Top Curr Chem (Z) (2018) 376:26
https://doi.org/10.1007/s41061-018-0204-5

REVIEW

Recent Developments in Acenaphthoquinone-Based Multicomponent Reactions: Synthesis of Spiroacenaphthylene Compounds

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Received: 1 November 2017 / Accepted: 10 May 2018 / Published online: 5 June 2018

Abstract This review characterizes the multicomponent reactions of acenaphthoquinone as building blocks for the synthesis of a variety of heterocyclic compounds with medicinal chemistry interest. There is a wide range of reactions that include acenaphthoquinone in the synthesis of heterocyclic compounds. Also this review gives an overview spirocyclic compounds has important applications in pharmacological during the period from 2000 to 2017. Spiro compounds having cyclic structures fused at a central carbon are of recent interest due to their interesting adjustable overall qualities and their structural implications on biological systems.

Keywords Multicomponent reaction · Acenaphthoquinone · Spiro compounds · Heterocyclic synthesis

1 Introduction

Acenaphthoquinones are interesting with regard to photochemistry [1, 2], synthetic photochemistry [3, 4], and versatile synthetic intermediates to polycyclic hydrocarbon [5] and heterocyclic compounds [6]. The most widely used methods for the preparation of acenaphthoquinone are the oxidation of acenaphthene with various oxidizing agents [7] and the Friedel–Crafts reaction of naphthalene derivatives with oxalyl chloride [8]. Multicomponent reactions (MCRs) play an increasingly important role in organic and medicinal chemistry because of their convergence, productivity, ease of execution, good to excellent yields, and broad applications in combinatorial chemistry [9–11]. Also, multicomponent reactions

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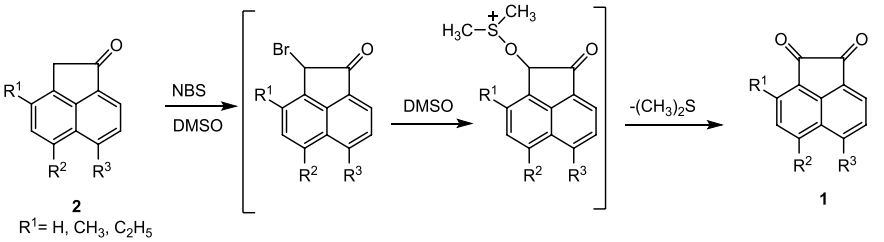
are generally defined as reactions where more than two starting materials react to form a product, incorporating essentially all of the atoms of the educts. Such reactions provide a number of valuable conceptual and synthetic advantages over stepwise sequential approaches towards complex and valuable molecules. They are atom economic, efficient, and extremely convergent. Such strategies reduce the number of steps in the reactions, thus avoiding the complicated purification procedures and allowing saving of both solvents and reagents [12, 13]. Acenaphthoquinone as privileged molecules in the design and synthesis of spiro-fused cyclic frameworks like spiro[4*H*-pyran] derivatives, spiro acenaphthylenes, dispiro oxindolopyrrolidines/pyrrolizidines, spiro[indoline-3,2′-quinazoline, dispirodihydrofuranyl oxindoles, spiro1*H*-pyrrolo[2,3-*b*]pyridines, spiro dihydropyridines, spiro[isoindoline-1,2′-quinazoline, etc. Also used in the preparation propellans as polycyclic pyrroles. 4*H*-pyrans derivatives have been considered because their pharmacological activity [14], which includes spasmolytic, diuretic, anti-coagulant, anti-anaphylactic activity [14–17], anti-cancer [18], cytotoxic [19], anti-HIV [20–22], anti-inflammatory [23], anti-malarial [24, 25], anti-microbial [26], anti-hyperglycemic and anti-dyslipidemic [27], and anti-neurodegenerative disorders like Alzheimer's, Parkinson's, and Huntington's disease [28–30]. Most the reaction in his review are atom-efficient, high yielding, short reaction time, environmental friendliness, easy work-upand follows a simple experimental procedure.

2 Acenaphthoquinone Synthesis

Synthesis of acenaphthoquinone **1** from 1-acenaphthenone **2** with *N*-bromosuccinimide was carried out in dimethyl sulfoxide at room temperature. Under similar conditions, several acenaphthoquinones were prepared from the corresponding 1-acenaphthenones in good yields (Scheme 1) [30].



Scheme 1 Acenaphthoquinone synthesis

3 Synthesis of Oxazo[3.3.3] Propellane

Yan et al. reported three-component synthesis of oxazo[3.3.3]propellane **5** using acenaphthylene-1,2-dione **1**, heterocyclic ketene aminals (HKAs) **4** and ethyl trifluoroacetylacetate **3**, bearing four consecutive quaternary stereo-centers (Scheme 2) [31].

4 Synthesis of Spiro[acenaphthylene-imidazo pyridine]carbonitrile Compounds

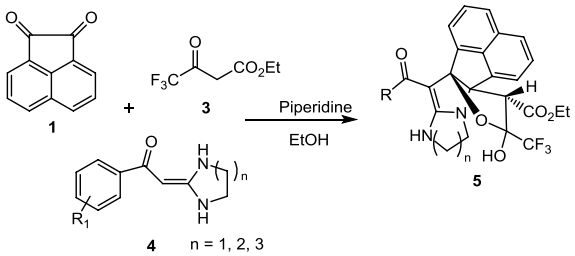
Shao and coworkers discovered that the reaction between ketene aminals **6**, acenaphthoquinone **1** and ethyl cyanacetate **7** in DMF, at 70 °C, resulted in the formation of 2-oxo-1,2-dihydropyridine-spiro 1,3-diaza heterocycles **8** with excellent yields (Scheme 3) [32]. A mechanism involving aza–ene, imine–enamine tautomerization followed by cyclization was proposed (Scheme 4).

5 Synthesis of Spiro-dihydropyridine Derivatives

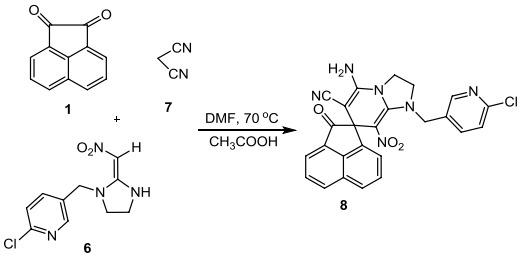
In 2016, Hasaninejad's group reported the synthesis of spiro-dihydropyridine derivatives **13** by one-pot multicomponent reaction of acenaphthoquinone derivatives **1** with malononitrile **7** and *N*,*N*′-substituted-2-nitroethene-1,1-diamines **12** in PEG-400 under catalyst-free conditions (Scheme 5) [33].

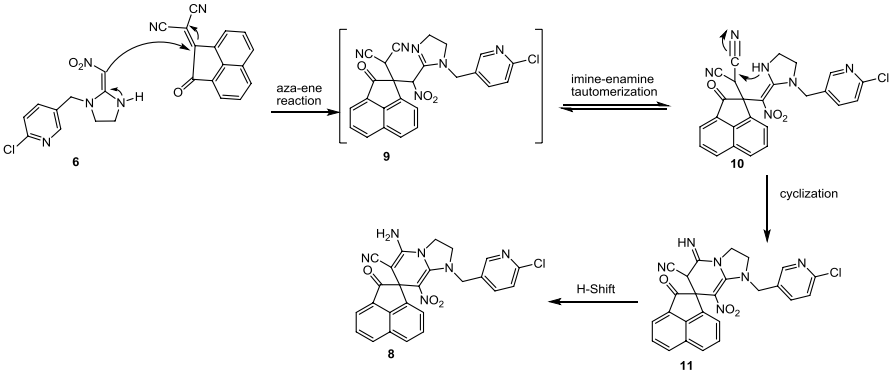
In 2014, Li and coworkers discovered synthesis of spiro-dihydropyridines derivatives **16** of acenaphthoquinone **1**, malononitrile **7** and HKAs **15** without the catalysts in CH_2CH_2/MeOH at room temperature (Scheme 6) [34].

Scheme 2 Synthesis of oxazo[3.3.3]propellane



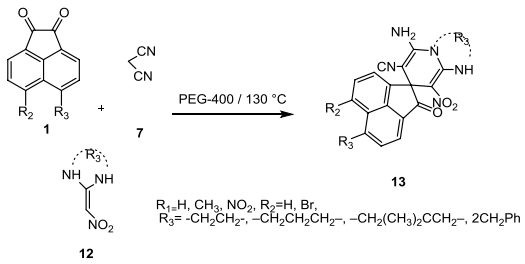
Scheme 3 Synthesis of spiro[acenaphthylene-1,7′-imidazo[1,2-a]pyridine]-6′-carbonitrile



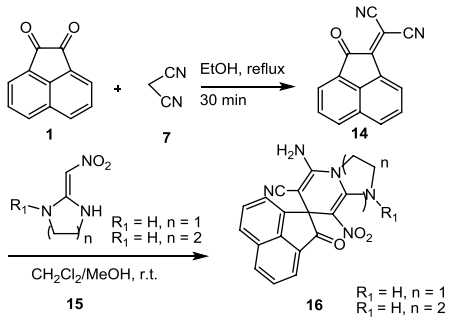


Scheme 4 Proposed mechanism for the formation of spiro[acenaphthylene-1,7′-imidazo[1,2-*a*]pyridine]-6′-carbonitrile

Scheme 5 Synthesis of spiro-dihydropyridine derivatives



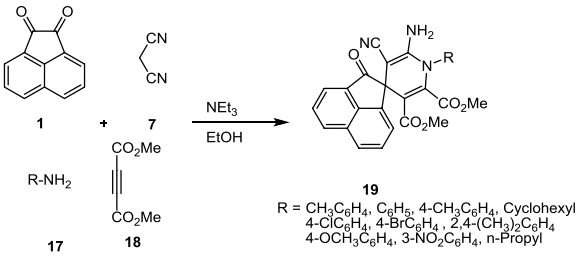
Scheme 6 Synthesis of spiro-dihydropyridines derivatives

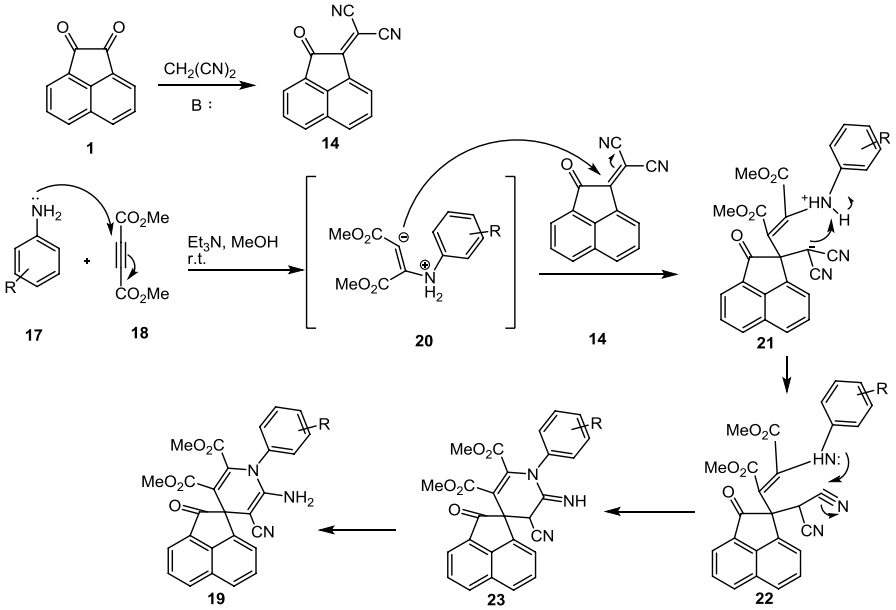


An efficient synthesis of a series of spiro dihydropyridine derivatives **19** was developed via one-pot four-component reaction of diketone **1**, malononitrile **7**, primary amines **17**, and acetylenic esters **18** in good yield (Scheme 7) [35]. A plausible mechanism of this four-component reaction is presented in Scheme 8.

Initially, acenaphthoquinone **1** undergoes Knoevenagel condensation with malononitrile **7** in the presence of Et_3N to afford component **14**. *m*-Toluidine **17** adds on to DMAD **18** to give the zwitterionic intermediate **20**, which undergoes Michael addition with **14** to form **21** and then through the migration of hydrogen atom obtained

Scheme 7 Synthesis of a series of spiro dihydropyridine derivatives



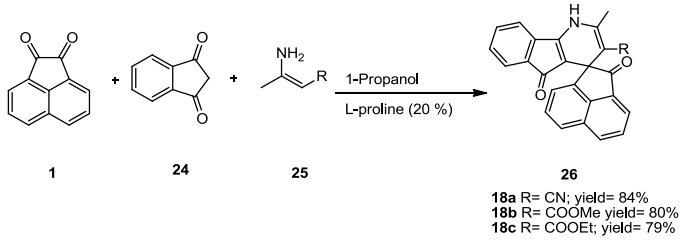


Scheme 8 Plausible mechanism for the formation of 2-oxospiro-[acenaphthyl-3,4′-(1′,4′-dihydropyridine)] derivatives

22. The intramolecular addition of the amino group to the cyano triple bond provides **23**, which tautomerizes to give **19** (Scheme 8).

6 Synthesis of Spiro-indenopyridine Derivatives

L-Proline was found to be a versatile organo-catalyst for the synthesis of new spiro[acenaphthylene-indeno[1,2-*b*]pyridine] derivatives **26** developed by Bazgir et al. in a one-pot, three-component (MCR) approach involving substituted acenaphthoquinone **1**, 1*H*-indole-2,3-diones **24**, enamines **25** under mild reaction conditions using 1-propanol as a solvent in good yields as shown in Scheme 9 [36].

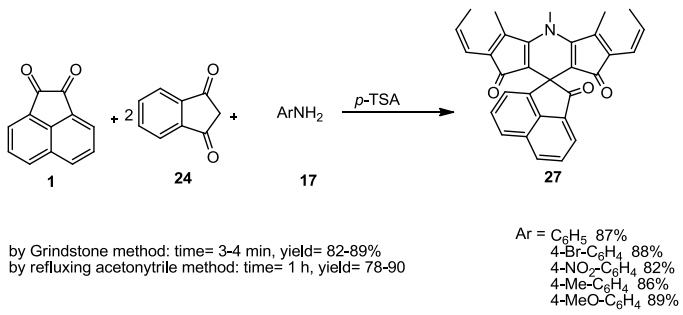


Scheme 9 Synthesis of spiro[acenaphthylene-indeno [1,2-*b*]pyridine] derivatives

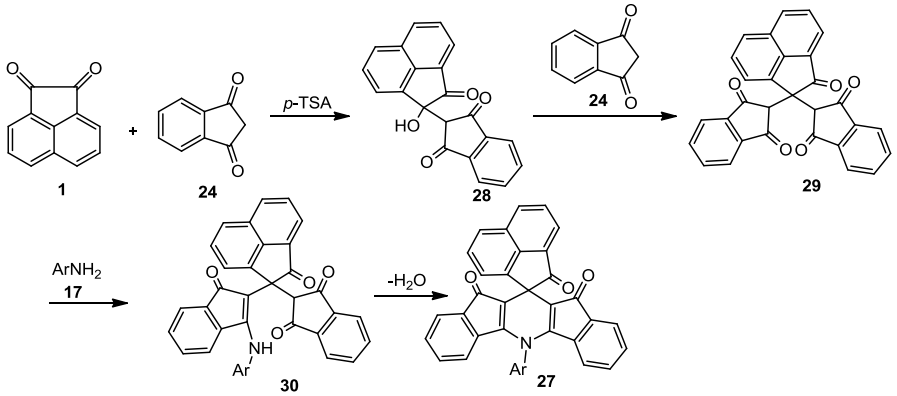
In a study by Ghahremanzadeh and coworkers, a synthetic route to highly functionalized spiro[acenaphthylene-diindenopyridine]triones **27** was developed via a one-pot, four-component domino reaction of 1,3-indandione **24**, aromatic amines **17**, acenaphthylene-1,2-dione **1** using a 'Grindstone Chemistry' method/ in refluxing acetonitrile conditions with *p*-TSA (Scheme 10) [37]. A reasonable mechanism for the formation of spiro[diindenopyridine-indoline]triones **27** is shown in Scheme 11. The mechanism involves the formation of intermediate **28** from 1,3-indanedione **24** to the acenaphthoquinone **1**, which reacted further with another molecule of **24**. Finally, addition of the substituted aniline **17** to the intermediate **29**, followed by cyclization afforded the product **27** (Scheme 11).

A new four-component synthesis of spiro-[acenaphthylene-1(2*H*),4′-[4*H*-indeno[1,2-*b*]pyridines] **33** was described by the reaction of acenaphthylene-1,2-dione **1**, indane-1,3-dione **24**, 1,3-dicarbonyl compounds **32**, and NH_4OH **31** in toluene at reflux. The preparation method is efficient and convenient and the presence of a catalytic amount of pyridine is required. (Scheme 12) [38].

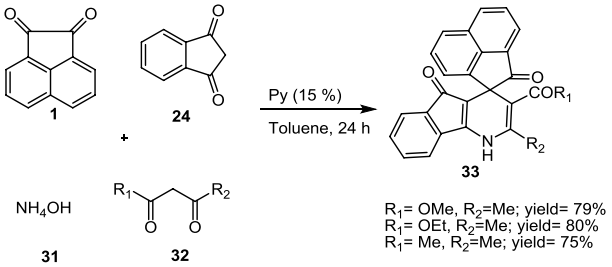
In 2002, Nair et al. accomplished the zwitterion generated from diisopropylaminoisocyanide **34** and dimethyl acetylenedicarboxylate (DMAD) **18** with acenaphthoquinone **1** in benzene under reflux in an atmosphere of argon to the synthesis of dimethyl 1′-(diisopropylamino)-2,5′-dioxo-1′,5′-dihydro-2*H*-spiro[acenaphthylene-1,2′-pyrrole]-3′,4′-dicarboxylate **35** (Scheme 13) [39].



Scheme 10 One-pot synthesis of spiro[acenaphthylene-diindenopyridine]triones



Scheme 11 Proposed mechanism for the synthesis of spirodiindenopyridine-indolines **27**

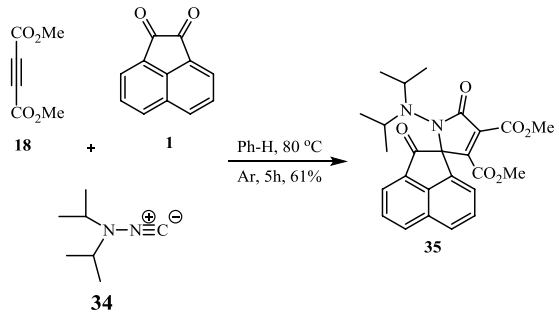


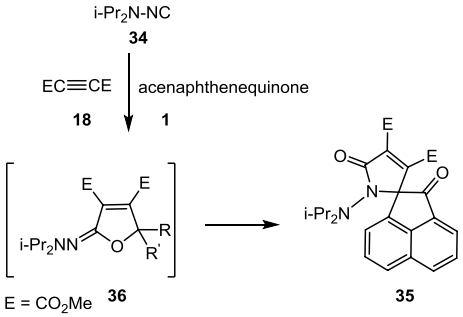
Scheme 12 Synthesis of spiro-[acenaphthylene-1(2*H*),4′-[4*H*-indeno[1,2-*b*]pyridines]

7 Synthesis of Spiro-pyrrole Derivatives

Reaction of acenaphthoquinone **1** and *N*-isocyano-*N*-isopropylpropan-2-amine **34** with dimethyl acetylenedicarboxylate (DMAD) **18** afforded synthesis of dimethyl 1′-(diisopropylamino)-2,5′-dioxo-1′,5′-dihydro-2*H*-spiro[acenaphthylene-1,2′-pyrrole]-3′,4′ dicarboxylate **35** (Scheme 14) [40].

Scheme 13 Synthesis of spiro[acenaphthylene-1,2′-pyrrole]-3′,4′-dicarboxylate

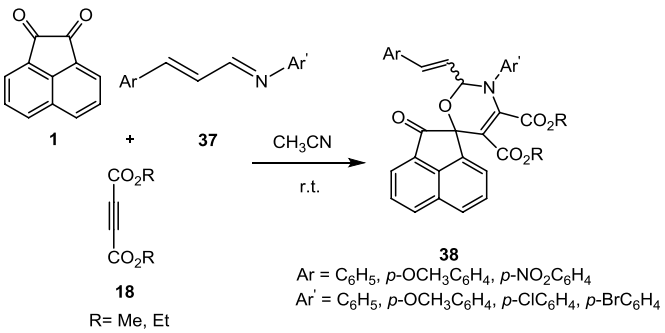




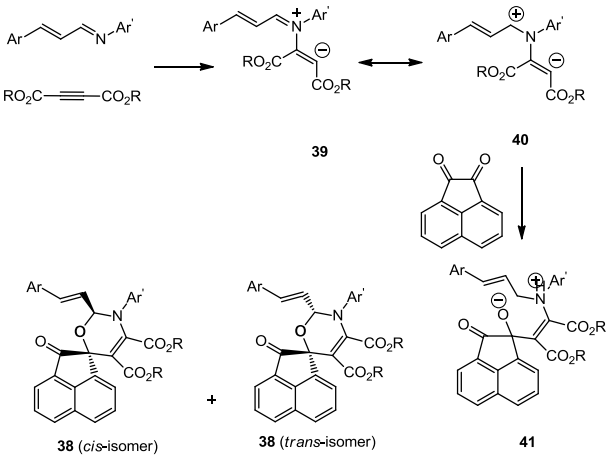
Scheme 14 Synthesis of spiro[acenaphthylene-1,2′-pyrrole]-3′,4′-dicarboxylate

8 Synthesis of Spiro-oxazine Derivatives

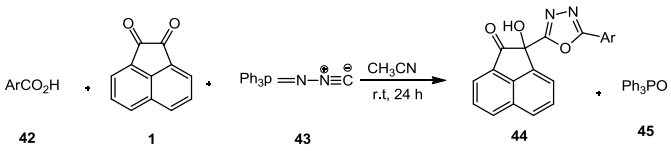
In 2015, Zhang and Yan described a reaction between α,β-unsaturated *N*-arylaldimines **37**, dialkyl acetylenedicarboxylate **18** and acenaphthenequinone **1** in dry acetonitrile without a catalyst for the synthesis of structurally diverse spirocyclic 1,3-oxazines **38** in good yields (Scheme 15) [41]. A proposed mechanism for the formation of spiro[acenaphthylene-1,6′-[1,3]oxazines] three-component reaction is shown in Scheme 16. The first step is the nucleophilic addition of aldimine to acetylenedicarboxylate affords the desired 1,4-dipole **39**. Secondly, this 1,4-dipolar intermediate **40** attacks one carbonyl group of 1,4-naphthoquinone and results in the zwitterionic intermediate **41**. Thirdly, the intramolecular attack of negative oxygen to the iminium salt in intermediate **41** gives the final spiro[acenaphthylene-1,6′-[1,3]oxazines] and a mixture of *cis*/*trans*-diastereoisomers **38** was obtained (Scheme 16).



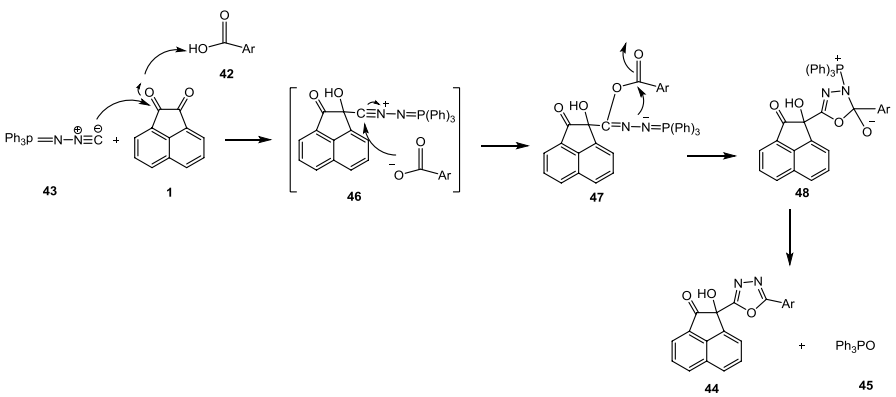
Scheme 15 Synthesis of spiro[acenaphthylene-1,6′-[1,3]oxazines]



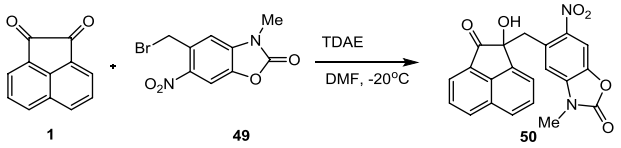
Scheme 16 A proposed mechanism for the formation of spiro[acenaphthylene-1,6′-[1,3]oxazines]



Scheme 17 Synthesis of 1,3,4-oxadiazole 2-hydroxyacenaphthylen-1(2*H*)-one



Scheme 18 Proposed mechanism for the synthesis of **29**



Scheme 19 Synthesis of 5-((1-hydroxy-2-oxo-1,2-dihydroacenaphthylen-1-yl)methyl)-3-methyl-6 nitrobenzo[d]oxazol-2(3*H*)-one

9 Synthesis of Spiro-oxadiazole and Oxazole Derivatives

Ramazani et al. discovered that reactions of (*N*-isocyanimino)triphenylphosphorane **43** with acenaphthoquinone **1** in the presence of aromatic carboxylic acids **42** proceed smoothly at room temperature and under neutral conditions to afford sterically congested 1,3,4-oxadiazole derivatives **44** in high yields (Scheme 17) [42]. A plausible mechanism for the reaction is shown in Scheme 18. The first step may involve nucleophilic addition of (*N*-isocyanimino) triphenylphosphorane **28** to acenaphthoquinone **1**, by the acid **42** as catalyst, leading to nitrilium intermediate **46**. This intermediate may be attacked by the conjugate base of acid to form 1:1:1 adduct **47**. This adduct under intramolecular aza-Wittig reaction of the iminophosphorane moiety with the ester carbonyl was obtained 1,3,4-oxadiazole derivatives **44** by elimination of triphenylphosphine oxide **45** from intermediate **48** (Scheme 18).

