

## Facile Synthesis of 2H-3-Chromeneimines and 3, 5-Dibenzylidene-1-Prop-2-Ynyl-Piperidin-4-Ones

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## Short Communication

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**Keywords:** Claisen-Schmidt condensation, 3,5-dibenzylidene-4-one, propargylbromide, 2H-3-chromenecarbaldehydes, aniline.**ABSTRACT**

The Claisen-Schmidt condensation of 3,5-dibenzylidene-4-one(1a-f) react with propargylbromide(2) in presence of  $K_2CO_3$  at room temperature to gave 3,5-dibenzylidene-1-prop-2-ynyl-piperidin-4-ones(3a-f), and 2H-3-chromenecarbaldehydes (4a-d) react with aniline (5a) and anhydrous  $Na_2SO_4$  to give 2H - chromene-3-(4'-phenyl) imine (6a-d) in good yields.

**INTRODUCTION**

Heterocyclic ring systems having piperidin-4-one nucleus have aroused great interest in the past and present years due to their wide range of biological activity such as anti viral, and anti microbial activity and their derivative piperidines are also biologically important and act as neurokinin receptor antagonists<sup>[1,2,3,4]</sup>. The bis (substituted benzyliden) cycloalkanones are very important precursors to potentially bioactive pyrimidine derivatives intermediates of agrochemicals, pharmaceuticals, and perfumes new organic materials for nonlinear optical applications, cytotoxic analogues and the units of liquid-crystalline polymers<sup>[5,6,7,1]</sup>. In addition these compounds undergo double 1,3-dipolar cycloaddition reaction with azomethine to give bis-spiropyrrolidines, which are often the central ring system of numerous natural products.

**EXPERIMENTAL****General Methods**

Melting points were determined on a Polmon instrument (model no. MP-96).IR spectra were recorded on Perkin-Elmer 337 spectrometer, and  $^1H$  NMR (400 MHz) and  $^{13}C$  NMR (100.6 MHz) were recorded on a Varian Gemini 200 spectrometer using TMS as internal standard (chemical shifts values were described in ppm  $\delta$ ). Mass spectra were recorded on a VG micromass LCMS 2010 instrument.

**I.General procedure for the synthesis of 3, 5 - dibenzylidene-1-prop-2-ynyl-piperidin-4-ones (3a-d)<sup>[8,9,10]</sup>.**

3,5-Dibenzylidene-piperidin-4-one (**1**) (6.87 gr,25 mmol) dissolved in acetone (25mL), propargylbromide (**2**) (4.13 gr, 35 mmol),  $K_2CO_3$  (6.9 gr, 50 mmol) was added and stirred at room temperature for 8 hours. Acetone was decanted, concentrated and then ice cold water was added. The solid obtained was separated on column chromatography with petroleum ether: ethyl acetate (9:2) to give 3,5-dibenzylidene-1-prop-2-ynyl-piperidin-4-one (**3a**).

Employing the similar procedure as mentioned **3a**, compounds **3b-f** were obtained from **1b-f**.

***i. 3,5-Dibenzylidene-1-prop-2-ynyl-piperidin-4-one(3a).***

Yield: 75%, mp: 157 °C

IR (KBr): 2900 cm<sup>-1</sup>, 2100 cm<sup>-1</sup>, 1650 cm<sup>-1</sup>.

<sup>1</sup>HNMR (400 MHz) δ 2.32(t, 1H, J=2.4Hz, -C=CH) 3.51 (d, 2H J=2.4 Hz, -CH<sub>2</sub>-C=), 3.89 (s, 4H, piperidinone ring-H), 7.38 (m, 10H, Ar-H), 7.75 (s 2H arylidene-H).

MS: m/z 314 (98) [M+H]<sup>+</sup>.

***ii. 3,5-Bis-(4-chloro-benzylidene)-1-prop-2-ynyl-piperidin-4-one(3b).***

Yield: 77%, mp, 136 °C

<sup>1</sup>HNMR (400 MHz) δ 2.51 (t, 1H, J = 2.6Hz, -C=CH), 3.53 (d 2H, J = 2.6Hz, -CH-C=), 3.84 (s, 4H, piperidinone ring-H), 7.54 (m, 8H, Ar-H), 7.60 (s, 2H, arylidene-H).

