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REVIEW OF SYNTHESIS AND APPLICATIONS OF HETEROCYCLIC COMPOUNDS FROM 3-AMINO-2-CYCLOHEXENONE

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Abstract

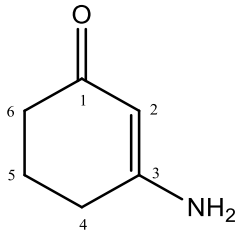
3-amino-2-cyclohexenone is an important intermediate to synthesize biologically important organic compounds such as dopamine autoreceptor agonists, antagonists of oxytocin and inhibitors of acetylcholinesterase. 3-amino-2-cyclohexenone is also used for the synthesis of heterocyclic compounds like pyridines, quinolines, acridines and indole derivatives. It facilitates cycloaddition reactions and provides a straightforward route to optically active compounds, which then can be converted to the alkaloid pumiliotoxin C. It can be used as UV filter, as well. We'll go into all of the essential 3-amino-2-cyclohexenone reactions and applications in this article.

Key words: 3-amino-2-cyclohexenone, β-enaminone, heterocyclic compounds synthesis, Carbolines, Acradines

1. Introduction

In organic synthesis, 3-aminocyclohex-2-en-1-one is a valuable intermediate (such as dopamine autoreceptor agonists) which is an enaminone with a cyclic structure [1], inhibitors of acetylcholinesterase [2], antagonists of oxytocin [3], KATP channel openers [4] and anticonvulsant drugs [5] and heterocyclic compounds of functional significance (such as quinolines or pyridines) [6-12], sesquiterpenes [13], azaazulenes [14], angucycilinone 5-aza-analogue and tetrahydro-1,3-oxazines [15]. The molecular formula is C_6H_9NO and the molecular weight is 111.14. Solid is the physical state. The Respiratory system is one of its target organs. It irritates the body chemically [11]. This chemical has the potential to irritate the skin and other mucous membranes. It irritates the eyes, skin, and respiratory system. If you come into contact with your pupils, rinse them thoroughly with water and seek medical attention right away.

This compound's structural formula is:



1.1 Computed Properties

Table 1: computational properties

Calculated Characteristics	Property Value	Reference
Hydrogen bond donor count	1	Computed by Cactvs 3.4.6.11 (PubChem release 2019.06.18)

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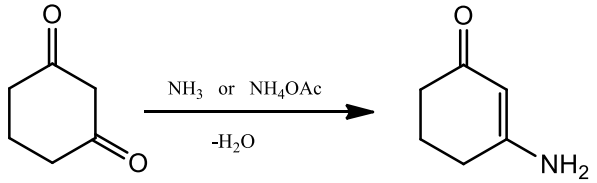
Molecular Wt.	111.14	Computed by PubChem 2.1 (PubChem release 2019.06.18)
Rotatable Bond Count	0	Computed by Cactvs 3.4.6.11 (PubChem release 2019.06.18)
Count of Hydrogen Bond Acceptors	2	Computed by Cactvs 3.4.6.11 (PubChem release 2019.06.18)
Heavy Atom Count	8	Computed by PubChem
Monoisotopic Mass	111.068414 g/mol	Computed by PubChem 2.1 (PubChem release 2019.06.18)
Formal Charge	0	Computed by PubChem

2. Chemistry of 3-amino-2-cyclohexenone

1, 3-binucleophiles are enamines that are unsubstituted at the nitrogen atom and are widely used in heterocyclic compound production. One method is to use cyclic enamines as a point of departure for the synthesis of condensed heterocycles in reactions with biselectrophiles. Condensing moderately priced 1, 3-cyclohexandione (2) with ammonium acetate or ammonia with azeotropic water removal under refluxing conditions using poisonous solvents like benzene yields the readily available 3-aminocyclohex-2-enone(1) [6, 16-22]. This is a good starting substrate for making heterocyclic compounds with different numbers of rings, heterocycle sizes, heteroatom numbers, and reciprocal arrangements.

Equation 1: The synthesis of 3-amino -2-cyclohexenone



2 1

N and C_2 atoms act as nucleophilic centres in an enamino ketone compound (1). The nucleophilicity of the carbon atoms has improved, according to published evidence. Despite the fact that the products of the initial reaction are rarely isolated, the carbon atom is attacked first at the most electrophilic core of the reagent in most biselectrophile reactions. Zymalkowski and Rimek first described compound (1) 5, 5-dimethyl derivative in 1961 whose chemistry is similar to that of compound (1), but its properties have never been systematically classified. The current study is the first to bring together previously published information on the application of enaminone (1) as a C, N-bisnucleophilic component in condensed heterocyclic synthesis [23].

3. Chemical reactions

a. Synthesis of indole derivatives

i. Synthesis of spirooxindole derivatives

MCRs are one-pot reactions that need at least three starting materials and produce a substance that includes almost all of the educts' atoms. Because of their inherent ability to generate a significant amount

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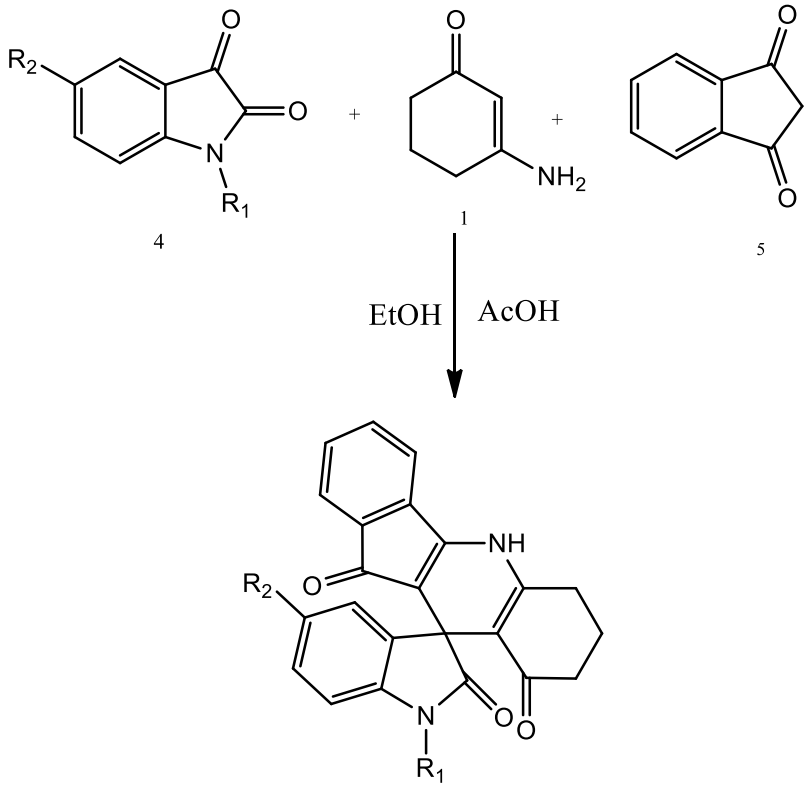
in a time and cost-effective manner of highly complex molecules, in synthetic organic chemistry, MCRs are gaining traction, especially in the prescription drugs industry.

In a three-component reaction catalysed by acetic acid in an ethanol solvent, isatins (4), 1,3-Indandione (5), and 3-Aminocyclohex-2-en-1-one (1) are combined to give active Synthesis of indenoquinoline–spirooxindole (3) derivatives in a single pot. The technique is useful in that it is both fast and easy to implement [24].



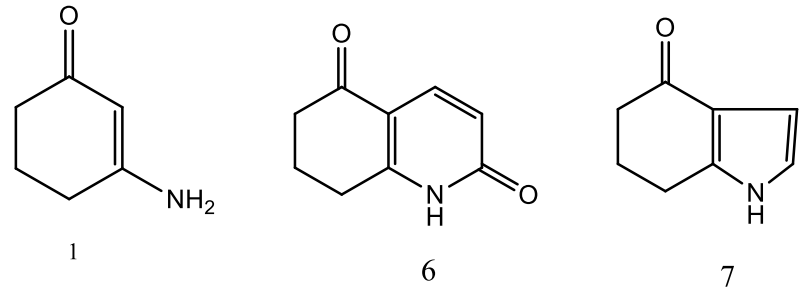
4 1 5

3 (87.4%)

Scheme 1: Spirooxindole derivatives synthesis

3.1.2 Cyclization of Cyanoethylated ketones

Molecule (1) is a popular beginning material for the manufacture of heterocycles of nitrogen including (6), (7) and (8) [12, 17, 25]



1 6 7

8

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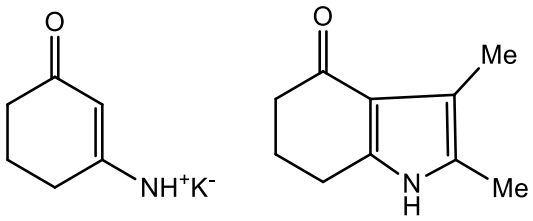
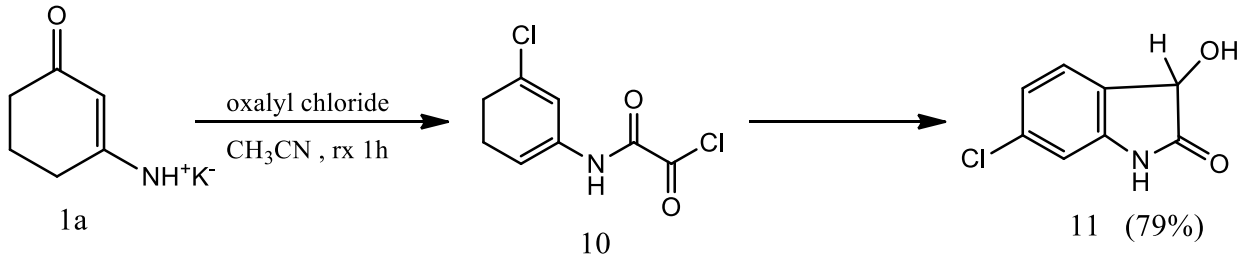
The predicted and widely recognised indole derivative (9) was obtained by alkylation of (1a) with 3-chloro-2-butanone, followed by heating.



1a 9

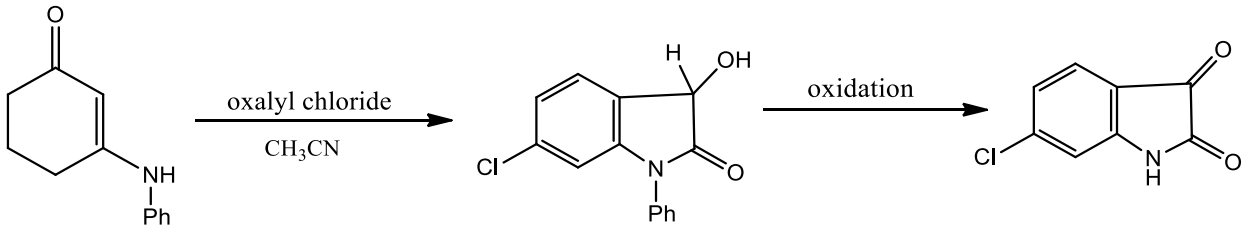
When compound (1a) or its acid, 3-Amino-2-cyclohexen-1-one, was mixed with oxalyl chloride (COCl), a 6-membered compound with an atom of Cl was formed. The ring of six membered of the proposed intermediate has chlorine atom as substitution. The intermediate can rather than cyclizing to the 2-position, cyclize to the 4-position after hydrogen atom translation, giving rise to the derivative of 6-chlorinated indole (11).



1a 10 11 (79%)

Scheme 2: 6-chlorinated indole derivative

Similar to the phenyl amino derivative 1, 3-cyclohexanedione and aniline are easily produced at 130 ^{0}C/5 min, the 6-chlorinated indole derivative (12) could be cyclized to form 6-chloroindoline-2,3-dione (13) on oxidation [26].



