Regioselective synthesis of isocoumarins by ruthenium-catalyzed aerobic oxidative cyclization of aromatic acids with alkynes

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Electronic Supplementary Information

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Experimental Section

General procedure for the oxidative cyclization of aromatic acids with alkynes catalyzed by ruthenium complex.

A 25-mL round bottom flask or a 15-mL pressure tube containing [{ $RuCl_2(p-cymene)$ }_2] (0.002 mmol, 2 mol %), AgSbF₆ (0.010 mmol, 10 mol %) and Cu(OAc)₂.H₂O (0.020mmol, 20 mol %) was evacuated and purged with nitrogen gas three times (Silver salt is moisture sensitive. Thus, the reaction mixture was purged with nitrogen gas). To the flask or tube were then added aromatic acids (1) (1.00 mmol), alkynes 2 (1.20 mmol) and 1,2-dichloroethane or *t*-BuOH (3.0 mL) via syringes and allowed the reaction mixture to stir at room temperature for 5 min. Then, the reaction mixture was allowed to stir at 100 °C for 12 h under open air (for a 15-mL pressure tube, a screw cap was used to cover the tube). After cooling to ambient temperature, the reaction mixture was diluted with CH₂Cl₂, filtered through Celite and silica gel, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexanes and ethyl acetate as eluent to give pure **3**. The reaction worked equally in the both reaction setups. For low boiling reactants (for example, alkynes **2d-e** and acids **1ij**), a 15-mL pressure tube setup is recommended in order to get more yields.

1.5 mmol of 2-methylacrylic acid (1i) was used for the reaction with an alkyne 2a (1.0 mmol). Yield was calculated based on 2a.

Similarly, 2.0 mmol of acrylic acid **1j** was used for the reaction with an alkyne **2c** (1.0 mmol).

Spectral data and copies of ¹H and ¹³C NMR spectra of all compounds **3a-u** are listed below (pages 7 - 53).

Mechanistic investigations:

The observed results for the mechanistic investigations of the present reaction were shown below.

a) To isolate a key five-membered metallacycle intermediate **5** (see the manuscript, Scheme 3), the reaction of 4-bromobenzoic acid (1.0 equiv), $[{RuCl_2(p-cymene)}_2]$ (1.0 equiv), AgSbF₆ (4.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) in 1,2-dichloroethane at 100 °C for 12 h was carried out. In the reaction, the expected five-membered metallacycle intermediate **5** cannot be isolated. However, a different type of intermediate **A** was isolated in the reaction mixture (complex **A** is highly stable at room temperature as well as under open atmosphere). The structure of intermediate **A** was determined by a single crystal X-ray diffraction (eq 1).



In order to get the key intermediate 5, the ratio of 4-bromobenzoic acid has been changed as:

i) 4-bromobenzoic acid (**1.0 equiv**), $[{RuCl_2(p-cymene)}_2]$ (1.0 equiv), AgSbF₆ (4.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) in 1,2-dichloroethane at 100 °C for 12 h.

ii) 4-bromobenzoic acid (**2.0 equiv**), [{ $RuCl_2(p-cymene)$ }₂] (1.0 equiv), AgSbF₆ (4.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) in 1,2-dichloroethane at 100 °C for 12 h.

iii) 4-bromobenzoic acid (**10.0 equiv**), [{ $RuCl_2(p-cymene)$ }₂] (1.0 equiv), AgSbF₆ (4.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) in 1,2-dichloroethane at 100 °C for 12 h.

In all these conditions, only intermediate **A** was observed. Again, the structure of intermediate **A** was determined by a single crystal X-ray diffraction. The expected key intermediate **5** was not observed in these reactions. Complex **A** was also isolated without $Cu(OAc)_2.H_2O$ under similar reaction conditions.

b) Next, the observed complex **A** was further treated with 1-phenyl-1-propyne (**2a**) (1.2 equiv), AgSbF₆ (2.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) in 1,2-dichloroethane at 100 °C for 12 h. Again, the expected key intermediate **5** cannot be isolated. But, the cyclization product **3a** was observed exclusively in 95% yield. The reaction of complex **A** with 1-phenyl-1-propyne (**2a**) (1.2 equiv) was also tried without AgSbF₆ under similar reaction conditions. In the reaction also, the expected cyclization product **3a** was observed in 92% yield.

