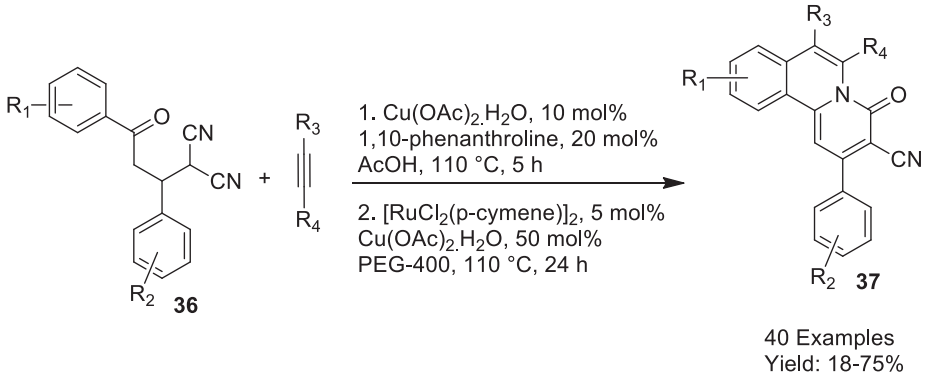
Scheme 13. Synthesis of the *4H*-quinolizin-4-ones by Ru(IV) catalyzed *C–H* activation of benzamide.



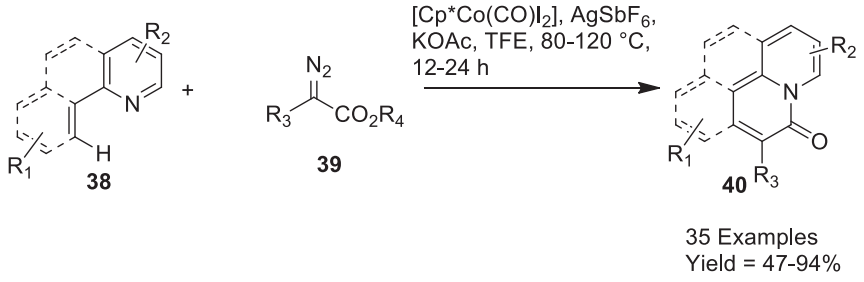
Scheme 14. Synthesis of the *4H*-quinolizin-4-ones by ruthenium coupling of isoquinoline and alkyne to quinolizinone.

Fe_3O_4-MNPs (magnetic iron oxide nanoparticles) serves as catalyst for the synthesis of 4*H*-pyrido[2,1-*a*]isoquinolin-4-one **63** via multicomponent reactions of the phthalaldehyde, methyl amine, methyl malonyl chloride, alkyl bromides, and triphenylphosphine. The reaction proceeds in aqueous sodium hydroxide at 80 °C. Alternatively the 2-aminobenzaldehyde is and acetaldehyde is used as substrates instead of the phthalaldehyde and methyl amine which gave access to 4*H*-pyrido[2,1-*a*]isoquinolin-4-one **63A** (Scheme 21) [33].

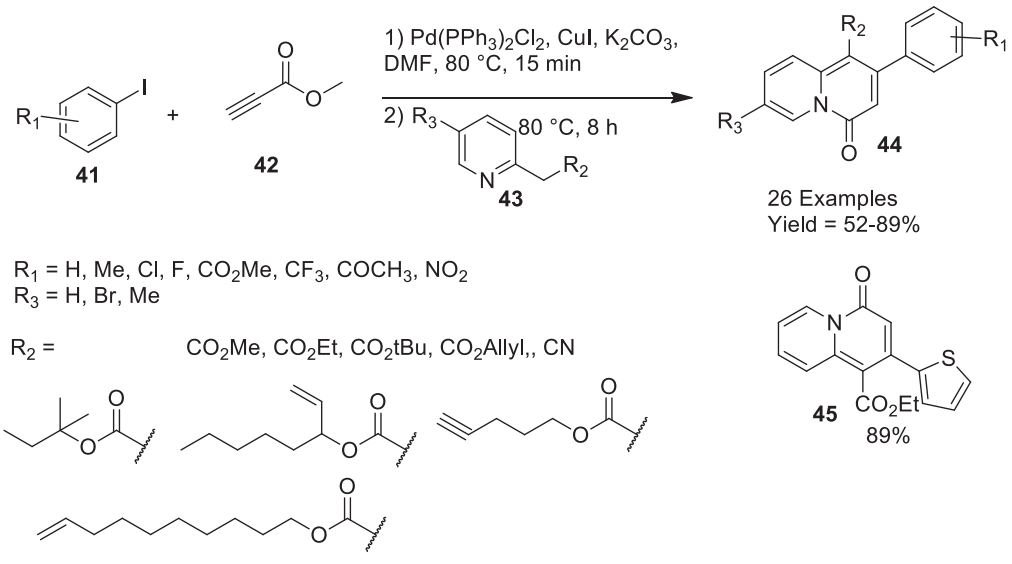
Baek Y. et al. synthesized acylmethyl-substituted 2-arylpyridine by rhodium catalyzed C–H activation reaction of 2-arylpyridines with 3-aryl-2H-azirines. Acylmethyl-substituted 2-arylpyridine 2-arylpyridine can be used as the starting material for the synthesis of isoquinoline using one pot procedure. Acyldiazo group can be