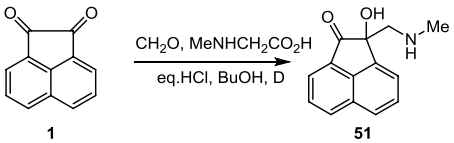
In 2015, Nadji-Boukrouche's group reported 5-(dibromomethyl)-3-methyl-6 nitrobenzoxazolone **49** reacted with acenaphthoquinone **1** catalyzed by tetrakis (dimethylamino) ethylene (TDAE) in DMF under stirred at 20 °C for 1 h and then warmed to room temperature for 2 h to yield for synthesis of 5-((1-hydroxy-2-oxo-1,2-dihydroacenaphthylen-1-yl)methyl)-3-methyl-6-nitrobenzo[*d*]oxazol-2(3*H*)-one **50** (Scheme 19) [43].

10 Synthesis of Acenaphthylen-1-one Derivatives

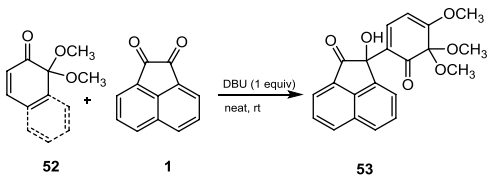
Acenaphthoquinone **1** was found to react smoothly with nonstabilized azomethine ylides, generated in situ from sarcosine/formaldehyde or *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine, to give 2-hydroxy-2-((methylamino)methyl) acenaphthylen-1(2*H*)-one **51**, which were converted into 2-alkylaminoethanols in moderate-to-good yields by heating in *n*-butanol with hydrochloric acid (Scheme 20) [44].

A series of 2-hydroxy-2-(4,5,5-trimethoxy-6-oxocyclohexa-1,3-dien-1-yl)acenaphthylen-1(2*H*)-one **53** was prepared by Chittimalla and coworkers who did reactions of

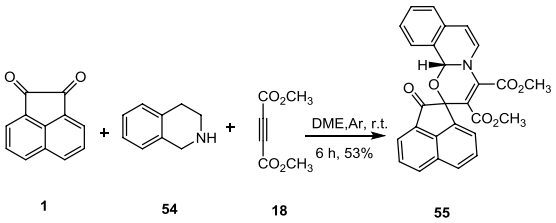
Scheme 20 Synthesis of 2-hydroxy-2-((methylamino) methyl)acenaphthylen-1(2*H*)-one



Scheme 21 Synthesis of 2-hydroxy-2-(4,5,5-trimethoxy-6-oxocyclohexa-1,3-dien-1-yl) acenaphthylen-1(2*H*)-one



Scheme 22 Synthesis of [1,3] oxazino isoquinoline



acenaphthoquinone **1**, *o*-benzoquinone (MOB; 6,6-dimethoxy-cyclohexa-2,4-dienone derivatives) derivatives **52** in THF/H_2O at room temperature (Scheme 21) [45].

11 Synthesis of Spiro-oxazino Isoquinoline Derivatives

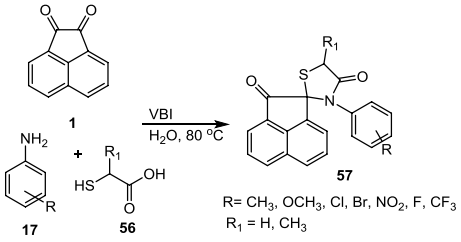
The reaction of 1,2,3,4-tetrahydroisoquinoline **54** and acenaphthoquinone **1** with dimethyl acetylenedicarboxylate **18** was investigated in a one-pot, three-component process for synthesis of a variety of [1,3]oxazino isoquinoline **55** via 1,4-dipolar cycloaddition (Scheme 22) [46].

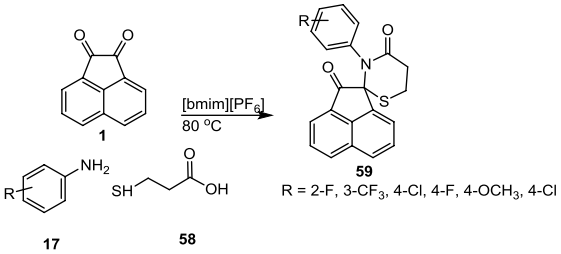
12 Synthesis of Spiro-thiazolidine and Thiazine–Dione Derivatives

Treatment of acenaphthylene-1,2-dione **1** with substituted anilines **17**, and a mercaptocarboxylic acid **56** in the presence of thiamine hydrochloride [vitamin B1 (VB1)] as catalyst was developed for the synthesis of spiro[acenaphthylene-1,2′[1,3]-thiazolidine]-2,4′(1*H*)-diones **57** in water at 80 °C temperature (Scheme 23) [47].

Anshu Dandia et al. developed a new synthesis of medicinally important spiro[acenaphthylene-1,2′-[1,3]thiazine]dione **59** via the one-pot reaction of acenaphthylene 1,2-dione **1**, substituted anilines **17** with 3-mercaptopropionic acid **58** in

Scheme 23 Synthesis of spiro[acenaphthylene-1,2′[1,3]-thiazolidine]-2,4′(1*H*)-diones





Scheme 24 Synthesis of spiro[acenaphthylene-1,2-[1,3] thiazine]-2,4-diones

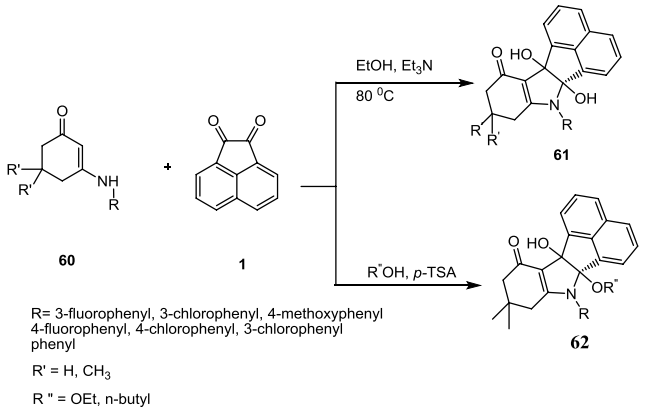
1-butyl-3 methylimidazolium hexafluorophosphate [bmim][PF_6] at 80 °C (Scheme 24) [48].

13 Synthesis of Acenaphtho[1,2-*b*]indole Derivatives

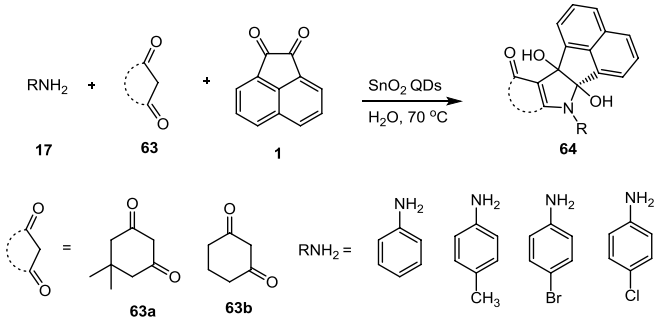
Chen et al. reported the preparation of acenaphtho[1,2-*b*]indoles, which can be accessed in a one-step, two-component reaction between enaminones **60** with acenaphthoquinone **1**. During the first pathway, product **61** was synthesized in the presence of Et_3N, while a second reaction in the presence of *p*-toluenesulfonic acid leads to compound **62** via intramolecular cyclization and highly regioselective SN_1-type reaction with alcohols under solvent-free conditions with excellent yields (Scheme 25) [49].

14 Synthesis of Dihydroxy Acenaphtho[1,2-*b*]indolone Derivatives

In 2015, Das et al. reported the procedure for the synthesis of dihydroxy acenaphtho[1,2-*b*]indolone derivatives **64** in aqueous medium catalyzed by a tin oxide (SnO_2) quantum dot (QD). The reaction was performed by the treatment of



Scheme 25 Synthesis of acenaphtho[1,2-b]indoles

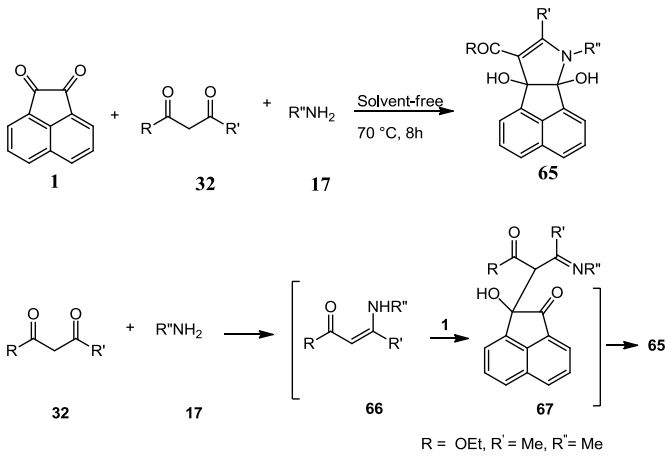


Scheme 26 Synthesis of dihydroxy acenaphtho[1,2-b]indolone derivatives

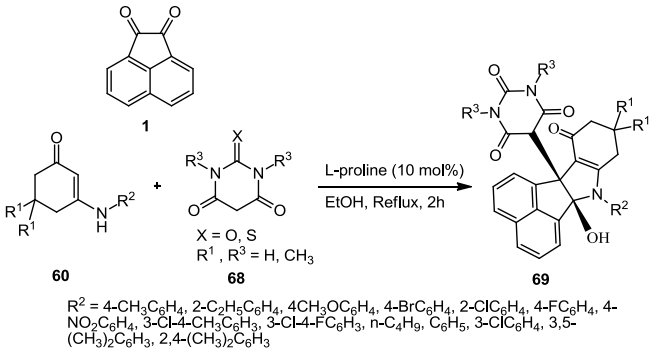
acenaphthenequinone **1**, 1,3-dicarbonyl compounds **63**, and aromatic amines **17** at 70 °C for 2-3 h (Scheme 26) [50].

15 Synthesis of Hydroxypyrrole Derivatives

A one-pot synthesis of pyrrole derivatives **65** via reaction between acenaphthoquinone **1**, 1,3-dicarbonyls **32**, and primary amines **17** under solvent-free conditions is described (Scheme 27) [51]. A tentative mechanism for this transformation is proposed in Scheme 28. It is conceivable that the reaction involves the initial formation of enaminones **66** between 1,3-dicarbonyls **32** and primary amines **17**. Enaminones that are formed under solvent-free conditions react with the carbonyl group of **1** and produced **67**. Cyclization of this intermediate leads to the compound **65** (Scheme 28).



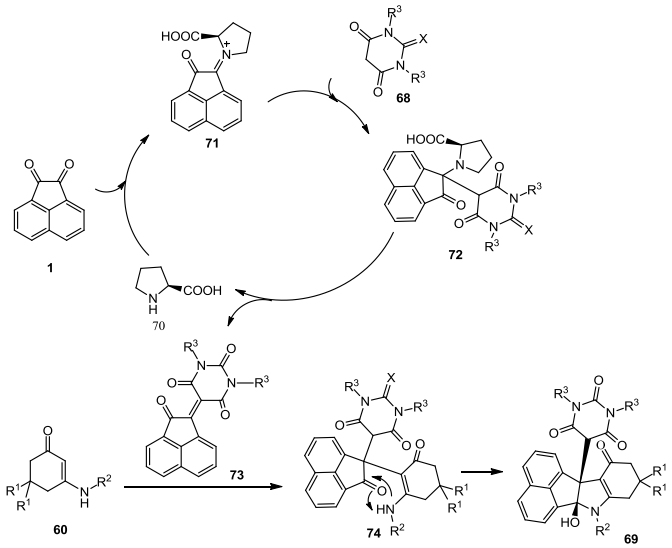
Scheme 27 and 28 Synthesis of pyrrole derivatives



Scheme 29 Synthesis of tetrahydroacenaphtho[1,2-*b*]indolone derivatives

16 Synthesis of Tetrahydroacenaphtho[1,2-*b*]indolone Derivatives

Three-component reaction of acenaphthoquinone **1**, enaminones **60**, was accomplished with barbituric acid **68** by Liu et al. using L-proline (10 mol%) as catalyst in refluxing ethanol. This efficient method gave the synthesis of tetrahydroacenaphtho[1,2-*b*]indolone derivatives **69** with good yields (Scheme 29) [52]. Mechanistic representation for synthesis of tetrahydroacenaphtho[1,2-*b*] indolone derivatives is shown in Scheme 30. Reaction of the acenaphthylene-1,2-dione **1** with L-proline to afford iminum ion **71**. The intermediate **72** was formed by the Knoevenagel condensation of iminum ion **71** with barbituric acid **68**, and



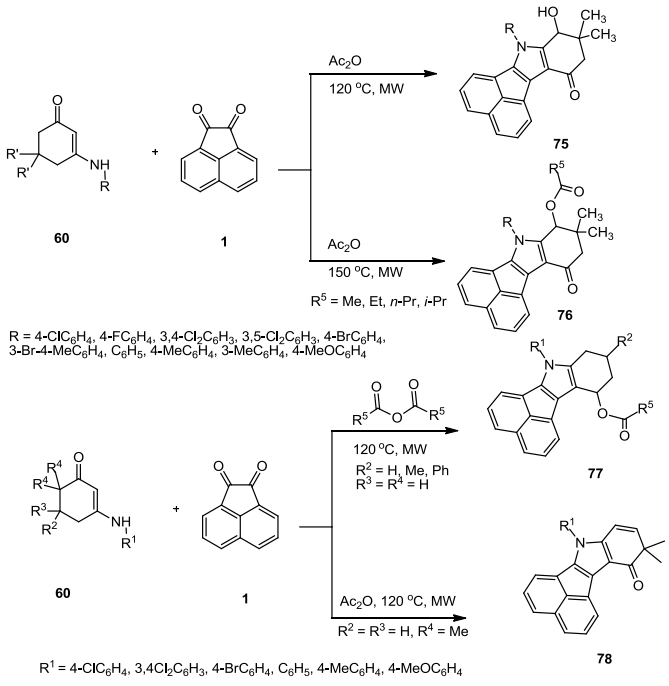
Scheme 30 Proposed mechanism for the synthesis of **49**

elimination of L-proline. Then the Michael addition of intermediate **73** with enaminones **60** would give the intermediate **72**, after with intramolecular cyclization to generated **69** (Scheme 30).

17 Synthesis of Pentacyclic and Tetracyclic Indole Derivatives

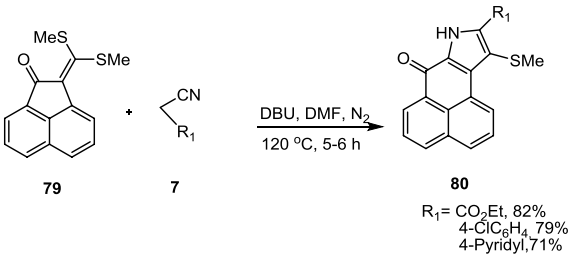
A new multicomponent domino reaction of cyclic enaminones **60** with acenaphthylene-1,2-dione **1** for synthesis of pentacyclic indoles **75**, **76**, **77**, **78** by Li and coworkers with good to excellent yields in an anhydride solvent has been established, providing selective protocol to pentacyclic indoles with different substituted patterns (Scheme 31) [53].

An efficient method has been developed by Yugandar and coworkers for the synthesis of novel tetracyclic indole derivatives **80** via a one-pot, three-component condensation reaction of tetracyclic indole derivatives **79** in high yields, in DMF at 120 °C in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) on treatment with various active methylene such as ethyl 2-cyanoacetate/4-pyridylmethyl nitrile/2-(4-chlorophenyl)nitrile **7**, respectively, under identical conditions (Scheme 32) [54].



Scheme 31 Synthesis of pentacyclic indoles

Scheme 32 Synthesis of tetracyclic indoles



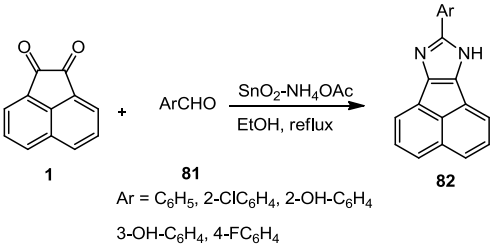
18 Synthesis of Imidazole Derivatives

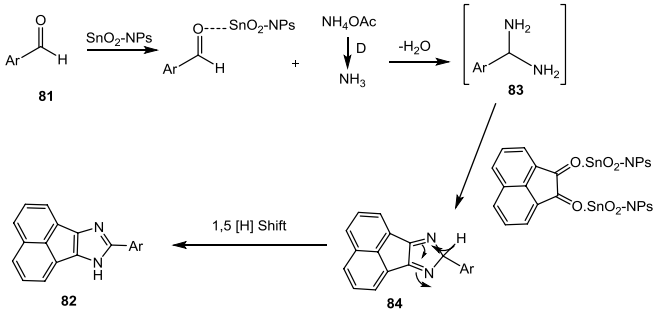
In 2015, Mokhtary et al. synthesized three-component condensation of acenaphthenequinone **1** with aryl aldehyde **81** and ammonium acetate to generate highly substituted imidazole derivatives **82** over tin oxide nanoparticles as catalyst in ethanol under reflux conditions (Scheme 33) [55].

In Scheme 34, it was assumed that the SnO_2 nanoparticles can be used to active the carbonyl group of aldehydes and facilitate the formation of a diamine intermediate. The later, the condensation of the diamine intermediate with acenaphthenequinone, intramolecular cyclization and then tautomeric [1,5] proton shift the corresponding 8-aryl-7*H*-acenaphtho[1,2-*d*]imidazole derivatives (Scheme 34).

Reaction of acenaphthoquinone **1** with benzaldehyde **81** in the presence of ammonia had been reported to afford 8-phenyl-7*H*-acenaphtho[1,2-*d*]imidazole **82** (Scheme 35) [56].

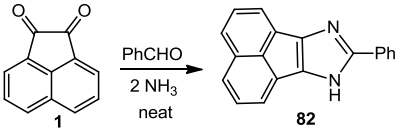
Scheme 33 Synthesis of imidazole derivatives





Scheme 34 Synthesis of imidazole derivatives

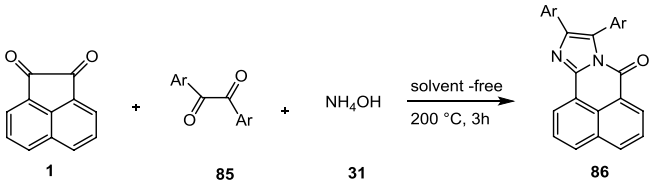
Scheme 35 Synthesis of phenyl-7*H*-acenaphtho[1,2-d] imidazole



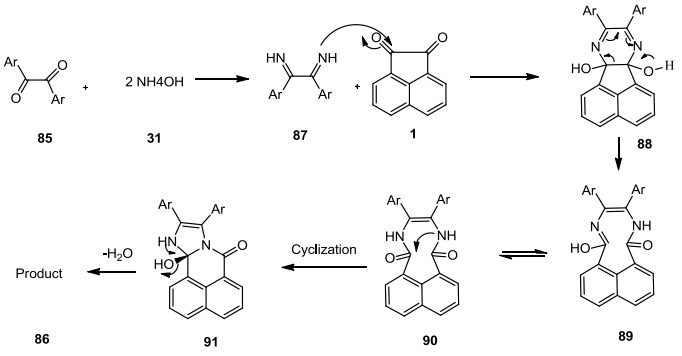
19 Synthesis of Spiro-benzoimidazoisoquinolin Quinazolinone Derivatives

Reaction of acenaphthoquinone **1** with benzyl **85**, and ammonium acetate **31** under solvent-free conditions had been reported to 9,10-diaryl-7*H*-benzo[*d*, *e*]imidazo[2,1-*a*]isoquinolin-7-ones **86** in good to excellent yields (Scheme 36) [57]. The suggested mechanism for the formation of products **86** is illustrated in Scheme 37.

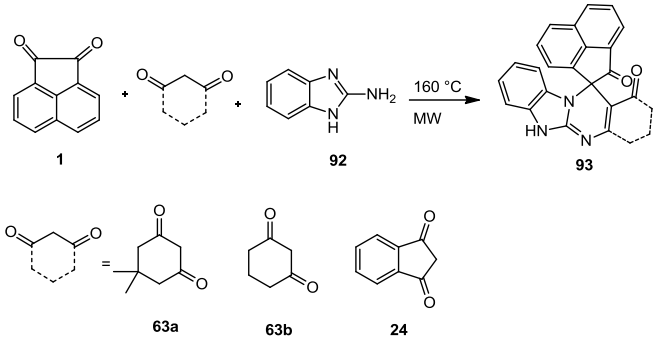
In 2016, Sawant's group a novel multicomponent route has been discovered for the synthesis of spiro-benzimidazoquinazolinones **93** under microwave irradiation. It involves a one-pot, three-component reaction of acenaphthoquinone **1**, 1,3-diketone (**63**, **24**) and 2-aminobenzimidazole **92** in ethanol at 180 W and 160 °C temperature (Scheme 38) [58]. A possible mechanism for the formation of **93** is proposed in Scheme 39. It is reasonable to assume that **93** results from initial formation



Scheme 36 Synthesis of benzo[d,e]imidazo[2,1-a]isoquinolin-ones



Scheme 37 Proposed mechanism for the synthesis of **59**

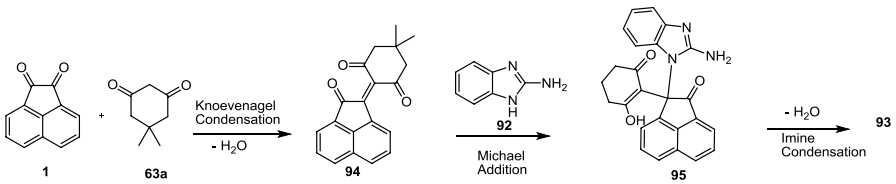


Scheme 38 Synthesis of spiro-benzimidazoquinazolinones

of a hetero-diene **94** by standard Knoevenagel condensation of the dimedone **63a** and acenaphthoquinone **1**. Then, the subsequent Michael-type addition of the 2-aminobenzimidazole **92** to the heterodyne **95**, followed by cyclization affords the corresponding products **93** (Scheme 39).

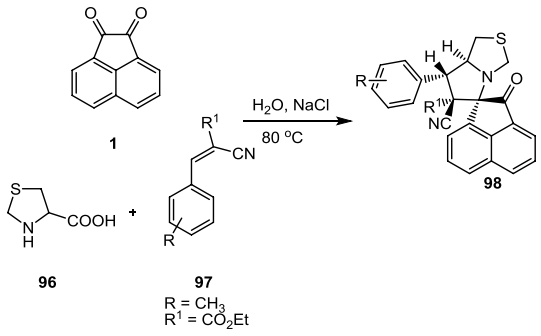
20 Synthesis of Spiro-pyrrolo-thiazole Derivatives

Synthesis of spiro[acenaphthylene-1,5′-pyrrolo[1,2-*c*]thiazole] derivatives **64** has been achieved by a one-pot, three-component reaction through 1,3-dipolar cycloaddition of acenaphthenequinone **1**, 1,3-thiazole-4-carboxylic acid **62** and Knoevenagel adduct **63** in aqueous medium in the presence of NaCl (Scheme 40) [59].



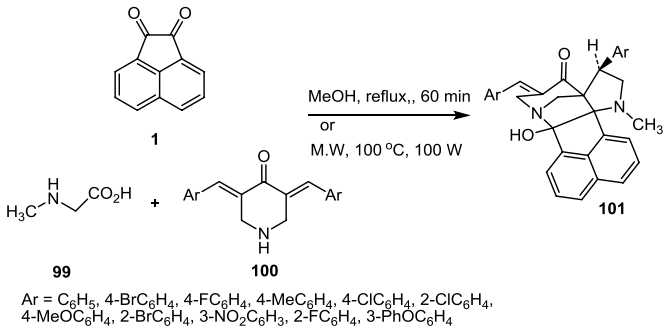
Scheme 39 Proposed mechanisms for the synthesis of spirobenzimidazoquinazolinone

Scheme 40 Synthesis of spiro[acenaphthylene-1,5′-pyrrolo[1,2-c]thiazole] derivatives

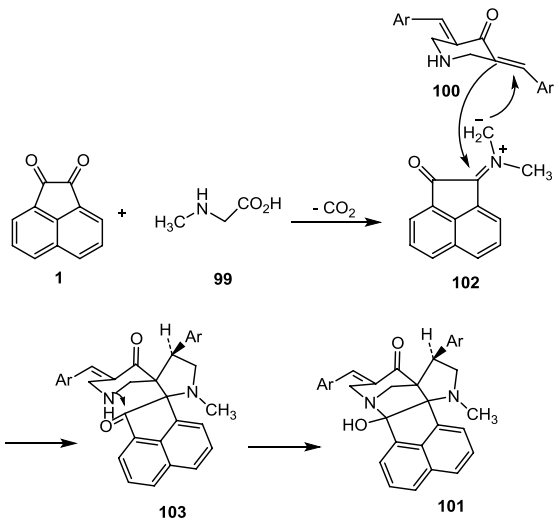


21 Synthesis of Diazahexacyclo-henicosa-pentaen-one Derivatives

Kumar and coworkers reported that the one-pot pseudo-three-component [3 + 2]-cycloaddition between the *N*-unsubstituted 3,5-bis[(*E*)-arylmethylidene] tetrahydro-4(1*H*)-pyridinones **100**, sarcosine **99** and acenaphthoquinone **1** afforded derivatives of diazahexacyclo-henicosa-pentaen-ones **101** in good to excellent yields and isolated as the sole reaction product. The ring systems thus generated contain as structural elements bridged, fused, and spiro rings and were obtained with complete selectivity through the creation of two C–C and two C–N bonds, which led to the generation of two azaheterocyclic rings, four carbon and one nitrogen adjacent stereo-centers, three of which are quaternary (Scheme 41) [60]. The proposed mechanism for the synthesis of **101** is summarized in Scheme 42 for the case of the diazapentacycle **101**. The reaction of acenaphthoquinone **1** and sarcosine **99** affords the azomethine ylide **102**, which adds to one of the C=C bonds of the bisdipolarophile **100** to form the corresponding cycloadduct **103**. The final attack an amino group to the neighboring carbonyl group led to formation component **101** (Scheme 42).