We have tried several times to isolate intermediate 5; unfortunately, we were not able to isolate it.

Based on these observations, we concluded that a five-membered metallacycle intermediate 5 was formed during the reaction in the presence of alkyne 2 and further undergo cyclization reaction rapidly with alkyne to give the cyclization product 3. It seems that intermediate 5 is highly reactive species and difficult to isolate under our reaction conditions. But, the reaction of 1-phenyl-1-propyne (2a) with complex A clearly revealed that complex A is one of the intermediate of the present reaction.

Procedure for the preparation of ruthenium complex A

A 15-mL pressure tube containing [{RuCl₂(p-cymene)}₂] (0.100 mg, 1.0 equiv), AgSbF₆ (4.0 equiv) and Cu(OAc)₂.H₂O (2.0 equiv) and 4-bromobenzoic acid (1.0 or 2.0 or 4.0 equiv) was evacuated and purged with nitrogen gas three times. Then, 1,2-dichloroethane (4.0 mL) was added via syringe to the tube and allowed the reaction mixture to stir at 100 °C for 12 h. After cooling to ambient temperature, the mixture was filtered through a short Celite pad and the Celite pad was washed with MeOH several times and the filtrate was concentrated by vacuum. Recrystallization from EtOAc/MeOH (9:1) gave single crystals suitable for X-ray analysis.



Table 1. Crystal data and structure refinement for RK 1.

Identification code	RK1
Empirical formula	$C_{27}H_{32}BrCl_2F_6O_2Ru_2Sb$
Formula weight	977.23
Temperature	200(2) K
Wavelength	0.71073 A
Crystal system	Orthorhombic
space group	Pnma

Unit cell dimensions $a = 12.7425(16) \text{ A}$ alpha = 90 deg.	
b = 23.711(3) A beta = 90 deg.	
c = 10.2862(13) A gamma = 90 deg.	
Volume 3107.8(7) A^3	
Z, Calculated density 4, 2.089 Mg/m ³	
Absorption coefficient 3.341 mm^-1	
F(000) 1888	
Crystal size 0.3 x 0.2 x 0.2 mm3	
Theta range for data collection 1.72 to 28.34 deg.	
Limiting indices -16<=h<=17, -31<=k<=31, -13<=l<=13	
Reflections collected / unique $28307 / 3962 [R(int) = 0.0704]$	
Completeness to theta = 28.34 99.9 %	
Refinement method Full-matrix least-squares on F ²	
Data / restraints / parameters 3962 / 0 / 199	
Goodness-of-fit on F^2 0.571	
Final R indices [I>2sigma(I)] R1 = 0.0373, wR2 = 0.0994	
R indices (all data) $R1 = 0.0701, wR2 = 0.1446$	
Largest diff. peak and hole 0.694 and -1.532 e.A^-3	

Spectral data of compounds 3a-u

6-Bromo-4-methyl-3-phenyl-1*H*-isochromen-1-one (3a).



Colorless solid; mp 130-132 °C; eluent (5% ethyl acetate in hexanes); 90% yield (0.282 gm).

IR (ATR) \tilde{v} (cm⁻¹): 3020, 2915, 1710, 1593, 1476 and 1214.

¹H NMR (CDCl₃, 400 MHz): δ 8.20 (d, *J*= 8.0 Hz, 1 H), 7.77 (s, 1 H), 7.64 (dd, *J*= 8.0, 4.0 Hz, 1 H), 7.56 – 7.53 (m, 2 H), 7.47 – 7.42 (s, 3 H), 2.27 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.9, 152.5, 140.5, 132.9, 131.5, 131.3, 130.6, 129.8, 129.6, 128.5, 126.5, 119.6, 108.4, 13.7.

HRMS (ESI): calc. for [(C₁₆H₁₁O₂Br)H] (M+H) 315.0020, measured 315.0034.

6-Chloro-4-methyl-3-phenyl-1*H*-isochromen-1-one (3b).



Colorless solid; mp 119-121 °C; eluent (5% ethyl acetate in hexanes); 86% yield (0.232 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 3033, 2925, 1699, 1610, 1593, 1174 and 1096.