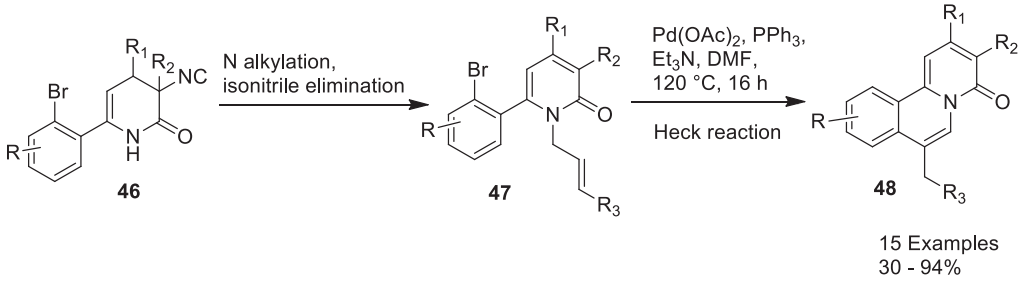
Scheme 15. Synthesis of the *4H*-quinolizin-4-ones by coupling of α-ketomalonitrile and alkyne to quinolizinone.



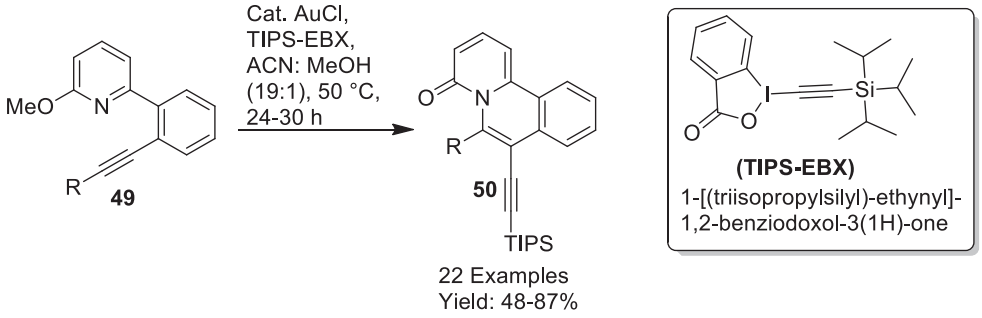
Scheme 16. Directed C−H bond functionalization with carbene precursors.



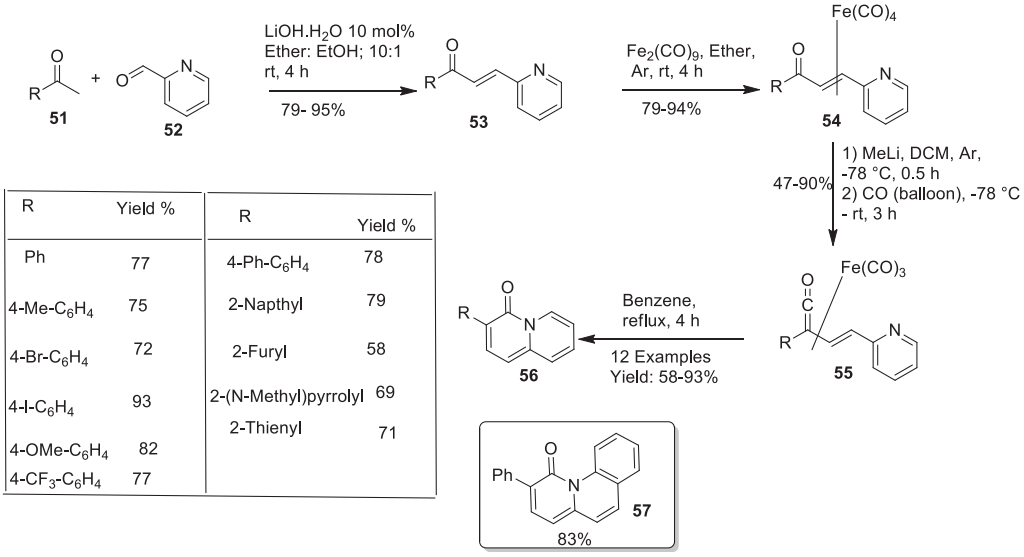
Scheme 17. The synthesis of 4*H*-quinolizin-4-ones via one-pot Sonogashira coupling and annulation reaction.