Scheme 41 Synthesis of hydroxy-tetrahydro-methanoacenaphtho[1,2-[1,2-*b*]]pyrrolo[2,3-c]azepin-one



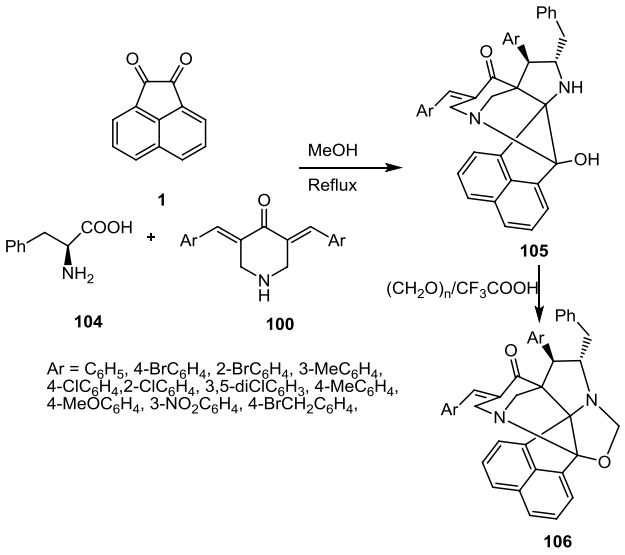
Scheme 42 Mechanistic proposal to explain the formation of compounds **67** through a domino sequence

22 Synthesis of Hybrid Heterocyclic Systems

Arumugam et al. has developed an expedient regio-stereo and product-selective synthesis of novel hybrid heterocyclic systems **105** comprising [1,2-*c*]oxazolidine, pyrrolidine and piperidine units, in good to excellent yields, via a three-component reaction of acenaphthoquinone **1** with L-phenylalanine **104** and 3,5-dibenzylidene-piperidin-4-one **100** in methanol under heating at reflux. Also, the reaction of **105** with *para*-formaldehyde proceeded in a highly product-selective manner furnishing solely the heptacyclic ring system **106** (Scheme 43) [61].

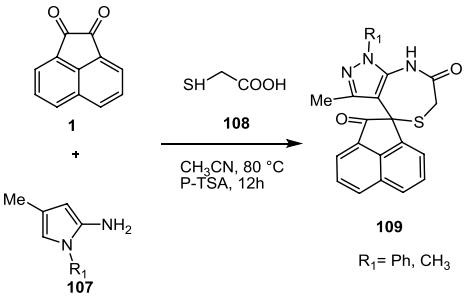
23 Synthesis of Spiro-pyrazolo-thiazepine Derivatives

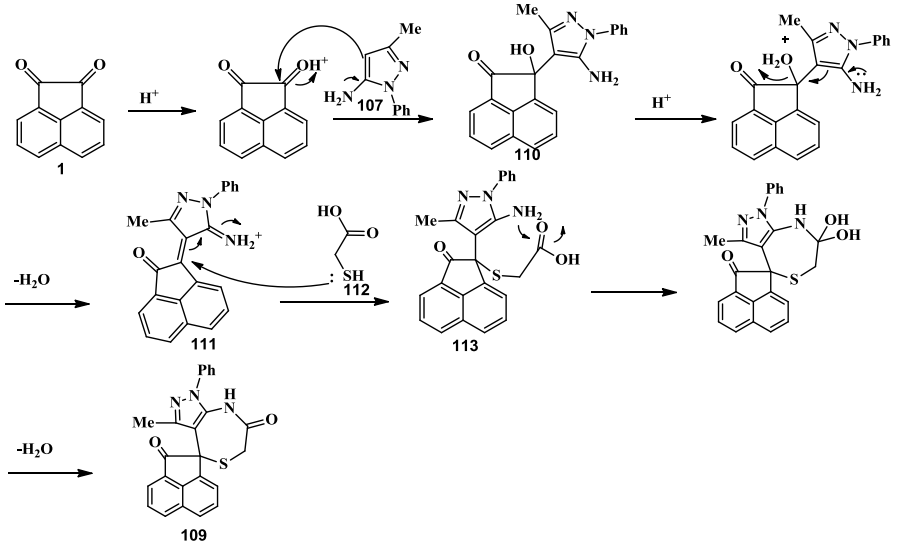
One-pot reaction of acenaphthoquinone **1**, 5-amino-3-methylpyrazole **107**, and thio-acid **108** in CH_3CN in the presence of catalyst *p*-TSA gave spiro[acenaphthylene-1,4′-pyrazolo[3,4-*e*][1,4]thiazepine]-2,7′ (1′ *H*)-dione derivatives **109** (Scheme 44) [62]. A plausible mechanism that could account for the three-component reaction is given in Scheme 45. The first step involves the formation of a Baylis–Hillman type adduct **110** by the nucleophilic addition of 5-amino-3-methylpyrazole **107** to acenaphthoquinone **1** as a intermediate, which may occur to afford **111**. Then, **111** is attacked via Michael addition of thioacid **108** to give the intermediate **112** followed by cycloaddition, dehydration, to form the corresponding product **109** (Scheme 45).



Scheme 43 Synthesis of hybrid heterocyclic

Scheme 44 Synthesis of spirocyclic acenaphthyleneones



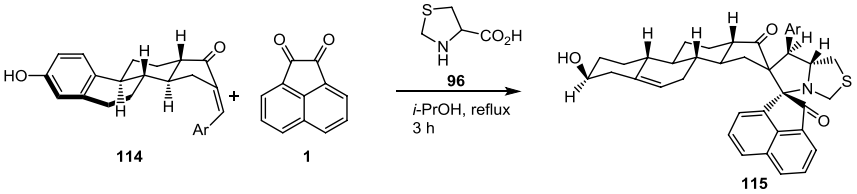


Scheme 45 Plausible mechanism for the formation of 2-oxospiro-[acenaphthyl-3,4′-(1′,4′-dihydropyridine)] derivatives

24 Synthesis of Dispiro-estrone-*trans*-androsterones Hybrid Heterocycle Derivatives

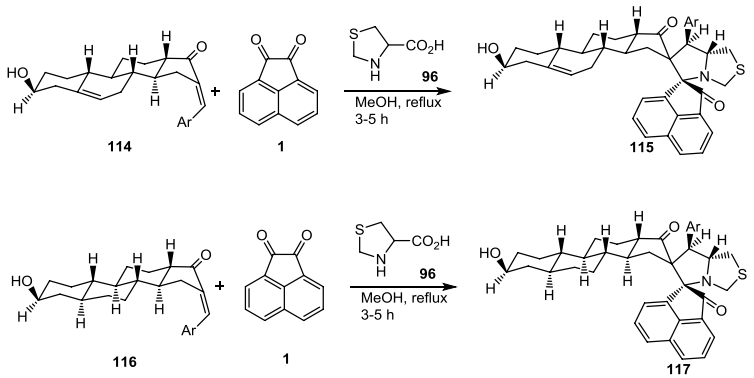
The 1,3-dipolar cycloaddition of azomethine ylides generated in situ from the reaction of acenaphthylene-1,2-dione **1** and 1,3-thiazolane-4-carboxylic acid **96** to various exocyclic dipolarophiles synthesized from estrone **114** at reflux *i*-PrOH for 3 h afforded a library of novel spiroacenaphthylene-1-one-7-(aryl)tetrahydro-1*H*-pyrrolo[1,2-*c*][1,3]thiazole estrone hybrid heterocycles **115** (Scheme 46) [63].

In 2013, Kumar et al. discovered the 1,3-dipolar cycloaddition of azomethine ylide derived in situ from the reaction of acenaphthylene-1,2-dione **1** and 1,3-thiazolane-4-carboxylic acid **96** to various exocyclic dipolarophiles from *trans*-androsterone **116** and *trans*-dehydroandrosterone **114** afforded a library of novel spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl) tetrahydro-1*H*-pyrrolo



Ar = 4-$CH_3C_6H_4$, 4$CH_3OC_6H_4$, 4-BrC_6H_4, 2-ClC_6H_4, 4-FC_6H_4, 4-$(CH_3)_2NC_6H_4$, C_6H_5, 3-ClC_6H_4, 3,5-$(CH_3O)_2C_6H_3$, C_6H_5, 3-FC_6H_4, 2-FC_6H_4, 2,4-di ClC_6H_4

Scheme 46 Synthesis of spiro-acenaphthylene-spiro-tetrahydro-1*H*-pyrrolo[1,2-c][1,3]thiazolo estrone hybrid heterocycles



Ar = C_6H_5, 4-Br-C_6H_4, 4-Cl-C_6H_4, 4-Me-C_6H_4, 4-MeO-C_6H_4, 4-FC_6H_4, 3-Br-C_6H_4, 2-Cl-C_6H_4, 2-Me-C_6H_4, 2-MeO-C_6H_4, Naphthyl

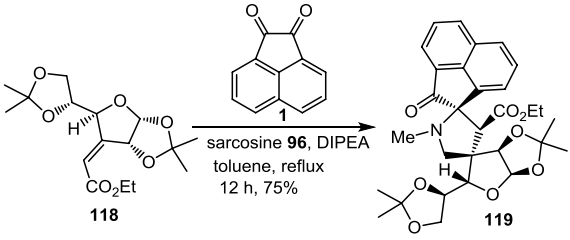
Scheme 47 Synthesis of spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl)-tetrahydro-1*H*-pyrrolo [1,2-c][1,3]thiazolo-*trans*-androsterone/dehydroandrosterone hybrid heterocycles

[1,2-*c*][1,3]thiazolo-trans-androsterone/dehydroandrosterone hybrid heterocycles **115** and **117**, respectively (Scheme 47) [64].

25 Synthesis of Bispiropyrrolidine Derivatives

Banerjee's group afforded an efficient synthesis of bispiropyrrolidine derivatives **119** through 1,3-dipolar cycloaddition reaction of a carbohydrate-derived exocyclic olefin **118** with in situ-generated nonstabilized azomethine ylides, formed by the reaction of sarcosine (a secondary α-amino acid) **96** with acenaphthenedione **1** and cycloalkanones in refluxing toluene, when DIPEA was used as a base (Scheme 48) [65].

Scheme 48 Synthesis of bispiropyrrolidine derivatives



26 Synthesis of Carbohydrate-Derived Spiro Heterocycles

In 2015. Raghunathan et al. reported a facile one-pot synthesis of carbohydrate-derived spiro heterocycles **123-126** via [3 + 2] cycloaddition reaction of azomethine ylides. A unique dipolarophile(4-oxo-2-glyco-4*H*-chromene-3-carboxylate) **120** synthesized from D-glucose reacted with azomethine ylide generated in situ from secondary α-amino acids (sarcosine **99**, proline **96**, or pipecolinic acid **121**, tetrahydroisoquinoline-3-carboxylic acid **122**) and 1,2-diketone (acenaphthoquinone) **1** to give their corresponding cycloadducts in good yield (Scheme 49) [66].

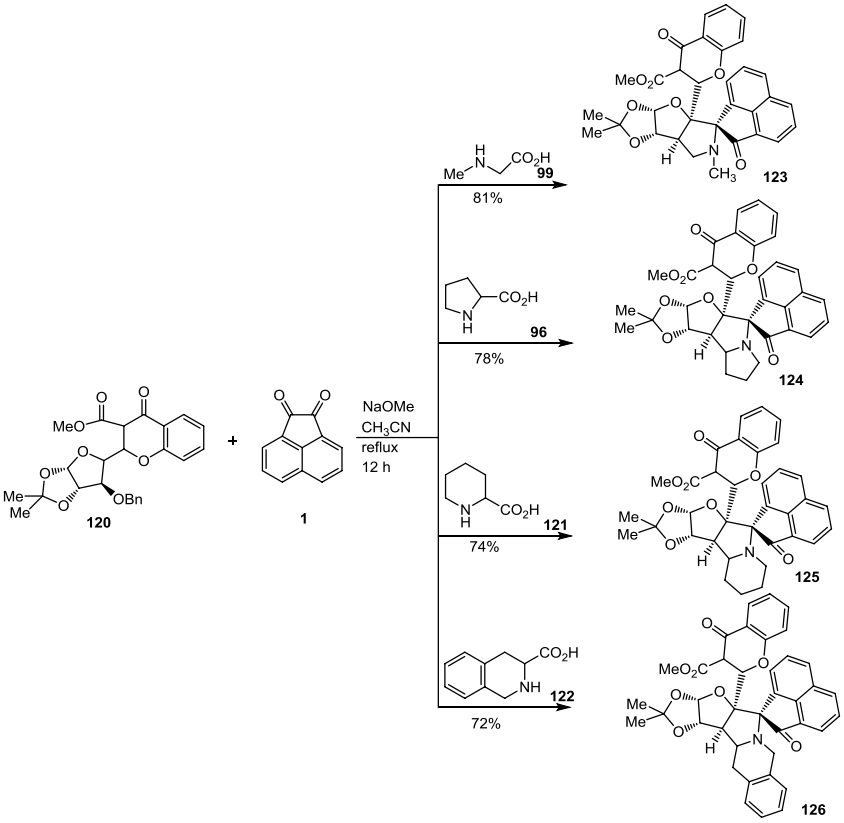
27 Synthesis of Spiropyrrolidine and Spiropyrrolizidine Derivatives

Tabatabaei Rezaei et al. studied the regio-selective synthesis of spiropyrrolidine and spiropyrrolizidine **127** and **128** via the multicomponent condensation of azomethine ylides (generated in situ from amino acids **96** and **99** viz. sarcosine/*N*-phenylglycine/proline and acenaphthenequinone **1**) with the Knoevenagel adduct derivatives **97** (preformed by the reaction of malononitrile with substituted benzaldehydes). The reactions were carried out under both conventional heating and ultrasonic irradiation conditions (Scheme 50) [67].

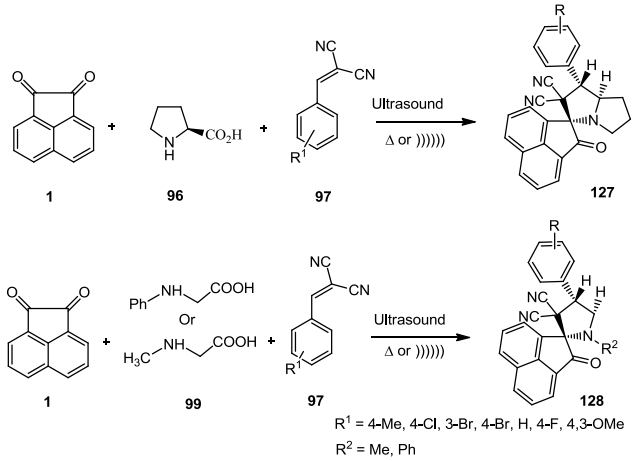
An efficient synthesis of novel spiro[acenaphthylene-1,2′-pyrrolidine] **127**, spiro[acenaphthylene-1,2′-pyrrolizidine] **128**, containing cyano group were successfully synthesized via a three-component 1,3-dipolar cycloaddition reaction of acenaphthenequinone **1**, sarcosine or proline **96** and **99**, and Knoevenagel adducts **97** in refluxing aqueous methanol (Scheme 51) [68].

The synthesis of novel glyco-spiro-pyrrolidines and glyco-spiro-pyrrolizidines **130**, **132**, and **133** has been accomplished through 1,3-dipolar cycloaddition reaction of various azomethine ylides derived from acenaphthoquinone **1** and secondary amino acids **99**, **96** with glycoacrylate **129**, **131** as dipolarophile (Schemes 52, 53) [69].

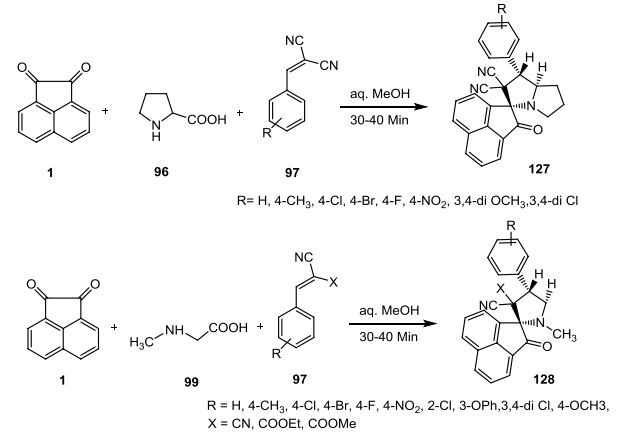
The synthesis of new spiropyrrolidines/pyrrolizidines **135**, **136** has been achieved by Ramesh and coworkers. Baylis–Hillman adduct (of ninhydrin with sarcosine/proline) as dipolarophiles **134** were reacted with azomethine ylides, generated in situ from sarcosine **99**, **96** and acenaphthoquinone **1**, to produce the corresponding cycloadducts in various condition. The other regioisomers **135a**



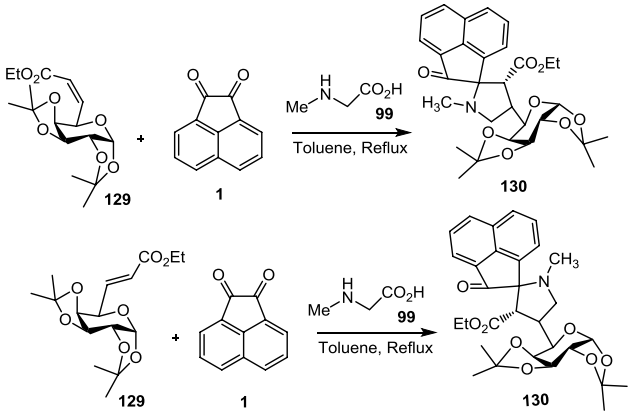
Scheme 49 Synthesis of carbohydrate-derived pyrrolidinyl-spiro acenaphthylenones



Scheme 50 Synthesis of spiropyrrolidine and spiropyrrolizidine



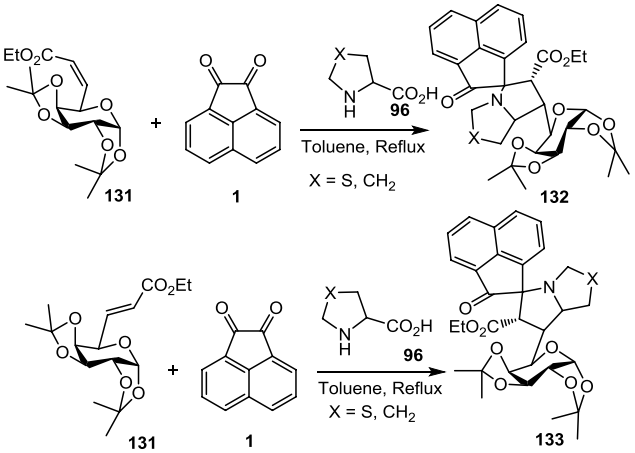
Scheme 51 Synthesis of spiro[acenaphthylene-pyrrolidine] **87**, spiro[acenaphthylene-pyrrolizidine] **88**



Scheme 52 Synthesis of glycopyrrolidine

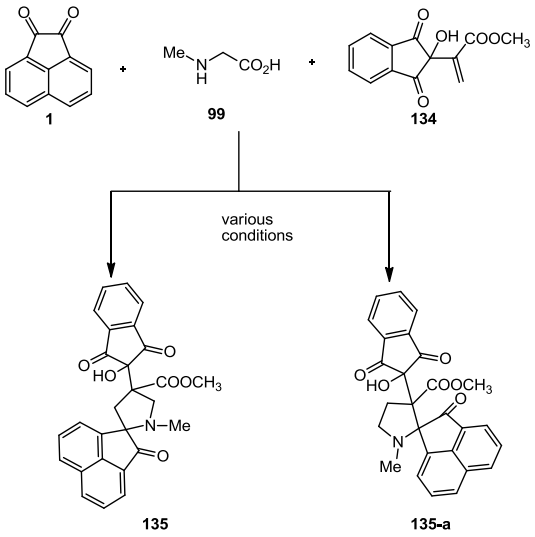
and **136a** were not formed (Method A: conventional methanol reflux, Method B: methanol/MW, Method C: K-10 Montmorillonite clay/MW) (Schemes 54, 55) [70].

Raghunathan et al. developed an efficient three-component protocol to synthesize acridine-dione-derived mono spiro-pyrrolidine and pyrrolizidine derivatives **138**, **139** by 1,3-dipolar cycloaddition reaction. The *o*-acryloylacridine-diones **137**, as dipolarophiles reacted with azomethine ylide derived from diketones **1**



Scheme 53 Synthesis of glycopyrrolizidines

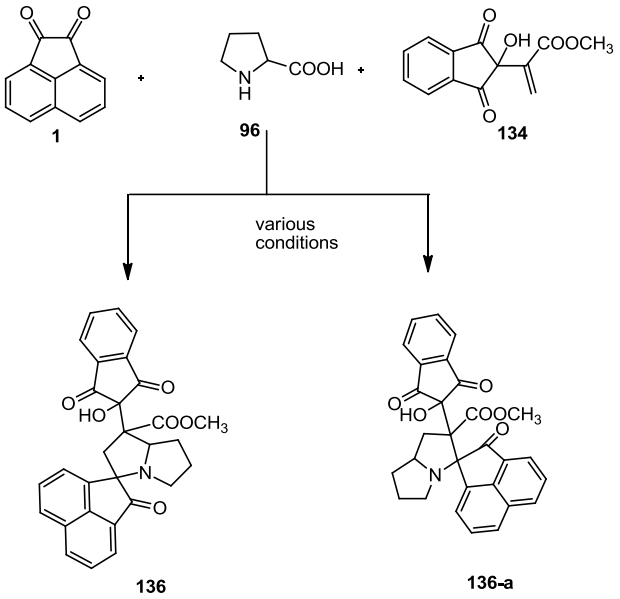
Scheme 54 Synthesis of novel spiropyrrolidines



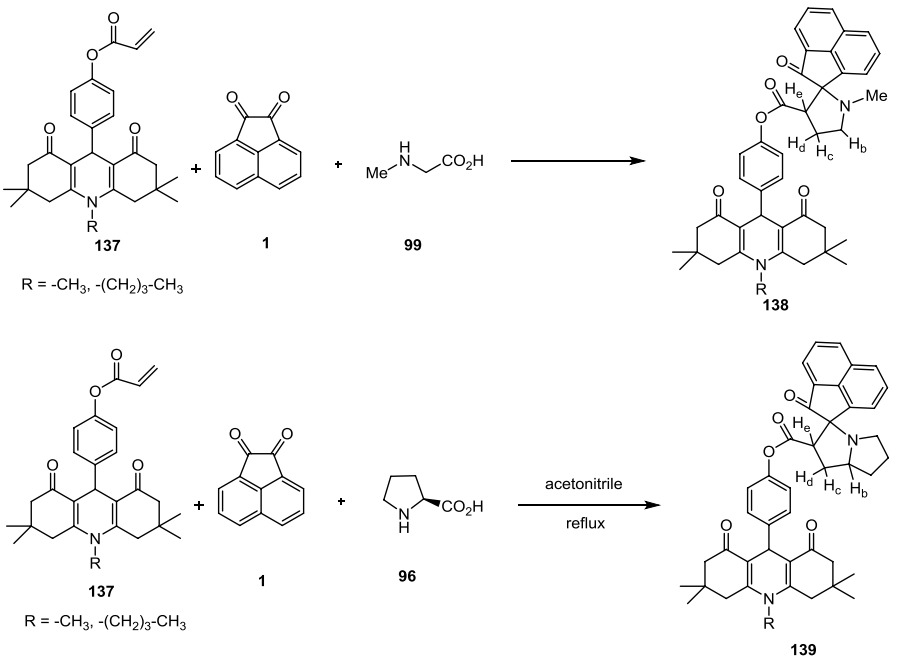
and *sec*-amino acids **99**, **96** to give acridinedione-derived mono spiropyrrolidine/pyrrolizidine derivatives in good yield (Scheme 56) [71].

Vijay et al. reported the reaction of isatin **140**, sarcosine **99**, and acenaphthenequinone **1** and 3,4-diphenyl cyclobutene-1,2-dione **142** in methanol:water (3:1) furnishing novel spiropyrrolidine derivatives **141** and **143** (Scheme 57) [72].

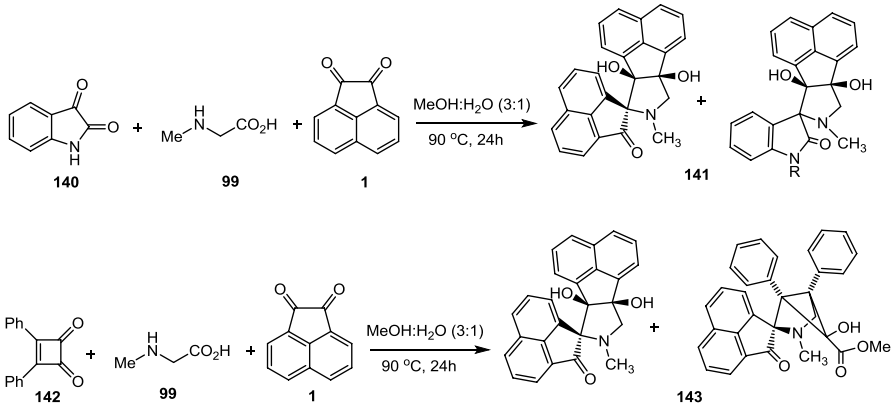
A novel spiro[acenaphthylene-1,2′-pyrrolidin]-2-one derivatives **146** was synthesized via the three-component, one-pot reaction of acenaphthenequinone **1**, arylmethyl amines **144**, and chalcones **145** with high regioselectivity in ethanol without any catalyst for 90 min (Scheme 58) [73].



