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# Lewis acid catalyzed Povarov reaction of pentafulvenes and spiro[2,4]-hepta-[4,6]-diene: An efficient access to cyclopentene fused quinolines

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**ABSTRACT**
An efficient protocol for the Lewis acid catalyzed three-component aza-Diels-Alder reaction of pentafulvenes as dienophile has been developed. Cyclopentene fused tetrahydroquinolines were formed in good yields with excellent diastereoselectivities. The method was extended to spiro[2,4]hepta-4,6-diene, by which 3,4-dihydroquinoline derivatives were obtained. The aromatization of cycloadducts furnished corresponding quinoline derivatives.
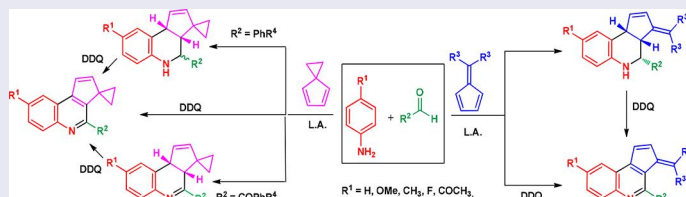
**GRAPHICAL ABSTRACT**



## Introduction

The development of highly selective methodologies affording biologically relevant molecules which are found as the privileged substructures in natural as well as synthetic pharmaceuticals is considered as one of the biggest challenges in the modern organic synthesis. Heterocycles are always counted at the top position among organic molecules owing to their abundance in nature along with their active role in many pharmaceutical leads. Among the nitrogen containing heterocycles, quinoline systems and their derivatives are observed to form the structural motif of many medicinally valuable compounds.[1,2] Berberine, sanguinarine, camptothecin, and helidonine are only some examples for fused quinoline derivatives which are known to possess anticancer, hypotensive, anti-HIV, analgesics, and anti-inflammatory activities.[2e] Besides, they have been extensively
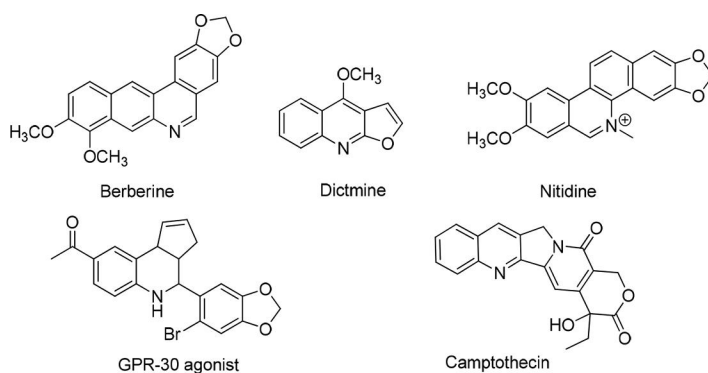
**Figure 1.** Biologically relevant quinoline derivatives.

examined for their modes of action in the inhibition of tyrosine kinases, DNA repair, and topoisomerase and tubulin polymerization (Fig. 1).[2f]

The inverse electron demand aza-Diels-Alder reaction between 2-azadienes and electronically rich olefins, known as Povarov reaction,[3] is considered as one of the most powerful and convenient route toward the synthesis of tetrahydroquinoline ring systems. Moreover, the reaction is a very useful tool, especially in its multicomponent variant,[4] for the preparation of natural products as well as biologically active agents.[4c,4d,5] Although discovered a century ago,[6] the cross-conjugated pentafulvenes, still fascinate the synthetic chemists, because of its excelling performance in the field of cycloaddition reactions by virtue of their ability to act as 2π, 4π, and 6π component.[7] Pentafulvenes engaged in [4 + 3],[8] [2 + 2],[9] [4 + 2],[10] [2 + 4],[11] [6 + 4],[12] and [6 + 2][13] cycloadditions and provided efficient approaches toward the synthesis of polycyclic systems and natural products containing cyclopentanoid ring, such as prostaglandins, β-vetinones, hinesol, capnellene, hirsutine, longifoline, viburtinal, etc.[14] Our group also extensively investigated cycloaddition profile of pentafulvenes by reacting with 3-oxidopyridinium/pyrylium betaines, which furnished the [6 + 3] and [3 + 2] products with a wide range of synthetic potential.[15] Moreover, we have successfully extended the chemistry of pentafulvenes through transition metal/Lewis acid catalyzed reactions.[16]

The Povarov reaction of cyclopentadiene as the dienophile has extensively been investigated by various groups regardless of the thermal instability of cyclopentadiene and the low yields of the product.[17] In spite of the extensive literature, there is only a sporadic report with pentafulvenes as dienophiles in Povarov reaction.[18] Hence we focused on utilizing pentafulvenes for expanding the chemical space using Povarov reaction. We undertook a detailed investigation by reacting imines generated from α-oxo aldehydes and aryl amines. Also, the biological potential of the quinoline scaffolds further prompted us to investigate this interesting cycloaddition reaction. Herein, we report an inverse electron demand aza-Diels Alder reaction of pentafulvenes with imines and the reaction was further extended to spiro-[2,4]-hepta-[4,6]-diene which ultimately afforded the ring fused tetrahydroquinoline derivatives.