12 13 (84%)

Scheme 3: 6-chlorinated indoline-2, 3-dione synthesis

3.1.3 Indoles and Carbolines Syntheses through Amino acetaldehyde Acetals

The 4-oxotetrahydroindole is synthesised using a surprisingly dione (2) is a stable molecule that undergoes intramolecular condensation [25]. In glacial acetic acid, the oxoindoles (7) were allowed to react with formaldehyde and methyl amino acetaldehyde dimethyl acetal give condensation product (15).The Mannich bases (15) were treated with dilute HCl to close the ring to the corresponding hydroxy compounds. Over palladium on carbon, various hydroxy compounds (16) undergo hydrogenolysis was achieved with some difficulty. In 66 percent of the cases, the recognised compound N-methyl-1, 2, 3, 4-tetrahydro-y-carboline (17) was obtained.

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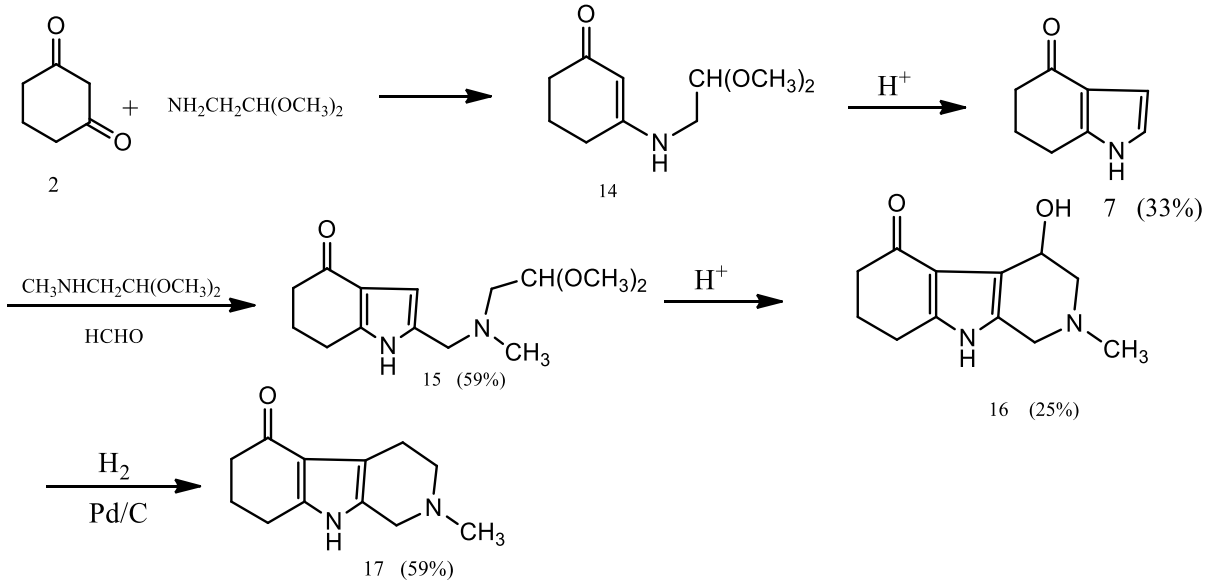
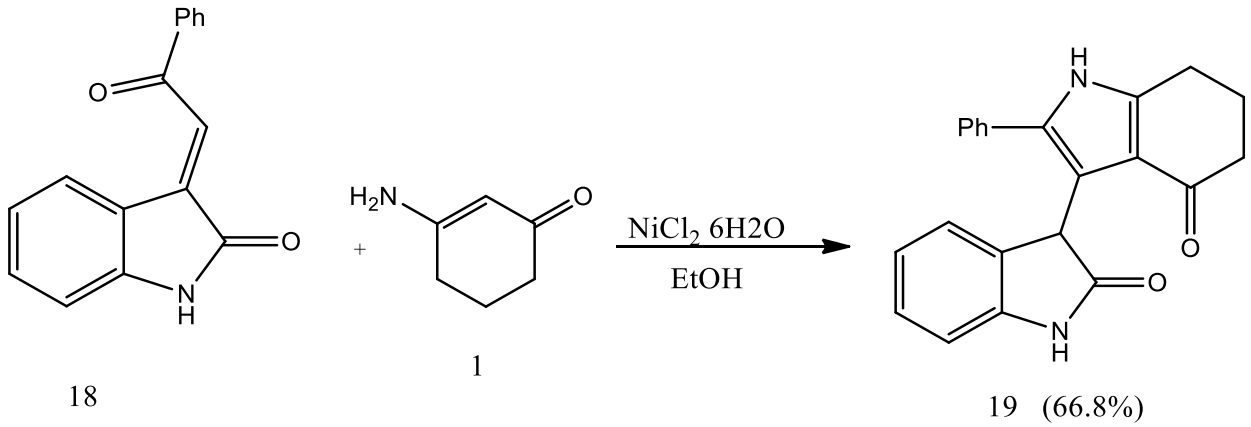


Scheme 4: Indoles and Carbolines synthesis

3.1.4 Synthesis of Derivatives of 3-(4-oxo-4,5,6,7-tetrahydro-1H-indol-3-yl)indolin-2-one

The reaction of 3-alkylideneoxindoles (18) with 3-aminocyclohex-2-enone (1) produces 3-(4-oxo-4, 5, 6, 7-tetrahydro-1H-indol-3-yl) indolin-2-one derivatives (19) with excellent yields, after a sequential Michael addition, nickel dichloride hexahydrate catalysed intramolecular condensation[27].



Scheme 5: 3-(4-oxo-4, 5, 6, 7-tetrahydro-1H-indol-3-yl) indolin-2-one synthesis

3.2 Synthesis of quinoline and its derivatives

3.2.2 Synthesis of polyfunctional octahydroquinolines

A new form of the Hantzsch reaction for the synthesis of 1, 2, 3, 4, 5, 6, 7, and 8-octahydroquinolines (21) has been established based on regioselective cascade recyclization of N-arylitaconimides (20) in reactions with 3-aminocyclohex-2-enones. C-nucleophilic attachment of enaminone to the active multiple bond of itaconimide and intramolecular transamidation with subsequent recyclization of the intermediate were the mechanisms of this domino effect [28].

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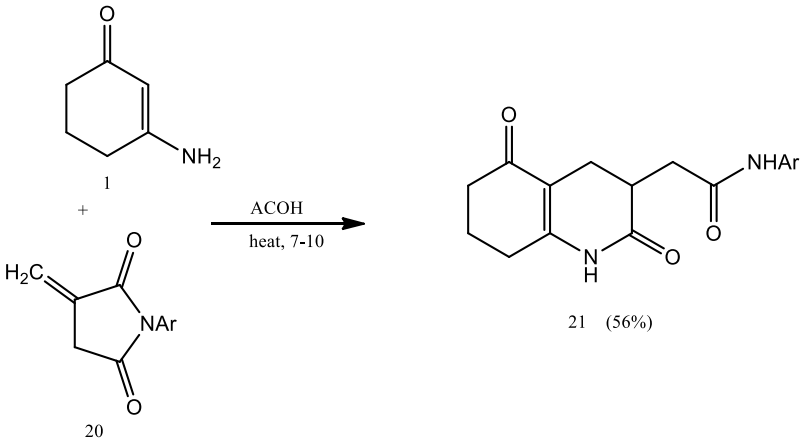
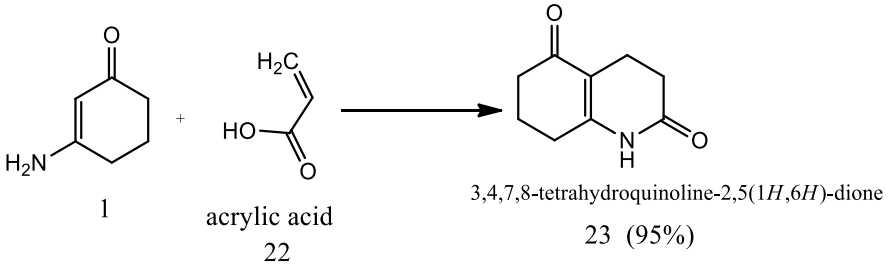


Scheme 6 : polyfunctional octahydroquinolines synthesis

3.2.3 Reaction with acrylic acid

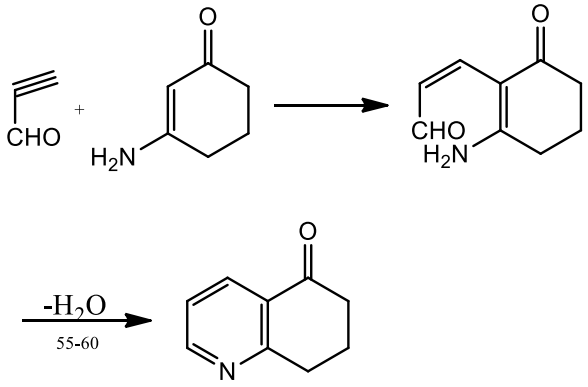
3-amino-2-cyclohexenone react with acrylic acid (22) to produce the (23) quinoline derivative with a good yield **[29].**



Scheme 7: tetrahydroquinoline synthesis

3.2.4 Synthesis of 7,8-dihydroquinoline-5(6H)-one

At room temperature, it can be used to render 7, 8-dihydro-6H-quinolin-5-one (34), this reaction will require the solvent dimethyl formamide and will take 12 hours to complete. The yield is approximately 54%.



Scheme 8: dihydroquinoline synthesis[30]

3.2.5 The preparation of 7, 8-dihydroquinoline -5(6H)-one.

Compound (25) is produced by combining (2) and 1, 1, 3, 3-tetraethoxylpropane, which is commercially available. Following that, the two synthetic phases were successfully merged. Both reactants and solvent

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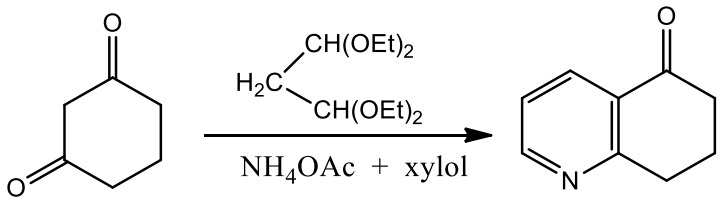
are applied to the reaction vessel and heated under reflux until the mixture is purified in vacuum to yield the substance (25) in a one-pot synthesis [21].

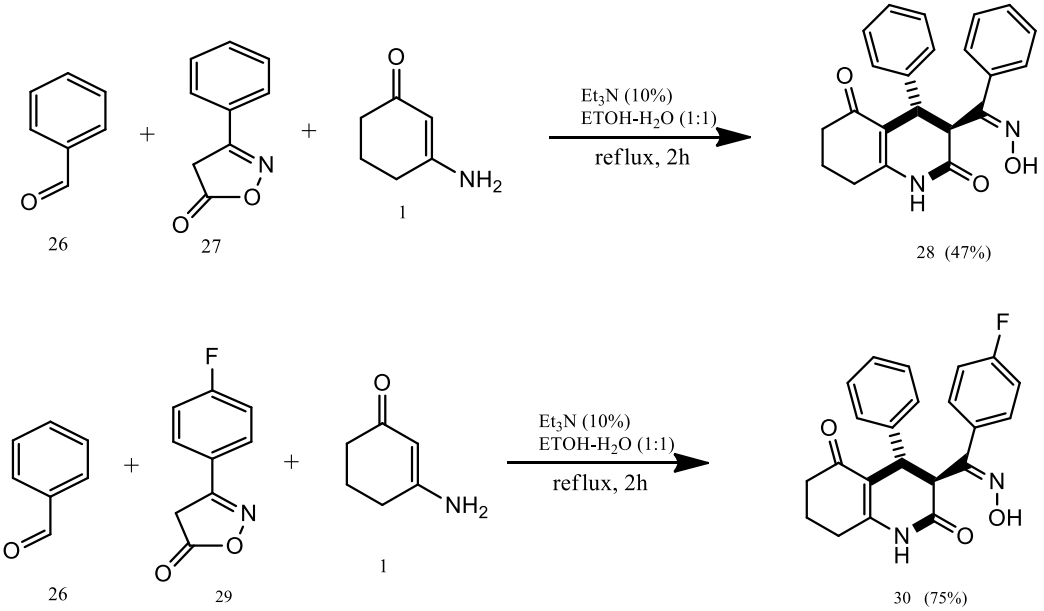


25

Scheme 9: Preparation of 7, 8- dihydro-quinoline -5(6H)-one

3.2.6 Amine-catalyzed knoevenagel–michael-cyclization–ring-opening cascade

Under the catalysis of triethylamine, a diastereoselective three-component cascade reaction occurs between aromatic aldehydes, 3-phenylisoxazol-5(4H)-one (27), and 3-aminocyclohex-2-enone (1), yielding (3S)-3-((E)-(hydroxyimino)(phenyl)methyl)-4-phenyl-3,4,7,8-tetrahydroquinoline-2,5(1H,6H)-dione (28) in a 45-85% yield. Knoevenagel/Michael addition, cyclism, and ring-opening reactions are believed to play a role in the transition. The procedure was done in green media (EtOH/water, 1:1–1:3) at reflux. Only filtration is used to separate the compounds since they crystallize directly from the reaction mixture [31].