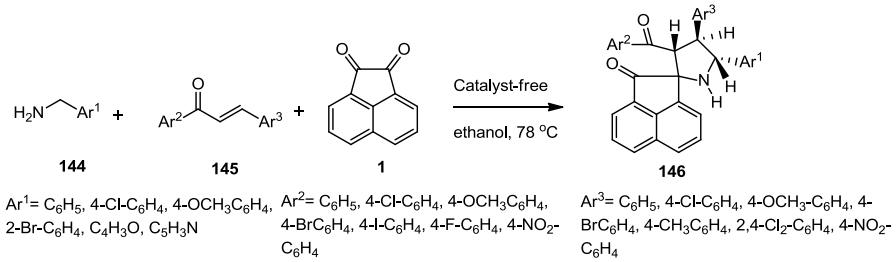
Scheme 55 Synthesis of novel spiropyrrolizidines



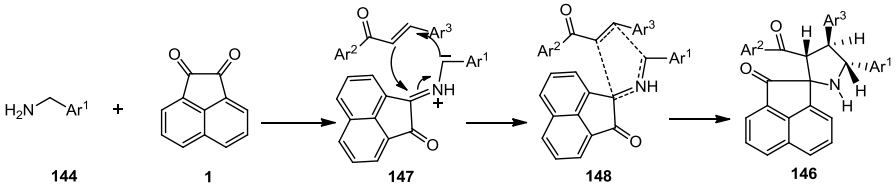
Scheme 56 Synthesis of mono spiroacenaphtheno/indano-pyrrolidine/pyrrolizidine derivatives



Scheme 57 Synthesis of spiropyrrolidine derivatives



Scheme 58 Synthesis of spiro[acenaphthylene-1,2′-pyrrolidin]-2-one derivatives



Scheme 59 Plausible mechanism for the synthesis of spiro[acenaphthylene-1,2′-pyrrolidin]-2-one derivatives

The suggested mechanism for the formation of product **146** is illustrated in Scheme 59. The reaction of acenaphthenequinone **1** with arylmethyl amines **144** led to the formation of the azomethine ylides **147**, which is used as dipoles. The carbanion of azomethine ylides **147** then assaulted the electrophilic *β*-carbon of chalcones, the products **146** were afforded (Scheme 59).

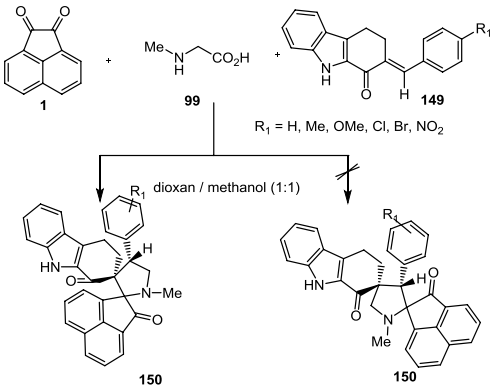
28 Synthesis of Dispiropyrrolidine/Pyrrolizidines Thiapyrrolizidine Derivatives

A series of novel dispiropyrrolidine derivatives **150** has been accomplished through 1,3-dipolar cycloaddition reaction of azomethine ylide generated from sarcosin **65** and acenaphthoquinone **1** with the dipolarophile (*E*)-2-arylidine-1-keto-carbazoles **149**. The cycloadducts ketocarbazalo spiro *N*-methyl pyrrolidines showed the most interesting antimicrobial activity at lower concentration (Scheme 60) [74].

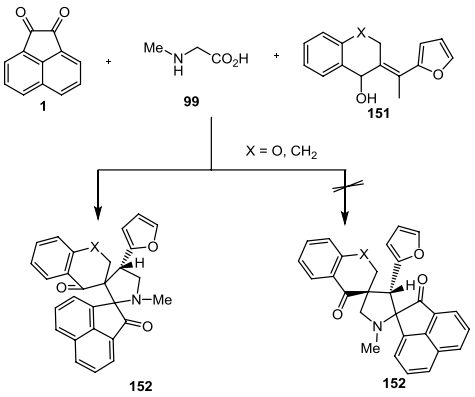
The synthesis of novel dispiroheterocycles **152** by the cycloaddition reaction of azomethine ylides generated from sarcosine **99** and acenaphthoquinone **1** with (*E*)-3-furfurylidene-4-chromanone/(*E*)-2-furfurylidene-1-tetralone **151** was described by Manian et al. (Scheme 61) [75].

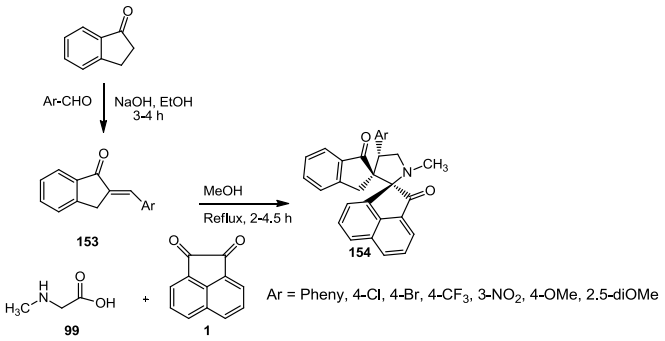
The reaction of 2-[(*E*)-1-arylmethylidene]-1-indanones **153** with acenaphthoquinone **1** and sarcosine **99** in MeOH at reflux afforded synthesis of highly functionalized dispiropyrrolidines **154** using [3 + 2]-cycloaddition by Ali et al. (Scheme 62) [76].

Scheme 60 Synthesis of novel dispiropyrrolidine derivatives



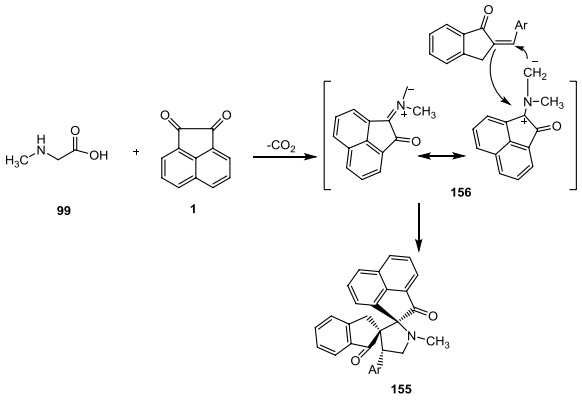
Scheme 61 Synthesis of novel dispiroheterocycles derivatives





Scheme 62 Synthesis of highly functionalized dispiropyrrolidines

Scheme 63 Mechanism for the regioselective formation of dispiropyrrolidine

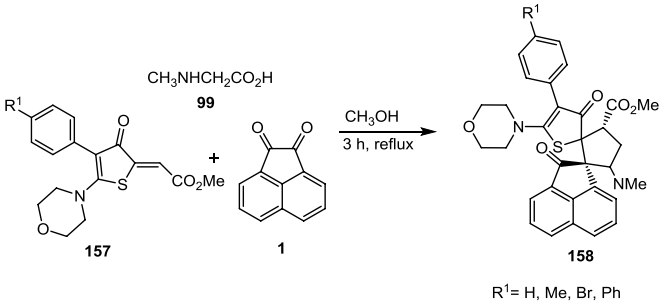


A plausible mechanism for the formation of the novel pyrrolidine derivative is given in Scheme 63. The reaction of acenaphthenequinone **1** and sarcosine **99** to give the azomethine ylide **156**, which adds to C=C bond of the dipolarophile from the bottom to form the desired cycloadduct. Eventually, only one stereoisomer of the cycloadduct despite of the presence of three stereocenters (Scheme 63).

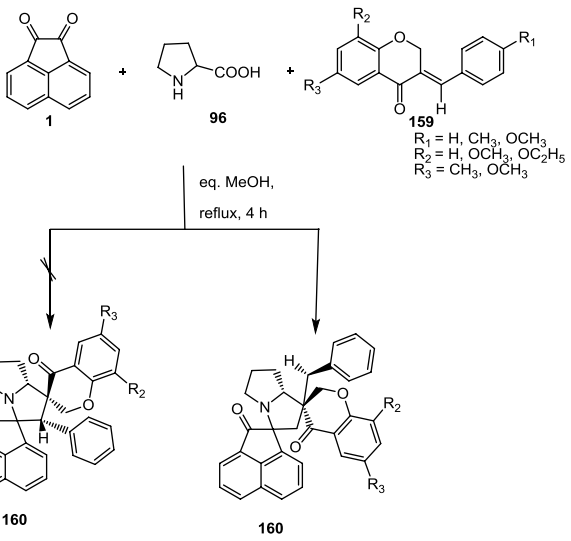
A new dispiro compound **158** was regioselectively synthesized by a one-pot, multicomponent reaction of acenaphthoquinone **1**, thiophenone ring **157**, and sarcosine **99**. Unsaturated thiophenone dipolarophiles were reacted with azomethine ylides, generated in situ from sarcosine, acenaphthoquinone, to produce the corresponding cycloadducts in good yields (70–90%) (Scheme 64) [77].

A synthetic route for the preparation of novel synthesis of novel dispiropyrrolidin/pyrrolizine derivatives **160** and **161** has been accomplished via 1,3-dipolar cycloaddition of azomethineylides generated in situ by the decarboxylative condensation of acenaphthenequinone **1** and sarcosine **99** and *L*-prolin **96** with the dipolarophile (*E*)-3-arylidene-4-chromanones **159** (Schemes 65, 66) [78].

A facile regio- and stereoselective synthesis of novel dispiroheterocyclic hybrids was developed by reaction of benzo[1,4]oxazine/benzo[1,4]thiazine **162** and acenaphthoquinone **1**, α-amino acids **96**, **99** via 1,3-dipolar cycloaddition reaction



Scheme 64 Synthesis of dispiro compound

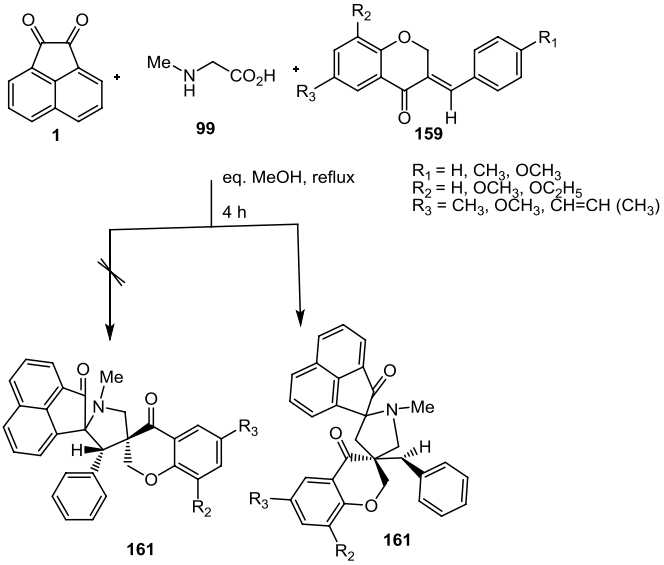


Scheme 65 Synthesis of novel dispiropyrrolizine derivatives

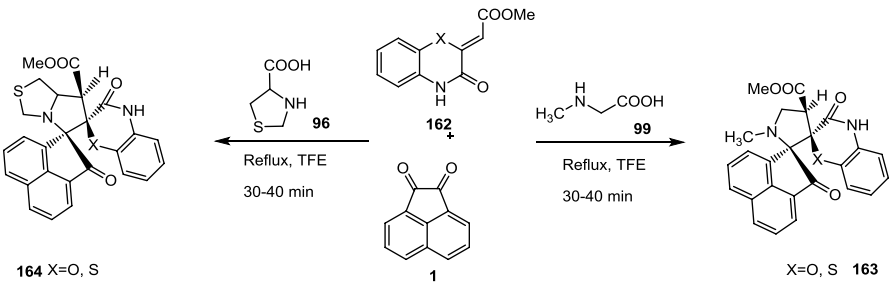
and using 2,2,2-trifluoroethanol as a new alternative and non-nucleophilic solvent for rapid access to construct a diversity-oriented library of regioselectivity dispiropyrrolidine/thiapyrrolizidines **163**, **164** were prepared (Scheme 67) [79].

Perumal and Thennarasu have developed the regioselective synthesis of a series of novel dispiropyrrolidines **166** through intermolecular 1,3-dipolar cycloaddition of azomethine ylides obtained from 1,2-diones like isatin **140** and sarcosine **99** with acenaphthenone-2-ylidine ketone **165** dipolarophiles in methanol under reflux conditions (Scheme 68) [80].

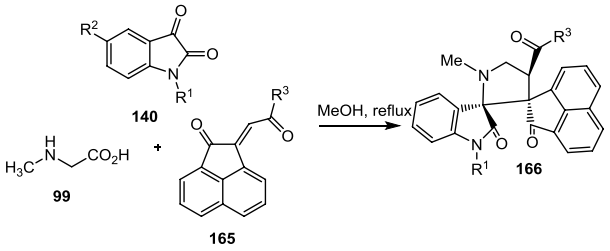
Perumal et al. has reported the reaction of isatin derivatives **140** and acenaphthenequinone **1** with α-amino acids **96** or **99**, and acenaphthenone-2-ylidine



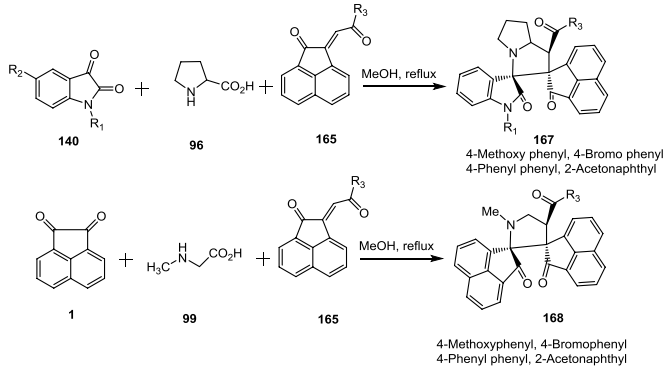
Scheme 66 Synthesis of novel dispiro compound



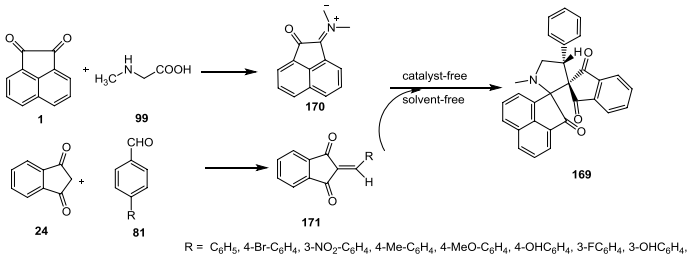
Scheme 67 Synthesis of acenaphthaquinone containing benzo[1,4]thiazine/oxazine based dispiroheterocycles via azomethine ylides



Scheme 68 Synthesis of novel dispiropyrrolidines



Scheme 69 Synthesis of novel dispiropyrrolizidines



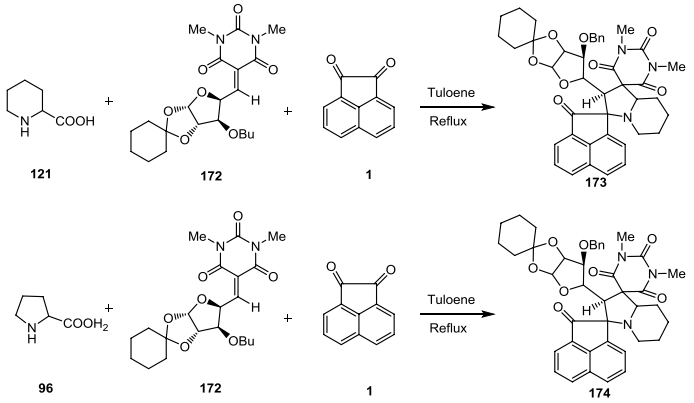
Scheme 70 Synthesis of dispiropyrrolidine derivatives

ketone **165** dipolarophiles in methanol at reflux conditions that led to synthesis of a series of novel dispiropyrrolizidines **167**, **168** (Scheme 69) [80].

Li and coworkers in 2008 developed a novel method for the synthesis of dispiropyrrolidine derivatives **169** by a tandem Knoevenagel-1,3-dipolar cycloaddition reaction sequence of acenaphthylene-1,2-dione **1**, sarcosine **99**, 1,3-indanedione **24**, and an aldehyde **81** without any catalyst and solvent-free (Scheme 70) [81].

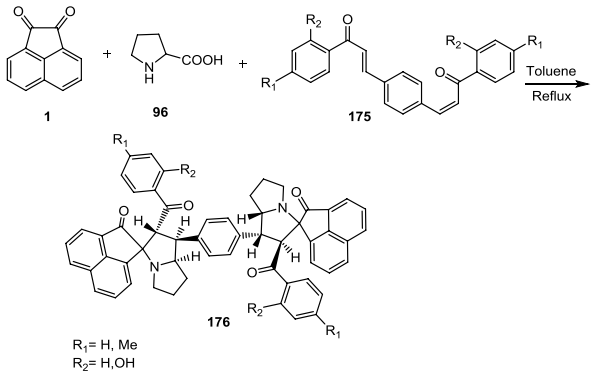
As shown in Scheme 71, this research group evaluated the synthesis of glyco dispiro pyrrolizidines **173**, **174** 1,3-dipolar cycloaddition reaction. The novel glycosyl dipolarophile derived **172** from dicyclohexylidine glucose underwent neat [3+2] cycloaddition reaction with the azomethine ylide generated from 1,2-diketones **1** and cyclic amino acid **96**, **121** to give the corresponding glycosidic heterocycles in good yields (Scheme 71) [82].

In 2013, synthesis of a series of novel dispiro pyrrolizidines **176** has been achieved by 1,3-dipolar cycloaddition reaction of azomethine ylide generated from secondary amino acids **96** and diketones **1** with bischalcones **175** (Scheme 72) [83].



Scheme 71 Synthesis of a new dispiro pyrrolizidines

Scheme 72 Synthesis of dispiro pyrrolizidines

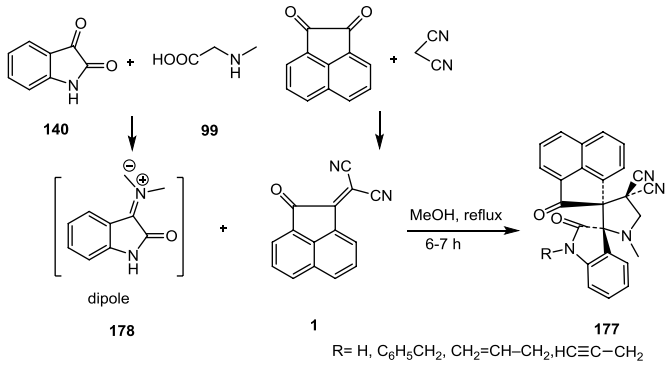


29 Synthesis of Dispirooxindole-pyrrolidine/Pyrrolizidine Derivatives

Dandia et al., reaction of the 1,3-dipolar cycloaddition of 2-oxo-(2*H*)-acenaphthylen-1-ylidene-malononitrile **1** as dipolarophiles have been investigated for the first time with the azomethine ylides generated in situ from *N*-substituted isatin **140** and sarcosine **99** to furnish novel dispiro heterocycles **177** (Scheme 73) [84].

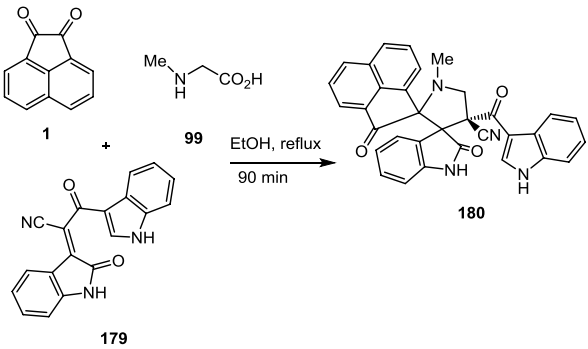
Perumal's group synthesized an efficient novel dispirooxindole-pyrrolidine derivative **180** through 1,3-dipolar cycloaddition of an azomethine ylide generated from acenaphthenequinone **1** and sarcosine **99** with the dipolarophile 3-(1*H*-indol-3-yl)-3-oxo-2-(2-oxoindolin-3ylidene)propanenitrile **179** in the absence of catalyst and in EtOH at reflux condition (Scheme 74) [85].

Bharitkar and coworker reported the facile, atomeconomic synthesis of novel spiro-pyrrolizidino-oxindole **182** adducts of withaferin-A **181** via the intermolecular cycloaddition of azomethine ylides generated in situ from L-proline **96** and acenaphthoquinone **1** withaferin-A (WA) has attracted the attention of chemists as well as biologists due to its interesting structure and various bio-activities (Scheme 75) [86].

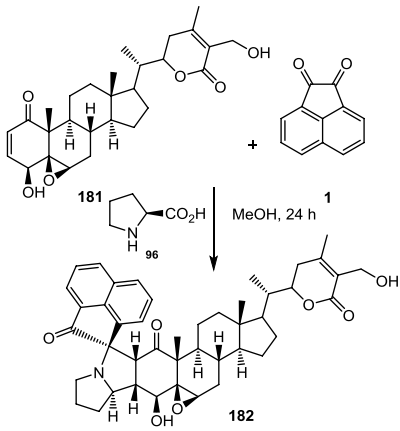


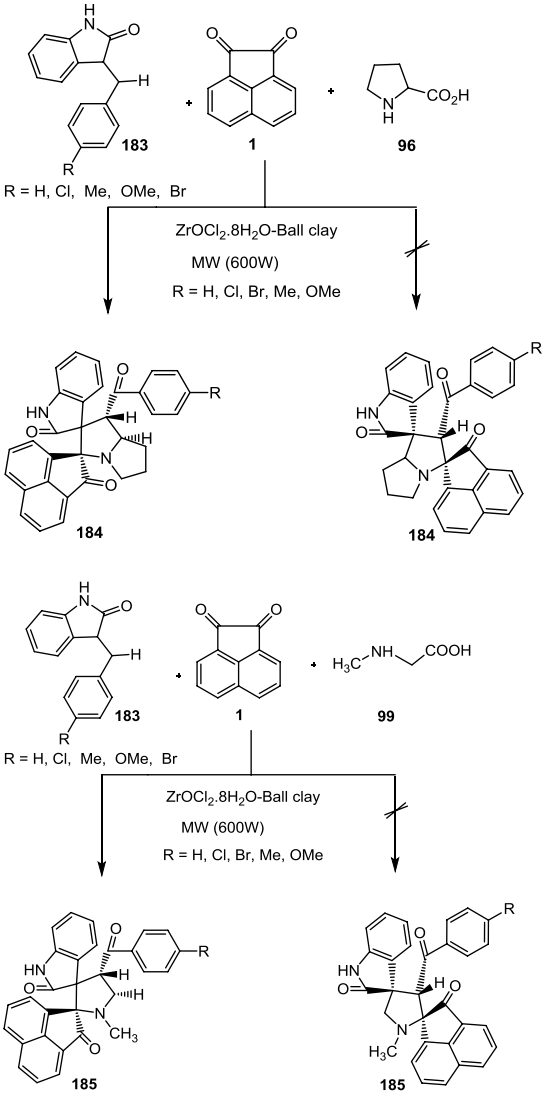
Scheme 73 Synthesis of dispiropyrrolidine oxindoles

Scheme 74 Synthesis of spirooxindole derivatives



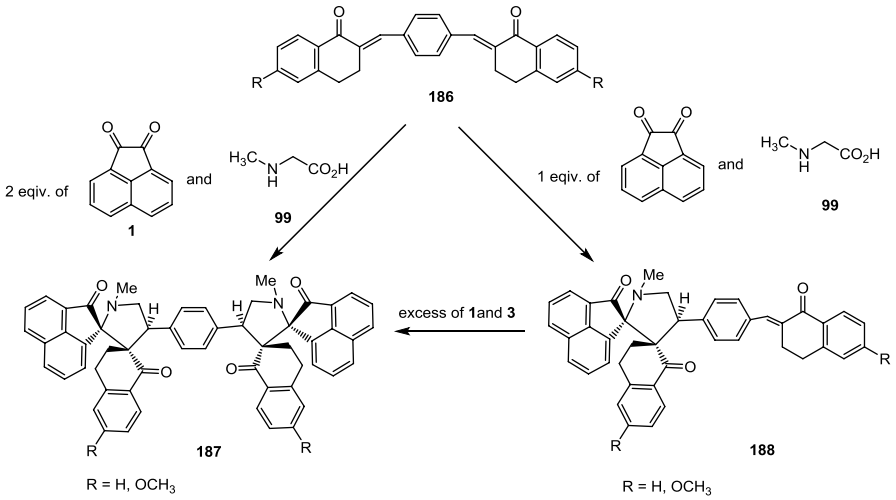
Scheme 75 Synthesis of novel spiro-pyrrolizidino-acenaphtho-quino withaferin-A





Scheme 76 Synthesis of novel dispiro-oxindolopyrrolidines and -pyrrolizidines

In 2007, Raghunathan et al. reported an efficient microwave-assisted $ZrOCl_2 \cdot 8H_2O$-mediated synthesis of novel dispiro-oxindolopyrrolidines/pyrrolizidines **184** and **185** through [3 + 2] cycloaddition reaction of azomethine ylides derived from acenaphthenequinone **1** and sarcosine/L-proline **96**, **99** with (*E*)-2-oxoindolino-3-ylidene acetophenones **183** as dipolarophiles in good yields (Scheme 76) [87].