## Results and discussion

We commenced our investigation by reacting the imine **1a**, generated from phenyl glyoxal monohydrate and *p*-anisidine, with diphenylfulvene **2a** in the presence of 10 mol%
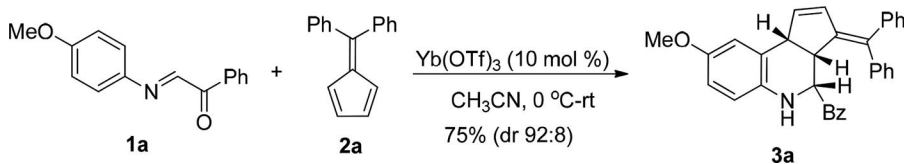
**Scheme 1.**　Reaction of aryl imine **1a** with diphenylfulvene **2a**.

Yb(OTf)$_3$ in acetonitrile at 0 °C for 12 h. The reaction afforded endo-alkylidenecyclopentene fused tetrahydroquinoline **3a** in 75% yield with a diastereomeric ratio of 92:8 (Scheme 1). The structure of the product was established using various spectroscopic techniques and finally the stereochemistry was unambiguously confirmed by single crystal X-ray analysis of compound **3b** (Fig. 2, a, CCDC No:1451008).

A detailed optimization study was performed to find the best catalyst system for the reaction. In this regard, several Brønsted and Lewis acid catalysts were screened and the results are summarized in Table 1. Among various lanthanide triflates screened, the initially used Yb(OTf)$_3$ was found to be the best catalyst for the reaction and is already proved to be an efficient catalyst for this type of reaction. BF$_3$·OEt$_2$ furnished the product in 69% yield. Brønsted acid catalyst such as TFA was also screened, but the yield was found to be lower as compared to Lewis acids. When the solvent was switched from acetonitrile to dichloromethane yield was further lowered to 52% and in the absence of catalyst, the reaction did not afford any product.

With the optimized reaction condition, we checked the viability of the reaction with different imines and fulvenes. In all cases, we obtained the product in moderate to good yields (Table 2).
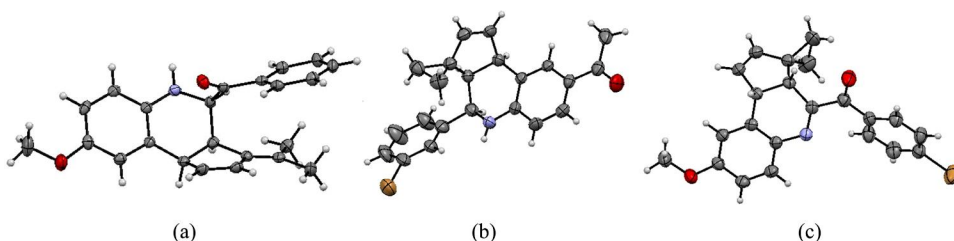


|  | (a) | | (b) | | (c) |

**Figure 2.**　ORTEP diagrams of (a) **3b**, (b) *endo*-**8b** and (c) **9e.**

**Table 1.**　Optimization studies.
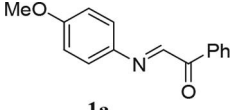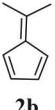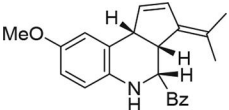
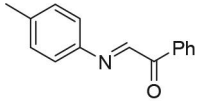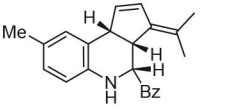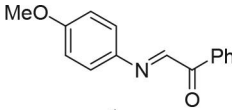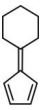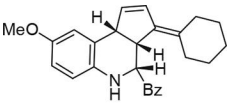| Entry | Catalyst | Solvent | Yield$^a$ (dr)$^b$ |
|---|---|---|---|
| 1 | Yb(OTf)$_3$ | CH$_3$CN | 75 (92:8) |
| 2 | Sc(OTf)$_3$ | CH$_3$CN | 58 (93:7) |
| 3 | Cu(OTf)$_2$ | CH$_3$CN | 46 (88:12) |
| 4 | BF$_3$·OEt$_2$ | CH$_2$Cl$_2$ | 69 (98:2) |
| 5 | TFA | CH$_3$CN | 31 (93:7) |
| 6 | Yb(OTf)$_3$ | CH$_2$Cl$_2$ | 52 (96:4) |
| 7 | – | CH$_3$CN | No Reaction |

Reaction conditions: imine (1.2 equiv.), fulvene (1 equiv.), catalyst (10 mol%), CH$_3$CN, 0 °C–rt, 12 h.
$^a$Isolated yield.
$^b$Determined through $^1$H NMR analysis of crude mixture.