26 27 1 28 (47%)

26 29 1 30 (75%)

Scheme 10: catalysed by amines Knoevenagel–Michael–ring-opening cyclization cascade

3.2.7 Synthesis of hydroquinolines

Hydroquinone is synthesized from 3-amino-2-cyclohexenone by following method [32].

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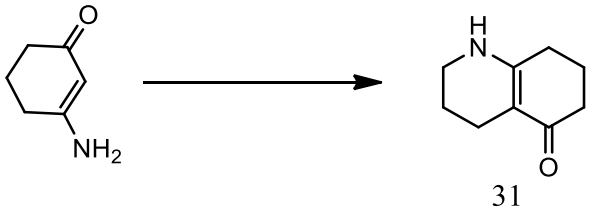
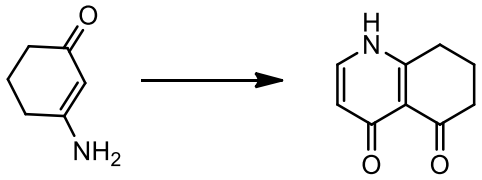


31

5, 6, 7, 8-tetrahydroquinoline derivatives as potential acetylcholinesterase inhibitors is also synthesized from 3-amino-2-cyclohexenone [2].



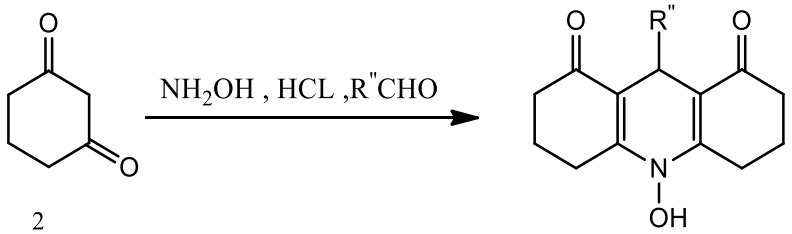
32

Scheme 11: Hydroquinolines synthesis

3.3. Synthesis of acridines derivatives

3.3.1 New Decahydroacridine-1,8-dione Derivatives Synthesis and Transformations

The structural fragment of decahydroacridinediones is a 1, 4-dihydropyridine ring, which can be made using various Hantzsch synthesis methods. The biological effects of these compounds are diverse. The better Decahydroacridine-1, 8-Dione was made from a three-component condensation of cyclohexane-1, 3-dione (2) with 1.2 equivalent of hydroxylamine and 1.1 equivalent of ample aldehyde in anhydrous pyridine. Diketones were heated with hydroxylamine in pyridine to produce the corresponding enamino ketone (1), then aldehyde was added to the reaction mixture and the mixture was heated further to yield the corresponding product (33)[33].



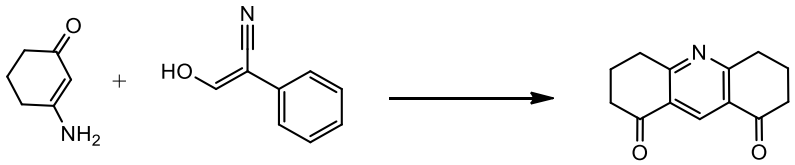
2

33 (86%)

Scheme 12: Decahydroacridine-1, 8-dione synthesis

3.3.2 Synthesis of 1, 2, 3, 4-tetrahydroacridine

3-amino-2-cyclohexenone react with 3-hydroxy-2-phenylacrylonitrile to produce tetrahydroacridine derivatives (35) [2].



34

35 (11%)

Scheme 13: Tetrahydroacridine synthesis

3.4 Synthesis of Pyridine derivatives

3.4.1 Reaction of 3-formylchromones with electron-rich amino heterocycles

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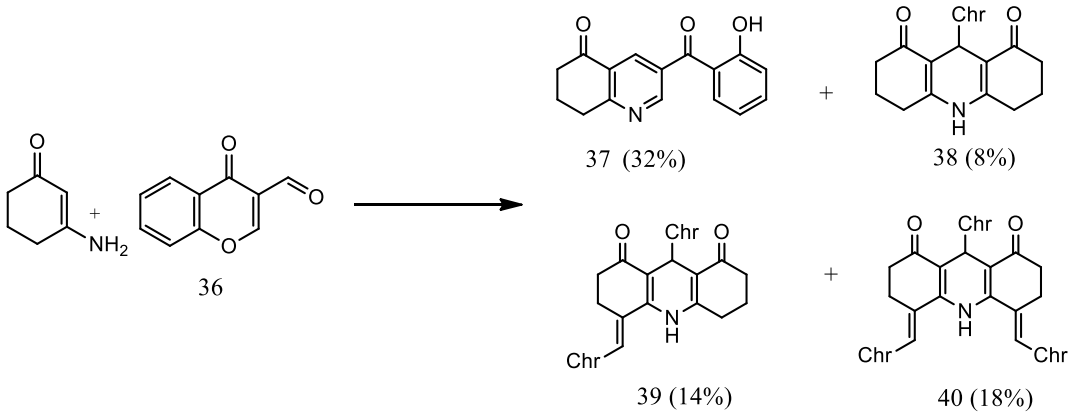
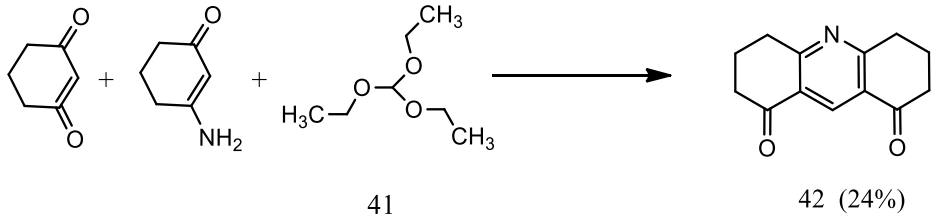
The electrophilic Carbon-4 atom, the formyl feature at Carbon-3, and the unsaturated Carbon-2 atom, all of these are nucleophile Michael added and all easily accessible in the structure of 3-formylchromones. By reacting with different binucleophiles, 3-formylchromones are used to make a variety of heterocyclic structures. 1, 2-binucleophiles like hydrazines and hydroxylamines, as well as 1, 3-NCN-binucleophiles like amidines and amino heterocycles, outperform pyrazoles, isoxazoles, and pyrimidines with a 2-hydroxybenzoyl group [34-36].

The reaction of 3-formylchromone (36) with electron-rich aminoheterocycles yields fused 3-(2-hydroxybenzoyl) pyridines as the only result. 2- Aminothiophene, 6-aminouracils, 5-aminoisothiazoles, 5-aminoisoxazoles, 5-aminofuran, and 5-aminopyrazoles all produce high yields of cyclization products when used under the conditions stated. In the meantime,3-amino-2-cyclohexenone(1) produces a difficult-to-separate mixture of at least four compounds, including the required pyridine (37) 32%, three other Hantzsch products (38) 8%, (39) 14%, and (40) 18% [37].



Scheme 14: The synthesis of pyridine

3.4.2 The three-component condensation method used to make pyridine derivatives.



Scheme 15[10]

3.5 Angucyclinone 5-Aza Analogues and the Synthesis of the First Angucyclinone

3.5.1 Angucyclinone formation

Diene (44) was generated by combining 3-amino-2-cyclohexenone (1) with a small amount of N-(dimethoxymethyl)-N, N-dimethylamine (43) to yield E, E: Z, E isomers in a 3/1 mixture. In 92 percent of cases, reflux-heating a toluene solution of this mixture provided the favoured and most reliable EE-isomer [16].

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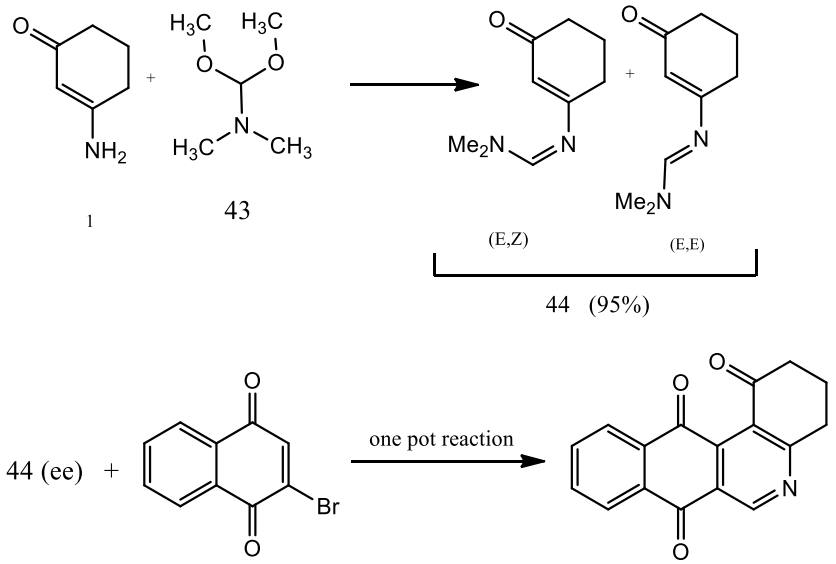
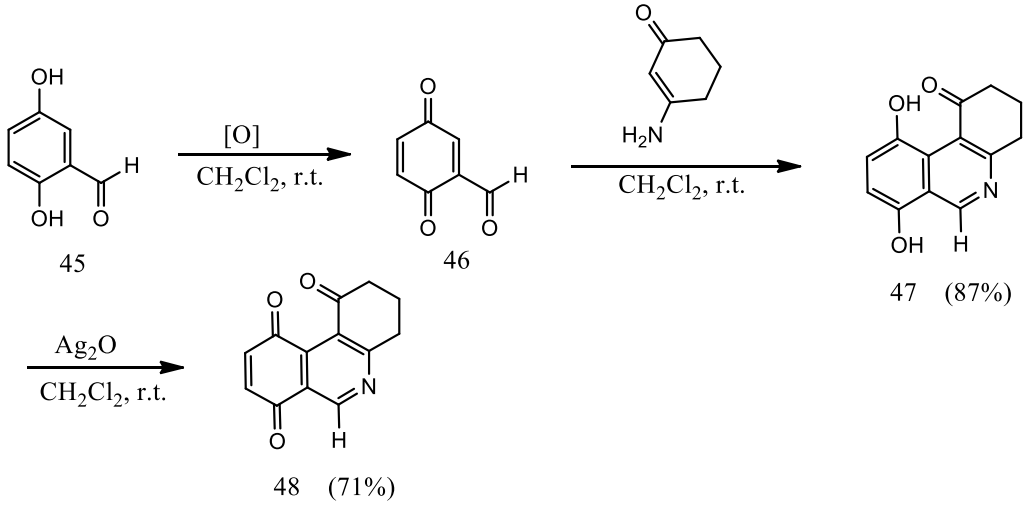


Scheme 16: angucyclinone synthesis

3.5.2 Analogues of Angucyclinone 5-Aza: Design and Synthesis

The N-congeners of the angucyclinone chromophore are made from 3-amino-2-cyclohexenone. This method will be used to synthesise a broad range of N-heterocyclic quinones, and the cytotoxic effects of these compounds on a variety of cancer cells will be studied.

At room temperature, formyl benzoquinone (46), obtained by oxidizing (45) with oxides of silver (I) [38], reacted with the enaminone (1) to give dihydroxyphenanthridine (47) in an 87 percent yield. The quinones (48) were then synthesised in a 71 percent yield by oxidizing dihydroxyphenanthridine (47) with silver (I) oxide.