¹H NMR (CDCl₃, 400 MHz): δ 8.23 (d, *J*= 8.0 Hz, 1 H), 7.54 – 7.50 (m, 3 H), 7.44 – 7.38 (m, 4 H), 2.22 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.8, 152.6, 141.8, 140.4, 132.9, 131.5, 129.7, 129.6, 128.5, 123.4, 119.2, 108.5, 13.7.

HRMS (ESI): calc. for [(C₁₆H₁₁O₂Cl)H] (M+H) 271.0525, measured 271.0532.

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6-Iodo-4-methyl-3-phenyl-1*H*-isochromen-1-one (3c).



Colorless solid; mp 163-165 °C; eluent (5% ethyl acetate in hexanes); 92% yield (0.332 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 3013, 2922, 1720, 1602, 1586, 1475, 1214 and 1096.

¹H NMR (CDCl₃, 400 MHz): δ 8.03 (d, *J*= 8.0 Hz, 1 H), 7.99 (s, 1 H), 7.87 (dd, *J*= 8.0, 4.0 Hz, 1 H), 7.57 – 7.54 (m, 2 H), 7.47 – 7.43 (s, 3 H), 2.26 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.2, 152.4, 140.2, 137.2, 133.0, 132.8, 131.1, 129.7, 129.6, 128.4, 120.1, 103.6, 95.6, 13.7.

HRMS (ESI): calc. for [(C₁₆H₁₁O₂I)H] (M+H) 362.9882, measured 362.9867.

6-Acetyl-4-methyl-3-phenyl-1*H*-isochromen-1-one (3d).



Colorless solid; mp 131-133 °C; eluent (8% ethyl acetate in hexanes); 81% yield (0.225 gm).

IR (ATR) \tilde{v} (cm⁻¹): 2925, 1740, 1695, 1605, 1593 and 1174.

¹H NMR (CDCl₃, 400 MHz): δ 7.75 (dd, *J*= 8.0, 4.0 Hz, 1 H), 7.62 (d, *J*= 4.0 Hz, 1 H), 7.51 – 7.49 (m, 2 H), 7.41 – 7.37 (m, 3 H), 7.23 (dd, *J*= 8.0, 4.0 Hz, 1 H), 2.52 (s, 3 H), 2.25 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 204.6, 161.1, 151.9, 145.9, 139.6, 134.9, 132.9, 129.7, 129.6, 128.4, 124.8, 124.3, 116.9, 109.8, 31.3, 13.8.

HRMS (ESI): calc. for [(C₁₈H₁₄O₃)H] (M+H) 279.1021, measured 279.1018.

6-Methoxy-4-methyl-3-phenyl-1*H*-isochromen-1-one (3e).



Colorless solid; mp 127-129 °C; eluent (8% ethyl acetate in hexanes); 93% yield (0.247 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 3003, 2932, 1708, 1602, 1488, 1362, 1230 and 1139.

¹H NMR (CDCl₃, 400 MHz): δ 8.23 (d, *J*= 8.0 Hz, 1 H), 7.52 – 7.49 (m, 2 H), 7.40 – 7.36 (m, 3 H), 7.01 (dd, *J*= 8.0, 4.0 Hz, 1 H), 6.92(s, 1 H), 3.88 (s, 3 H), 2.20 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 164.9, 162.4, 152.9, 141.2, 133.4, 132.2, 129.6, 129.4, 128.3, 115.4, 114.0, 109.6, 106.7, 55.8, 13.8.

HRMS (ESI): calc. for [(C₁₇H₁₄O₃)H] (M+H) 267.1021, measured 267.1018.

4-Methyl-3-phenyl-1*H*-isochromen-1-one (3f).



Colorless Semi solid; eluent (5% ethyl acetate in hexanes); 75% yield (0.117 gm).

IR (ATR) \tilde{v} (cm⁻¹): 2922, 1690, 1634, 1605, 1486 and 1317.

¹H NMR (CDCl₃, 400 MHz): δ 8.36 (d, *J*= 8.0 Hz, 1 H), 7.78 (t, *J*= 8.0 Hz, 1 H), 7.62 (d, *J*= 8.0 Hz, 1 H), 7.59 – 7.52 (m, 2 H), 7.53 (t, *J*= 8.0 Hz, 1 H), 7.48 – 7.41 (m, 3 H), 2.20 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.7, 151.3, 138.4, 134.9, 133.3, 129.8, 129.6, 129.4, 128.5, 128.0, 123.5, 120.9, 109.3, 13.7.