**Table 2.** Two component Povarov reaction of pentafulvenes.

| Entry | Imine | Fulvene | Product (Yield) (dr)[a] |
|-------|-------|---------|------------------------|
| 1 | **1a** | **2b** | **3b** (55%) (91:9) |
| 2 | **1b** | **2b** | **3c** (43%) (92:8) |
| 3 | **1a** | **2c** | **3d** (64%) (90:10) |

Reaction conditions: imine (1.2 equiv.), fulvene (1 equiv.), Yb(OTf)$_3$ (10 mol%), CH$_3$CN, 0 °C–rt, 12 h.
[a]Determined through $^1$H NMR analysis of crude mixture.

Encouraged from these results, further we focused on performing out this reaction in a multicomponent one-pot fashion which was highly desirable over the multistep procedure with respect to atom-economic transformation of easily available starting materials. To our delight, we obtained comparable results when we set up a three-component reaction of *p*-anisidine **4a**, phenylglyoxal monohydrate **5a**, and diphenylfulvene **2a** under the optimized reaction conditions (Scheme 2).

The scope of the reaction was then explored with several substituted anilines and various pentafulvenes. Evaluation of the reactivity of a series of fulvenes such as dimethyl, cyclohexyl, cyclopentyl, etc., revealed that the hetero Diels–Alder reaction with imines which is generated *in situ* is effective under the optimal catalyst system. Phenyl glyoxals bearing different substituents on the phenyl ring furnished the corresponding products in good yields. After successful attempts with phenyl glyoxal, we extended the reaction using ethyl glyoxylate as aldehyde component. The structures of all the products were established by usual spectral analyses. The results obtained are summarized in Table 3.

The success in employing different fulvenes in Povarov reaction encouraged us to investigate the reaction with related substrates. This led us to choose spirocyclopropane appended cyclopentadiene, the system in which the exocyclic double bond of pentafulvene is replaced by a cyclopropane ring, as the 2π component. We initiated our studies with a three-component reaction of 2 equiv. of spiro[2,4]hepta-4,6-diene **7**, 1 equiv. of aromatic
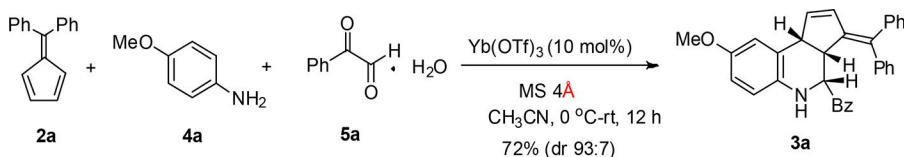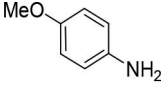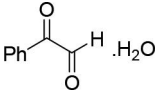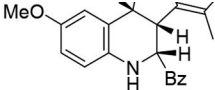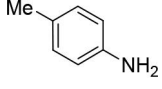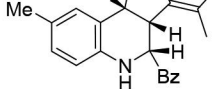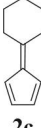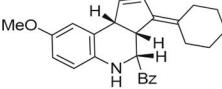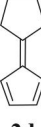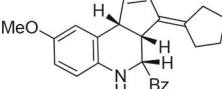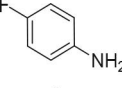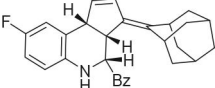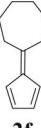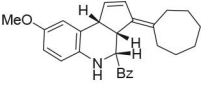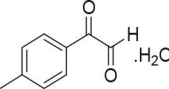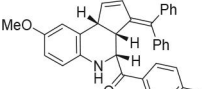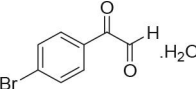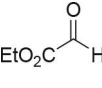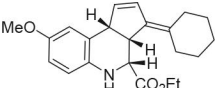


**Scheme 2.** Three-component aza-Diels Alder reaction of amine **4a**, aldehyde **5a**, and diphenylfulvene **2a**.

**Table 3.** Three-component Pavarov reaction of pentafulvenes.

| Entry | Amine | Aldehyde | Fulvene | Product (yield) (dr)[a] |
|---|---|---|---|---|
| 1 | **4a** | **5a** | **2b** | **3b (78%) (90:10)** |
| 2 | **4b** | **5a** | **2b** | **3c (52%) (89:11)** |
| 3 | **4a** | **5a** | **2c** | **3d (56%) (89:11)** |
| 4 | **4a** | **5a** | **2d** | **3e (77%) (96:4)** |
| 5 | **4c** | **5a** | **2e** | **3f (40%) (91:9)** |
| 6 | **4a** | **5a** | **2f** | **3g (45%) (90:10)** |
| 7 | **4a** | **5b** | **2a** | **3h (46%) (91:9)** |
| 8 | **4a** | **5c** | **2a** | **3i (58%) (96:4)** |
| 9 | **4a** | **5d** | **2c** | **3j (35%) (92:8)** |