Scheme 17: Synthesis of Angucyclinone 5-Aza Analogues

After successfully synthesising phenanthridinequinones, these dienophiles undergo a Diels–Alder reaction with (E)-1-trimethylsilyloxybuta-1, 3-diene (49). At room temperature, the quinone cycloaddition (49) utilizing the diene in dichloromethane went smoothly, yielding the adduct (50) as the sole regioisomer. Diels–Alder adducts (50) were reacted with hydrochloric acid to produce the corresponding benzo[j]phenanthridinequinones (51a) (method A). The respective 8-hydroxy benzo[j]phenanthridinequinones (51b) were obtained after mild hydrolysis of the adduct (50) with and oxidation of the alcohol intermediaries with pyridinium chlorochromate (PCC) (method B)[39].

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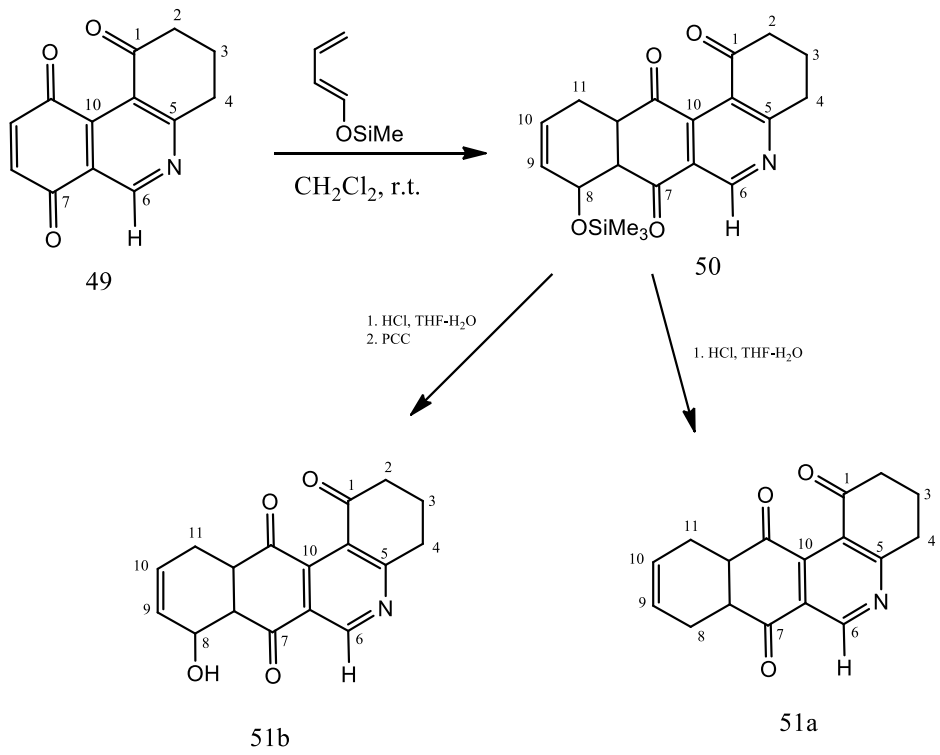

49 50 51b 51a

Scheme 18

3.6 The tetrahydro-6H-pyrido [3, 2-b] azepin-6-on scaffold

The 4-(trifluoromethyl)-8, 9-dihydro-5H-pyrido [3, 2-b] azepin-6(7H)-one synthesised for the first time. In this procedure, the Beckmann rearrangement is the main step in the synthesis of azepin-6-ones. Under Dean–Stark conditions, 3-amino-2-cyclohexenone (1) was formed by condensing cyclohexane1, 3-dione (2) with 1 equiv of acetate of ammonia. The yield of pure compound obtained is 70% following the process of recrystallization from ethyl acetate.

In refluxing acetic acid, the β-enaminone (1) was treated with 1.5 equiv of various 1-substituted-4-trifluoro-1,3-diones for 7 hours to yield the respective (52) [40]. To make the 4-(trifluoromethyl)-8, 9-dihydro-5H-pyrido [3, 2-b] azepin-6(7H)-one (55a), a ring expansion with a nitrogen atom was performed on the (52). The Beckmann rearrangement was chosen to convert the ring to a seven-membered ring. Using hydroxylamine hydrochloride as a starting material, the Beckmann rearrangement was used to create the oximes (53).

After several days of refluxing in an ethanol–water mixture, the departing group tosylate was extracted, and after rearrangement, the desired 4-(trifluoromethyl)-8, 9-dihydro-5H-pyrido [3, 2-b] azepin-6(7H)-ones (55a) were formed in (6:4) ratio. Potassium acetate (2.1 equivalents) was used as required. Imidates were formed when the cosolvent ethanol invaded the intermediate nitrilium ion (55b) [41].

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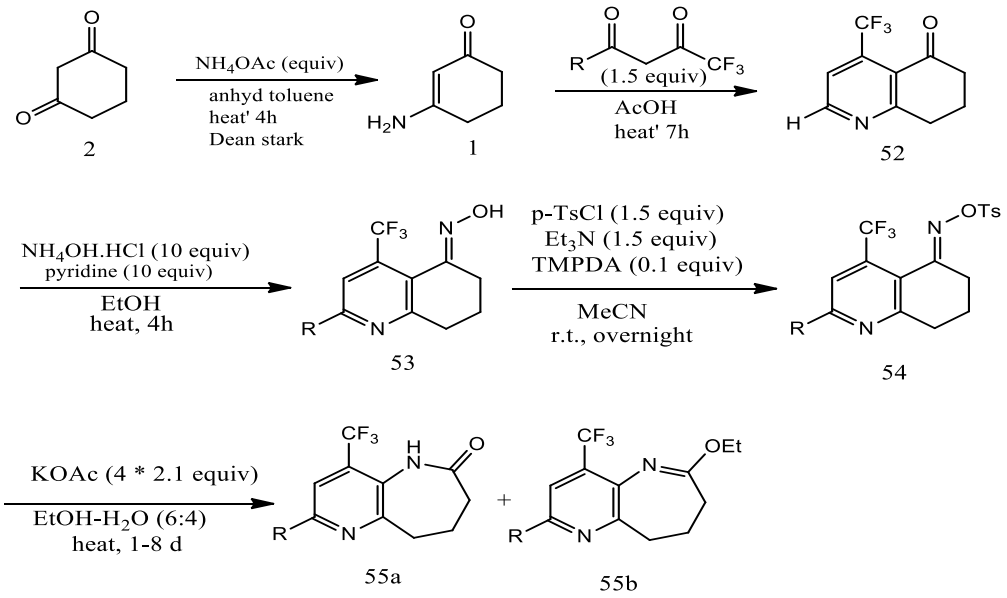
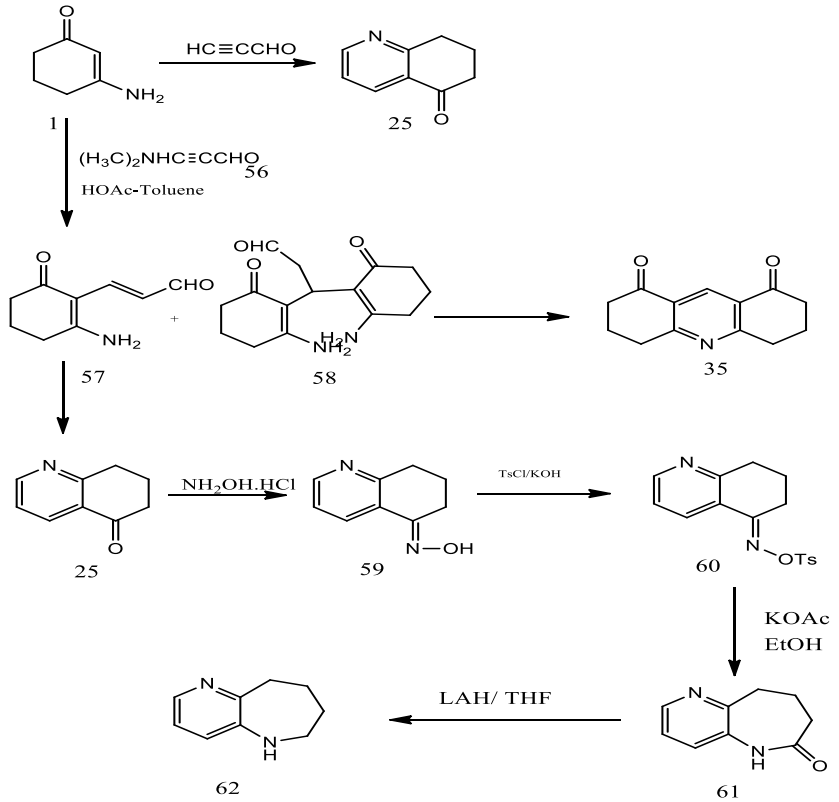


Scheme 19: Tetrahydro-6H-pyrido [3, 2-b] azepin-6-on

3.6.1 1, 4, 5, 6-tetrahydropyrazolo [3, 4d] pyrido [3, 2b] azepine syntheses

In a 23 percent yield, 7,8dihydro5 (6H) quinolinone (25) is synthesised from commercially available 3amino2cyclohexen1one (1) and 3(dimethylamino) acrolein (56) to prevent the preparation of propynal [42]. It was previously used as a reactant in the difficult process of synthesising 7, 8-dihydro5 (6H) quinolinone. It explains how to make tricyclic azepine in a straight forward manner (70) [12].



Scheme 20: Synthesis of 5 (4methylphenylsulfonyl) 6, 7, 8, 9tetrahydro5Hpyrido [3, 2b] azepine

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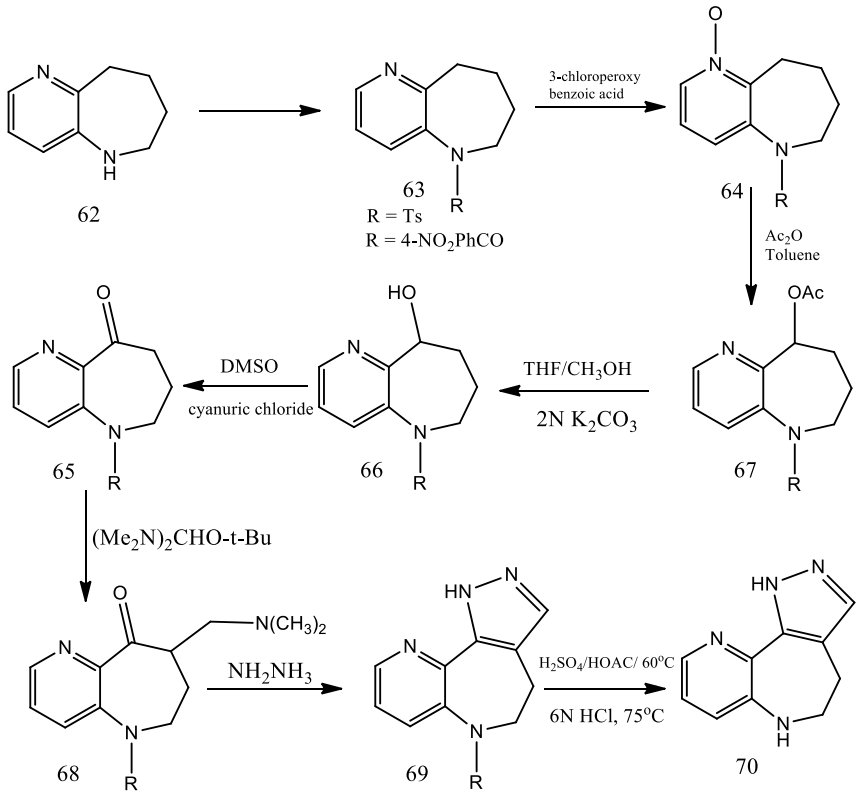
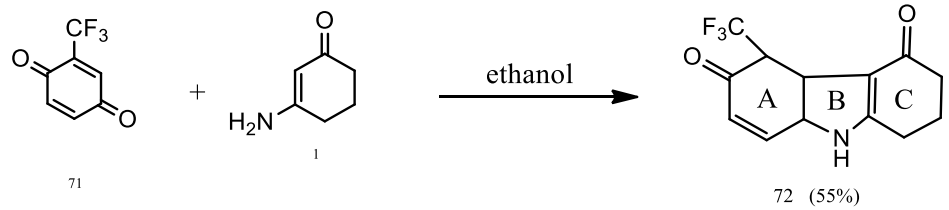
How to make 6(4methylphenylsulfonyl)1,4,5,6tetrahydropyrazolo[3,4d]pyrido[3,2b]azepine(69) from 5(4methylphenylsulfonyl)6,7,8,9tetrahydro5Hpyrido[3,2b]azepine (62). The tricyclic azepine (70) was synthesised by removing the N (4methylphenylsulfonyl) group by treating with 40 percent H_2SO4 in acetic acid. A similar reaction chain was used to synthesise 6(4nitrobenzoyl)1,4,5,6tetrahydropyrazolo[3,4d]pyrido[3,2b]azepine (69) from 5(4nitrobenzoyl)6,7,8,9tetrahydro5Hpyrido[3,2b]azepine (63).