HRMS (ESI): calc. for [(C₁₆H₁₂O₂)H] (M+H) 237.0915, measured 237.0924.

6-Bromo-4-ethyl-3-phenyl-1*H*-isochromen-1-one (3g).



Colorless solid; mp 129-131 °C; eluent (5% ethyl acetate in hexanes); 87% yield (0.285 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2987, 1710, 1593, 1476, 1214.

¹H NMR (CDCl₃, 400 MHz): δ 8.16 (d, *J*= 12.0 Hz, 1 H), 7.72 (s, 1 H), 7.58 (d, *J*= 8.0 Hz, 1 H), 7.49 – 7.47 (m, 2 H), 7.41 – 7.39 (s, 3 H), 2.62 (q, *J*= 8.0 Hz, 2 H), 1.21 (t, *J*= 8.0 Hz, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.9, 152.7, 139.4, 133.1, 131.7, 131.3, 130.5, 129.8, 128.9, 128.5, 126.5, 120.1, 114.5, 20.2, 14.7.

HRMS (ESI): calc. for [(C₁₇H₁₃O₂Br)Na] (M+Na) 350.9996, measured 350.9981.

4-Methyl-3-phenylpyrano[4,3-b]indol-1(5H)-one (3h).



Colorless solid; mp 279-281 °C; eluent (30% ethyl acetate in hexanes); 56% yield (0.154 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 3359, 2947, 1690, 1567, 1477, 1360 and 1078.

¹H NMR (CDCl₃, 400 MHz): δ 7.66 (d, *J*= 8.0 Hz, 1 H), 7.46 – 7.36 (m, 5 H), 7.28 (dd, *J*= 8.0, 4.0 Hz, 2 H), 7.13 (t, *J*= 8.0 Hz, 1 H), 2.26 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 158.1, 152.5, 145.6, 135.8, 132.3, 128.9, 128.6, 127.8, 127.5, 127.4, 126.0, 123.7, 121.5, 120.7, 119.5, 13.9.

HRMS (ESI): calc. for [(C₁₈H₁₃NO₂)H] (M+H) 276.1024, measured 276.1037.

4-Methyl-5-phenyl-7*H*-thieno[2,3-*c*]pyran-7-one (3i).



Colorless solid; mp 93-95 °C; eluent (8% ethyl acetate in hexanes); 80% yield (0.193 gm).

IR (ATR) \tilde{V} (cm⁻¹): 2988, 1685, 1522, 1427, 1281, 1043.

¹H NMR (CDCl₃, 400 MHz): δ 7.78 (d, *J*= 4.0 Hz, 1 H), 7.51 – 7.48 (m, 2 H), 7.38 – 7.33 (m, 3 H), 7.20 (d, *J*= 4.0 Hz, 1 H), 2.29 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 158.8, 153.3, 150.0, 135.0, 132.6, 129.3, 128.4, 128.2, 123.8, 123.0, 109.0, 14.6.

HRMS (ESI): calc. for [(C₁₄H₁₀O₂S)H] (M+H) 243.0479, measured 243.0489.

3,5-Dimethyl-6-phenyl-2*H*-pyran-2-one (3j).



Colorless oil; eluent (5% ethyl acetate in hexanes); 78% yield (0.156 gm).

IR (ATR) \tilde{v} (cm⁻¹): 2987, 1685, 1577, 1425, 1320 and 1178.

¹H NMR (CDCl₃, 400 MHz): δ 7.50 – 7.48 (m, 2 H), 7.38 – 7.33 (m, 3 H), 7.04 (s, 1 H), 2.07 (s, 6 H).

¹³C NMR (CDCl₃, 100 MHz): δ 163.7, 155.0, 144.9, 132.7, 129.5, 128.7, 128.4, 123.9, 111.5, 16.8, 16.5.

HRMS (ESI): calc. for [(C₁₃H₁₂O₂)H] (M+H) 201.0915, measured 201.0918.

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6-Chloro-3,4-diphenyl-1*H*-isochromen-1-one (3k).



Colorless solid; mp 168-170 °C; eluent (5% ethyl acetate in hexanes); 71% yield (0.228 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2937, 1701, 1573 and 1134.