Reaction conditions: amine (1.0 equiv.), aldehyde (1.0 equiv.), fulvene (1.2 equiv.), Yb(OTf)$_3$ (10 mol%), 4 Å MS, CH$_3$CN, 0 °C–rt, 12 h.
[a]Determined through $^1$H NMR analysis of crude mixture.
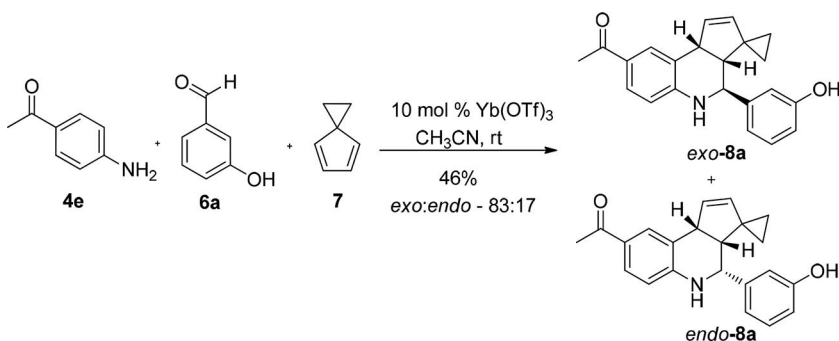
**Scheme 3.** Three-component aza-Diels Alder reaction of amine **4e**, aldehyde **6a**, and spiro[2,4]hepta-4,6-diene **7**.

amine **4e** and 1 equiv. of aromatic aldehyde **6a** in the presence of 10 mol% of Yb(OTf)$_3$ as the Lewis acid in acetonitrile at room temperature.

The reaction afforded spirocyclopentene appended tetrahydroquinoline as a mixture of *endo* and *exo* diastereomers in 46% overall yield (Scheme 3).

The best catalyst system for the reaction was found by detailed optimization studies. The results are summarized in Table 4. The best yield was obtained in the presence of 20 mol% of Sc(OTf)$_3$ in acetonitrile solvent at room temperature (Table 4, Entry 7).

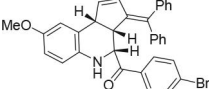With the optimal reaction condition in hand, the scope of the reaction was explored using different aromatic aldehydes and amines. Aromatic amine having electron withdrawing substituent (Table 5, Entries 1, 2) gave better yield compared to that having electron donating substituent (Table 5, Entry 3) and the results obtained are summarized in Table 5. Most of the diastereomers were separable by silica gel column chromatography. The single crystal structure of *endo*-**8b** is given in Figure 2 (b, CCDC No: 1438981). It is noteworthy that the compound **8f** is a synthetic derivative of the GPR 30 selective agonist (G-1) (Fig. 1).[5b,19]

The scope of α-oxo aldehydes in the Povarov reaction of spiro[2,4]hepta-4,6-diene was also investigated in detail. When the reaction of *p*-toluidine **4e**, phenyl glyoxal monohydrate **5a**, and spiro[2,4]hepta-4,6-diene **7** was conducted in presence of 20 mol% of Sc(OTf)$_3$ in acetonitrile at room temperature for 12 h, to our delight, 3,4-dihydroquinoline **9a** was formed in 44% yield along with tetrahydroquinoline **10a** (10%) in minor amount (Scheme 4).
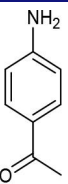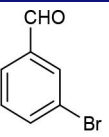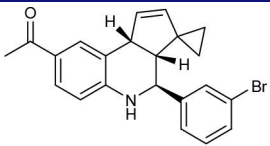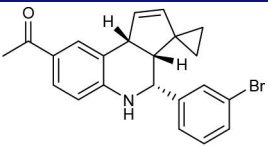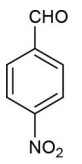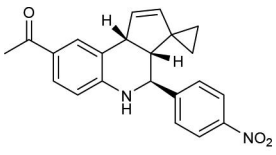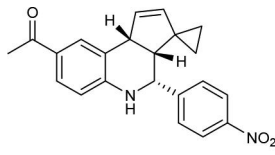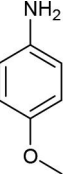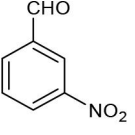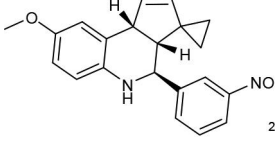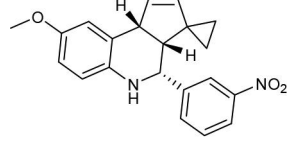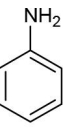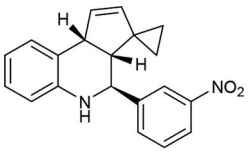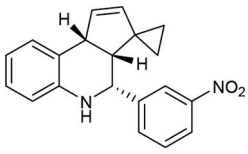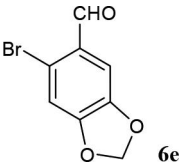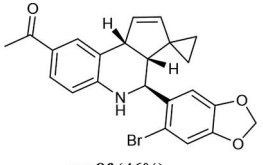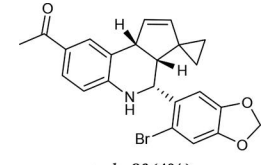
The reaction was found to be general with many aromatic aldehydes and anilines, and 3,4-dihydroquinolines were formed in good yields along with minor amounts of