Scheme 21: 1, 4, 5, 6-tetrahydropyrazolo [3, 4-d] pyrido [3, 2-b] azepine synthesis

3.7 Preparation of Carbazoles

Making carbazole derivatives by combining quinones derivatives with enamines may be a good option. We show how to produce carbinolamines(72) from substituted 1, 4-benzoquinones (71) and 3-amino-2-cyclohexenone using acetic acid as a catalyst [43].



Scheme 22: Carbazoles synthesis

3.8 Heterocyclic systems synthesis via 3-amino-2-cyclohexenone

Although low yields of the necessary piperidone (73) were obtained when the enamine ketone (1) was treated with alkyl (methyl) propiolate at a moderate temperature, it was discovered that carrying out the reaction at a higher temperature (140-150 ^{0}C) in dimethylformamide or carbitol as preferred solvent, with filtration on occasion of the precipitate generated. A 45 percent yield (73) was achieved using this approach.

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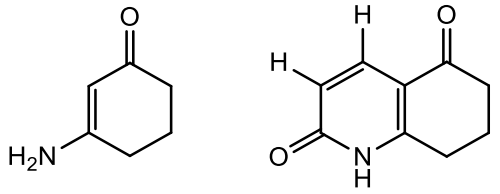
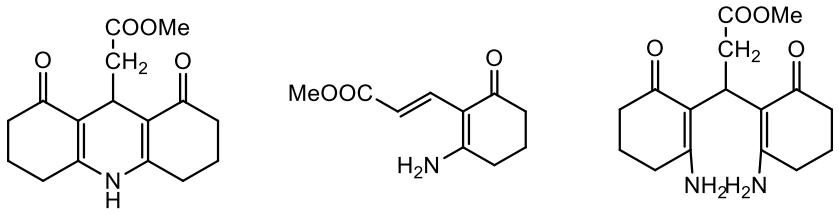


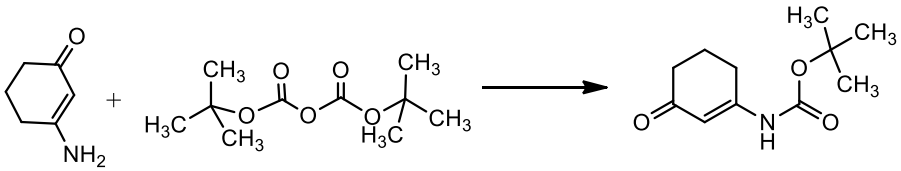
1 73 (45%)

The mother-liquors from the crystallisation of (73) were painstakingly worked up into a new product, which was assigned structure (74) based on its spectroscopic findings. When a second ketone mole of (1) is added to the ester intermediate, it cyclizes when the NH3 is removed, forming the hypothetical intermediate (76) [17].



74 75 76

3.8.1 Carbamate synthesis.

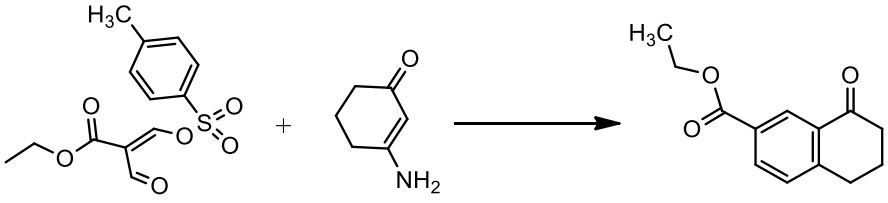


77 78 (38%)

Scheme 23: carbamate synthesis[44]

3.8.2 Tetrahydronaphthalene synthesis

Tetrahydronaphthalene (80) is prepared by reacting (79) with 3amino2cyclohexenone (1) [45].



79 80

Scheme 24: synthesis Tetrahydronaphthalene

3.8.3 5-hydroxy-3, 4-dihydrocarbostyril, and 5-hydroxycarbostyril synthesis.

A new and functional synthesis of (82) and 5-hydroxycarbobristil (83) has been developed using 3-amino cyclohex-2-en-1-one, which can be obtained in a 95 percent yield from 1, 3-cyclohexanedione. Compound (81) was dehydrogenated to compound (82) in 95 percent yield by refluxing 10% Pd-charcoal and (81) mixture in decalin for 3 hours. Refluxing the same mixture for 24 hours, on the other hand,

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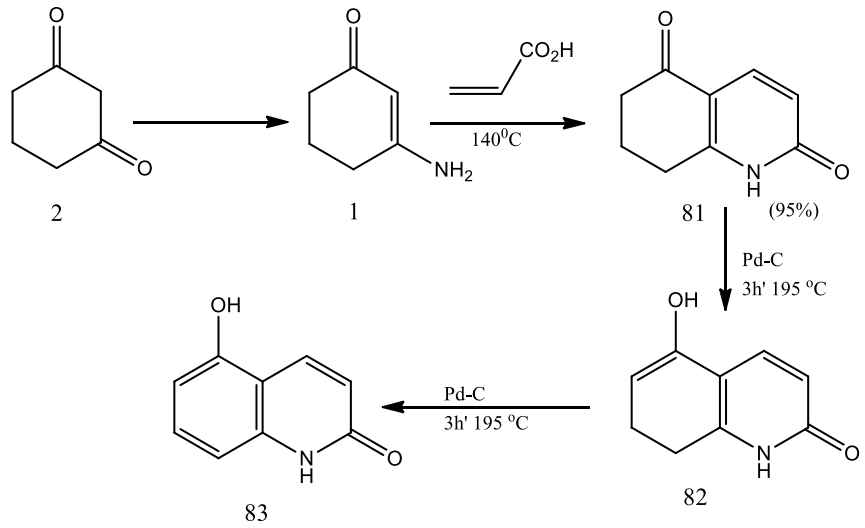
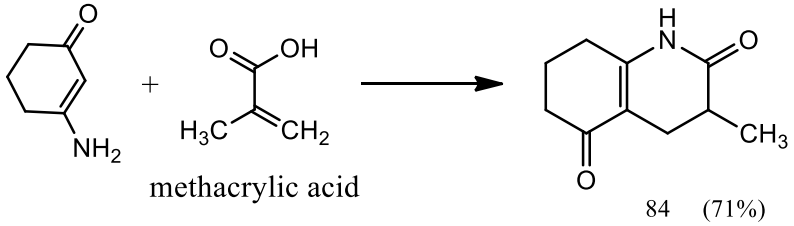
produced an overwhelmingly bitter mixture (83). To isolate (82) and (84), recrystallization was used. As a result, using a relatively simple process, both products (82) and (83) could be generated in high yields.



Scheme 25: Synthesis of the 5-hydroxy-3, 4-dihydrocarbostyril, and the 5-hydroxycarbostyril

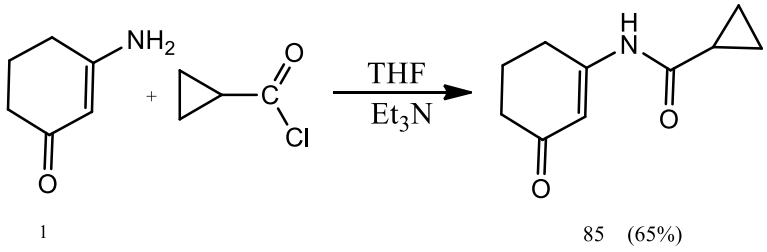
The result was comparable when meth acrylic acid was used instead of acrylic acid because a higher temperature was needed for the reaction than in the synthesis of (82).The compound (82) did not react with ethyl acrylate or crotonic acid [29].



Scheme 26

3.9 Synthesis of N-(3-Oxo-cyclohex-1-enyl)-cyclopropanecarboxamide

In the presence of triethylamine as a precursor, 3-amino-2-cyclohexenone (1) reacts with cyclopropanecarbonyl chloride in THF solvent to form the compound (85)[22].



Scheme 27: cyclopropanecarboxamide synthesis

3.10 N-alkenoyl p – enaminone's [2+2] photocycloaddition.

The N-alkenoyl β-enaminone's intramolecular cycloaddition exhibits strong diastereoselectivity and regioselectivity, resulting in fascinating synthons for the complete synthesis of various sesquiterpenes or triquinanes.

Deprotonation in tetrahydrofuran with NaHMDS as a base at low temperatures, accompanied by incorporation of the readily available unsaturated acid chloride, conveniently prepared in accordance with

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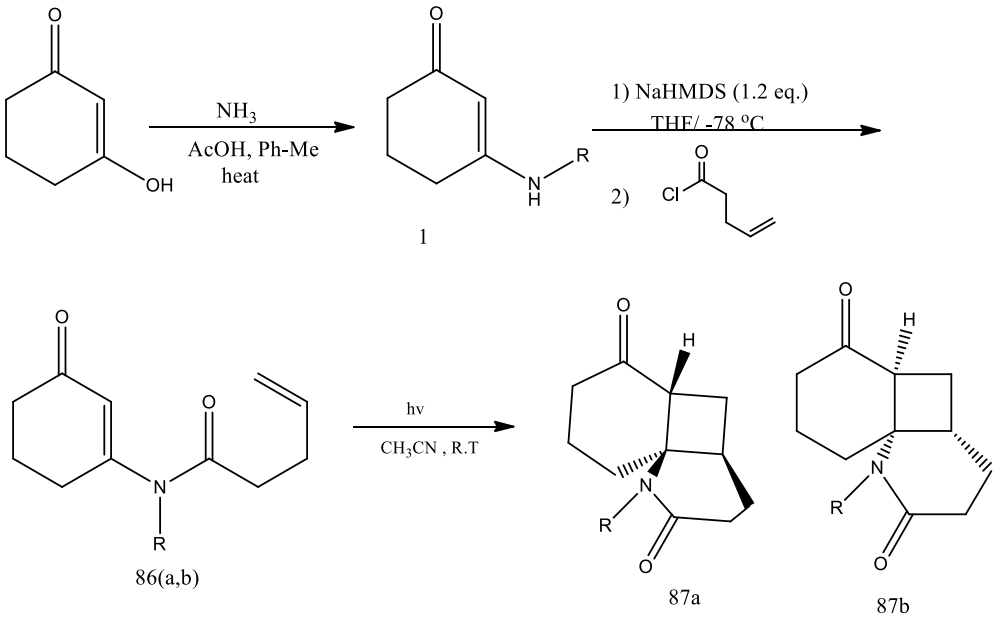
protocol, yielded high yields of enaminones (1). No reaction was observed when (86) was irradiated at 313 nm in an Argon flushed acetonitrile solution for an extended period of time (Pyrex vessel, medium pressure lamp). This lack of reactivity may be due to radical cyclisation processes or to an unfavourable exocyclic chain conformation, as with unsaturated oxoamides. When the N-atom is replaced, by an alkyl alternative, the conformational behavior of the beginning p-enaminones is expected to change. As a result, high yields of the [2+2] cycloadducts (87a) and (87b) were obtained [13].