Scheme 18. The synthesis of 4*H*-quinolizin-4-ones by multicomponent alkylation, Heck reaction procedure.

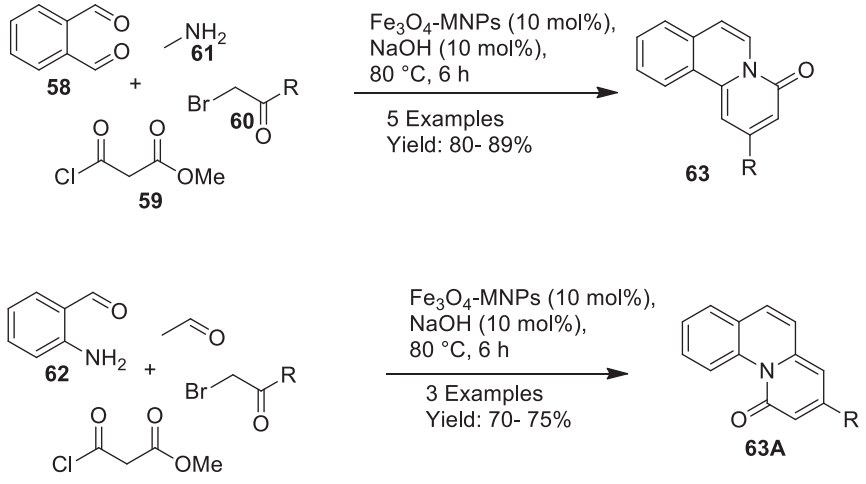


Scheme 19. Gold catalyzed synthesis of 4*H*-quinolizin-4-ones.



R	Yield %	R	Yield %
Ph	77	4-Ph-C_6H_4	78
4-Me-C_6H_4	75	2-Napthyl	79
4-Br-C_6H_4	72	2-Furyl	58
4-I-C_6H_4	93	2-(N-Methyl)pyrrolyl	69
4-OMe-C_6H_4	82	2-Thienyl	71
4-CF_3-C_6H_4	77		

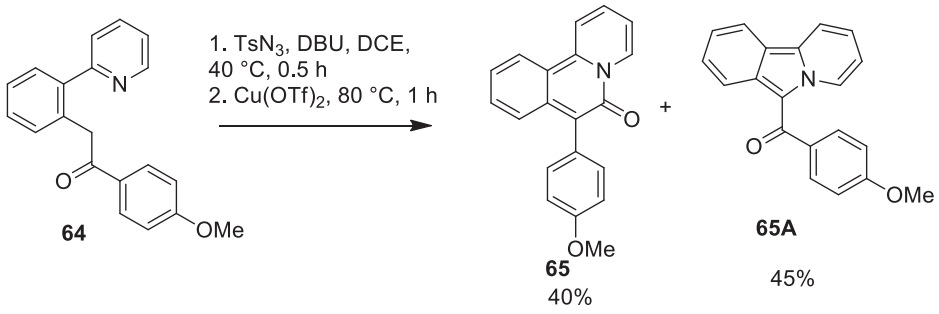
Scheme 20. 3-substituted 4H-quinolizin-4-ones via (η4-vinylketene)-Fe(CO)$_3$ complexes.



Scheme 21. Multicomponent reaction for the synthesis of pyrido[2,1-*a*]isoquinoline.

easily obtained from the diazotization of the corresponding acylmethyl-substituted 2-arylpyridine, which undergoes intramolecular cyclization of in situ generated diazo intermediate via Curtious rearrangement in presence of 1 mol% of copper triflate catalyst, leading to formation of pyridoisoquinolinone **65** (40%) and pyridoisoindole **65A** (45%) (Scheme 22) [34].

Dialkylthioether gold complexes serves as the source for the formation of the gold catalyst of the different oxidation states through photo reduction, which serves as an efficient catalyst for the synthesis of indolino-4H-benzoquinolizin-4-one **69** from **66** via the two sequential chemo-selective cyclization. The mono-substituted alkyne is activated by the gold (III) chloride catalyst



Scheme 22. One pot synthesis of 4*H*-quinolizin-4-ones.

whereas the disubstituted alkyne reacts in the presence of cationic gold (I). The first step is a 6-exo-dig cyclization followed by isomerization leading to the new β−carbolinone derivative **67** which undergoes 6-endo-dig cyclization towards 4*H*-quinolizin-4-one **69**. Different dialkylthioether gold complexes proved the effective for the transformation, however, we have shown below representative ligand **68** which yield the highest yield of 4*H*-quinolizin-4-one **69** (Scheme 23) [35].