Scheme 77 Synthesis of tetraspiro-bispyrrolidines and tetraspiro-bisoxindolopyrrolidines

30 Synthesis of Tetraspiro-bispyrrolidines and Tetraspiro-bisoxindolopyrrolidines

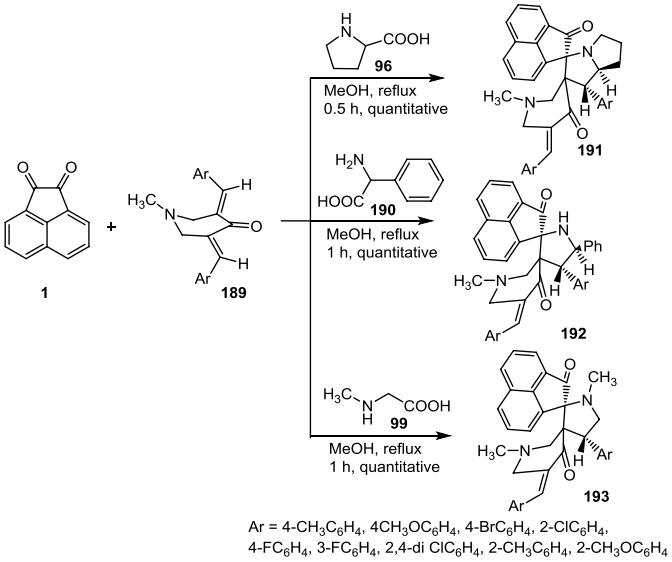
Raghunathan and Rajesh has reported an efficient approach to the synthesis of a new class of tetraspiro-bispyrrolidines and tetraspiro-bisoxindolopyrrolidines **187**, **188** through 1,3-dipolar cycloaddition reaction and under solvent-free microwave conditions (Scheme 77) [88].

31 Synthesis of Spiro-pyrido-pyrrolizines and Pyrrolidines

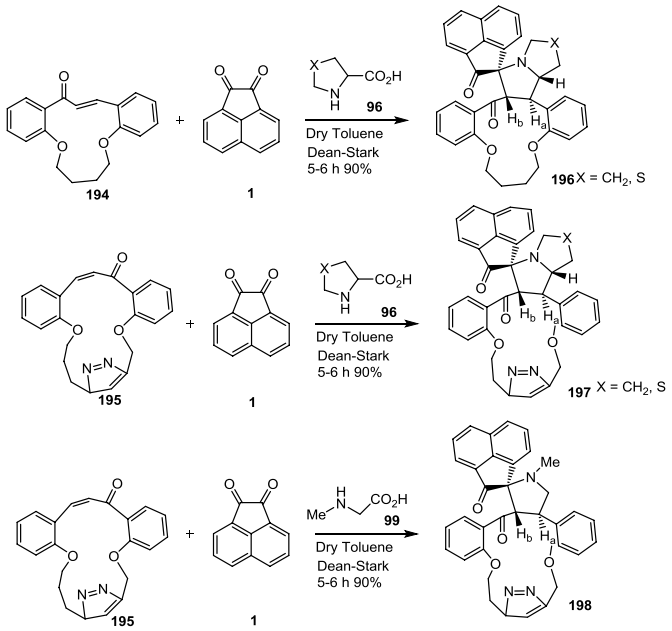
In 2008, Kumar et al. reported the 1,3-dipolar cycloaddition of azomethine ylides derived from acenaphthenequinone **1** and α-amino acids viz. proline **96**, phenylglycine **190** and sarcosine **99** to a series of 1-methyl-3,5-bis[(*E*)-arylmethylidene]tetrahydro-4(1*H*)-pyridinones **189** for synthesis of novel spiro-pyrido-pyrrolizines and pyrrolidines **191**, **192**, **193** in quantitative yields (Scheme 78) [89].

32 Synthesis of Spiro Pyrrolidine-grafted Macrocycles

In 2013, Raghunathan accomplished the synthesis of 13- and 16-membered macrocyclic enone **196**, **197**, **198** with alkyl ether and triazole as a linker using intramolecular aldol condensation. The newly synthesized macrocyclic enone was successfully utilized as a dipolarophile in 1,3-dipolar cycloaddition. The dipole generated from acenaphthenequinone **1** with various secondary amino acids (sarcosine, *L*-proline, and thiazolidine-4-carboxylic acid) **96**, **99** were reacted with macrocyclic enone

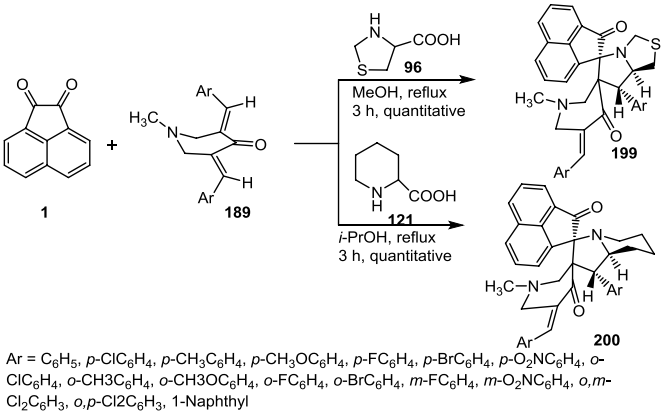


Scheme 78 Synthesis of novel spiro-pyrido-pyrrolizines and pyrrolidines



Scheme 79 Synthesis of spiroacenaphthenone pyrrolidine-grafted macrocycles

194, **195** to give a new class of spiropyrrolidine-grafted macrocycles **196**, **197**, **198** in good yield (> 85%) (Scheme 79) [90].



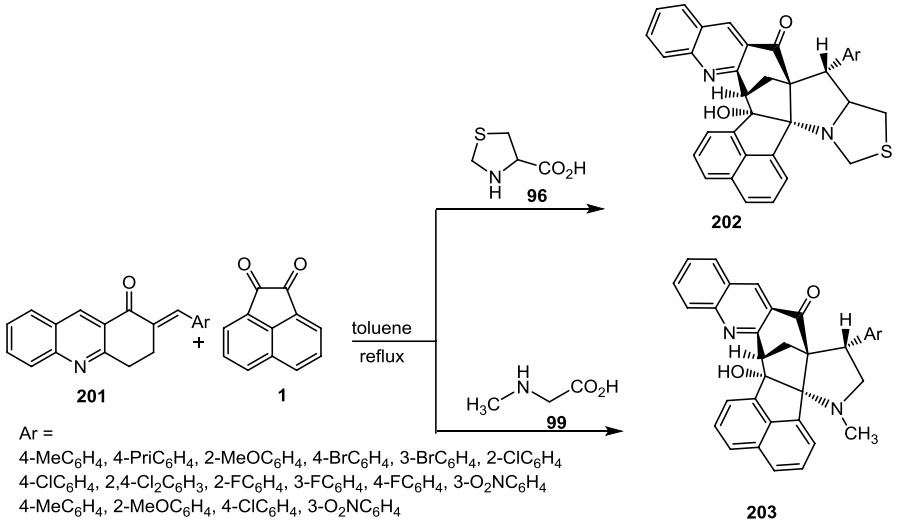
Scheme 80 Synthesis of dispiroacenaphthene

33 Synthesis of Dispiro-pyrrolo-thiazole

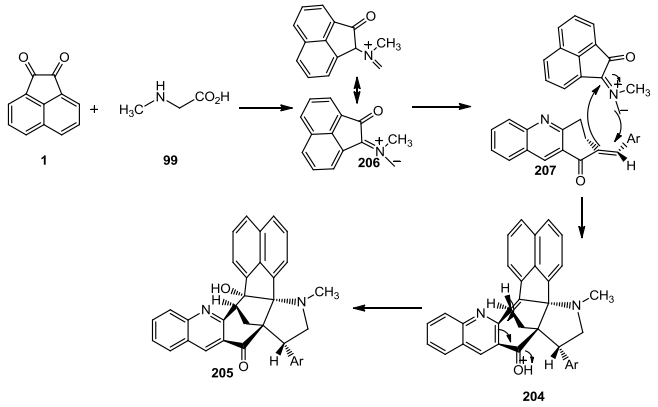
An efficient synthesis of spiroacenaphthene1″-one spiro[-arylmethylidene-1′-methylpiperidin-4′-one-7-aryltetrahydro-1*H*-pyrrolo[1,2-*c*][1,3]thiazoles **199** and spiroacenaphthene-1″-one spiro-arylmethylidene-1′-methylpiperidin-4′- one-4-aryloctahydroindolizines **200** was developed by reaction of 1,3-dipolar cycloaddition of azomethine ylides generated in situ from acenaphthenequinone **1** and α-amino acids **96**, **121** viz. 1,3-thiazolone-4-carboxylic acid and piperidine-2-carboxylic acid to a series of 1-methyl-3,5-bis[(*E*)-arylmethylidene]tetrahydro-4(1*H*)-pyridinones **189** in good yield (Scheme 80) [91].

34 Synthesis of Polycyclic Hybrid Heterocycles

The synthesis of polycyclic hybrid heterocycles **202**, **203** by utilizing a 1,3-dipolar cycloaddition of azomethine ylides, generated in situ via decarboxylative condensation of acenaphthoquinone **1** and *N*-substituted sarcosine/thiazolidine-4-carboxylic acid **96**, **99** with 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinones **201** in a three-component fashion was reported by Perumal and coworkers (Scheme 81) [92]. The reaction, via initial formation of azomethine ylide **206**, generated by the condensation of sarcosine **99** and acenaphthoquinone **1** followed by decarboxylation. Concomitant cycloaddition of the azomethine ylide **206** to 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinones **207** affords the cycloadducts **204**, which undergose intramolecular via the reaction of the methylene group of the carbocyclic ketone fused to the quinoline moiety with the remaining acenaphthoquinone carbonyl of **204** furnishes **205** (Scheme 82).



Scheme 81 Synthesis of polycyclic hybrid heterocycles

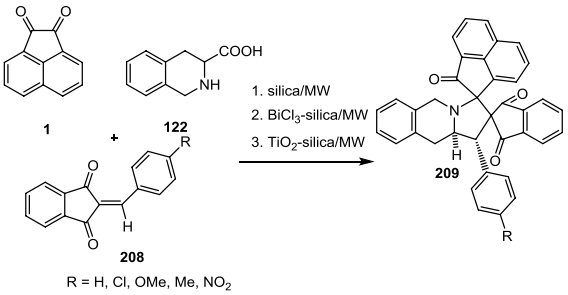


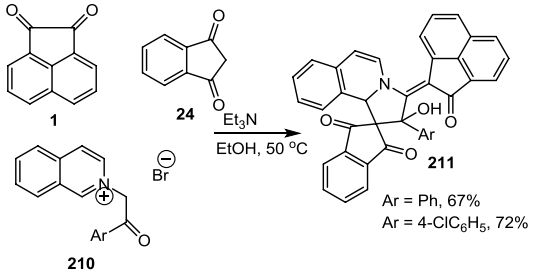
Scheme 82 Plausible mechanism for the formation of polycyclic hybrid heterocycles **159**

35 Synthesis of Dispiro-acenaphthen-pyrroloisoquinoline

The dipolarophiles 2-arylidene-indanediones **208** can be easily obtained via a two-component condensation of indandione with various benzaldehydes. The reaction of tetrahydroisoquinoline-3-carboxylic acid **122** with acenaphthenequinone **1** under different conditions to give an azomethine ylide. The ylide intermediate undergoes a 1,3-dipolar cycloaddition with 2-arylidene-indanediones **208** in a one-pot, three-component reaction led to the formation hexahydro-1-phenyl-spiro[2.2′]-indane-1,3-dione-spiro[3.2″] acenaphthen-1-one-pyrrolo[1,2-*a*]isoquinoline **209**. This group carried out this reaction using different methods: silica, $BiCl_3$–silica or TiO_2–silica under MW irradiation. The best results were obtained by the last method (TiO_2–silica). TiO_2–silica is used as an efficient solid-supported catalyst (Scheme 83) [93].

Scheme 83 Synthesis of dispiroheterocyclic





Scheme 84 Synthesis of 2′-acenaphthylidenespiro[indane-2,1′-pyrrolo[2,1-*a*]isoquinolines]

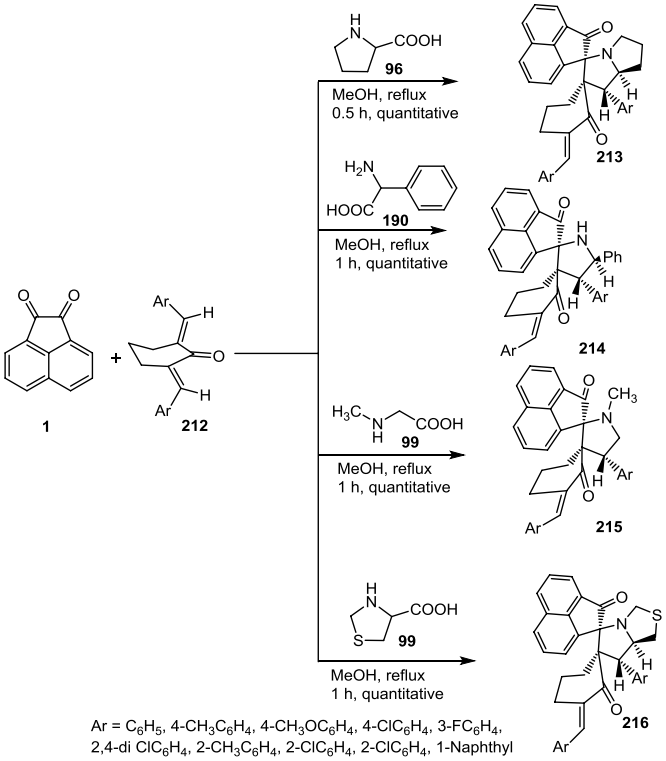
In 2014, Yan et al. described the synthesis of 2′-acenaphthylidenespiro[indane-2,1′-pyrrolo[2,1-*a*]isoquinolines] **211** were efficiently synthesized by three-component reactions of in situ-generated *N*-phenacylisoquinolinium bromides **210** with indane-1,3-dione **24** and acenaphthoquinone **1** in ethanol using triethylamine as the base (Scheme 84) [94].

36 Synthesis of Acenaphthylene Dispiro Heterocycles

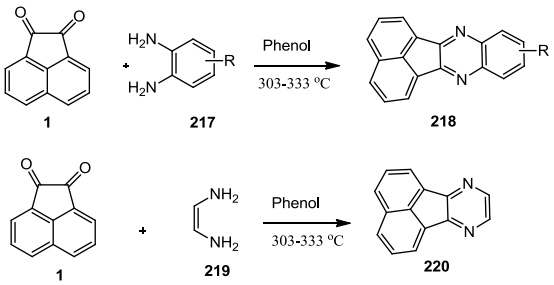
Synthesis of novel acenaphthylene dispiro heterocycles **213**, **214**, **215**, **216** has been achieved by a one-pot, three-component 1,3-dipolar cycloaddition reaction. The azomethine ylides generated in situ from *N*-substituted acenaphthoquinone **1** and α-amino acids **96**, **99**, **190** viz. sarcosine, phenylglycine, 1,3-thiazolane-4-carboxylic acid and proline reacted with 2,6-bis[(*E*) arylmethylidene] cyclohexanones **212** as a dipolarophile to give acenaphthylene dispiro heterocycles in quantitative yields (Scheme 85) [95].

37 Synthesis of Acenaphtho[1,2-*b*]quinoxaline Derivatives and Acenaphtho[1,2-*b*]pyrazine

The reaction of acenaphthoquinone **1** with diamines **217**, **219** in phenol afforded the synthesis of acenaphtho[1,2-*b*]quinoxaline **218** and acenaphtho[1,2-*b*]pyrazine **220** (Scheme 86) [96].



Scheme 85 Synthesis of spiro-cyclohexanones

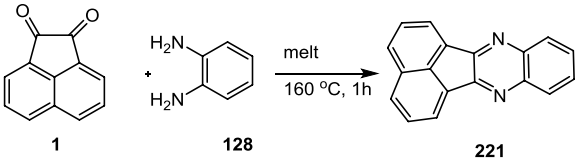


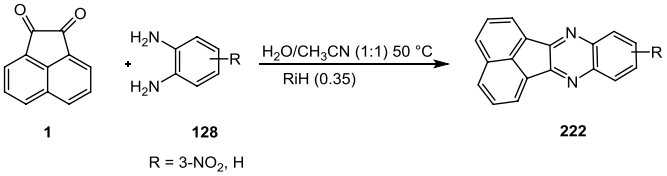
Scheme 86 Synthesis of acenaphtho[1,2-*b*]quinoxaline **218** and acenaphtho[1,2-*b*] pyrazine **220**

In 2014, an efficient synthesis of quinoxaline scaffolds **221** was developed by reaction of acenaphthoquinone **1** with diamines **128** under solid-state melt reaction (SSMR) with excellent yields (Scheme 87) [97].

Shirini et al. synthesized quinoxaline derivatives **222** in a mixture of H_2O and CH_3CN at 50 °C and in the presence of rice husk (RiH) with excellent yields with acenaphthoquinone **1** and diamines **128** (Scheme 88) [98].

Scheme 87 Synthesis of quinoxaline





Scheme 88 Synthesis of quinoxaline

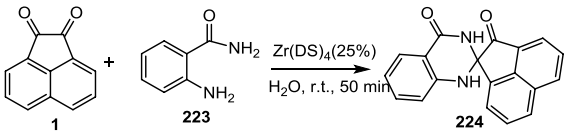
38 Synthesis of Spiroisoindoline-1,2′-quinazoline

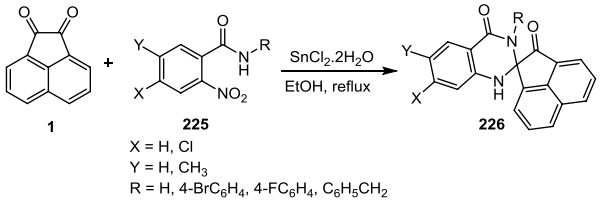
Shekouhy et al. suggested an efficient synthesis of 1-*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-diones **224** via the reaction of acenaphthoquinone **1** with 2-aminobenzamide **223** in H_2O using of zirconium tetrakis(dodecyl-sulfate) [$Zr(DS)_4$] at room temperature (Scheme 89) [99].

One-pot reaction of 2-nitrobenzamides **225** and acenaphthoquinone **1** in the presence of a catalytic amount of $SnCl_2{\cdot}2H_2O$ and in EtOH as solvent gave 10*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-dione derivatives **226** in good yield (Scheme 90) [100].

The synthesized 1-*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-diones **227** by Pore and coworkers via the reaction of acenaphthoquinone **1** with 2-aminobenzamide **223** in EtOH in the presence of Solfamic acid at room temperature (Scheme 91) [101]. A plausible mechanism for the reaction is shown in Scheme 92. At beginning,

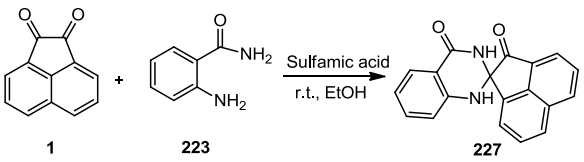
Scheme 89 Synthesis of quinazoline derivatives

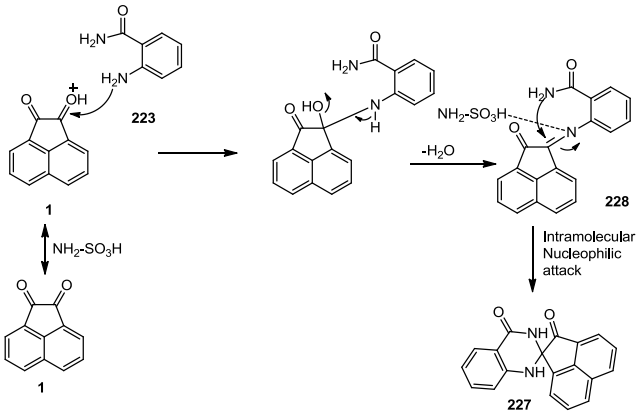




Scheme 90 Synthesis of 10-*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-dione derivatives

Scheme 91 Synthesis of spiro[isoindoline-1,2′-quinazoline]-diones





Scheme 92 Plausible mechanism for the synthesis of 1-*H*-spiro [isoindoline-1,2-quinazoline]-3,4 (3*H*)-diones

acenaphthoquinone **1** was activated by sulfamic acid, then the carbonyl unit of the acenaphthoquinone **1** undergoes nucleophilic attack by amine of anthranilamide **223** to afford an imine intermediate **228**, which undergoes intramolecular cyclization involving nucleophilic attack by $–CONH_2$ moiety on –C=N– was obtain the corresponding product **227**(Scheme 92).

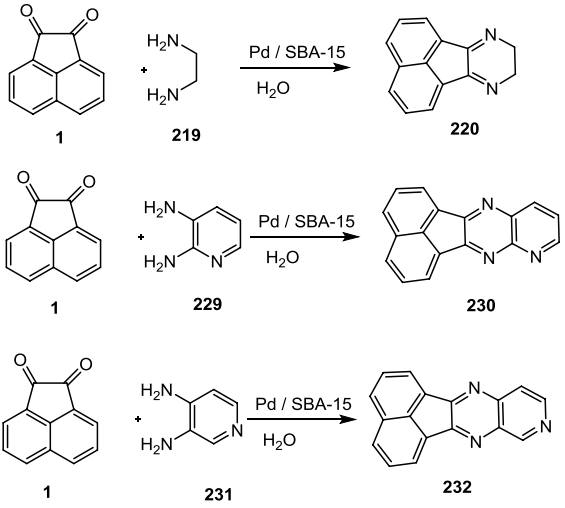
39 Synthesis of Dihydroacenaphtho[1,2-*b*]pyrazine/Pyridopyrazine

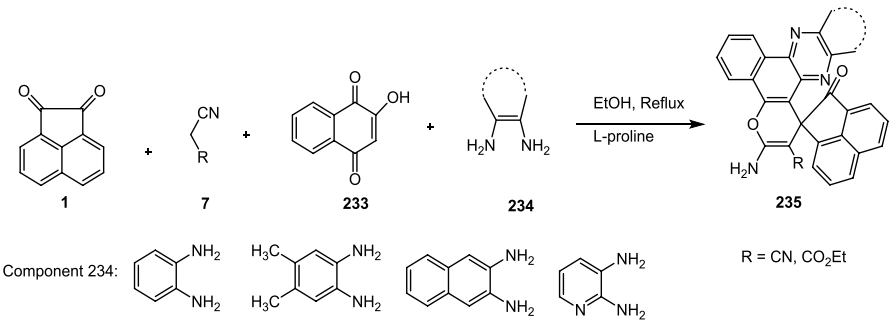
The reaction of acenaphthoquinone **1** with diamines **219**, **229**, **231** in the presence of catalyst Pd/SBA-15 as nanocatalyst to afford synthesis of dihydroacenaphtho[1,2-*b*]pyrazine **220** and acenaphtho[1,2-*b*]pyrido[2,3-*e*]pyrazine **230** and acenaphtho[1,2-*b*]pyrido[3,4-*b*]pyrazine **232** heterocycles with good to excellent yields under green conditions (Scheme 93) [102].

40 Synthesis of Spiro[benzo[*c*]pyrano[3,2-*a*]phenazine] Derivatives

Hasaninejad and coworkers prepared a novel multicomponent reaction for the synthesis of spiro[benzo [*c*]pyrano[3,2-*a*]phenazine] derivatives **235** by acenaphthoquinone **1**, activated methylene reagent **7**, 2-hydroxy-1,4-naphthoquinone **233** with aromatic 1,2-diamines **234** in the presence of L-proline (30 mol%) as a bifunctional organocatalyst in EtOH under reflux conditions (Scheme 94) [103].

Scheme 93 Synthesis of dihydroacenaphtho[1,2-*b*]pyrazine **172** and acenaphtho[1,2-*b*]pyrido-pyrazine **181**, **183**





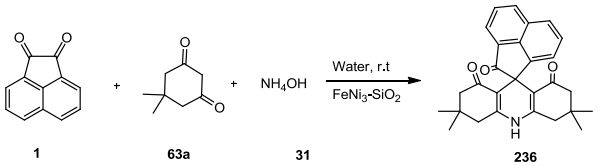
Scheme 94 One-pot, four-component synthesis of novel spiro[benzo[c]pyrano[3,2-a]phenazine] derivatives

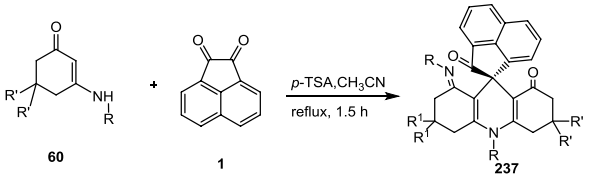
41 Synthesis of Spiroacridine Derivatives

Spiroacridine **236** were prepared from the reaction of acenaphthoquinone **1**, dimedone **63a**, and ammonium hydroxide **31** in the presence of $FeNi_3$–SiO_2 as the nanocatalyst at room temperature in water is reported (Scheme 95) [104].