MS: m/z 382 (78) [M+H]<sup>+</sup>

***iii. 3,5-Bis-(4-methoxy-benzylidene)-1-prop-2-ynyl-piperidin-4-one (3c).***

Yield: 80%, mp: 130 °C

<sup>1</sup>HNMR (400 MHz) δ 2.67 (t, 1H, J = 2.0 Hz, -C=CH), 3.85 (d, 8H, J = 2.4 Hz, -OCH<sub>3</sub>, & -CH<sub>2</sub>-C=), 3.89 (s, 4H, piperidinone ring-H), 6.99 (d, 4H, Ar-H), 7.40 (d, 4H, Ar-H) 7.66 (s, 2H, arylidene-H).

MS: m/z 374 (89) [M+H]<sup>+</sup>.

***iv. 3,5-Bis-(4-Bromo-benzylidene)-1-prop-2-ynyl-piperidin-4-one(3d).***

Yield: 77%, mp: 136 °C

<sup>1</sup>HNMR (400 MHz) δ 2.53 (t, 1H, J = 2.6Hz, -C=CH), 3.53 (d 2H, J = 2.6Hz, -CH-C=), 3.84 (s, 4H, piperidinone ring-H), 7.38 (m, 8H, Ar-H), 7.19 (s, 2H, arylidene-H).

MS: m/z 487 (98) [M+H]<sup>+</sup>

***v. 3,5-Bis-(4-methyl-benzylidene)-1-prop-2-ynyl-piperidin-4one (3e).***

Yield: 80%, mp: 130 °C

<sup>1</sup>HNMR (400 MHz) δ 2.12 (t, 1H, J = 2.0 Hz, -C=CH), 3.25 (d, 8H, J = 2.4 Hz, -CH<sub>3</sub>), 3.89 (s, 4H, piperidinone ring-H), 6.95 (d, 4H, Ar-H), 7.01 (d, 4H, Ar-H) 7.66 (s, 2H, arylidene-H).

MS: m/z 357 (89) [M+H]<sup>+</sup>.

***vi. 3,5-Bis-(4-ethoxy-benzylidene)-1-prop-2-ynyl-piperidin-4-one (3f).***

Yield: 80%, mp: 130 °C

<sup>1</sup>HNMR (400 MHz) δ 2.67 (t, 1H, J = 2.0 Hz, -C=CH), 1.33 (d, 8H, J = 2.4 Hz, -CH<sub>3</sub>, & -CH<sub>2</sub>), 3.89 (s, 4H, piperidinone ring-H), 6.72 (d, 4H, Ar-H), 7.190 (d, 4H, Ar-H) 7.66 (s, 2H, arylidene-H).

MS: m/z 417 (100) [M+H]<sup>+</sup>.

**II. General procedure for the synthesis of 2H-3-chromeneimines (6a-d)**<sup>[11,12,13,14,15,16,17,18,19, 20]</sup>

A mixture of 2H-3-chromenecarbaldehyde (**4a**) (1.6g, 10mmol), aniline (**5a**) (1.23g, 10mmol) and anhydrous Na<sub>2</sub>SO<sub>4</sub> (3.0g) was refluxed in dry methanol (50mL) on water bath for 6 h. After completion of the reaction the solution was decanted and methanol was evaporated under reduced pressure. The crude brown colored reaction mass was subjected to column chromatography over neutral alumina and elution with pet.ether:ethyl acetate (9:1) gave 2H-chromene-3-(4'-phenyl) imine (**6a**) as a light brown solid (2.1g, 80% yield), mp 117 °C

Employing the similar procedure as mentioned **6a**, compounds **6b-d** were obtained from **4b-d**.

vii. Synthesis of 2H-chromene-3-(4'-phenyl) imine (6a)

IR (KBr): 1630cm<sup>-1</sup>(C=N) and 1578cm<sup>-1</sup>(C=C).

UV (MeOH): 334 nm (log ε 4.2), 281 nm (log ε 4.5) and 248 nm (log ε 4.3).