**Table 4.** Optimization studies for the best reaction condition.

| Entry | LA | Equiv. of LA (mol%) | Solvent | Yield (%) |
|---|---|---|---|---|
| 1 | Yb(OTf)$_3$ | 10 | CH$_3$CN | 46 |
| 2 | Yb(OTf)$_3$ | 15 | CH$_3$CN | 50 |
| 3 | Yb(OTf)$_3$ | 20 | CH$_3$CN | 55 |
| 4 | Sc(OTf)$_3$ | 20 | DCM | 13 |
| 5 | Sc(OTf)$_3$ | 20 | MeOH | 15 |
| 6 | La(OTf)$_3$ | 20 | CH$_3$CN | 19 |
| 7 | Sc(OTf)$_3$ | 20 | CH$_3$CN | 65 |
| 8 | BF$_3$·OEt$_2$ | 20 | CH$_3$CN | 24 |

Reaction conditions: spiro[2,4]hepta-4,6-diene (2 equiv.), aldehyde (1 equiv.), amine (1 equiv.), solvent (4 mL), rt, 12 h.

**Table 5.** Reaction of spiro[2,4]hepta-4,6-diene with various aromatic aldehydes and aromatic amines.
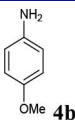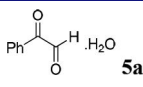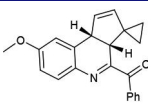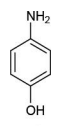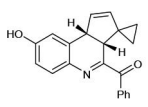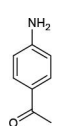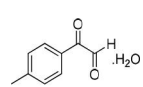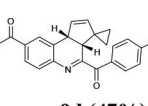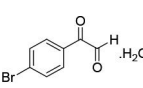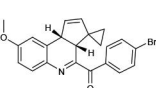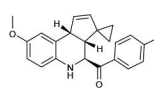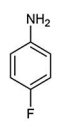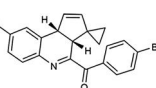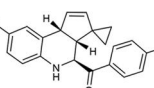
| Entry | Amine | Aldehyde | Product-yield (%) | |
|-------|-------|----------|-------------------|---|
| 1 | 4e | 6b | exo-8b (28%) | endo-8b (40%) |
| 2 | 4e | 6c | exo-8c (33%) | endo-8c (53%) |
| 3 | 4a | 6d | exo-8d (13%) | endo-8d (25%) |
| 4 | 4c | 6d | exo-8e (14%) | endo-8e (53%) |
| 5 | 4e | 6e | exo-8f (46%) | endo-8f (4%) |

Reaction conditions: spiro[2,4]hepta-4,6-diene (2 equiv.), aldehyde (1 equiv.), amine (1 equiv.), Sc(OTf)$_3$ (20 mol%), CH$_3$CN (4 mL), rt, 12 h.
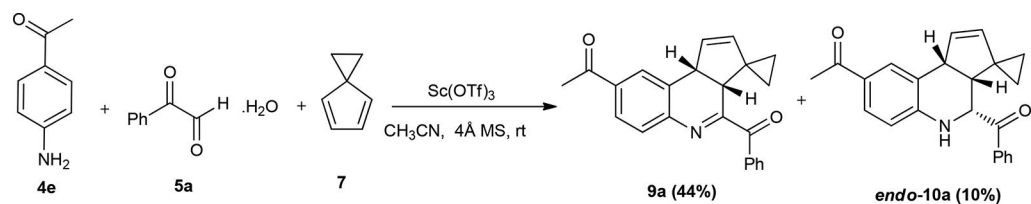


**Scheme 4.** Three-component aza-Diels Alder reaction of amine **4e**, phenyl glyoxal monohydrate **5a**, and spiro[2,4]hepta-4,6-diene **7**.