¹H NMR (CDCl₃, 400 MHz): δ 8.26 (d, *J*= 8.0 Hz, 1 H), 7.40 (d, *J*= 8.0, 4.0 Hz, 1 H), 7.37 – 7.35 (m, 3 H), 7.25 (s, 1 H), 7.23 (d, *J*= 8.0 Hz, 1 H), 7.18 – 7.16 (m, 2 H), 7.14 – 7.12 (m, 2 H), 7.10 (t, *J*= 8.0 Hz, 1 H), 7.08 (d, *J*= 4.0 Hz, 1 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.6, 152.3, 141.7, 140.5, 133.7, 132.6, 131.3, 131.2, 129.4, 129.3, 129.2, 128.7, 128.6, 128.0, 125.0, 118.8, 116.2.

HRMS (ESI): calc. for [(C₂₁H₁₃O₂Cl)H] (M+H) 333.0682, measured 333.0682.

6-Acetyl-3,4-diphenyl-1*H*-isochromen-1-one (3l).



Colorless solid; mp 175-177 °C; eluent (8% ethyl acetate in hexanes); 66% yield (0.224 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2940, 1735, 1688, 1609 and 1154.

¹H NMR (CDCl₃, 400 MHz): δ 7.58 (dd, *J*= 8.0, 4.0 Hz, 1 H), 7.37 – 7.35 (m, 2 H), 7.26 – 7.21 (m, 3 H), 7.19 – 7.16 (m, 4 H), 7.15 – 7.10 (m, 3 H), 2.58 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 204.6, 160.9, 145.7, 134.8, 132.5, 131.3, 129.4, 129.3, 129.2, 129.1, 129.0, 128.6, 128.4, 128.3, 128.0, 126.3, 125.0, 116.8, 31.4.

HRMS (ESI): calc. for [(C₂₃H₁₆O₃)H] (M+H) 341.1177, measured 341.1180.

6-Methoxy-3,4-diphenyl-1*H*-isochromen-1-one (3m).



Colorless solid; mp 170-173 °C; eluent (8% ethyl acetate in hexanes); 72% yield (0.236 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2922, 2850, 1715, 1599, 1487, 1364, 1230 and 1072.

¹H NMR (CDCl₃, 400 MHz): δ 8.27 (d, *J*= 8.0 Hz, 1 H), 7.35 – 7.31 (m, 3 H), 7.25 (dd, *J*= 8.0, 4.0 Hz, 2 H), 7.19 – 7.15 (m, 3 H), 7.14 – 7.09 (m, 2 H), 7.00 (dd, *J*= 8.0, 4.0 Hz, 1 H), 6.50 (d, *J*= 4.0 Hz, 1 H), 3.69 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 164.7, 162.1, 151.6, 141.3, 133.1, 132.0, 131.3, 129.3, 129.2, 129.1, 129.0, 128.2, 127.9, 116.9, 115.7, 113.8, 108.6, 55.6.

HRMS (ESI): calc. for [(C₂₂H₁₆O₃)H] (M+H) 329.1177, measured 329.1180.

4,5-Diphenyl-7*H*-thieno[2,3-*c*]pyran-7-one (3n).



Colorless solid; mp 165-167 °C; eluent (8% ethyl acetate in hexanes); 70% yield (0.212 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2922, 2850, 1707, 1576, 1424, 1405 and 1076.

¹H NMR (CDCl₃, 400 MHz): δ 7.69 (d, *J*= 4.0 Hz, 1 H), 7.33 – 7.30 (m, 3 H), 7.29 (t, *J*= 8.0 Hz, 1 H), 7.27 (d, *J*= 4.0 Hz, 1 H), 7.21 – 7.19 (m, 2 H), 7.17 (t, *J*= 8.0 Hz, 1 H), 7.15 – 7.11 (m, 2 H), 6.88 (d, *J*= 4.0 Hz, 1 H).

¹³C NMR (CDCl₃, 100 MHz): δ 158.3, 153.5, 149.6, 136.4, 134.9, 132.4, 130.4, 129.4, 129.3, 129.2, 128.3, 128.1, 125.3, 122.9, 115.9.

HRMS (ESI): calc. for [(C₁₉H₁₂O₂S)H] (M+H) 305.0636, measured 305.0648.

5,6-Diphenyl-2*H*-pyran-2-one (30).