6. RCM metathesis

Thomas A. Alanine et al. used the Ring-Closing Metathesis strategy for the construction of quinolizin-4-ones. The required key intermediate **75** was synthesized via Scheme 24. This involves the regioselective *N*-alkylation followed by Stille coupling. This protocol gives access to substituted quinolizin-4-ones **76** which were difficult to prepare by another method [36].

Hue Thi My Van et al. constructed quinolizin-4-ones **84** using the RCM strategy which is the starting material of 8-oxypseudopalmatine and 8-oxypseudoberberine (Scheme 25) [37].

7. Metal free protocol

Calum W. Muir et al. used the one pot Horner−Wadsworth−Emmons olefination/cyclization strategy for the construction of the 4*H*-quinolizin-4-ones **87** starting from β-ketopyridine **85** and triethylphosphinoacetate **86**. β-ketopyridine **85** undergo the Horner−Wadsworth−Emmons olefination by triethylphosphinoacetate **86** in the presence of the sodium hydride in toluene at 0 °C − rt in 15 min, the formed olefin cyclized to 4*H*-quinolizin-4-ones **87** on heating to reflux for 20 h (Scheme 26). This process offers the 2-substituted-4*H*-quinolizin-4-ones in good to excellent yield with range of the substituent tolerated [38].

α-hydroxy ketones **88** and dimethyl but-2-ynedioate undergoes cascade cyclization in the presence of the DBU as a base in DMF to gives access to pyrano[4,3-*a*]quinolizine-1,4,6(2*H*)-triones **89** in 40−94% yield (Scheme 27) [39].

Iwao Hachiya et al. have synthesized 4*H*-quinolizin-4-ones **92** and **93** in 14−77% yield by the addition reactions of malonic esters **91** to alkynylpyridines **90** (Scheme 28) [40].

The condensation of 2-pyridylderivative **95** with methyl-bis(methylsulfanyl)methylene -cyanoacetate **94** in the presence of potassium carbonate at room temperature for 4−5 h yields 3-cyano-4-oxo-4*H*-quinolizine **96** while the condensation of the **94** With the 3 equivalent of **95** formation of **97** is observed (Scheme 29) [41].

Hue T.B. Bui et al. used the one pot Stobbe condensation followed by cyclization strategy for the synthesis of the 4-Oxo-4H-quinolizine **199** from the commercially available pyridine 2-carboxaldehyde **98** (Scheme 30)[42].

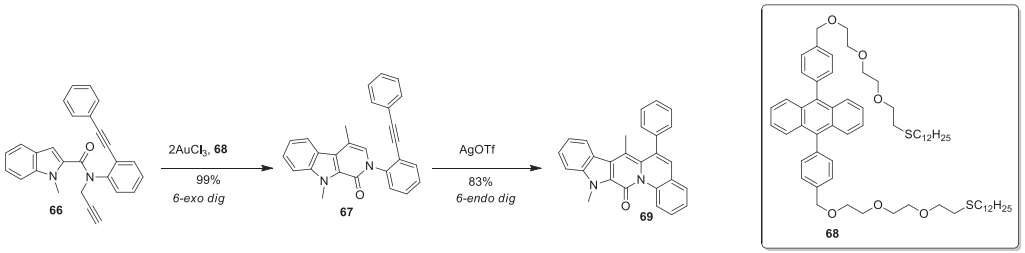
Quinolizinone **103** is synthesized in excellent yield using the flow technique, 2-Pyridiocyclobuenone **102** underwent the rearrangement at 100 °C in 10 min (Scheme 31)[43].

(*E*)-ethyl 3-(dimethylamino)-2-(1,3-dioxoisoindolin-2-yl)acrylate synthesized **105** from the ethyl 2-(1,3-dioxoisoindolin-2-yl) acetate **104** which on refluxing with 2-pyridylacetonitrile or ethyl 2-(pyridin-2-yl)acetate in acetic acid gives access to quinolizinones **106** (Scheme 32) [44].