**Table 6.** Reaction of spiro[2,4]hepta-4,6-diene with α-oxo aldehydes and aromatic amines.

| Entry | Amine | α-Oxo aldehyde | Products-yield (%) | |
|---|---|---|---|---|
| | | | Dihydroquinoline | tetrahydroquinoline |
| 1 |  4b |  5a |  9b (70%) | |
| 2 |  4f | 5a |  9c (59%) | |
| 3 |  4e |  5b |  9d (47%) | |
| 4 | 4b |  5c |  9e (52%) |  *endo*-10e (14%) |
| 5 |  4c | 5c |  9f (49%) |  *endo*-10f (13%) |

Reaction conditions: spiro[2,4]hepta-4,6-diene (2 equiv.), α-oxo aldehyde (1 equiv.), amine (1 equiv.), Sc(OTf)$_3$ (20 mol%), 4 Å MS, CH$_3$CN (4 mL), rt, 12 h.

corresponding tetrahydroquinolines. The scope of the reaction was successfully extended to various substituted α-oxo aldehydes also. The results obtained are summarized in Table 6. The 3,4-dihydroquinoline structure was explicitly confirmed by the single crystal X-ray analysis of **9e** (Fig. 2c, CCDC No: 1438980).
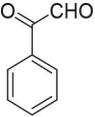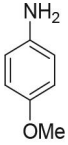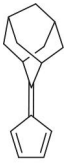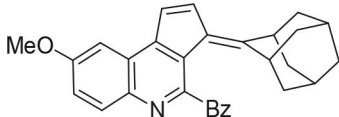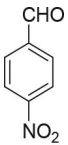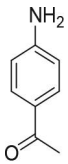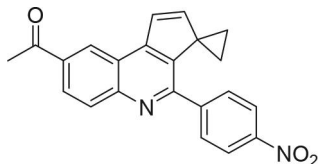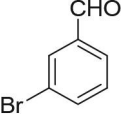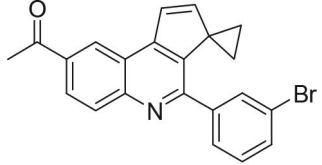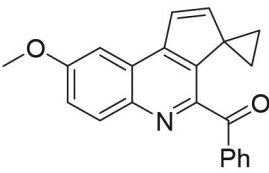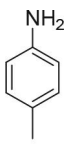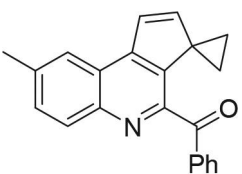
Furthermore, we synthesized quinoline derivatives by oxidation of tetrahydroquinolines and dihydroquinolines obtained through the Povarov reaction. When tetrahydroquinoline **3a** was oxidized with 2 equiv. of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in chloroform at room temperature, the quinoline **11a** was furnished in 95% yield (Scheme 5). The synthesis of quinoline was achieved in a single step by adding DDQ into the Povarov reaction condition. The reaction of pentafulvene **2a**, *p*-anisidine **4a**, and phenylglyoxal monohydrate **5a** in the
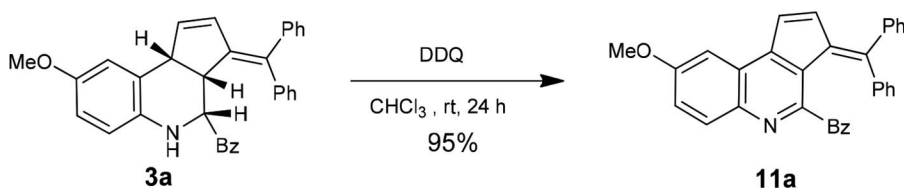


**Scheme 5.** Oxidation of tetrahydroquinoline **3a**.
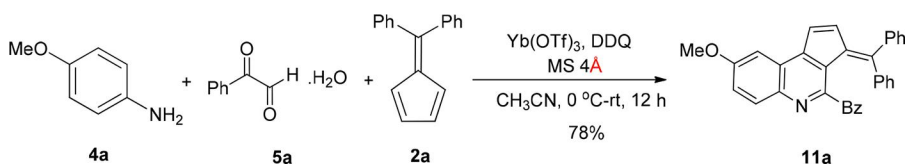
**Scheme 6.** Synthesis of quinoline **11a** from amine **4a**, aldehyde **5a**, and fulvene **2a**.

**Table 7.** Synthesis of quinoline derivative from amine, aldehyde and dienophile.

| Entry | Aldehyde | Amine | Dienophile | Product-Yield (%) |
|---|---|---|---|---|
| 1[a] | 5a | 4a | 2c | 11b (71%) |
| 2[b] | 1d | 4e | 7 | 11c (52%) |
| 3[b] | 1c | 4e | 7 | 11d (47%) |
| 4[b,c] | 5a | 4a | 7 | 11e (72%) |
| 5[b,c] | 5a | 2b | 7 | 11f (67%) |