Colorless solid; mp 83-85 °C; eluent (5% ethyl acetate in hexanes); 85% yield (0.210 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2966, 1692, 1579, 1415 and 1167.

¹H NMR (CDCl₃, 400 MHz): δ 7.40 (d, *J*= 12.0 Hz, 1 H), 7.30 – 7.28 (m, 2 H), 7.27 – 7.23 (m, 4 H), 7.19 – 7.15 (m, 2 H), 7.10 (dd, *J*= 8.0, 4.0 Hz, 2 H), 6.31 (d, *J*= 8.0 Hz, 1 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.3, 154.5, 147.9, 136.3, 132.2, 130.1, 129.3, 129.2, 129.1, 128.3, 128.0, 117.8, 114.1.

HRMS (ESI): calc. for [(C₁₇H₁₂O₂)H] (M+H) 249.0915, measured 249.0927.

6-Chloro-3,4-diethyl-1*H*-isochromen-1-one (3p).



Colorless solid; mp 82-84 °C; eluent (5% ethyl acetate in hexanes); 87% yield (0.205 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2973, 1705, 1563, 1433 and 1147.

¹H NMR (CDCl₃, 400 MHz): δ 8.16 (d, *J*= 8.0 Hz, 1 H), 7.42 (s, 1 H), 7.32 (dd, *J*= 8.0, 4.0 Hz, 1 H), 2.57 – 2.51 (m, 4 H), 1.21 (d, *J*= 8.0 Hz, 3 H), 1.12 (d, *J*= 8.0 Hz, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.2, 156.5, 141.6, 139.4, 131.7, 127.6, 122.4, 112.5, 24.3, 19.4, 14.3, 12.5.

HRMS (ESI): calc. for [(C₁₃H₁₃O₂Cl)H] (M+H) 237.0682, measured 237.0690.

3,4-Diphenyl-1*H***-benzo**[*h*]**isochromen-1-one** (**3q**).



Colorless solid; mp 182-184 °C; eluent (5% ethyl acetate in hexanes); 54% yield (0.187 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2989, 1709, 1592, 1453, 1290, 1108.

¹H NMR (CDCl₃, 400 MHz): δ 9.85 (d, *J*= 8.0 Hz, 1 H), 8.00 (d, *J*= 8.0 Hz, 1 H), 7.88 (d, *J*= 8.0 Hz, 1 H), 7.79 (d, *J*= 8.0 Hz, 1 H), 7.63 (d, *J*= 8.0 Hz, 1 H), 7.45 – 7.42 (m, 3 H), 7.37 (d, *J*= 8.0 Hz, 2 H), 7.30 – 7.28 (m, 2 H), 7.26 – 7.18 (m, 4 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.3, 152.6, 141.1, 135.8, 134.7, 132.8, 132.7, 131.5, 131.4, 129.3, 129.2, 129.1, 129.0, 128.5, 128.2, 127.8, 127.1, 122.8, 117.3, 114.0.

HRMS (ESI): calc. for [(C₂₅H₁₆O₂)H] (M+H) 349.1228, measured 349.1236.

3,4-Dimethyl-1*H*-benzo[*h*]isochromen-1-one (3r).



Colorless solid; mp 127-129 °C; eluent (5% ethyl acetate in hexanes); 88% yield (0.197 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2924, 1697, 1592, 1508 and 1297.

¹H NMR (CDCl₃, 400 MHz): δ 9.76 (d, *J*= 8.0 Hz, 1 H), 8.11 (d, *J*= 8.0 Hz, 1 H), 7.88 (t, *J*= 8.0 Hz, 1 H), 7.73 (d, *J*= 8.0 Hz, 1 H), 7.58 – 7.51 (m, 2 H), 2.37 (s, 3 H), 2.33 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.3, 152.2, 141.1, 134.7, 134.0, 132.2, 131.9, 131.7, 129.4, 128.8, 128.5, 126.4, 120.3, 17.7, 13.0.

HRMS (ESI): calc. for [(C₁₅H₁₂O₂)H] (M+H) 225.0916, measured 225.0923.

8,9-Dimethyl-6*H*-[1,3]dioxolo[4,5-*f*]isochromen-6-one (3s).



Colorless solid; mp 88-90 °C; eluent (10% ethyl acetate in hexanes); 93% yield (0.202 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 3020, 1709, 1626, 1450, 1288, 1214 and 1051.