Scheme 28: Photocycloaddition of N-Alkenoyl p – Enaminones

Table 2:

	substrate		cycloadduct	
86	R	Yield	87	yield
a	H	51%	a	No yield
b	benzyl	67%	b	60%

4 Applications

4.1 Transfer hydrogenations catalysed by asymmetric brønsted acid

Compounds of the stereocenter includes hydrogen are popular natural ingredients that are biologically active. Unsaturated molecules that undergo asymmetric hydrogenation like, carbonyls, and olefins is the popular and practical path to optically active materials. Using dihydropyridine (B) and 5 mol Brønsted acid (A) as hydrogen sources, we capable to obtain a wide variety of (89) by reacting 3-amino-2-cyclohexenone (1) with hex-1-yn-3-one (88) in strong yields with excellent enantioselectivities. We also discovered that hexahydroquinolinone, which is rapidly converted to the alkaloid (90), can be hydrogenated [46].

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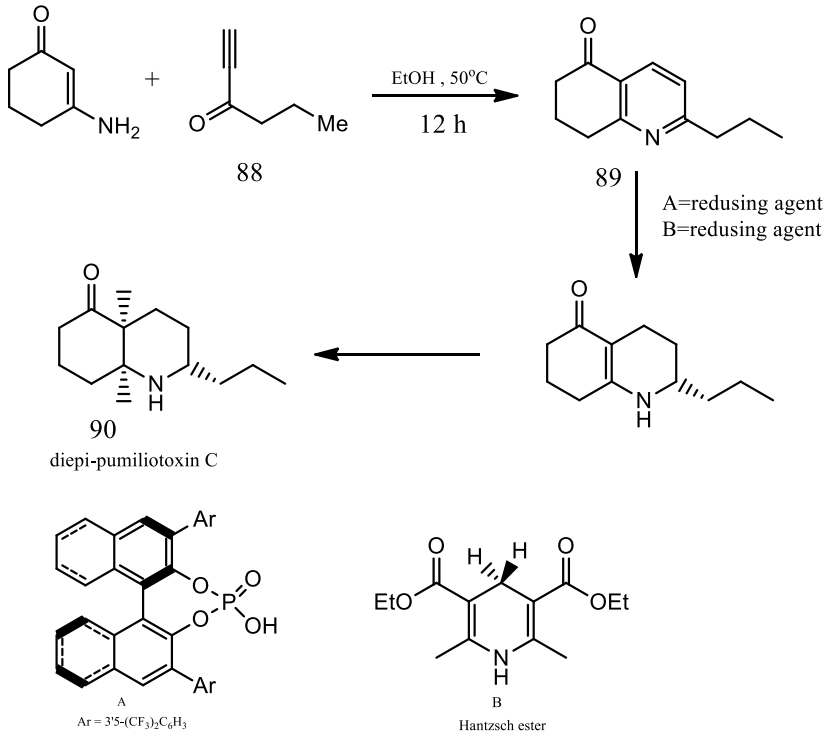
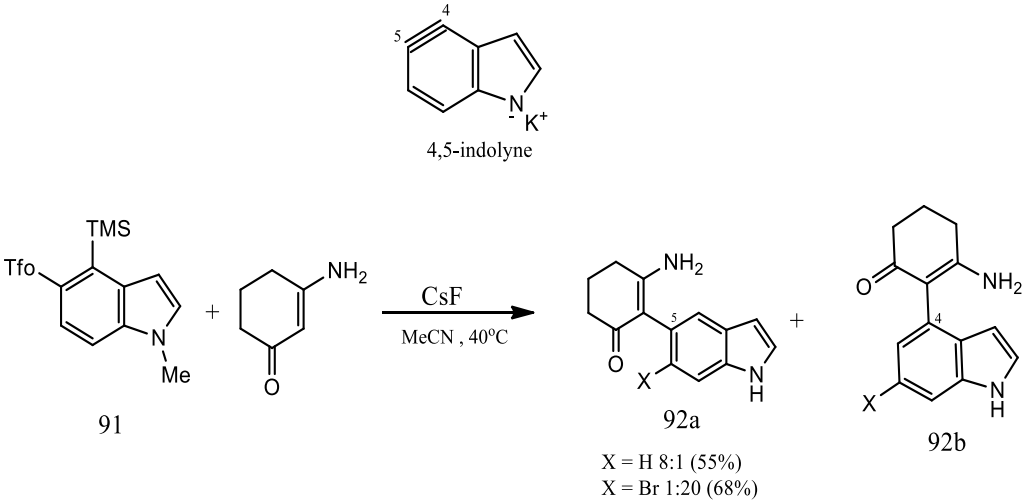


Scheme 29: Transfer Hydrogenations Catalyzed by Asymmetric Brnsted Acid

4.2 Understanding and modulating indolyne regioselectivities

For modern synthetic chemistry, heterocyclic arynes hold a lot of promise. One form of hetaryne is (i.e., indolynes), one derived from the indole. These highly reactive intermediates can be produced using silyltriflate precursors under mild fluoride-based reaction conditions. Compound (91) is a short-term precursor for the synthesis of 4, 5-indolyne. To learn more about indolyne generation and reactivity, researchers used a series of trapping experiments. The following reaction, which yields two isomers (92a) and (92b), demonstrates a wide range of nucleophiles and cycloaddition partners undergoing a smooth reaction with the assumed indolyne intermediate. It demonstrates that indolynes can be used as electrophilic indole surrogates with synthetically useful regioselectivity. Easy formulas can be used to estimate Regioselectivities before experiments, allowing selectivities to be modulated by careful design [47, 48].



Scheme 30: Modulating Indolyne Regioselectivities

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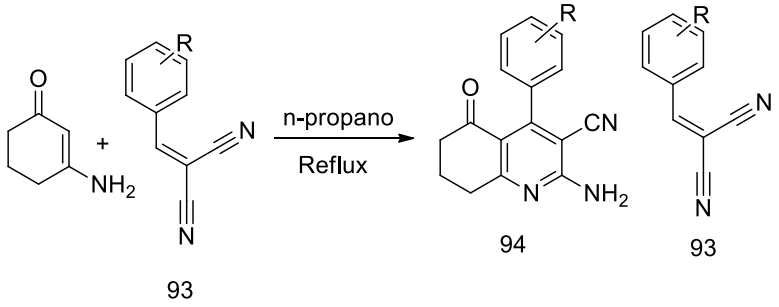
4.3 The photoprotection properties of myosporine amino acid motifs

Mycosporines and their amino acids derivatives are found in cyanobacteria, fungi, macro-and microalgae, and other species. "Mycosporines" and "mycosporine-like amino acids" are used interchangeably in the literature. Mycosporines, on the other hand, are cyclohexenone-based molecules, mycosporine-like amino acids are cyclohexenimine-based molecules. MAAs include mycosporines as well as mycosporine-like amino acids. MAAs have a good UVA and UVB absorbance band, as well as excellent photostability, making them a promising UV filter candidate. Synthetic MAA motifs have been investigated as an alternative to natural MAAs since natural MAAs are derived from natural sources and synthesised in small quantities; these molecules have shown promising levels of photostability.

Given the increasing concern ultraviolet (UV) filters that commercially available are damaging the atmosphere, new UV filters are urgently needed. Natural UV filters used in these cells include “mycosporines” and “mycosporine-like amino acids”. We begin with a basic analogue of an MAA, 3-aminocyclohex-2-en-1-one, and work our way up to get a greater understanding of the properties of photoprotection of MAAs (ACyO). After photoexcitation, ACyO gets stuck in the bare minimum of an S1 condition for long periods of time (>2.5 ns), according to previous experiments on ACyO using (TEAS) technique. Due to experimental constraints, the magnitude of ACyO's recovery of the electronic ground state could not be calculated within 2.5 ns. To assess the degree of recovery of electronic ground state ACyO within this time period, we used a combination of transient vibrational absorption spectroscopy (TEAS), FTIR, and DFT. By 1.8 ns, ACyO had recovered more than 75% of its electronic ground state, with the remainder presumably remaining in the excited state. In experiments of long-term irradiation, after 2 hours of irradiation with ACyO, researchers discovered that a small percentage of the substance degrades, which may be due to any stuck ACyO forming a photoproduct. These findings suggest that a basic MAA building block already has UV filtering abilities [49].

4.4 The analogues of 2-amino-5-oxo-4-phenyl-5, 6, 7, 8-tetrahydroquinoline-3-carbonitrile

Pyridine is a typical N-heteroaromatic used in a wide range of pharmaceuticals. The synthesis of 2-amino-5-oxo-4-phenyl-5, 6, 7, 8-tetrahydroquinoline-3-carbonitrile with alkane (1:1) ratio (94) with inhibitory activity in excellent isolated yields is identified for the first time (90-95 percent). Both compounds were obtained by adding various arylidene malononitriles to 3-amino-2-cyclohexen-1-one and then aromatizing them without the use of any catalyst. Antifungal development was then checked on them.[50].



Scheme 31: The 2-amino-5-oxo-4-phenyl-5, 6, 7, 8- tetrahydroquinoline-3-carbonitrile synthesis

4.5 Fused-Ring Oxazolopyrrolopyridopyrimidine Systems with Gram-Negative Activity

The annulation of a tetramate scaffold produces fused polyheterocyclic derivatives with antibacterial action against Gram-negative bacteria but not Gram-positive bacteria. Some acyclic enamine systems ((Z)-3-amino-1, 3-diphenylprop-2-en-1-one, 3-aminocyclopent-2-en-1-one, amino pyrimidines, 2-aminocyclopent-2-en-1-one,) had little impact when this strategy was applied to other enamine-containing systems. Enaminones have been used for nucleophilic displacement ring annulation for a long time [51].

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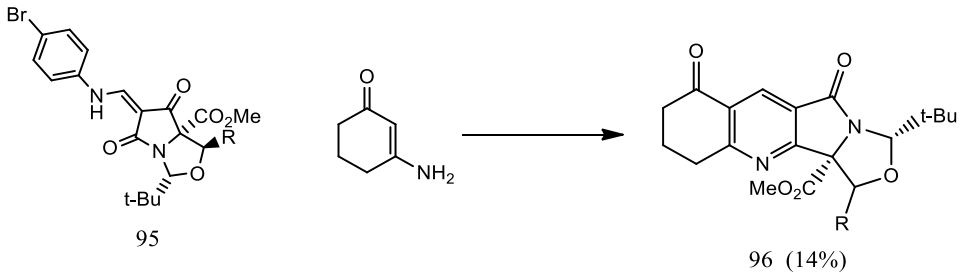
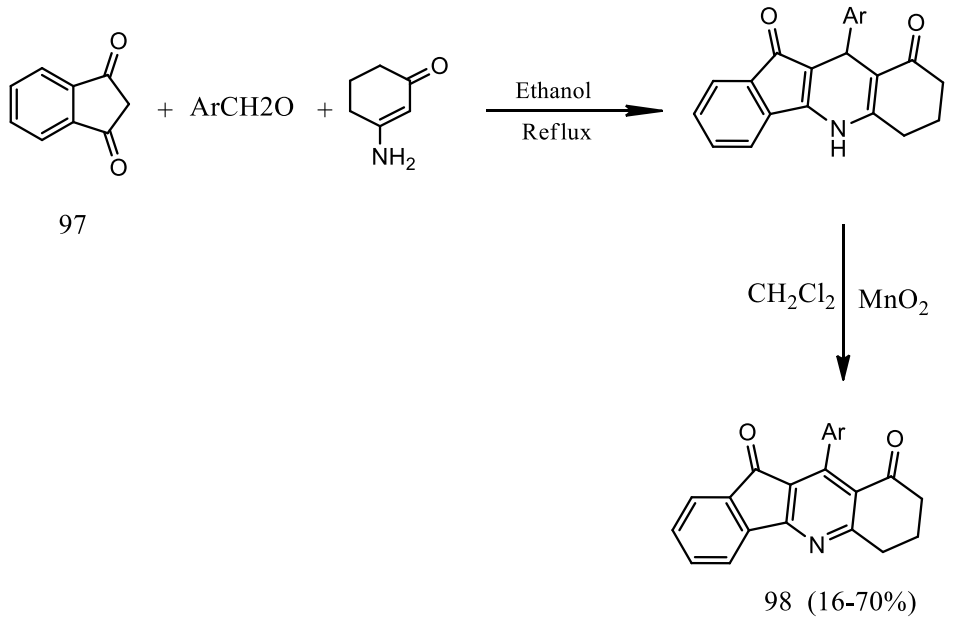


Scheme 32

4.6 Imidazole-based indeno [1, 2-b] quinoline-9,11-dione derivatives: synthesis and antiproliferative action

Molecular condensation of equivalent concentrations of associated enamines, aldehydes, and 1, 3-indandione (97) results in indeno [1, 2-b] quinoline-9, 11-dione derivatives. The aromatized 10-argio-7, 8-dihydro-6H-indeno [1, 2-b] quinoline-9, 11-dione (98) were then generated by oxidative aromatization with MnO2. Anticancer properties can be found in compounds containing imidazole-based indeno [1, 2-b] quinoline-9, 11-dione [52].