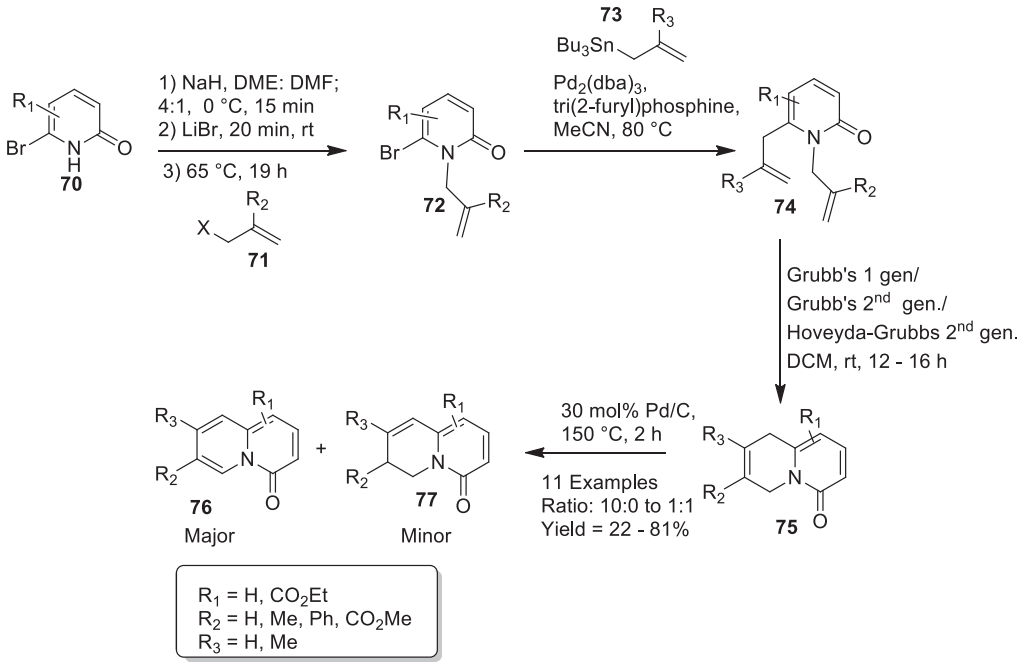
N-hetaryl substituted heptynone esters **107** undergo ring closure to give **108** which undergo a further anionic cyclization to provide tri- and tetracyclic quinolizinone derivatives **109** (Scheme 33) [45].

Anton J. Stasyuk et al. synthesized the naphthoquinolizines **111** via intramolecular Houben−Hoesch reaction of the **110** which showed interesting optical properties and high fluorescence quantum yield (Scheme 34) [46].

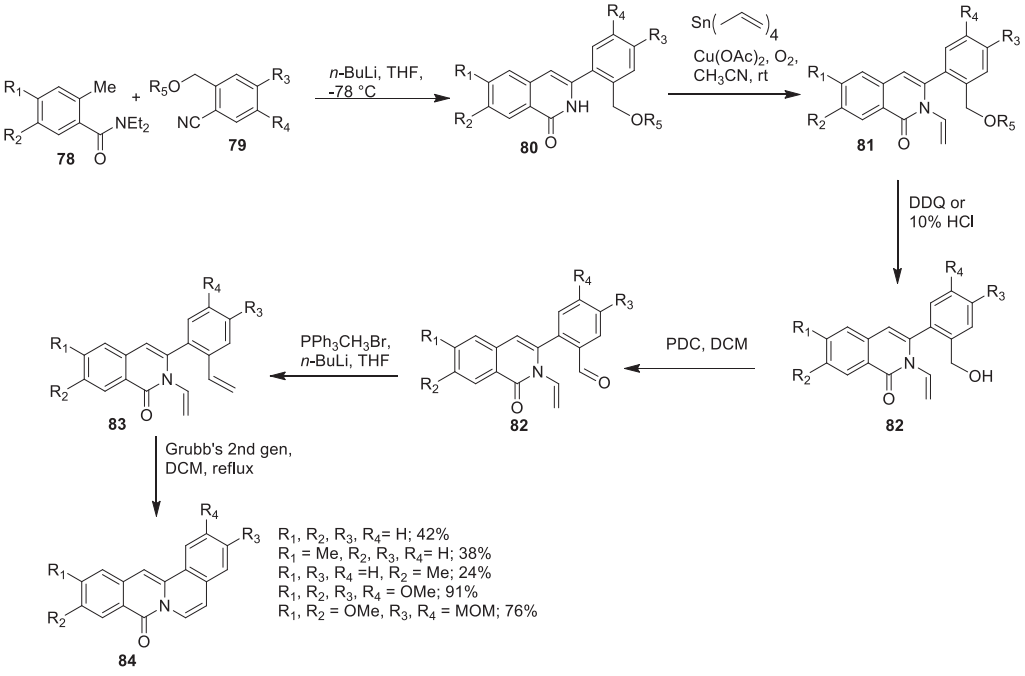
The orthoalkylnylaniline **112** and β-keto ester **113** on refluxing in ethanol in the presence of PTSA yields tetracyclic isoquinolinone



Scheme 23. Gold catalyzed synthesis of 4*H*-quinolizin-4-ones.