An efficient synthesis of 9-spiroacridine derivatives **237** was developed by reaction of enaminones **60** and acenaphthoquinone **1** in CH_3CN in the presence of *para*-toluenesulfonic acid in good yield by Chen's group (Scheme 96) [105]. A plausible mechanism is shown in Scheme 97. The first step, the aza-ene addition

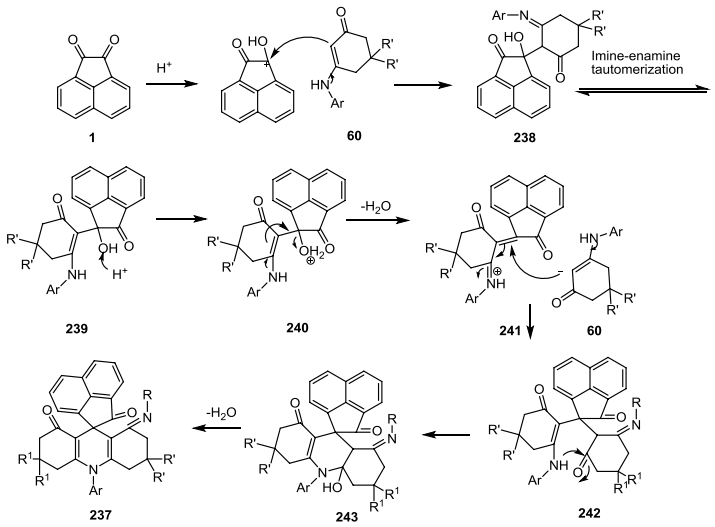
Scheme 95 Synthesis of spiroacridine





[R/R^1] = 4-FC$_6$H$_4$/H, 3-FC$_6$H$_4$/H, 4-ClC$_6$H$_4$/H , 3-ClC$_6$H$_4$/H, 4-BrC$_6$H$_4$/H , 3-BrC$_6$H$_4$/H, C$_6$H$_5$/H, 4-CH$_3$C$_6$H$_4$/H , 3-CH$_3$C$_6$H$_4$/H , 2-CH$_3$C$_6$H$_4$/H, 4-CH$_3$OC$_6$H$_4$/H, 4-FC$_6$H$_4$/CH$_3$, 3-FC$_6$H$_4$/CH$_3$, 4-ClC$_6$H$_4$/CH$_3$, 3-ClC$_6$H$_4$/CH$_3$, 4-BrC$_6$H$_4$/CH$_3$, 3-BrC$_6$H$_4$/CH$_3$, C$_6$H$_5$/CH$_3$, 4-CH$_3$C$_6$H$_4$/CH$_3$, 3-CH$_3$C$_6$H$_4$/CH$_3$, 4-CH$_3$OC$_6$H$_4$/CH$_3$

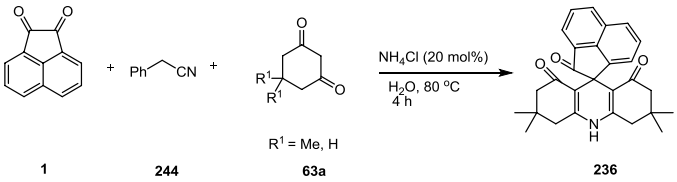
Scheme 96 Synthesis of 9-spiroacridine derivatives



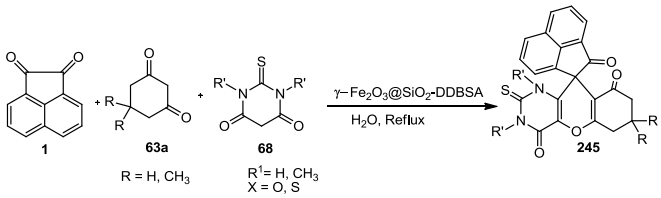
Scheme 97 Proposed mechanism for the synthesis of spiroacridines

of enaminone **60** to acenaphthoquinone **1**, leads to intermediate **238**, which undergoes a rapid imine–enamine tautomerization to give intermediate **239**. Afterwards, intermediate **239** accepts one proton to form **240**, and the elimination of H_2O from intermediate **240** gives iminium ion **241** enaminone **60** then in a Michael addition with compound **241** to afford intermediate **242**, the –NH group of which under an intramolecular attack of the carbonyl group, resulting in a cyclization reaction that to form **243**. Finally, intermediate **243** loses a molecule of water to lead to the formation of acridine **237** (Scheme 97).

The combination of acenaphthoquinone **1**, an activated methylene reagent **244**, and 1,3-dicarbonyl compounds **63** in the presence of catalytic ammonium chloride was found to be a suitable and efficient method for the synthesis of the spiro acenaphthylene **236** (Scheme 98) [106].



Scheme 98 Synthesis of spiroacridine



Scheme 99 Spiro[acenaphthylene-1,5-chromeno[2,3-d]pyrimidine] derivatives

42 Synthesis of Spiro Chromeno-pyrimidine

The spiro acenaphthylene derivative **245** was obtained by reaction of acenaphthoquinone **1**, cyclohexane-1,3-diones **63** and barbituric acids **68** in H_2O containing a catalytic amount of dodecyl benzenesulfonic acid functionalized silica-coated magnetic nanoparticles (γ-Fe_2O_3@SiO_2-DDBSA) at reflux temperature (Scheme 99) [107].

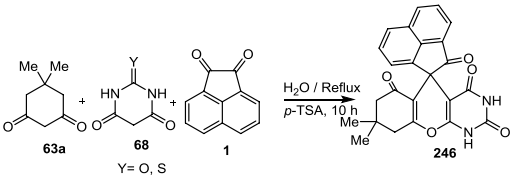
In 2010, Jadidi and coworkers reported an efficient one-pot synthesis of novel synthesis of spiro[acenaphthylene-1,5′-chromeno[2,3-*d*]pyrimidine] derivatives **246** by a three-component condensation reaction of barbituric acids **68** and acenaphthoquinone **1** with 5,5-dimethyl-cyclohexane-1,3-dione **63a** refluxing water in the presence of *p*-TSA for 10 h (Scheme 100) [108].

43 Synthesis of Spirochromene-spiropyran-spiropyranopyrazole

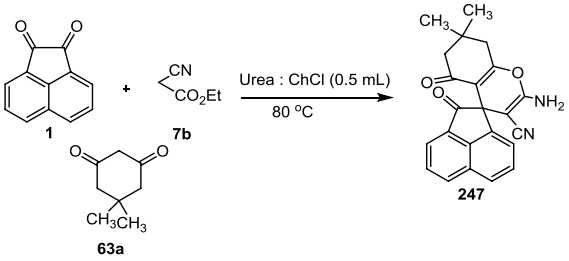
In 2014, Azizi and coworkers reported a simple and efficient synthesis of spiro acenaphthylene **247** by one-pot, three-component reaction of acenaphthoquinone **1**, malononitrile **7** and different nucleophiles **63a** in biodegradable choline chloride-based deep eutectic solvent in good yields 50–95% (Scheme 101) [109].

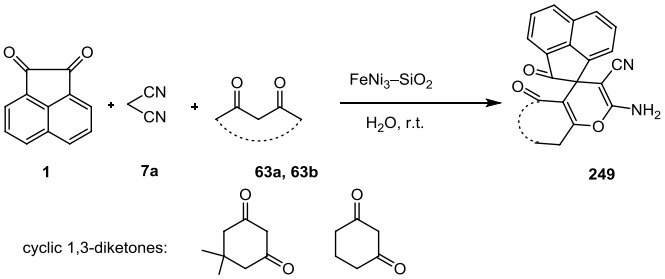
A green and efficient method for the synthesis of various spirochromenes **249** is reported by one-pot, three-component domino reaction of acenaphthoquinone

Scheme 100 Synthesis of spiro[acenaphthylene-1,5′-chromeno[2,3-d]pyrimidine] derivatives

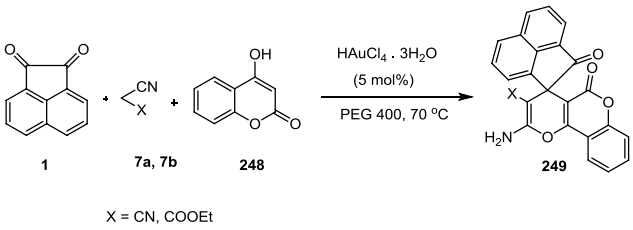


Scheme 101 One-pot, three-component synthesis of spiro acenaphthylene in DES





Scheme 102 Synthesis of spirochromene derivatives



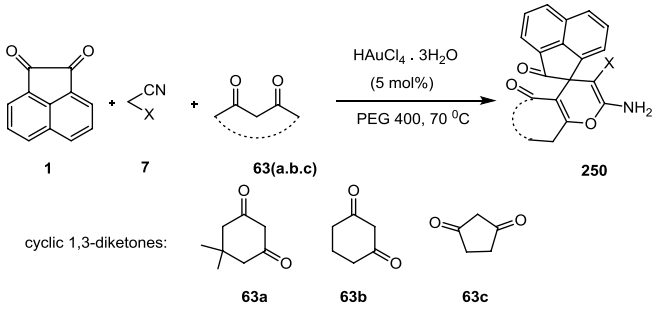
Scheme 103 Synthesis of spirochromene derivatives

1, malononitrile **7** and 1, 3-dicrbonyl compounds **63(a**, **b)** in the presence of $FeNi_3$–SiO_2 as the nano-catalyst at room temperature in water with high-product yields (Scheme 102) [104].

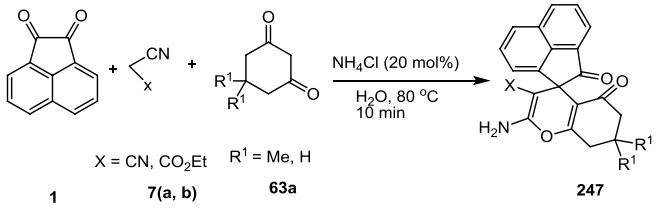
Synthesis of new spirochromene derivatives **249**, **250** by an organo-catalyzed via one-pot three-component condensation reaction of acenaphthoquinone **1**, active methylene compounds **7** and cyclic 1,3-diketones/4-hydroxycoumarin **63(a-c)**, **248** in refluxing PEG 400 in the presence of Gold(III) chloride ($HAuCl_4{\cdot}3H_2O$) was reported by Kidwai et al. (Schemes 103, 104) [110].

The combination of acenaphthoquinone **1**, an activated methylene reagent **7**, and 1,3-dicarbonyl compounds **63** in the presence of catalytic ammonium chloride was found to be a suitable and efficient method for the synthesis of the spiro acenaphthylene **247** (Scheme 105) [106].

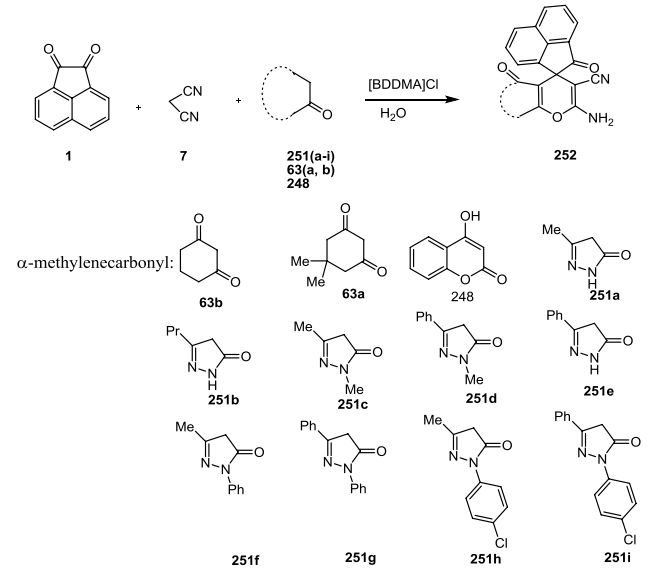
Reaction of compound **1** with malononitrile **7** and α-methylenecarbonyl compounds (β-diketones, pyrazolones) in the presence of (benzyl)(dimethyl)



Scheme 104 Synthesis of spiroacenaphthylene derivatives

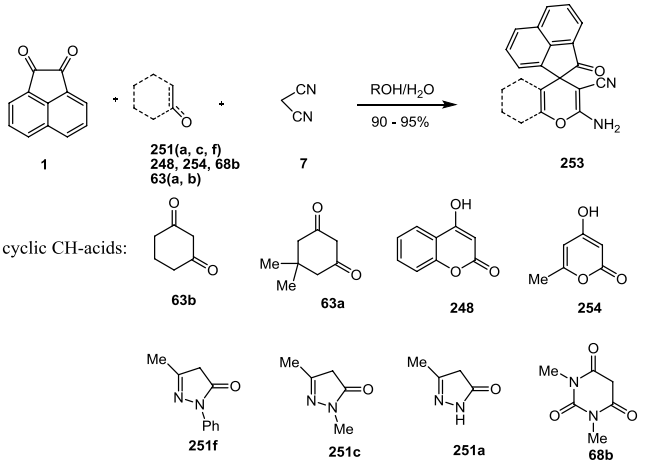


Scheme 105 Synthesis of spirochroman

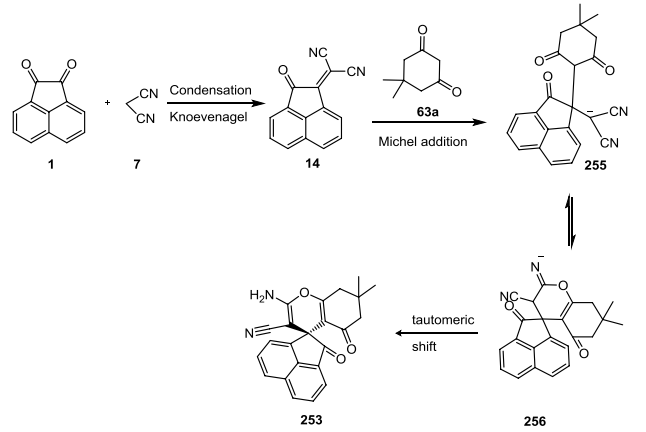


Scheme 106 One-pot synthesis of the spiroacenaphthylene derivatives

(*N*,*N*-dimethylaminoethyl) ammonium chloride as the basic ionic liquid an efficient and reusable catalyst for the synthesis of spiro acenaphthylenes **252** in water (Scheme 106) [111].



Scheme 107 Synthesis of spiro[acenaphthylene-1,4-pyrano [3,2-c]chromene]-3-carbonitrile

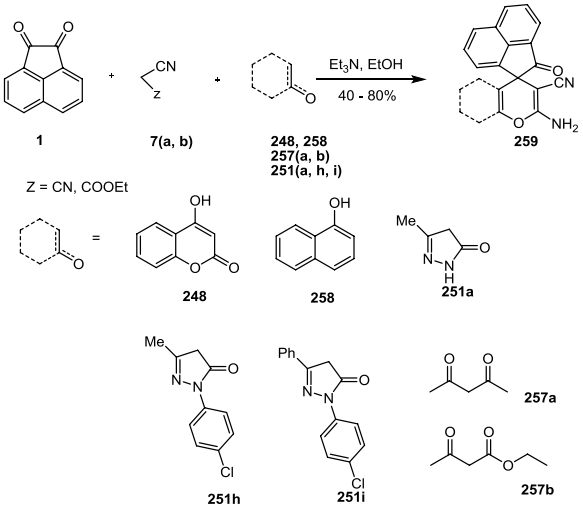


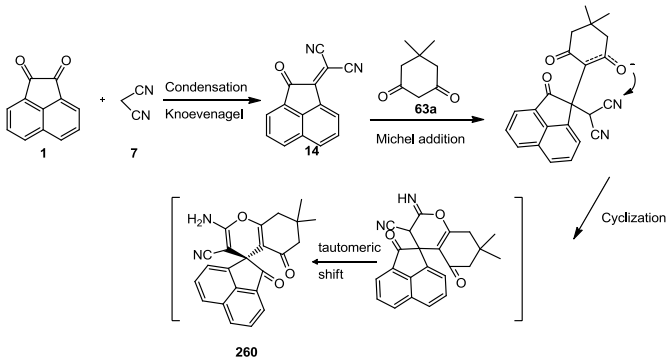
Scheme 108 Plausible mechanism for the synthesis of spiro acenaphthylene heterocycles

Elinson and coworkers condensed acenaphthoquinone **1** with a number of cyclic CH-acids in ROH/water at 80 °C with 90–95% yields. Then malononitrile **7** was added to form spiro acenaphthylene heterocycles **253**. Thus, a new simple and efficient green 'one-pot' method to synthesize substituted spiroacenaphthylene frameworks was found directly from simple starting compounds. The application of this convenient green multicomponent method is also beneficial from the viewpoint of diversity-oriented large-scale processes (Scheme 107) [112]. In the proposed mechanism for this reaction, the Michael addition of cyclic CH-acid **63a** to the Knoevenagel adduct **14** followed by intramolecular cyclization leads to the desired spiroacenaphthylene **253** (Scheme 108).

Heravi et al. have described the one-pot, three-component synthesis of the spiro acenaphthylene derivatives **259** via the reaction of acenaphthoquinone

Scheme 109 One-pot, three-component synthesis of the spiroacenaphthylene derivatives



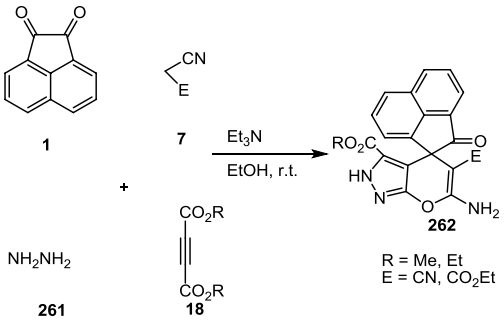


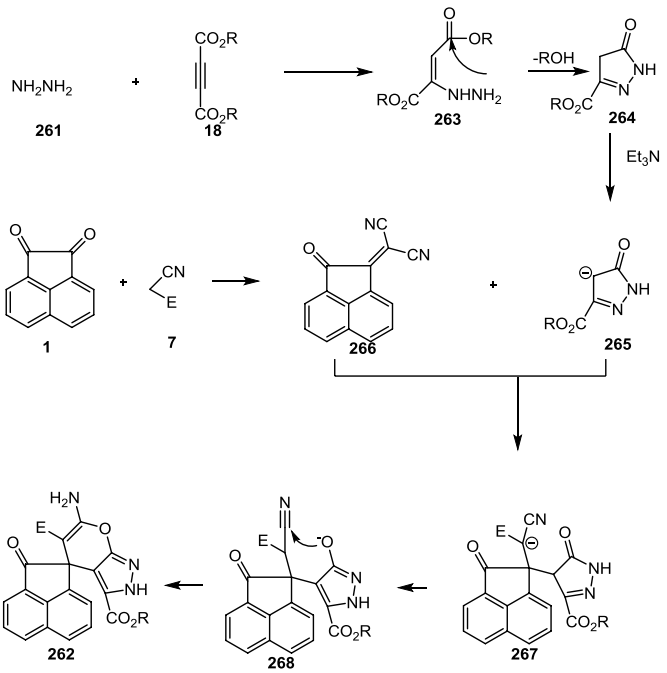
Scheme 110 Plausible mechanism for the synthesis of spiro acenaphthylene heterocycles

1, malononitrile/ethylcyanoacetate **7**, and various reagents including α-methylencarbonyl compounds/enols in EtOH and Et_3N as catalyst (Scheme 109) [113]. A plausible mechanism of the reaction is proposed in Scheme 110. Compound **1** undergoes Knoevenagel condensation with malononitrile/ethylcyanoacetate and leads to the formation **14**. Reactant **63a** with Michael addition to reagent **14** is followed by cycloaddition on to the nitrile. Finally, after tautomeric proton shift, the corresponding products **260** is formed (Scheme 110).

Spiro[acenaphthyl-3,4′-pyrano[2,3-*c*]pyrazole] derivatives **262** were prepared from the reaction of hydrated hydrazine **261**, dimethyl acetylenedicarboxylate **18**, acenaphthenequinone **1** and malononitrile or ethyl cycanoacetate **7** in ethanol in the presence of triethylamine with good yields (Scheme 111) [114]. A sequential reaction mechanism is proposed for this four-component reaction based on the previous reported synthetic reactions of Huisgen's 1,4-dipoles and the spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole]. Firstly, the addition of hydrazine to acetylenedicarboxylate

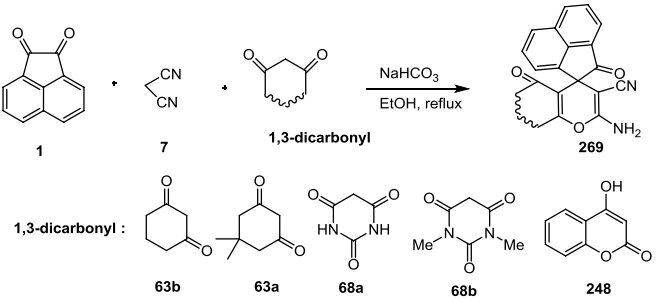
Scheme 111 Four-component reaction for synthesis of spiro[acenaphthyl-3,4′-pyrano[2,3-*c*]pyrazoles]



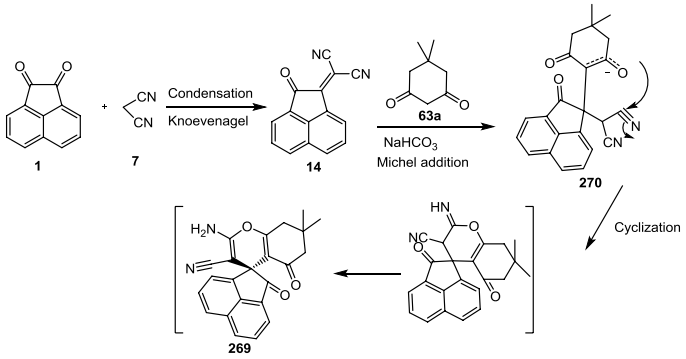


Scheme 112 Plausible mechanism for the synthesis of component **262**

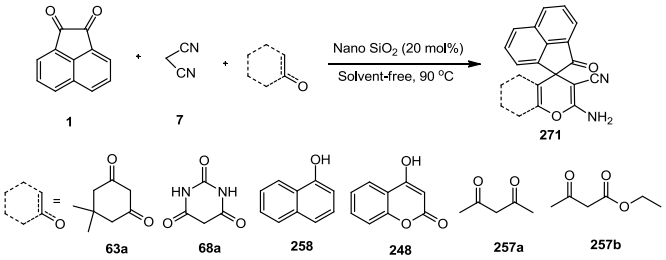
forms the 2-hydrazinyl substituted but-2-enedioate **263**. Secondly, the intramolecular hydrazinolysis of one ester affords a pyrazolone intermediate **264**, which in turn was deprotonated by triethylamine to transform a carbanium ion **265**. In the meantime, the triethylamine-catalyzed condensation of acenaphthoquinone with malononitrile produces the 2-(2-oxoacenaphthylen-1(2*H*)-ylidene)malononitrile **266**. Thirdly, a Michael addition of the carbanium ion **265** to component **266** gives the adduct **267**. Then, the adduct **267** transforms to a emulate **268** through the keto-enol tautomerization. Finally, the intramolecular addition of enolate to the cyano group results in the obtained spiro[acenaphthyl-3,4′-pyrano[2,3-*c*]pyrazole] derivatives **262** with an imine-enamine tautomerization (Scheme 112).



Scheme 113 Synthesis of spiro-pyran derivatives



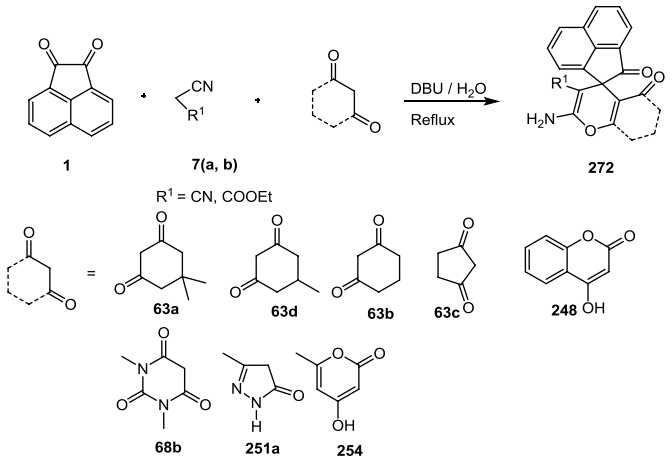
Scheme 114 Proposed mechanism for the synthesis of **269**



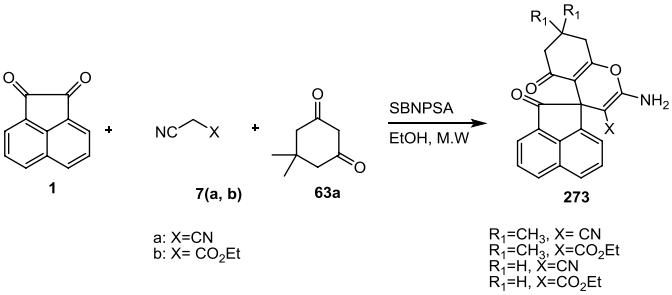
Scheme 115 Synthesis of spiroacenaphthylenes derivatives

A one-pot, three-component reaction has been reported for the synthesis of spiro-pyran derivatives **269** with acenaphthenequinone **1**, malononitrile **7**, and 1,3-dicarbonyl compounds such as cyclohexane-1,3-dione, dimedone, and barbituric acid in ethanol with $NaHCO_3$ as the catalyst. (Scheme 113) [115]. A proposed mechanism for the synthesis of component **269** is shown in Scheme 114.

A series of new spiro[4*H*-pyran] derivatives **271** were obtained by one-pot, three-component domino reaction of acenaphthoquinone **1**, malononitrile **7**, and different reagents including 1, 3-dicrbonyl compounds, β-naphthol and 4-hydroxycumarin the presence of nano SiO_2 at 90 °C temperature, solvent-free without any prior activation or modifications (Scheme 115) [116].



Scheme 116 Synthesis of spiroacenaphthylenes derivatives

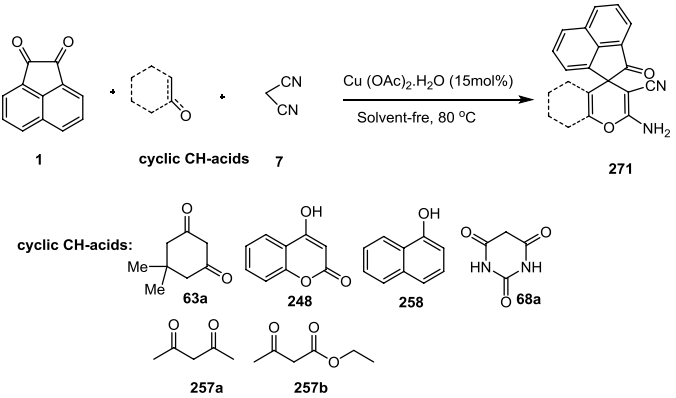


Scheme 117 Synthesis of spiropyran

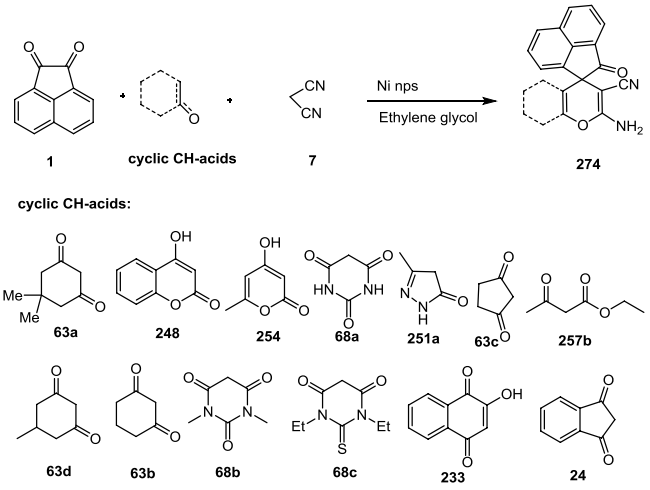
In 2013, Saluja's group developed an efficient synthesis of biologically and pharmacologically important spiropyrans derivatives **272** from condensation of malononitrile/ethyl cyanoacetate **7**, 1,3-dicarbonyl compounds, and acenaphthoquinone **1** in water using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as catalyst in good yields (Scheme 116) [117].