Reaction conditions:
[a]amine (1 equiv.), aldehyde (1 equiv.), fulvene (1.2 equiv.), Yb(OTf)$_3$ (10 mol%), DDQ (2 equiv.), 4 Å MS, CH$_3$CN, 0 °C–rt, 12 h.
[b]Dienophile (2 equiv.), aldehyde (1 equiv.), amine (1 equiv.), Sc(OTf)$_3$ (20 mol%), DDQ (2 equiv.), CH$_3$CN (4 mL), rt, 12 h.
[c]4 Å MS.
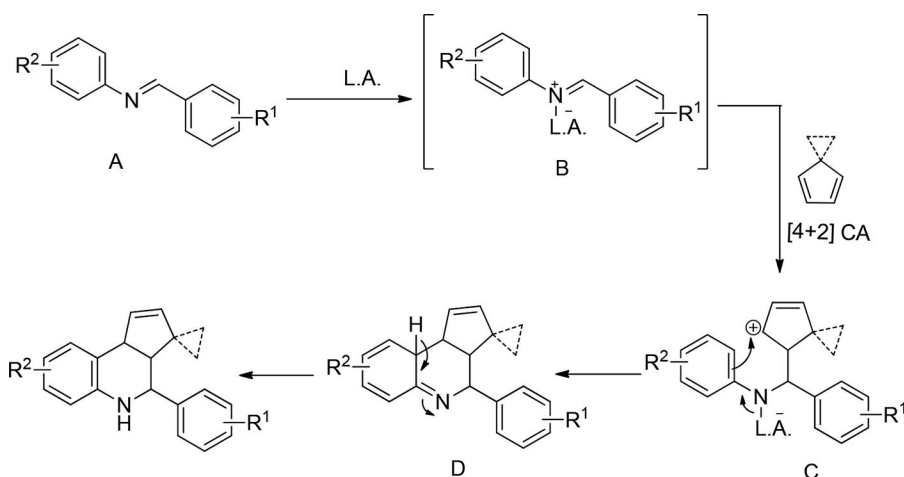
**Scheme 7.** A general mechanism involved in the synthesis of quinoline derivatives.

presence of 10 mol% Yb(OTf)$_3$ and 2 equiv. DDQ in acetonitrile at room temperature yielded 78% of the quinoline **11a** (Scheme 6). The reaction was further elaborated using spiro[2,4] hepta-4,6-diene as the dienophile to get spirocyclopentene fused quinoline derivatives (Table 7).

A general mechanism in the synthesis of quinoline derivatives is shown in Scheme 7. In the first step, Lewis acid co-ordinates to the imine nitrogen, yielding iminium intermediate B. The addition of B to the endocyclic double bond of the dienophile gives carbenium ion C. Friedel-craft-type cyclization occurs to give the intermediate D by the concurrent regeneration of Lewis acid. Further the proton transfer from D affords the tetrahydroquinoline derivative. The proton on carbon adjacent to nitrogen in tetrahydro-quinoline derived from α-oxo aldehydes is acidic due to the presence of carbonyl group. Consequently, this proton can be easily abstracted by the triflate anion from Lewis acid, providing 3,4-dihydroquinoline. Thus, 3,4-dihydroquinolines are formed in the presence of high mol% of Lewis acid.

## Conclusion

In summary, we have developed the Lewis acid-catalyzed three-component aza-Diels Alder reaction of pentafulvenes and of spiro-[2,4]-hepta-[4,6]-diene. Alkylidenecyclopentene fused tetrahydroquinolines were formed from pentafulvenes in good yields with excellent diastereoselectivities. Spiro-[2,4]-hepta-[4,6]-diene provided spirocyclopentene fused tetrahydroquinolines as well as 3,4-dihydroquinolines when reacted under different aldehydic condition. The synthetic utility is further highlighted by the synthesis of quino-line derivatives by DDQ mediated oxidation. The synthesis of quinolines was also achieved in a three-component fashion in presence of Lewis acid and oxidant. Moreover, all the compounds synthesized from spiro-[2,4]-hepta-[4,6]-diene possess a vinylcyclopropane moiety making them suitable substrates for the vinyl-cyclopropane rearrangement. Such a synthetic transformation would furnish differently functionalized quinoline derivatives and increase the synthetic importance of the synthesized molecules.

## Experimental

All reactions were performed in oven dried glass wares under inert atmosphere. All commercially available chemicals used were of the best grade and were used without further purification. All solvents used for the experiments were purified and dried according to the literature methods. Progress of the reactions was monitored by thin layer chromatography, which was performed on precoated plates (Silica gel 60 $F_{254}$, 0.25 mm, Merck) and visualized with UV light. Gravity column chromatography was performed using 100–200 mesh silica gel and appropriate mixtures of hexane-ethyl acetate were used for elution.