Scheme 24. Synthesis of substituted quinolizin-4-ones by Ring-Closing Metathesis.

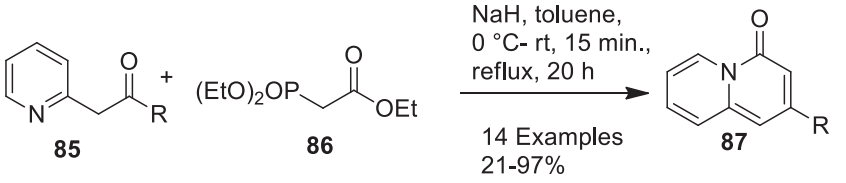


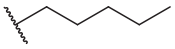
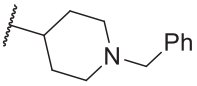
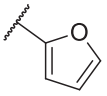
Scheme 25. Synthesis of polycyclic quinolizin-4-ones by Ring-Closing Metathesis.

114 in 35–96% yield. The reaction proceeds via hydration, condensation and double cyclization in one pot (Scheme 35) [47].

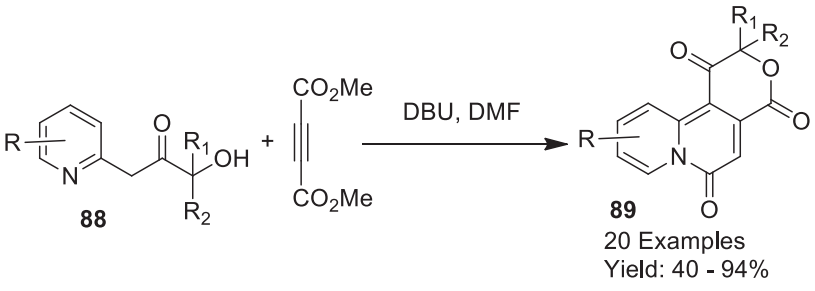
8. Conclusion

In this review, we have summarized the methods for the synthesis of 4*H*-quinolizin-4-one which is an important heterocyclic compound having nitrogen atom at the ring junction having polar zwitterionic character. Despite of the attractive physicochemical properties and interesting biological activities, due to the non-availability of a general method of the synthesis, *4H*-quinolizin-4-one's small molecule library under-represented in medicinal chemistry programs. Therefore, the development of the general methods for the constructions of this core is an area of interest.

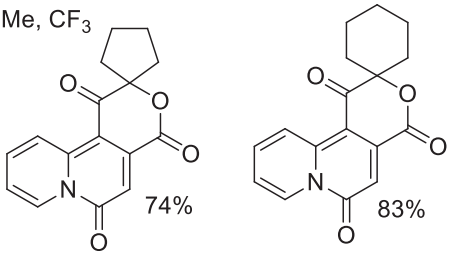


R	Yield	R	Yield
	95%	-4-F-C_6H_4	99%
		-4-Cl-C_6H_4	97%
	83%	-4-Br-C_6H_4	96%
	71%	-4-OMe-C_6H_4	97%
	48%	-4-OTBS-C_6H_4	21%
		-4-n-Bu-C_6H_4	76%
	62%	-4-N(Bn)$_2$-C_6H_4	92%
-C_6H_5	92%	-2-Me-C_6H_4	78%

Scheme 26. Horner–Wadsworth–Emmons olefination/ cyclization strategy for the construction of the 4*H*-quinolizin-4-ones.

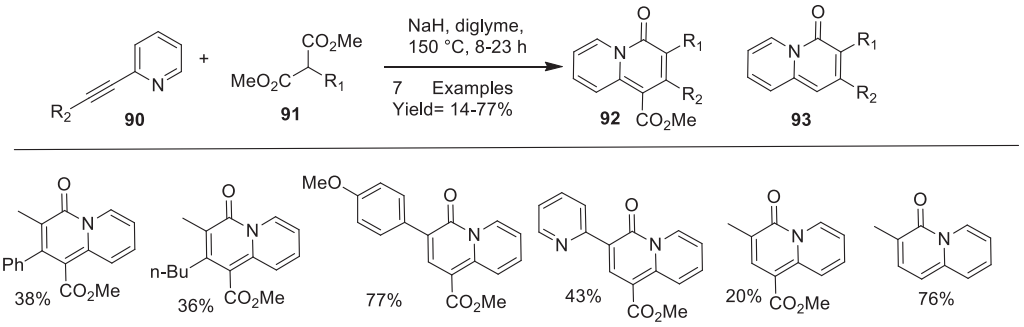


R = H, Me, OMe, F, Cl, Br, CN, COMe, CF_3
CO_2Et, NO_2
R_1, R_2 = Me, Et, $(CH_2)_5CH_3$, Ph