<sup>1</sup>H NMR (400 MHz): δ 8.13(s, CH=N), 7.01-7.18(m, H-5, 7; H-2', 6'), 6.78-6.90(m, H-4, 6, 8; H-3', 5'), 5.22(s, 2-OCH<sub>2</sub>).

<sup>13</sup>C NMR (100.6 MHz): δ 158.4(C-4'), 155.7(CH=N), 155.2(C-8a), 144.4(C-1), 132.0(C-7), 131.7(C-3), 130.8(C-5), 127.9(C-4), 122.2(C-2', 6'), 121.8(C-4a), 121.5(C-6), 116.0(C-8), 114.4(C-3', 5'), 65.0(C-2).

MS: m/z 235(M<sup>+</sup>) (100).

viii) 6-Chloro-2H-chromene-3-(4'-chlorophenyl)imine (6b)

Light yellow needles; yield 80-85%, mp 98 °C.

IR (KBr): 1629 cm<sup>-1</sup>(C=N) and 1574 cm<sup>-1</sup>(C=C).

UV (MeOH): 343 nm (log ε 4.4), 276 nm (log ε 4.3) and 241 nm (log ε 4.5).

<sup>1</sup>H NMR (400 MHz): δ 8.15(s, CHN), 7.15-7.31(m, 14-5, 7; H-2', 6'), 6.89-7.00(m, H-4, 8), 6.85(d, J=9.0Hz, H-3', 5'), 4.57(s, 2-OCH<sub>2</sub>).

<sup>13</sup>C NMR (100.6 MHz): δ 158.4(C-4'), 155.0(CH=N), 153.4(C-8a), 143.9(C-1), 132.5(C-3), 130.4(C-7), 1.30.0(C-5), 126.9(C-4), 125.9(C-4a), 122.9(C-6), 122.1(C-2', 6'), 114.117. 1 (C-8), 114.2(C-3', 5'), 65.0(C-2), 55.2(C-4-CH<sub>2</sub>).

MS: m/z 305 [M+H]<sup>+</sup>

ix) 6-Bromo-2H-chromene-3-(4'-bromophenyl) imine (6c)

Light brown needles; yield 85-87%, mp 137 °C.

IR (KBr): 1638 cm<sup>-1</sup>(C=N) and 1576 cm<sup>-1</sup> (C=C).

UV (MeOH): 355 nm (log ε 4.1) and 272 nm (log ε 4.6).

<sup>1</sup>H NMR (400 MHz): δ 8.15 (s, CH=N), 7.19-7.32(m, H-5, 7), 7.17(d, J=9.0Hz, H-2', 6'), 6.90(d, J=9.0Hz, H-3', 5'), 6.74(m, H-4, 8), 5.25(s, 2-OCH<sub>2</sub>).

<sup>13</sup>C NMR (100.6 MHz): δ 156.8(C-4'), 153.6(CH=N), 152.2(C-8a), 142.0(C-1), 137.8(C-7), 133.5(C-5), 131.3(C-3), 128.4(C-4), 122.1(C-4a), 120.8(C-2', 6'), 116.1(C-8), 112.7(C-3', 5'), 111.3(C-6), 63.2(C-2).

MS: m/z 392 [M+H].

x) 6-Methyl-2H-chromene-3-(4'-methylphenyl)imine (6d)

Yellow needles, yield 83-86%, mp 109 °C.

IR (KBr): 1635 cm<sup>-1</sup> (C=N) and 1578 cm<sup>-1</sup> (C=C).