Refluxing of acenaphthoquinone **1**, an activated methylene reagent **7**, and 1,3-dicarbonyl compounds **63a** in the presence of catalytic silica bonded *N*-propyl sulfamic acid (SBNPSA) in ethanol under irradiation microwave conditions was found to be a suitable and efficient method for the synthesis of the biologically important spiropyran **273** (Scheme 117) [118].

The multicomponent efficient synthesis of biologically active spiro-4*H*-pyran derivatives **271** was successfully developed by the three-component reaction of acenaphthoquinone **1**, malononitrile **7**, and various reagents including



Scheme 118 Synthesis of biologically active spiro-4*H*-pyran derivatives

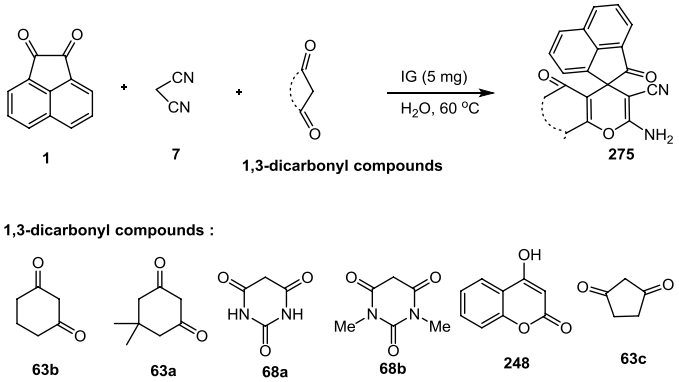


Scheme 119 Synthesis of biologically and pharmacologically important spiro-pyrans

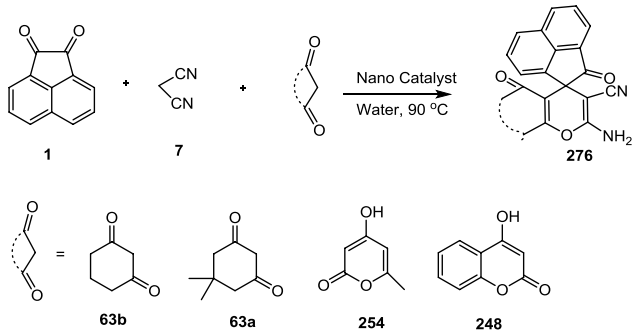
α-methylencarbonyl compounds/enols in the presence of a catalytic amount of copper(II) acetate monohydrate with good yields (Scheme 118) [119].

A convenient and efficient synthesis of biologically and pharmacologically important spiro-pyrans **274** from the condensation of malononitrile **7**, 1,3-dicarbonyl compounds, and acenaphthoquinone **1** has been reported using recyclable heterogeneous polyethylene glycol (PEG)-stabilized Ni nanoparticles in ethylene glycol (Scheme 119) [120].

Reaction of acenaphthenequinone **1**, activated methylene reagent **7**, and 1,3-dicarbonyl compounds in the presence of Isinglass (IG) as a biopolymer has



Scheme 120 Synthesis of spiroacenaphthylenes



Scheme 121 Synthesis of spiro acenaphthylene derivatives

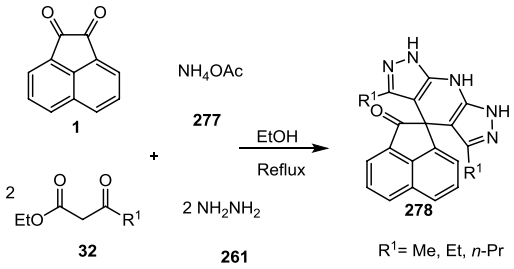
considerable catalytic efficiency for the synthesis of biologically important functionalized spiroacenaphthylenes **275** in water (Scheme 120) [121].

Shirini et al. have described the one-pot, three-component synthesis of the spiro acenaphthylene derivatives **276** via the reaction of acenaphthoquinone **1**, malononitrile **7**, and various reagents including α-methylencarbonyl compounds/enols in water and using $C_4(DABCO\text{-}SO_3H)_2{\cdot}4Cl$ as a nano, efficient, cheap, and reusable catalyst under mild and homogeneous conditions. (Scheme 121) [122].

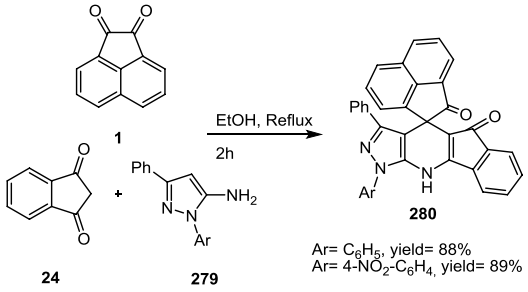
44 Synthesis of Spiro-tetrahydropyrazolopyridine Derivatives

Dabiri et al. conducted a catalyst-free, one-pot, $2A+2B+C+D$ four-component process employing 1,3-dicarbonyl compound **32**, an acenaphthoquinone **1**, hydrazine **261** and ammonium acetate **277** in ethanol as a green media for the synthesis of some tetrahydropyrazolopyridine derivatives **278** (Scheme 122) [123].

Scheme 122 Synthesis of tetrahydropyrazolopyridine derivatives



Scheme 123 Synthesis of spiro[acenaphthylene-1,4′-indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine]-dione



45 Synthesis of Spiroacenaphthyleneindeno-pyrazolo-pyridine]dione

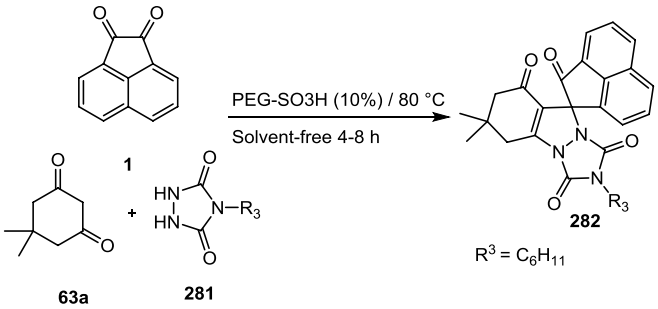
In 2011, Bazgir et al. reported the synthesis of spiro[acenaphthylene-indeno[1,2-*b*] pyrazolo[4,3-*e*]pyridine]diones **280** by the three-component reaction of 1,3-indandione **24**, pyrazol-5-amines **279** and acenaphthylene-1,2-dione **1** in ethanol at reflux (Scheme 123) [124].

46 Synthesis of Triazolo[1,2-*a*]indazole-trione Derivatives

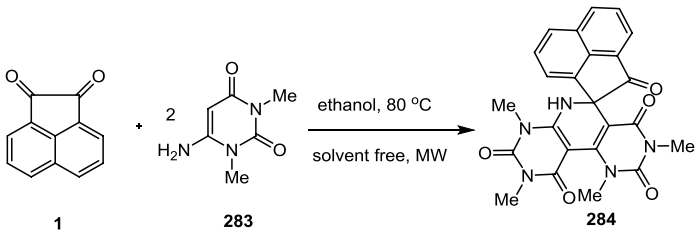
Hasaninejad et al. discovered the synthesis of triazolo[1,2-*a*]indazole-triones **282** by the condensation reaction between dimedone **63a**, acenaphthoquinone **1**, and ueazoles **281** in the presence of a catalytic amount of sulfonated polyethylene glycol (PEG-SO_3H) under solvent-free conditions at 80 °C. That as a highly stable and reusable eco-friendly degradable polymeric catalyst is described (Scheme 124) [125].

47 Synthesis of Spiro Pyridodipyrimidines

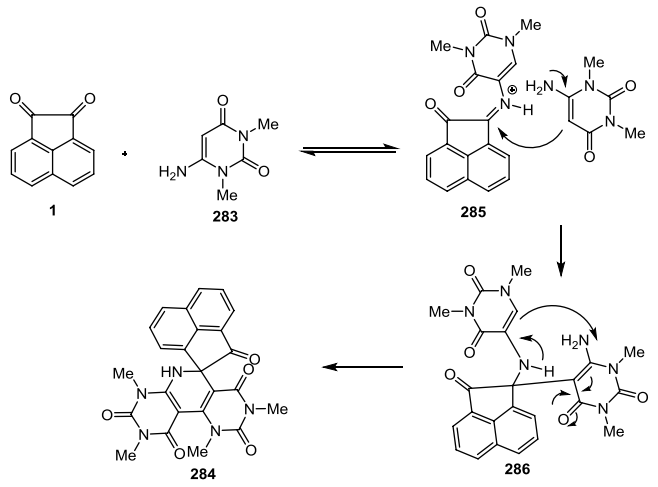
In 2008, Mohammadizadeh et al. reported that spiro pyridodipyrimidines **284** could react with acenaphthoquinone **1**, 1,3-dimethyl-6-aminouracil **283** under classical or microwave-assisted solvent-free conditions in good yields (Scheme 125) [126]. Mechanistic representation for synthesis of spiro pyridodipyrimidines **284** was shown in Scheme 126.



Scheme 124 Synthesis of triazolo[1,2-a]indazole-triones



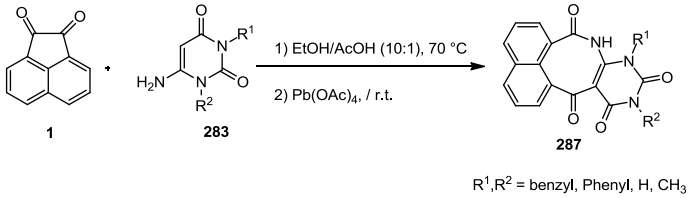
Scheme 125 Synthesis of spiro pyridodipyrimidines



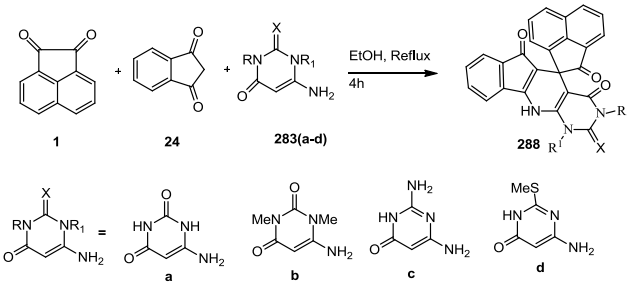
Scheme 126 Mechanistic representation for synthesis of spiro pyridodipyrimidines

48 Synthesis of Pyrimido-azocine Derivatives

In 2014, Mohammadizadeh et al. reported the synthesis of new naphtho[1,8-*ef*] pyrimido[4,5-*b*]azocine-7,10,12,13(8*H*,9*H*,11*H*)-tetraones **287** by the addition reaction of acenaphthoquinone **1** and 6-aminouracil derivatives **283** in the presence of



Scheme 127 Synthesis of azocine derivatives



Scheme 128 Synthesis of spiroacenaphthylene-1,4′-indeno-1,5′-pyrido[2,3-d]pyrimidines

lead(IV) acetate at room temperature/in EtOH at room temperature (Scheme 127) [127].

49 Synthesis of Spiro-indeno-pyrido-pyrimidines

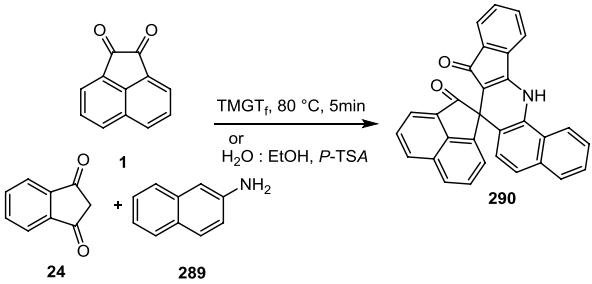
Bazgir et al. described the synthesis of spiroacenaphthylene-1,4′-indeno-1,5′-pyrido[2,3-*d*]pyrimidines **288** under reflux in ethanol and catalyst-free by the three-component reaction of acenaphthylene-1,2-dione **1**, 1,3-indandione **24**, amino uracils **283(a–d)** (Scheme 128) [128].

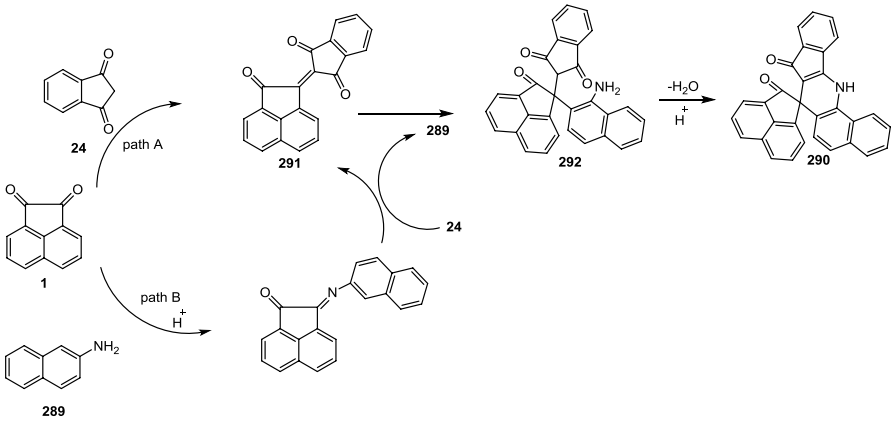
50 Synthesis of Spiro-indeno-benzoquinoline

Rad-Moghadam's researcher group established a novel synthesis of spiro[1*H*-indeno[1,2-*b*]benzo[*f*]quinolin-13,1′(20*H*)- acenaphthylene]-7,13-dihydro-12,2′-dione **290** expediently through three-component reactions between 2*H*-indene-1,3-dione **24**, 2-naphthalenamine **289** and acenaphthylene-1,2-dione **1** under catalysis of the ionic liquid *N,N,N,N*- tetramethylguanidinium triflate/H_2O–EtOH (5:1), *p*-TSA, 60 °C (Scheme 129) [129, 130].

The first step may involve a Knoevenagel condensation between the 2*H*-indene-1,3-dione **24** and acenaphthoquinone **1** for the formation of the stable intermediate **291**, which Michael addition of naphthalen-2-amine **289** followed by cyclocondensation

Scheme 129 Synthesis of spiro[1*H*-indeno[1,2-*b*]benzo[f]quinolin-13,1′(2′*H*)-acenaphthylene]-7,13-dihydro-12,2′-dione





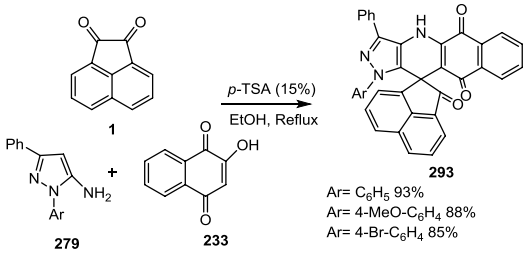
Scheme 130 Proposed mechanism for the formation of compound **290**

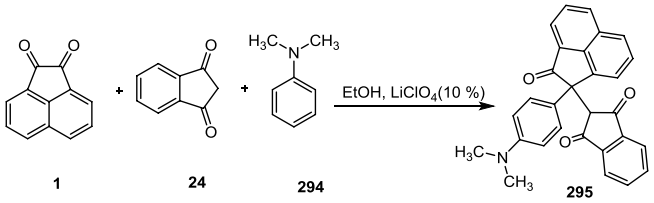
of the resultant adducts **292** give the corresponding products **290** (pathway A). Alternatively, the key intermediates **291** may be produced by condensation of 2*H*-indene-1,3-dione **24** with the preformed imine derived from the reaction between acenaphthoquinone **1** and naphthalen-2-amine **289** (pathway B) (Scheme 130).

51 Synthesis of Spiro-benzo-pyrazoloquinoline

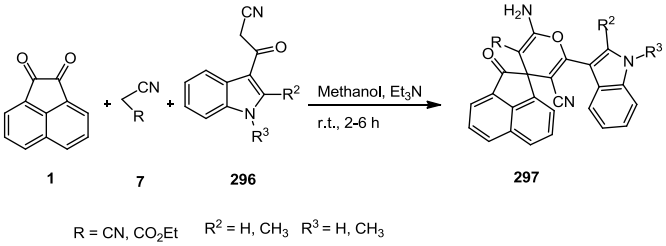
In 2012, Bazgir et al. developed a convenient synthesis of spiro[acenaphthylene-1(2*H*),11′-[11*H*]-benzo[*g*]pyrazolo[4,3-*b*]quinoline]-2,5′,1″-triones **293** by a three-component condensation reaction of 2-hydroxy-1,4-naphthoquinone **233**, pyrazol-5-amines **279**, and acenaphthylene-1,2-dione **1** in the presence of *p*-TSA as an inexpensive and available catalyst in refluxing ethanol (Scheme 131) [131].

Scheme 131 Synthesis of spiro [acenaphthylenebenzopyrazolo quinoline]triones





Scheme 132 Synthesis of 2-oxo-1,2-dihydroacenaphthylen-1-yl)-1*H* indene-dione



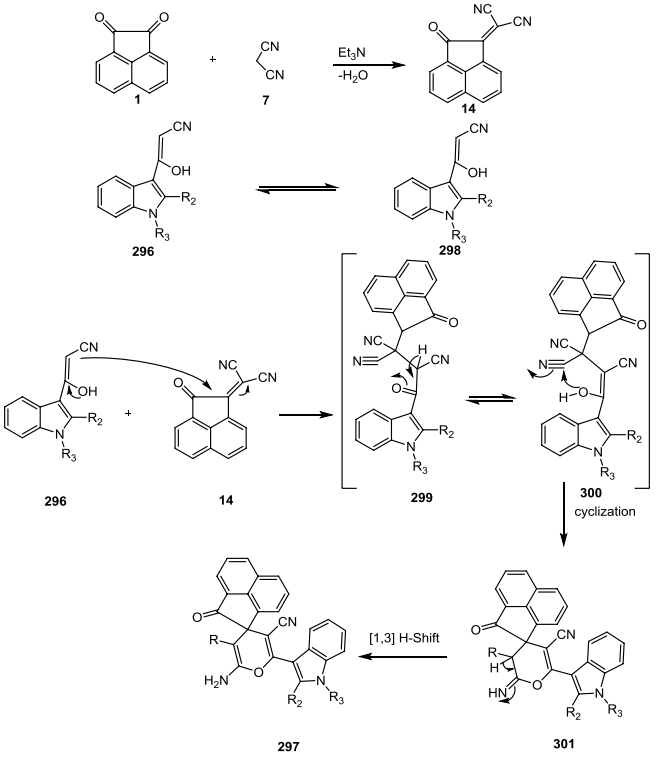
Scheme 133 Synthesis of spiroxindole derivatives from acenapthenequinone precursor

52 Synthesis of Dihydroacenaphthylen-indene-dione

Bazgir et al. described the synthesis of 2-(1-(4-(dimethylamino)phenyl)-2-oxo-1,2-dihydroacenaphthylen-1-yl)-1*H*-indene-1,3(2*H*)-dione **295** as new unsymmetrical oxindoles via a Friedel–Crafts-type three-component reaction of acenaphthoquinone **1**, 1,3-indandion **24**, *N,N*-dimethylaniline **294** in ethanol in the presence of $LiClO_4$ (Scheme 132) [132].

53 Synthesis of Spiroxindole

Nandakumar's group has accomplished a concise and efficient route for the synthesis of highly substituted spiroxindole derivatives from acenaphthenequinone precursor **297** by a reaction mixture of acenaphthoquinone **1**, malononitrile **7**, and 3-cyanoacetyl indole **296** and triethyl amine (20 mol%) in methanol under ambient temperature (Scheme 133) [133].

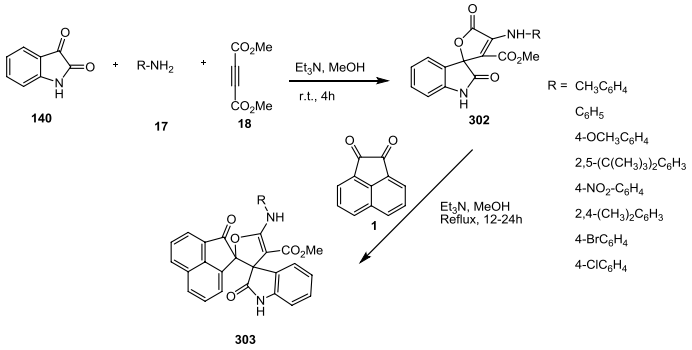


Scheme 134 Proposed mechanism for the synthesis of **297**

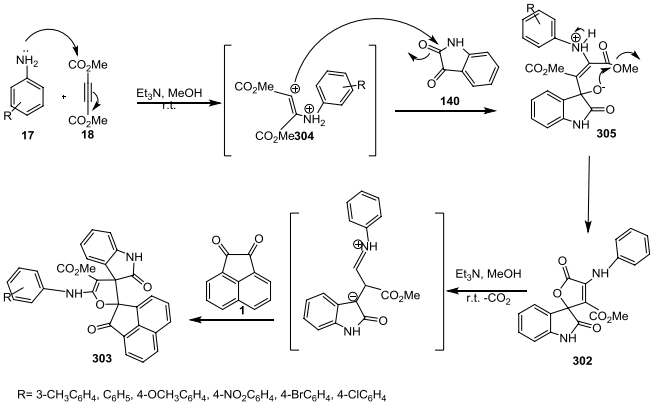
A plausible mechanism is propose. At beginning, acenaphthoquinone **1** reacts with malononitrile **301** to give a 2-(2-oxoacenaphthylen-1(2*H*)-ylidene)malononitrile adduct **14** and 3-cyanoacetyl indole **296** in the presence of base (Et_3N) enolise to give **298**; **298** further reacts with **14** to give intermediates **299** and **300**. The intermediate further rearranges via proton transfer to give **301**. Finally, the intermediate **301** affords to yield a spiroxindole derivative from acenaphthenequinone precursor **297** via proton transfer (Scheme 134).

54 Synthesis of Dispiro Dihydrofuranyl Acenaphthyl Oxindole Derivatives

Perumal's group developed an efficient synthesis of dispiro dihydrofuranyl acenaphthyl oxindole derivatives **303** via reaction between spirolactones **302** and acenaphthoquinone **1** catalyzed by Et_3N (triethylamine) in reflux MeOH. Also, spirolactones **302** from isatin **140**, primary amines **17**, and DMAD **18** through Huisgen dipolar additions are discussed (Scheme 135) [134]. A plausible mechanism of the reaction is proposed in Scheme 67. Initially, *m*-toluidine **17** adds on to DMAD **18** to provide the zwitterionic intermediate **304**, which adds on to isatin **140** to form **305** and then undergoes



Scheme 135 Synthesis of dispirodihydrofuranyl oxindoles

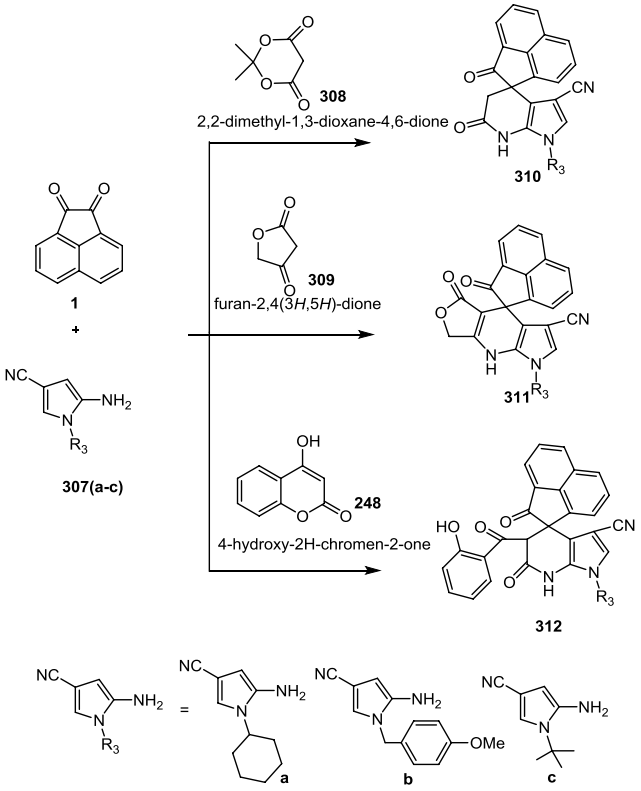


Scheme 136 Plausible mechanism for the formation of **228**

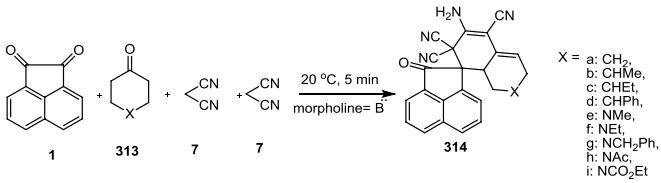
intramolecular addition with MeOH elimination to give the spiro lactone **302**, then adds on to acenaphthoquinone **1** to form **303**) Scheme 136).

55 Synthesis of Spiro-pyrrolo-pyridine Derivatives

As shown in Scheme 137, Langer's research group in 2013 established a three-component reaction of acenaphthoquinone **1**, *N*-substituted 5-amino-3-cyanopyrroles **307** and active methylene compounds **308**, **309**, and **248** under mild conditions using ethanol, acetic acid, or 1,4-dioxane as solvent for the synthesis of 4,7-dihydro-spiro1*H*-pyrrolo[2,3-*b*]pyridines **312** (Scheme 137) [135].