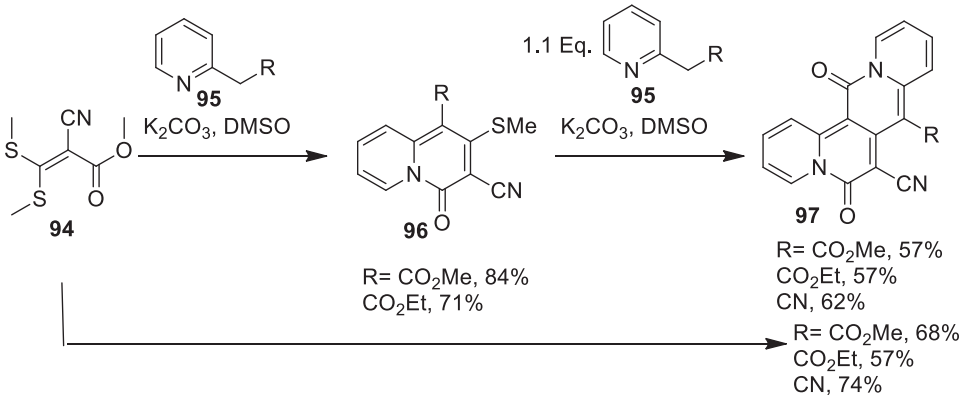


Scheme 27. Synthesis of pyrano[4,3-*a*]quinolizine-1,4,6(2*H*)-triones.

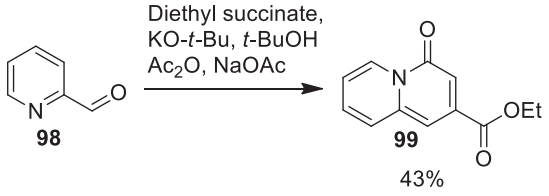
Over the year the traditional approaches are replaced with the new methods for synthesis of functionalized 4*H*-quinolizin-4-one. Mostly the procedure for the synthesis involves metal catalyzed intramolecular cyclocarbonylation, metal catalyzed/(double) *C–H* activation protocol and metal free methods such as Horner–Wadsworth–Emmons olefination/cyclization strategy, base



Scheme 28. Synthesis of 4*H*-quinolizin-4-ones base promoted annulation of 2-alkyl pyridine.

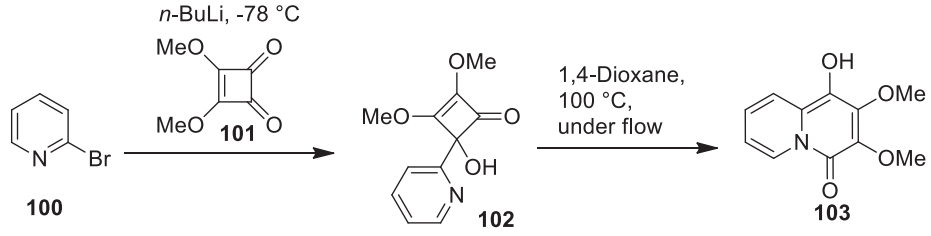


Scheme 29. Synthesis of 4*H*-quinolizin-4-ones by base promoted condensation of 2-pyridylderivative **95** with methyl-bis(methylsulfanyl)methylene −cyanoacetate.

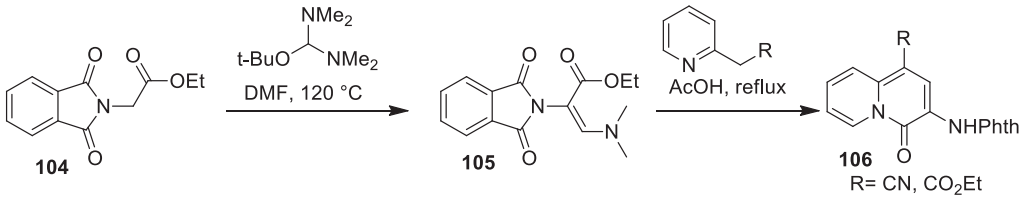


Scheme 30. Synthesis of 4*H*-quinolizin-4-ones by reaction of pyridyl-2-carboxyldehdye and diethylsuccinate