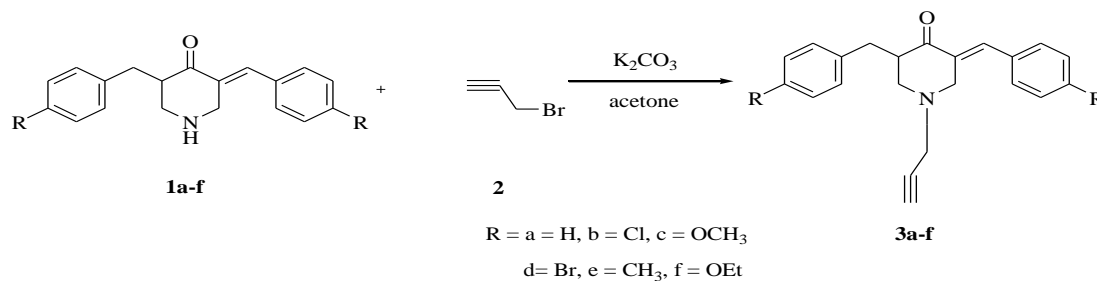
UV (MeOH): 349 nm (log ε 4.3), 266 nm (log ε 4.2) and 251 nm (log ε 4.7).

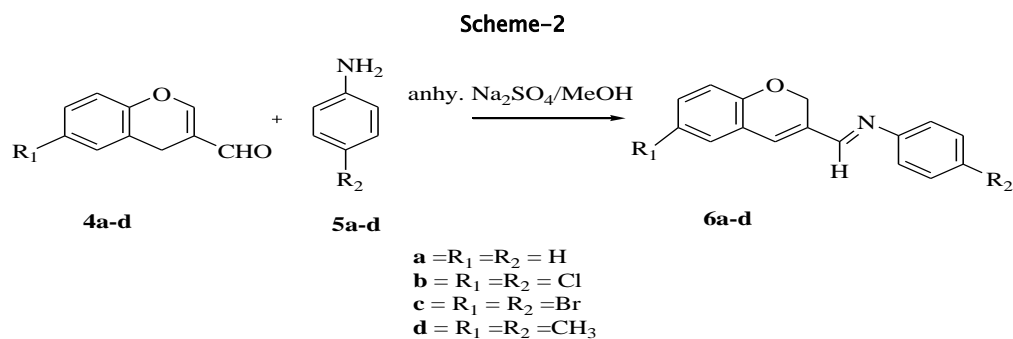
<sup>1</sup>H NMR (400 MHz): δ 8.12(s, CH=N), 7.10(d, J=9.0Hz, H-2', 6'), 6.84(d, J=9.0Hz, H-3', 5'), 6.74(s, H-4), 6.67-6.78(m, H-7, 8), 6.58(d, J=3.0Hz, H-5), 5.16(s, 2-OCH<sub>2</sub>), 2.35(s, 4'-CH<sub>3</sub>), 2.76(s, 6-CH<sub>3</sub>).

<sup>13</sup>C NMR (100.6 MHz): δ 158.5(C-4'), 155.1(CH=N), 154.2(C-6), 149.2(C-8a), 144.4(C-1'), 132.6(C-3), 132.2(C-4), 122.5(C-4a), 122.3(C-2', 6'), 116.6(C-7), 116.4(C-5), 114.4(C-3', 5'), 112.4(C-8), 65.0(C-2), 55.7(6-CH<sub>3</sub>), 55.2(4'-CH<sub>3</sub>).

MS: m/z 265(M<sup>+</sup>) (85).

Scheme-1





## RESULTS AND DISCUSSION

### Synthesis of 3, 5 -dibenzylidene-1-prop-2-ynyl-piperidin-4-ones (3a-f).

3,5-Dibenzylidene-piperidin-4-one (**1**) dissolved in acetone, propargylbromide (**2**) K<sub>2</sub>CO<sub>3</sub> was added and stirred at room temperature for 8 hours, to give 3,5-dibenzylidene-1-prop-2-ynyl-piperidin-4-one (**3a-f**). The structure of 3, 5-dibenzylidene-1-prop-2-ynyl-piperidin-4-one characterized from its spectral data. In the IR spectrum **3a**, the peak at 2900 (C-N), 1650 (C=O). The <sup>1</sup>H NMR of 3,5-dibenzylidene-1-prop-2-ynyl-piperidin-4-one was newly formed triazol ring appeared at around δ 7.60 as a singlet and phenyl protons appeared at δ 7.23-7.47 as multiplet. The N-CH<sub>2</sub> protons appeared at around δ 3.83, benzylic CH<sub>2</sub> protons appeared at around δ 5.50 as singlet.

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