Scheme 33: imidazole-based indeno [1, 2-b] quinoline-9, 11-dione derivatives synthesis

4.7 Photo rearrangement of N-alkanoyl β-enaminones

The corresponding diketones yield B-enaminones, which are very appealing molecules. Their photochemical reactivity has been thoroughly investigated, and there are a variety of synthetic applications available. Small variations in nitrogen alternatives have been shown to result in dramatically different photo processes. Photo-Fries rearrangements or electrocyclizations have been discovered depending on the substitution. Photo cyclization of N-aryl-enaminones, for example, yields the indole backbone [53], which is then rearranged into isoquinoline derivatives [54].

Like the De Mayo reaction of diketones the [2+2] photocycloadditions have been found in the presence of alkenes. We recently investigated the preparative significance of intra-molecular [2+2] photo-cycloadditions of N-alkenoyl β-enaminones, due to cyclobutane adducts have a wide range of possible applications as polycyclic structure precursors. Using enones (99) with (n=l, 2), the reaction was shown to be efficient and stereoselectively and regio-selectively, yielding the expected compound (100). Surprisingly, (99) with alkenoyl longer chain (n=3, 7) have a greater chance of rearranging to cyclohexenones alkylated at C-3 (101).

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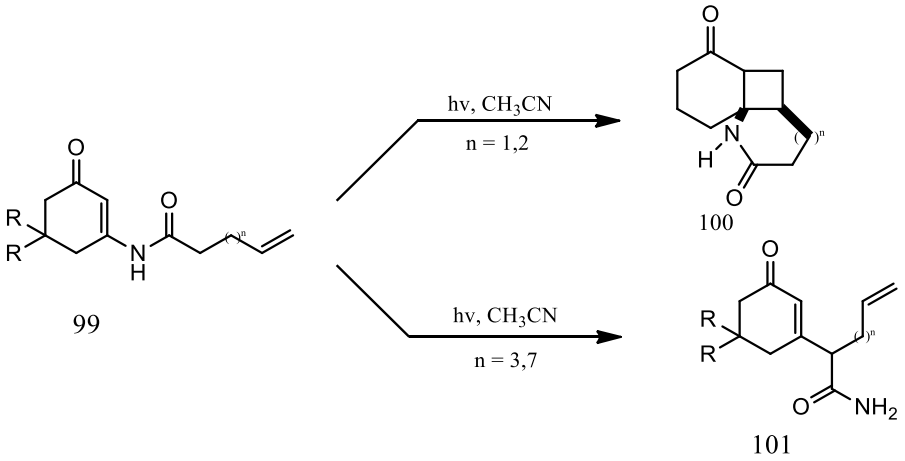
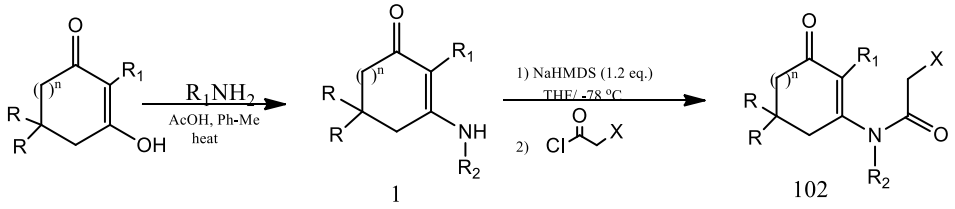


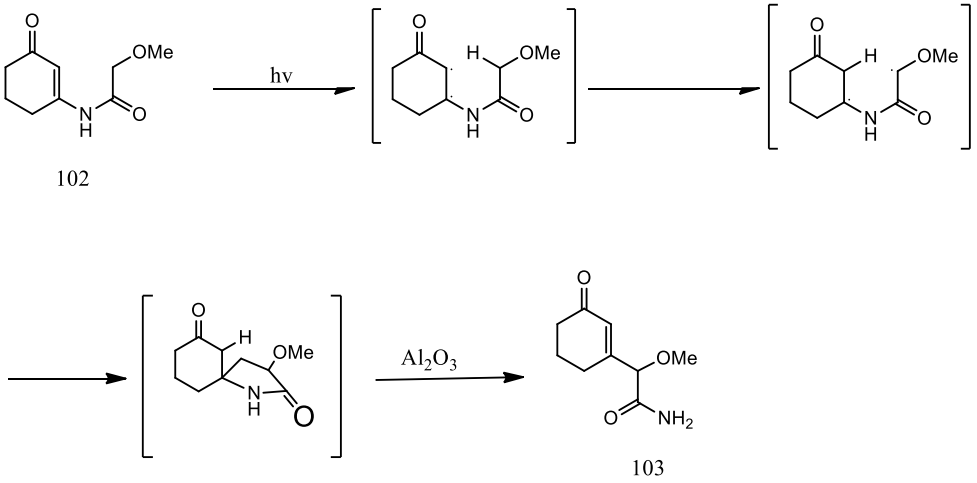
Scheme 34: Photo rearrangement of N-Alkanoyl β-Enaminones

Following the reaction, the starting materials (102) are synthesised in a series of steps. When a primary amine is blended with 1, 3-diones, -enaminones are formed quantitatively (1). The requisite N-alkanoyl enaminones (73) are isolated in high yields following removal of hydrogen with NaHMDS and treatment with the necessary hydrochloric acid.



Scheme 35

In terms of mechanism, we assume there is a hydrogen atom abstraction that leads, for example, from compound (102), to a spiranic keto-lactam (103) by subsequent reactions. This spiranic keto-lactam is highly susceptible to foundation due to amido-ketone structure and the pressure exerted by the ring of four-members, and it may undergo β-elimination when chromatography is done on alumina. According to this theory, the captodative effect could stabilize after initial hydrogen abstraction, the 1, 4-biradical intermediate forms by substituting the chain on the side with an electron-rich(X=OMe) substituent. Intramolecular H-abstractions by the excited enones have previously observed, and spiranic derivatives of high preparative value can be made in this manner [55, 56].



Scheme 36:

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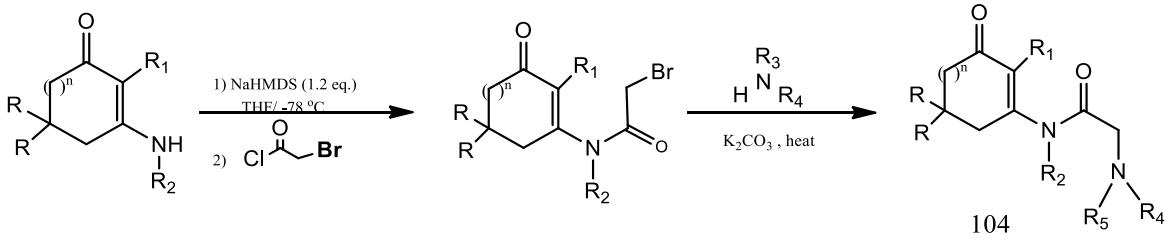
Various irradiation conditions (solvent form and wavelength value) on substrate (102) have been analysed, with the results outlined in Table 3. The key product was the rearranged compound (103) in both cases, but yields were higher in acetonitrile when the irradiation was performed at 366 nm.

Table 3:

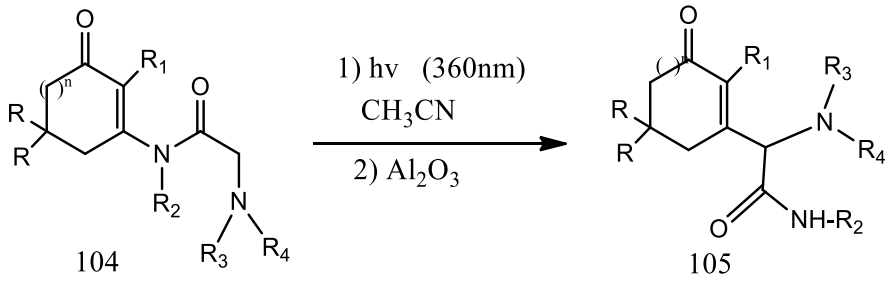
Solvent	CH3CN	CH3CN	MeOH	CH2C12	Ph-H
Wavelength	313nm	366nm	366nm	366nm	366nm
Chemical Yields	51%	68%	65%	55%	47%

We explored the possibility of obtaining α-amino β, γ-unsaturated acids (104) and their derivatives by photo rearrangement of β-enaminones. Substrates containing the bis (allyl) amino group have received special consideration. Depending on the circumstances, like palladium, catalysis, isomerization with rhodium catalysts, or oxidation conditions, this well-known protective category of the amino function may be cleaved easily. To synthesise the starting materials (104) with fair to high yields, a method close to that used to make -enaminones was used.



Scheme 37:

Table 4 summarises the results of irradiating Compounds (104) in acetonitrile solutions at 366 nm. Photo rearrangement happens regardless of the size or shape of the substituents in the starting materials, yielding cycloalkenones 12 with the expected α-amino-β, γ-unsaturated amide functionality. Furthermore, 10g, which yields 12g in fair yields, demonstrates that access to such abnormal dipeptides is possible.



Scheme 38

Table 4: photochemical preparation of α-Amino-β, γ-Unsaturated Acid Derivatives

77	**n**	**R**	**R_1**	**R_2**	**R_3**	**R_4**	**78**	**Yield (%)**
a	1	H	H	H	Allyl	Allyl	a	0
b	0	H	Me	$PhCH_2$	Allyl	Allyl	b	54

Conclusion

It is concluded that 3-amino-2-cyclohexxenone the compound of interest is an important synthon for the synthesis of many drugs such as anticancer, antifungal, antioxidant and other antiproliferative compounds. 3-amino-2-cyclohexenone is also used for the synthesis of heterocyclic compounds like pyridines, quinolines, acridines and indole derivatives. It give cycloaddition reactions and provide a

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convenient route to optically active products which is Diepi-pumiliotoxin C. It also has its applications as UV filter. Further study on its applications is in progress which proved it as a important future compound.

Conflict of Interest

Authors declare no conflict of interest.