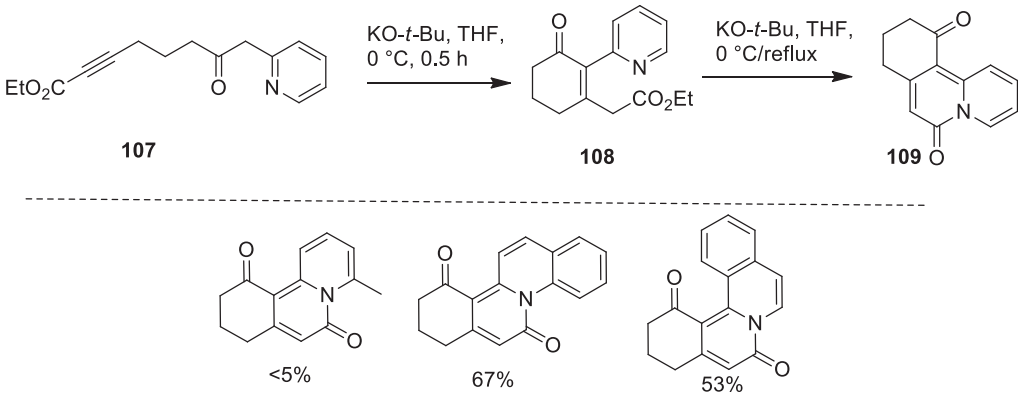
and acid catalyzed annulation reactions. In this review, the results of the synthetic efforts towards the synthesis of the quinolizinone since 2000 are reviewed. This helps the researcher to have the literature available methods at a glance and may helpful to researchers to explore the *4H*-quinolizin-4-one scaffold for the development of pharmacological agent.



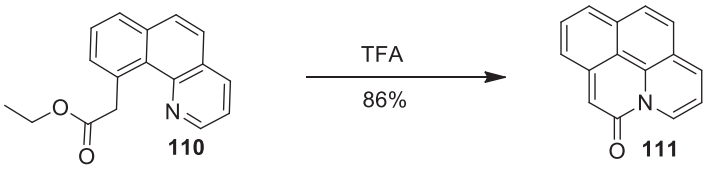
Scheme 31. Synthesis of 4*H*-quinolizin-4-ones from 2-Pyridiocyclobuenone using flow technique.



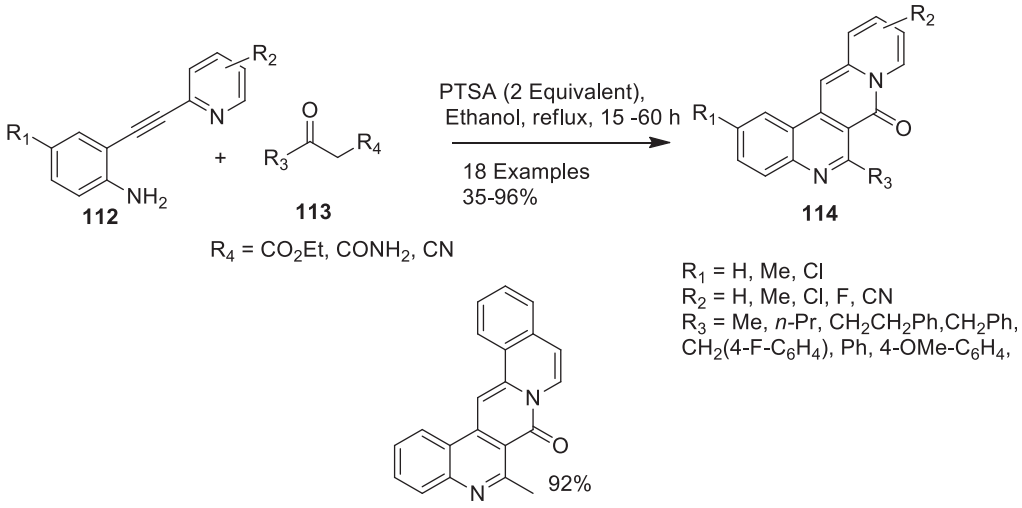
Scheme 32. Synthesis of 4*H*-quinolizin-4-ones from (*E*)-ethyl 3-(dimethylamino)-2-(1,3-dioxoisoindolin-2-yl)acrylate.



Scheme 33. Synthesis of 4*H*-quinolizin-4-ones from *N*-hetaryl substituted heptynone esters.



Scheme 34. Synthesis of 5H-benzo[*d*]pyrido[3,2,1-*i*]quinolin-5-one.



Scheme 35. Synthesis of 4*H*-quinolizin-4-ones by reaction of orthoalkylnylaniline and β-keto ester.

Declaration of competing interest

The authors declare no financial involvement or conflict.

Acknowledgements

Authors are thankful to Dr. V. B. Gaikwad (Principal) K.R.T. Arts, B.H. Commerce and A.M. Science College, Gangapur Road, Nashik 422 002, MS, India for continuous support and encouragement.

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