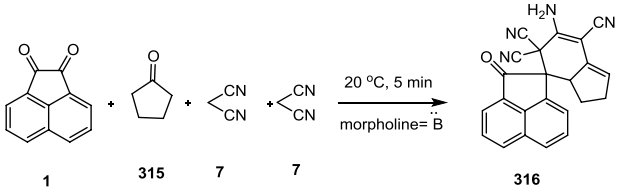
Scheme 137 Synthesis of 4,7-dihydro-1*H*-pyrrolo[2,3-*b*]pyridines



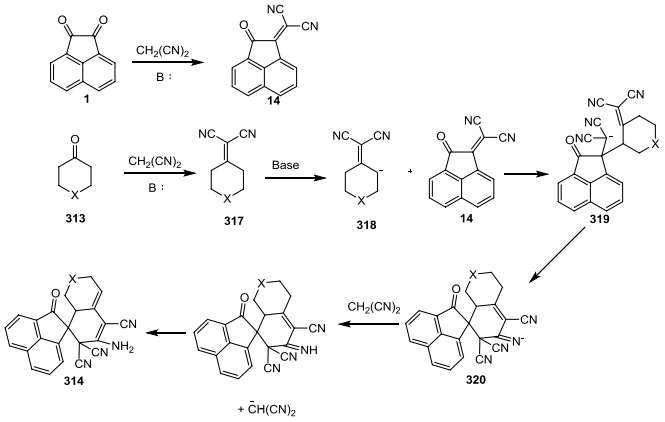
Scheme 138 Synthesis of spiroacenaphthylene derivatives

56 Sythesis of Spiro Acenaphthylene

Elinson and coworkers discovered that cyclic ketones **313**, **315**, and two molecules of malononitrile reacted to acenaphthylene-1,2-dione **1** to afford spiro acenaphthylene pentacyclic and pentaheterocyclic **314**, **316** in 70–95% yields (Schemes 138, 139) [136].



Scheme 139 Synthesis of spiroacenaphthylene pentacyclic systems



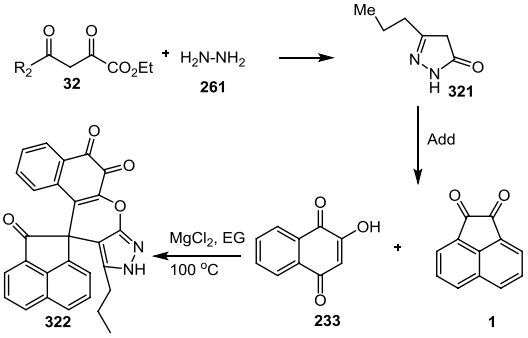
Scheme 140 Proposed mechanism for the synthesis of **233**

The first step may involve a Knoevenagel condensation between the malononitrile and acenaphthenequinone **1** for the formation of the Knoevenagel adduct **14** in base condition. A similar Knoevenagel condensation of cyclohexanone and malononitrile anion lead to Knoevenagel adduct **317**. Under basic conditions, Knoevenagel adduct **317** forms anion **318**, which adds to the activated double bond of Knoevenagel adduct **14** with further cyclization into anion **320**. Finally, after tautomeric proton shift, compound spiroacenaphthylene **314** is formed (Scheme 140).

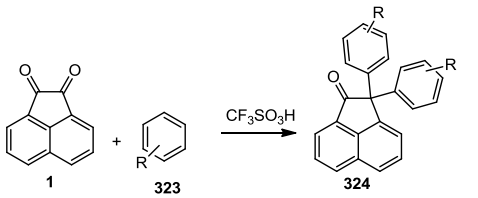
57 Synthesis of Spiroacenaphthylene Pyrazolo-chromene

Refluxing of hydrazine derivatives **261** with ethyl acetoacetate **32** by $MgCl_2$ in ethylene glycol afforded pyrazolinone derivative **321**. Treatment of **321** with 2-hydroxy-1,4-naphthoquinone **233** and acenaphthoquinone **1** in ethylene glycol in the presence of $MgCl_2$ gave spiro acenaphthylene **322** (Scheme 141) [137].

Scheme 141 Synthesis of spiroacenaphthylene catalyzed by $MgCl_2$ in EG



Scheme 142 Synthesis of 2,2-diphenylacenaphthylen-1(2*H*)-one

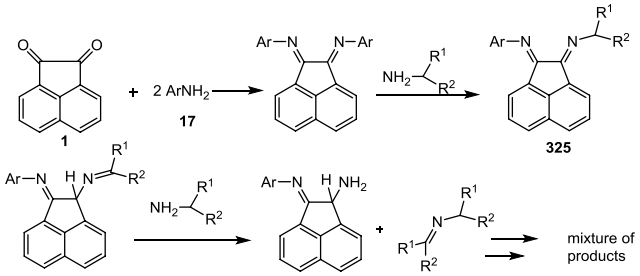


58 Synthesis of 2,2-Diphenylacenaphthylen-1(2*H*)-one

In 2008, Klumpp et al. described the synthesis of 2,2-diphenylacenaphthylen-1(2*H*)-one **324**. These compounds were obtained via the two-component reactions of acenaphthenequinone **1** with a series of arenes **323** in benzene using CF_3SO_3H (triflic acid) as catalyst in good yields 58–99% with high regioselectivity (Scheme 142) [138].

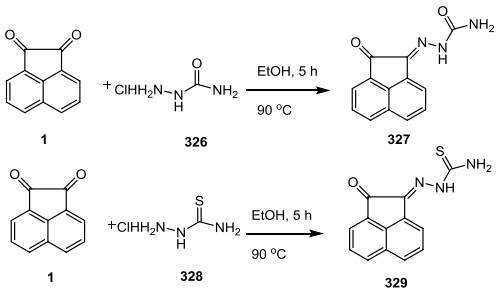
59 Synthesis of Acenaphthenequinonediimine Derivative

Ragaini et al. have reported the reaction of acenaphthoquinone **1** with amines **17** in methanol, at 60 °C, which gave alkyl-BIAN = bis(alkyl) acenaphthenequinonediimine derivative **325**. Ragaini et al. have investigated the reason for earlier failures and identified it as an isomerization of the initially formed CQN double bond. This isomerization is driven by a release of ring strain in the five-membered ring of the acenaphthene moiety. The use of amines in which the $–NH_2$ group is bound to a quaternary carbon atom cannot be employed to avoid the isomerization because these amines are too sterically encumbered to react at all. However, the use of amines in which the amino group is bound to a strained ring solves the problem, because the isomerization would cause an even larger strain than the one that is released. Cyclopropylamine (Cypr-NH_2) is the ideal amine, with no isomerization being observed at all. The best synthetic procedure involves a *trans* imination reaction from a [$ZnCl_2$(Ar-BIAN)] complex, where Ar contains electron-withdrawing groups, but



Scheme 143 Synthesis of bis(alkyl)acenaphthenequinonediimine derivative

Scheme 144 Synthesis of oxoacenaphthylen-2(1*H*)-ylidene)semicarbazide/isothiourea



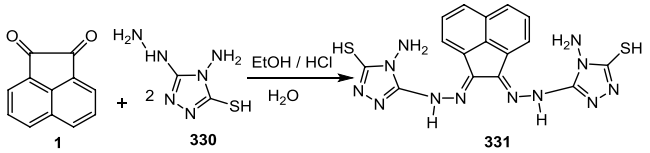
the direct synthesis from acenaphthenequinone and the amine is also possible in the case of Cypr-BIAN. (Scheme 143) [139].

60 Synthesis of Oxoacenaphthylen-ylidene Semicarbazide/Ylidene Amino-isothiourea

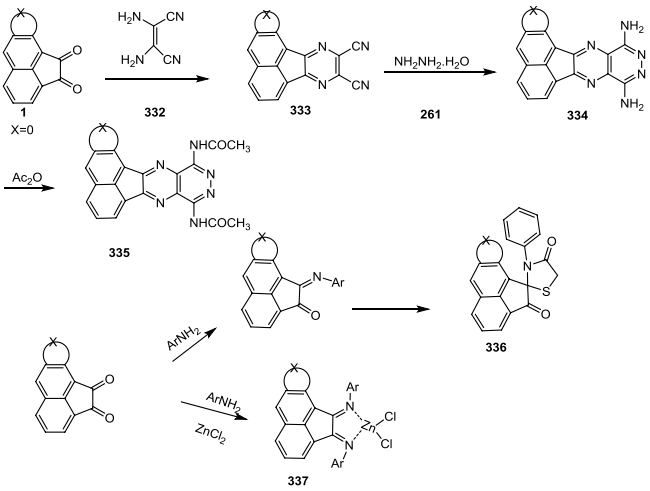
Novel (Z)-1-(1-oxoacenaphthylen-2(1H)-ylidene)semicarbazide **327** and 1-(1-oxoacenaphthylen-2(1*H*)-ylidene amino)isothiourea **329** were synthesized via a two-component reaction of acenaphthoquinone **1** with hydrazinecarboxamide hydrochloride **326**/hydrazinecarbothioamide hydrochloride **328** in EtOH at 90 °C for 5 h (Scheme 144) [140].

61 Synthesis of Diamine Acenaphtohydrazinomercaptotriazole

A diamine acenaphtohydrazinomercaptotriazole (AHTD) **331** was synthesized in one step from acenaphthoquinone **1** and 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole **330** in EtOH and in the presence of concentrated HCl (Scheme 145) [141].



Scheme 145 Synthesis of acenaphtohydrazinomercaptotriazole



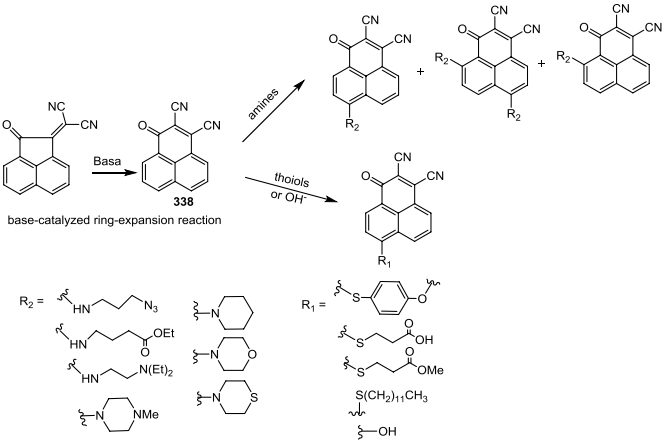
Scheme 146 Reaction of acenaphthenequinone with various reagents

62 Synthesis of Spiro-aceanthrene-thiazolidine-dione Derivatives

Reaction of acenaphthenequinone **1** with diaminomaleonitrile **332** at reflux temperature gave acenaphtho[1,2-*b*]pyrazine-8,9-dicarbonitrile **333**. The reaction of **333** with hydrazine hydrate **261** afforded the corresponding cyclic products, 8,11-diaminoacenatho[1,2-*b*]pyrazino[2,3-*d*]pyridazine **334**. The reaction of **1** with *p*-bromoaniline in presence of $ZnCl_2$ afforded complexes bis(*p*-bromophenylimino)acenaphthene **337**. Amer et al. have also described the synthesis of spiro[2*H*-aceanthrene-2,2′-thiazolidine]-1,4′-dione derivatives **336** (Scheme 146) [142].

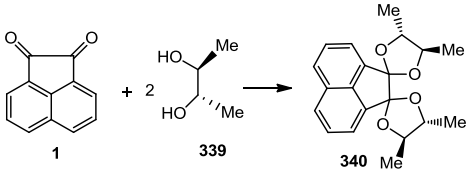
63 S_NAr^H Reactions

Li et al. have revisited the synthesis of a series of ICT fluorophores, which were reported to have a core structure of 8-oxo-8*H*-acenaphtho[1,2-*b*]pyrrol-9-carbonitrile. Their core structure was corrected as 1-oxo-1*H*-phenalene-2,3-dicarbonitrile **338**. The oxidative S_NAr^H reaction of **338** with mercaptopropionic acid was very slow and less efficient. After refluxing in CH_3CN for 2 days, only a small fraction of **338** was converted to the product as a single regioisomer. Due to the strong electron-withdrawing groups on **338**, its naphthalene ring shows a highly electron-deficient



Scheme 147 S_NAr^H reactions of 1 with different nucleophiles

Scheme 148 Synthesis of bis-ketal



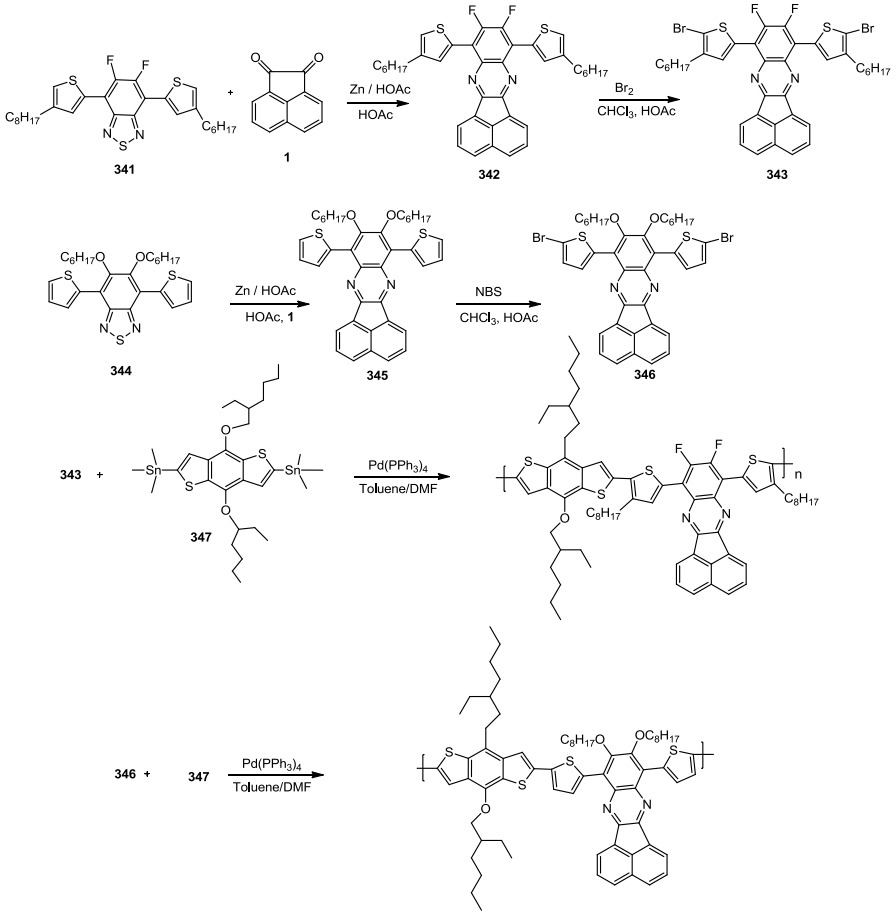
nature and oxidative S_NAr^H reactions can precede smoothly under very mild conditions. Several nucleophiles, such as thiols, hydroxide, and amines, were used for the structural modification of **338** (Scheme 147) [143].

64 Synthesis of Bis-1,4-dioxane

Reaction of acenaphthoquinone **1** with butane-2,3-diol **339** led to formation bis-1,4-dioxane (bis-ketal) **340** (Scheme 148) [144].

65 Synthesis of Acenaphtho[1,2-*b*]quinoxaline-Based Low-Band-Gap Polymer

Reaction of **341** with acenaphthoquinone **1** in acetic acid afforded compound **342** and reaction with Br_2 in $CHCl_3$ was developed acenaphtho[1,2-*b*]-quinoxaline **343**. Compound **344** reacted with acenaphthoquinone **1** as a 1,2-dicarbonyl in the presence zinc dust and acetic acid to afford compound **345** and reaction with NBS in $CHCl_3$ was developed acenaphtho[1,2-*b*]-quinoxaline **346**. Bis(trimethyltin) BDT monomer **347** and **343** or **346** were mixed in toluene and DMF. After being purged with nitrogen, $Pd(PPh_3)_4$ to be synthesized corresponding products (Scheme 149) [145].

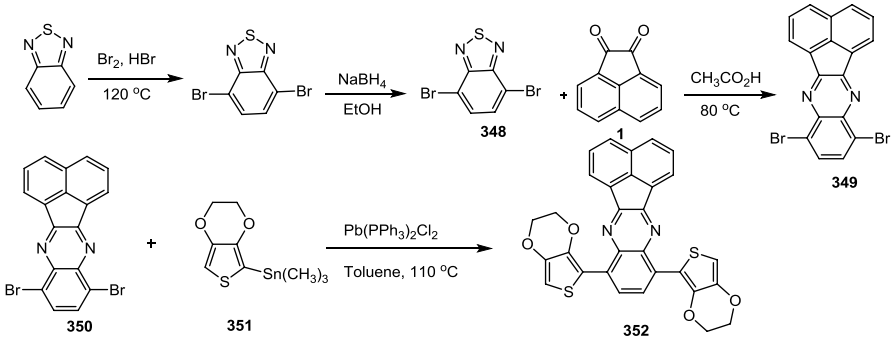


Scheme 149 Synthesis of acenaphtho[1,2-*b*]-quinoxaline and polycondensation reaction

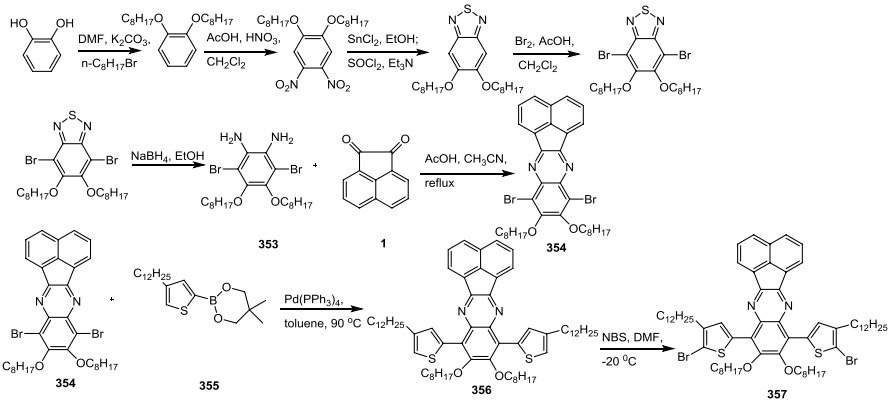
66 Synthesis of Bis-acenaphtho[1,2-*b*]quinoxaline

An efficient synthesis of 8,11-dibromoacenaphtho[1,2-*b*]quinoxaline **349** has been developed with the reaction of acenaphthoquinone **1** and 4,7-dibromobenzo[*c*][1,2,5]thiadiazole **348.** The reaction of **352** with (2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)trimethylstannane **350** led to formation 8,11-bis(2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)acenaphtho[1,2-*b*]quinoxaline **351** (Scheme 150) [146].

The synthesis of 3,6-dibromo-4,5-bis(octyloxy)benzene-1,2-diamine **353** with 4,7-dibromo-5,6-bis(octyloxy)benzo[*c*][1,2,5]thiadiazole and $NaBH_4$ in EtOH has been reported. Reaction of 4,7-dibromo-5,6-bis(octyloxy)benzo[*c*][1,2,5]thiadiazole with acenaphthoquinone **1** in the presence of catalyst AcOH in reflux CH_3CN to afford synthesis of 8,11-dibromo-9,10 bis(octyloxy)acenaphtho[1,2-*b*]quinoxaline **354.** Reaction of **354** with 2-(4-dodecylthiophen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane **355** in the presence of $Pd(PPh_3)_4$ in toluene at 90 °C for synthesis



Scheme 150 Synthesis of 8,11-bis(2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)acenaphtho[1,2-*b*]quinoxaline

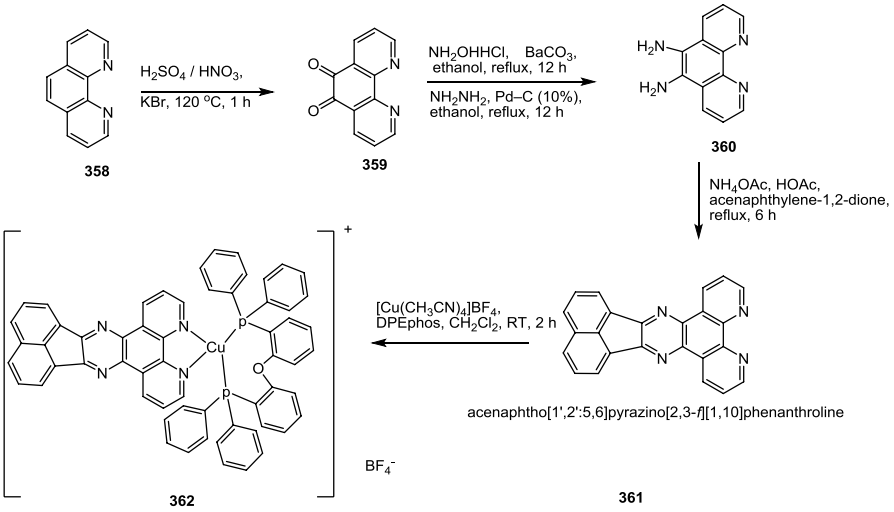


Scheme 151 Synthesis of 8,11-bis(5-bromo-4-dodecylthiophen-2-yl)-9,10-dioctyloxyacenaphtho[1,2-*b*]quinoxaline

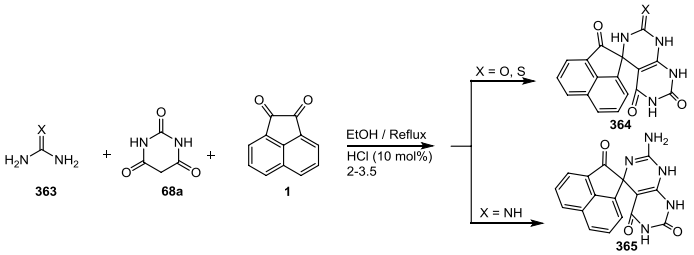
of 8,11-bis(4-dodecylthiophen-2-yl)-9,10-bis(octyloxy)acenaphtho[1,2-*b*]quinoxaline **356**. A solution of *N*-bromosuccimide (NBS) in DMF was added to **356** for synthesis of 8,11-bis(5-bromo-4-dodecylthiophen-2-yl)-9,10-bis(octyloxy) acenaphtho[1,2-*b*]quinoxaline **357** (Scheme 151) [147].

67 Diimine Cu(I) Complex with Acenaphthoquinone

A novel diimine Cu(I) complex [Cu(ABPQ)(DPEphos)]BF_4 [ABPQ and DPEphos are acenaphtho[1,2-*b*]bipyrido[2,3-h;3,2-*f*]quinoxaline and bis(2-(diphenylphosphanyl)phenyl) ether, respectively] is synthesized with acenaphtho[1′,2′:5,6]pyrazino[2,3-*f*][1,10]phenanthroline in the presence of [Cu(CH_3CN)$_4$]BF_4 and DPEphos in CH_2Cl_2 at room temperature for 2 h (Scheme 152) [148].



Scheme 152 Synthesis of diimine Cu(I) complex [Cu(ABPQ)(DPEphos)]BF_4



Scheme 153 Synthesis of spiro[quinazoline/pyrimidine]ones

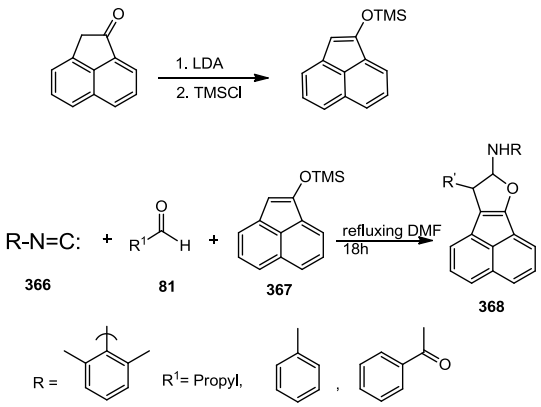
68 Synthesis of Spiro-quinazoline/Pyrimidine Derivatives

Synthesis of novel the biologically important spiro[quinazoline/pyrimidine]ones **364**, **365** was described using HCl (10 mol%) in a one-pot, three-component condensation of barbituric acid **68a**, acenaphthoquinone **1**, and urea or thiourea **363** in refluxing EtOH (Scheme 153) [149].

69 Synthesis of 9-(Alkyl or aryl)acenaphtho[1,2-*b*]furan-8-(alky or aryl)amine Compounds

In 2012, Sandaroos and coworkers described the synthesis of 9-(alkyl or aryl) acenaphtho[1,2-*b*]furan-8-(alky or aryl)amine compounds **368** by one-pot reaction of (acenaphthylen-1-yloxy)trimethylsilane **367**, alkyl and aryl aldehydes **81**, and aryl and alky isocyanides **366** in refluxing DMF (Scheme 154) [150].

Scheme 154 Synthesis of 9-(alkyl or aryl)acenaphtho[1,2-*b*]furan-8-(alky or aryl)amine compounds



70 Conclusions

This review has summarized the use of acenaphthoquinone in the synthesis of heterocyclic compounds with respect to the number of atoms in heterocyclic rings, taking into consideration the heteroatom. We have shown that acenaphthoquinone is a very versatile substrate, as it can be used for the synthesis of a large variety of heterocyclic compounds. Acenaphthoquinone has been developed in the synthesis of spiro[4*H*-pyran] derivatives, spiro acenaphthylenes, dispiro oxindolopyrrolidines/pyrrolizidines, spiro[indoline-3,2′-quinazoline, dispirodihydrofuranyl oxindoles, spiro1*H*-pyrrolo[2,3-*b*]pyridines, spiro dihydropyridines, spiro[isoindoline-1,2′-quinazoline and etc. Many synthetic compounds also exhibit potential antimicrobial activities. There is a wide range of multicomponent reactions that include acenaphthoquinone in the synthesis of various organic compounds. This review purpose to show deputation examples of these multicomponent reactions in recent years. We can still expect many further developments of this compound in synthetic chemistry.

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