References

1. Caprathe, B.W., et al., Dopamine autoreceptor agonists as potential antipsychotics. 3. 6-Propyl-4, 5, 5a, 6, 7, 8-hexahydrothiazolo [4, 5-f] quinolin-2-amine. Journal of medicinal chemistry, 1991. **34**(9): p. 2736-2746.
2. Gatta, F., et al., Synthesis of 1, 2, 3, 4-tetrahydroacridine and 5, 6, 7, 8-tetrahydroquinoline derivatives as potential acetylcholinesterase inhibitors. Heterocycles (Sendai), 1992. **34**(5): p. 991-1004.
3. Bell, I.M., et al., Development of Orally Active Oxytocin Antagonists: Studies on 1-(1-{4-[1-(2-Methyl-1-oxidopyridin-3-ylmethyl) piperidin-4-yloxy]-2-methoxybenzoyl} piperidin-4-yl)-1, 4-dihydrobenz [d][1, 3] oxazin-2-one (L-372,662) and Related Pyridines. Journal of medicinal chemistry, 1998. **41**(12): p. 2146-2163.
4. Carroll, W.A., et al., Synthesis and Structure− Activity Relationships of a Novel Series of 2, 3, 5, 6, 7, 9-Hexahydrothieno [3, 2-b] quinolin-8 (4 H)-one 1, 1-Dioxide KATP Channel Openers: Discovery of (−)-(9 S)-9-(3-Bromo-4-fluorophenyl)-2, 3, 5, 6, 7, 9-hexahydrothieno [3, 2-b] quinolin-8 (4 H)-one 1, 1-Dioxide (A-278637), a Potent KATP Opener That Selectively Inhibits Spontaneous Bladder Contractions. Journal of medicinal chemistry, 2004. **47**(12): p. 3163-3179.
5. Foster, J.E., et al., Synthesis, characterization and anticonvulsant activity of enaminones. Part 6: Synthesis of substituted vinylic benzamides as potential anticonvulsants. Bioorganic & medicinal chemistry, 1999. **7**(11): p. 2415-2425.
6. Zymalkowski, F. and J. Rimek, Synthese des Bz-Tetrahydrochinolins. Naturwissenschaften, 1960. **47**(4): p. 83-83.
7. Nitta, M., H. Soeda, and Y. Iino, On the Reaction of N-[(3-Oxo-2-cyclohexenyl) imino] triphenylphosphorane with α-Bromo Ketones and α, β-Unsaturated Ketones. Bulletin of the Chemical Society of Japan, 1990. **63**(3): p. 932-934.
8. Mulamba, T., et al., Synthesis of compounds with the novel 2, 3, 7-triazaphenalene ring system. Heterocycles, 1995. **1**(41): p. 29-36.
9. Singh, K., J. Singh, and H. Singh, Carbon transfer reactions of functionalized oxazolidines and their open chain enamine tautomers to enamine nucleophiles. A facile synthesis of substituted pyridines and ring annulated derivatives. Tetrahedron, 1998. **54**(5-6): p. 935-942.
10. Pyrko, A.N., Synthesis of pyridine derivatives by the three-component condensation of a β-dicarbonyl compound, β-enaminocarbonyl compound, and ethyl orthoformate. Chemistry of Heterocyclic Compounds, 1999. **35**(6): p. 688-694.
11. Sajiki, H., T. Ikawa, and K. Hirota, A Practical and One-Pot Procedure for the Synthesis of 3-Amino-2-cyclohexen-1-one from 3-Aminophenol. Organic process research & development, 2005. **9**(2): p. 219-220.
12. Albright, J.D. and X. Du, Synthesis of 1, 4, 5, 6-tetrahydropyrazolo [3, 4-d] pyrido [3, 2-b] azepine. Journal of Heterocyclic Chemistry, 2000. **37**(1): p. 41-46.
13. Amougay, A., J.-P. Pete, and O. Piva, Intramolecular [2+ 2] photocycloaddition of N-alkenoyl β-enaminones. Tetrahedron letters, 1992. **33**(48): p. 7347-7350.
14. Nitta, M., S. Mori, and Y. Iino, A novel route to 1-azaazulenes by the reaction of β-amino enones with activated tropones. Heterocycles (Sendai), 1991. **32**(1): p. 23-28.
15. Blue, E.D., Synthesis and Reactivity of Copper Complexes Possessing Non-dative Ligands. 2007.
16. Collet, S.C., et al., A hetero Diels–Alder approach to the synthesis of the first angucyclinone and angucycline 5-aza-analogues. Tetrahedron letters, 2004. **45**(25): p. 4911-4915.
17. Dubas-Sluyter, M.A.T., W.N. Speckamp, and H.O. Huisman, Heterocylic synthesis via 1-amino-3-oxo-1-cyclohexene. Recueil des Travaux Chimiques des Pays-Bas, 1972. **91**(2): p. 157-160.
18. Iida, H., A convenient synthesis of m-aminophenols by mercury (II) acetate oxidation of 3-amino-2-cyclohexenones. 1982.
19. Baraldi, P.G., D. Simoni, and S. Manfredini, An improved preparation of enaminones from 1, 3-diketones and ammonium acetate or amine acetates. 1983.
20. Montes, I.F. and U. Burger, The cyanide catalyzed isomerization of enol esters derived from cyclic 1, 3-diketones. Tetrahedron letters, 1996. **37**(7): p. 1007-1010.

21. Huang a, Y. and R.W. Hartmann, The Improved Preparation of 7, 8-Dihydro-Quinoline-5 (6 H)-One and 6, 7-Dihydro-5 H-1-Pyrindin-5-one. Synthetic communications, 1998. **28**(7): p. 1197-1200.
22. Lin, Y.-L., et al., SAR studies of 3-cyclopropanecarbonyloxy-2-cyclohexen-1-one as inhibitors of 4-hydroxyphenylpyruvate dioxygenase. Bioorganic & medicinal chemistry, 2002. **10**(3): p. 685-690.
23. Rudenko, D.A., S.N. Shurov, and Y.G. Stepanyan, 3-Amino-5, 5-dimethylcyclohex-2-enone in the synthesis of heterocyclic compounds. Chemistry of Heterocyclic Compounds, 2011. **47**(6): p. 661.
24. Yang, P.H., C.T. Qu, and W.Z. Wang, AcOH catalyzed three-component synthesis of spirooxindole derivatives. Research on Chemical Intermediates, 2013. **39**(2): p. 463-468.
25. Bobbitt, J.M., et al., Syntheses of indoles and carbolines via aminoacetaldehyde acetals. The Journal of Organic Chemistry, 1978. **43**(18): p. 3541-3544.
26. Bergman, J. and B. Stensland, Cyclization of Cyanoethylated Ketones as a Route to 6-Substituted Indole Derivatives. Journal of Heterocyclic Chemistry, 2014. **51**(1): p. 1-10.
27. Yang, P.H., Synthesis of 1, 3, 1′, 5′, 6′, 7′-hexahydro-3, 3′-biindolyl-2, 4′-dione derivatives by cyclization of 3-alkylideneoxindoles with enaminone. Research on Chemical Intermediates, 2014. **40**(1): p. 425-430.
28. Kovygin, Y.A., et al., Cascade recyclization of N-arylitaconimides as a new approach to the synthesis of polyfunctional octahydroquinolines. Chemistry of Heterocyclic Compounds, 2019. **55**(8): p. 748-754.
29. Shono, T., Y. Matsumura, and S. Kashimura, New practical synthesis of 5-hydroxy-3, 4-dihydrocarbostyril and 5-hydroxycarbostyril. The Journal of Organic Chemistry, 1981. **46**(18): p. 3719-3719.
30. Zymalkowski, F. and H. Rimek, Eine neue Synthese des Bz-Tetrahydrochinolins. Archiv der Pharmazie, 1961. **294**(12): p. 759-765.
31. Vereshchagin, A.N., et al., High diastereoselective amine-catalyzed Knoevenagel–Michael-cyclization–ring-opening cascade between aldehydes, 3-arylisoxazol-5 (4 H)-ones and 3-aminocyclohex-2-en-1-ones. Molecular diversity, 2018. **22**(3): p. 627-636.
32. LeBel, N.A. and B.W. Caprathe, Nitrones by heterolytic fragmentation of. gamma.-N-hydroxyamino sulfonates. Conversion of a decahydroquinoline to a perhydroazaazulene. The Journal of Organic Chemistry, 1985. **50**(20): p. 3938-3940.
33. Pyrko, A.N., Synthesis and transformations of new 1, 2, 3, 4, 5, 6, 7, 8, 9, 10-decahydroacridine-1, 8-dione derivatives. Russian Journal of Organic Chemistry, 2008. **44**(8): p. 1215-1224.
34. Ghosh, C.K., Chemistry of 4-Oxo-4H-[1] benzopyran-3-carboxaldehyde. Journal of heterocyclic chemistry, 1983. **20**(6): p. 1437-1445.
35. Sabitha, G., Aldrichim. 1996, Acta.
36. Bruno, O., et al., Synthesis and pharmacological evaluation of 2, 5-cycloamino-5H-[1] benzopyrano [4, 3-d] pyrimidines endowed with in vitro antiplatelet activity. Bioorganic & medicinal chemistry letters, 2001. **11**(11): p. 1397-1400.
37. Ryabukhin, S.V., et al., Chlorotrimethylsilane-mediated synthesis of functionalized fused pyridines: Reaction of 3-formylchromones with electron-rich aminoheterocycles. Synthesis, 2007. **2007**(12): p. 1861-1871.
38. Ruiz, V.M., et al., Studies on quinones. VII. Synthesis of some benzo [b] thiophene-4, 7-diones. Journal of Heterocyclic Chemistry, 1981. **18**(6): p. 1161-1164.
39. Valderrama, J.A., et al., Design and synthesis of angucyclinone 5-aza analogues. Synlett, 2006. **2006**(17): p. 2777-2780.
40. Volochnyuk, D.M., Pushechnikov AO. Krotko DG. Sibgatulin DA. Kovalyova SA. Tolmachev AA. Synthesis, 2003. **1531**.
41. Muylaert, K., et al., Synthesis and Early ADME Evaluation of a Novel Scaffold, Tetrahydro-6H-pyrido [3, 2-b] azepin-6-one. Synlett, 2014. **25**(10): p. 1443-1447.
42. Jössang-Yanagida, A. and C. Gansser, Tetrahydropyridoazepines and tetrahydropyridoazepinones from the corresponding dihydroquinolones. Journal of Heterocyclic Chemistry, 1978. **15**(2): p. 249-251.
43. Littell, R., G.O. Morton, and G.R. Allen, Observations on the mechanism of the nenitzescu indole synthesis. Journal of the Chemical Society D: Chemical Communications, 1969(19): p. 1144-1144.
44. Shepard, M.S. and E.M. Carreira, Enantioselective allene/enone photocycloadditions: The use of an inexpensive optically active 1, 3-disubstituted allene. Tetrahedron, 1997. **53**(48): p. 16253-16276.
45. Torii, S., T. Inokuchi, and M. Kubota, A facile synthesis of polyfunctionally substituted pyridines from ethoxycarbonylmalonaldehyde. Synthesis (Stuttgart), 1986(5): p. 400-402.
46. Rueping, M., E. Sugiono, and F.R. Schoepke, Thieme chemistry journal awardees-Where are they now? Asymmetric Brønsted acid catalyzed transfer hydrogenations. Synlett, 2010. **2010**(06): p. 852-865.

ISSN- 2394-5125 VOL 8, ISSUE 02, 2021

47. Bronner, S.M., K.B. Bahnck, and N.K. Garg, Indolynes as electrophilic indole surrogates: fundamental reactivity and synthetic applications. Organic letters, 2009. **11**(4): p. 1007-1010.
48. Bronner, S.M., A.E. Goetz, and N.K. Garg, Understanding and modulating indolyne regioselectivities. Synlett, 2011. **2011**(18): p. 2599-2604.
49. Whittock, A.L., et al., Reinvestigating the Photoprotection Properties of a Mycosporine Amino Acid Motif. Frontiers in chemistry, 2020. **8**.
50. Gholap, A.R., et al., Synthesis and evaluation of antifungal properties of a series of the novel 2-amino-5-oxo-4-phenyl-5, 6, 7, 8-tetrahydroquinoline-3-carbonitrile and its analogues. Bioorganic & medicinal chemistry, 2007. **15**(21): p. 6705-6715.
51. Chen, Y., et al., Fused-Ring Oxazolopyrrolopyridopyrimidine Systems with Gram-Negative Activity. Antibiotics, 2017. **6**(1): p. 2.
52. Sarkarzadeh, H., et al., Synthesis and antiproliferative activity evaluation of imidazole-based indeno [1, 2-b] quinoline-9, 11-dione derivatives. Archives of pharmacal research, 2013. **36**(4): p. 436-447.
53. Benchekroun-Mournir, N., D. Dugat, and J.-C. Gramain, A short Synthesis of (±) N-benzyl aspidospermiden. Tetrahedron letters, 1992. **33**(28): p. 4001-4004.
54. Amougay, A., et al., Photorearrangement of N-alkanoyl β-enaminones. Application to the synthesis of α-amino-β, γ-unsaturated acid derivatives. Tetrahedron, 1996. **52**(7): p. 2405-2420.
55. Kohmoto, S., et al., Asymmetric type-II photocyclization of acrylylureas. The Journal of Organic Chemistry, 1992. **57**(12): p. 3490-3492.
56. Ikeda, M., et al., Photochemical synthesis of spiro-β-lactams. Journal of the Chemical Society, Chemical Communications, 1984(12): p. 758-759.