Melting points were determined using a Fisher Johns melting point apparatus and were uncorrected. IR spectra were recorded on Bruker FTIR spectrometer. Proton and carbon nuclear magnetic resonance spectra were recorded at 500 and 125 MHz, respectively, on a Bruker AMX 500 spectrophotometer. Chemical shifts for 1H NMR spectra were reported as δ in units of parts per million (ppm) with SiMe4 (δ 0.0) as the internal standard and relative to the signal of chloroform-*d* (δ 7.25, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (double doublet), and m (multiplet). Coupling constants are reported as *J* values in Hz. $^{13}$C NMR spectra are also reported as δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.03, triplet). Mass spectra were recorded under ESI/HRMS at 60,000 resolution using Thermo Scientific Exactive mass spectrometer.

### *Procedures*

### *General experimental procedure for two component aza-Diels Alder reaction of imine and pentafulvenes (method A)*

Yb(OTf)$_3$ (10 mol%) and imine (1.2 equiv.) were stirred in acetonitrile at 0 °C. To this reaction mixture, fulvene (50 mg, 1.0 equiv.) in acetonitrile was added and stirred at room temperature for 8 h. The solvent was evaporated *in vacuo* and the residue on silica gel (100–200 mesh) column chromatography using hexane-ethyl acetate mixtures yielded tetrahydroquinoline derivatives.

### *General experimental procedure for three-component aza-Diels Alder reaction of aromatic amine, aldehyde, and pentafulvenes (method B)*

To a suspension of 10 mol% Yb(OTf)$_3$ and 4 Å molecular sieves in dry acetonitrile was added a solution of aldehyde (50 mg, 1.0 equiv.) and aromatic amine (1.0 equiv.) in acetonitrile followed by addition of fulvene (1.2 equiv.) in acetonitrile solution at 0 °C. The reaction mixture was stirred for 8 h at room temperature. The reaction was monitored by TLC and quenched with water. The aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue on column chromatography (silica gel) using hexane-ethyl acetate mixtures yielded tetrahydroquinolines in good yields.

### *General procedure for the Lewis acid catalyzed three-component aza-Diels Alder reaction of spiro[2,4]hepta-4,6-diene*

The amine (50 mg, 1 equiv.) and aldehyde (1 equiv.) were weighed into a schlenk tube and 2 mL of acetonitrile was added (4 Å MS was also added, when monohydrates of α-oxo

aldehydes were used). Spiro[2,4]hepta-4,6-diene (2 equiv.) was added into the reaction mixture, followed by a solution of Sc(OTf)$_3$ (20 mol%) in 2 mL of acetonitrile. The reaction mixture was stirred at room temperature for 12 h. Then the solvent was removed *in vacuo* and the residue was subjected to silica gel column chromatography using hexane-ethyl acetate mixtures to afford the desired products.

### General procedure for the oxidation of tetrahydroquinolines to quinolines (method C)

The tetrahydroquinoline derivative (50 mg, 1 equiv.) was taken in a 50 mL round bottom flask and dissolved in 3 mL of chloroform. DDQ (2 equiv.) was added and stirred at room temperature for 24 h. After completion of the reaction (monitored by TLC), the solvent was removed *in vacuo*. An aqueous saturated NaHCO$_3$ solution (10 mL) was added, and the resulting mixture was extracted with CHCl$_3$ (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The reaction mixture was purified by column chromatography (hexane-ethyl acetate) to afford the desired product.

### General procedure for the one pot synthesis of quinoline derivatives of pentafulvene (method D)

The aldehyde (50 mg, 1 equiv.), amine (1 equiv.), Yb(OTf)$_3$ (10 mol%), and 4 Å molecular sieves were weighed into a Schlenk tube and 2 mL of acetonitrile was added. After cooling the reaction mixture to 0 °C, a solution of fulvene (1.2 equiv.) in 2 mL acetonitrile was added, followed by DDQ (2 equiv.). The reaction mixture was, then, stirred at room temperature for 24 h. Then the solvent was removed *in vacuo*. An aqueous saturated NaHCO$_3$ solution (10 mL) was added, and the resulting mixture was extracted with CHCl$_3$ (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The reaction mixture was purified by column chromatography (hexane-ethyl acetate) to afford the desired product.

### General procedure for the one-pot synthesis of quinoline derivatives of spiro[2,4]hepta-4,6-diene

The aldehyde (50 mg, 1 equiv.), amine (1 equiv.), and DDQ (2 equiv.) were weighed into a Schlenk tube and 2 mL of acetonitrile was added. Spiro[2,4]hepta-4,6-diene (2 equiv.) was syringed into the reaction mixture, followed by Sc(OTf)$_3$ (20 mol%) dissolved in 2 mL of acetonitrile (4 Å MS was also added, when monohydrates of α-oxo aldehydes were used). The reaction mixture was stirred at room temperature for 24 h. Then the solvent was removed *in vacuo*. An aqueous saturated NaHCO$_3$ solution (10 mL) was added, and the resulting mixture was extracted with CHCl$_3$ (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The reaction mixture was purified by column chromatography (hexane-ethyl acetate) to afford the desired product.

## Funding

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