¹H NMR (CDCl₃, 400 MHz): δ 7.87 (d, *J*= 8.0 Hz, 1 H), 6.87 (d, *J*= 8.0 Hz, 1 H), 6.03 (s, 2 H), 2.19 (s, 3 H), 2.17 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.2, 152.7, 149.9, 141.9, 126.1, 122.9, 115.4, 108.8, 105.8, 101.9, 17.0, 14.0.

HRMS (ESI): calc. for [(C₁₂H₁₀O₄)H] (M+H) 219.0657, measured 219.0668.

9-Methyl-8-phenyl-6*H*-[1,3]dioxolo[4,5-*f*]isochromen-6-one (3t).



Colorless solid; mp 170-174 °C; eluent (10% ethyl acetate in hexanes); 87% yield (0.243 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2964, 2917, 2855, 1714, 1620, 1577, 1497, 1455, 1361 and 1267.

¹H NMR (CDCl₃, 400 MHz): δ 7.94 (d, *J*= 8.0 Hz, 1 H), 7.51 – 7.48 (m, 2 H), 7.39 – 7.35 (m, 3 H), 6.95 (d, *J*= 12.0 Hz, 1 H), 6.07 (s, 2 H), 2.31 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 161.9, 152.9, 150.7, 142.9, 133.1, 129.6, 129.4, 128.3, 126.2, 123.1, 115.0, 109.5, 107.4, 102.1, 15.7.

HRMS (ESI): calc. for [(C₁₇H₁₂O₄)H] (M+H) 281.0813, measured 281.0821.

8-Methyl-7-phenyl-5*H*-[1,3]dioxolo[4,5-g]isochromen-5-one (3t').



Colorless solid; eluent (10% ethyl acetate in hexanes); 4% yield (0.112 gm).

¹H NMR (CDCl₃, 400 MHz): δ 7.65 (s, 1 H), 7.51 – 7.49 (m, 2 H), 7.39 – 7.36 (m, 3 H), 6.95 (s, 1 H), 6.07 (s, 2 H), 2.20 (s, 3 H).

6,7-Dimethoxy-4-methyl-3-phenyl-1*H*-isochromen-1-one (3u).



Colorless solid; mp 177-179 °C; eluent (10% ethyl acetate in hexanes); 88% yield (0.264 gm).

IR (**ATR**) \tilde{v} (cm⁻¹): 2938, 2868, 1706, 1607, 1508, 1464, 1391, 1266 and 1228.

¹H NMR (CDCl₃, 400 MHz): δ 7.73 (s, 1 H), 7.55 (dd, *J*= 8.0, 4.0 Hz, 2 H), 7.46 – 7.40 (m, 3 H), 6.94 (s, 1 H), 4.02 (s, 3 H), 3.99 (s, 3 H), 2.29 (s, 3 H).

¹³C NMR (CDCl₃, 100 MHz): δ 162.9, 155.1, 149.5, 134.6, 133.5, 129.6, 129.2, 128.3, 115.0, 114.1, 109.8, 108.9, 104.3, 56.4, 56.3, 13.9.

HRMS (ESI): calc. for [(C₁₈H₁₆O₄)H] (M+H) 297.1126, measured 297.1128.

5,6-Dimethoxy-4-methyl-3-phenyl-1*H*-isochromen-1-one (3u').



Colorless solid; eluent (10% ethyl acetate in hexanes); 2% yield (0.059 gm).

¹H NMR (CDCl₃, 400 MHz): δ 8.18 (d, *J*= 8.0 Hz, 1 H), 7.55 (dd, *J*= 8.0, 4.0 Hz, 2 H), 7.45 – 7.41 (m, 3 H), 7.12 (d, *J*= 8.0 Hz, 1 H), 3.99 (s, 3 H), 3.85 (s, 3 H), 2.43 (s, 3 H).



NOESY experiments spectra of compound 3a.



























DEPT (135) NMR Spectrum of Compound 3c.







DEPT (135) NMR Spectrum of Compound 3d.





















¹H and ¹³C NMR Spectra of Compound **3h.**

































DEPT (135) NMR Spectrum of Compound 3m.



¹H and ¹³C NMR Spectra of Compound **3n.**

















¹H and ¹³C NMR Spectra of Compound **3q.**



























¹H NMR Spectrum of Compound **3u'.**





