ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis of Substituted 2-styryl chromones from 7-hydroxy-2-styrylchromones

C Srinivas Rao, K Naresh, C Jyotsna, Shakil S Sait*

Department of Chemistry, JNTU, Kukatpally, Hyderabad - 500085, Andhra Pradesh, India

ABSTRACT

A mixture of 8-allyl-7-hydroxy-3- methyl-2-styrylchromones (**1a-d)** react with allyl bromide and potassium carbonate to gives 3,8-dimethyl-2[(E)-2-phenyl-1ethenyl]-4H-furo[2,3-h] chromone-4-ones**(3a-d)** in section-A, and 7-hydroxy-8-allyl-3 -methyl-2-styrylchromones**(5a-d)** with ,3-dichloro-5,6-dicyano-1,4-benzoquinontetr(DDQ) gives 3-methyl-2[(E)-2-phenyl-1-etheny1]-4H,8H-pyrono[2,3-f]chromen-4,8-diones**(6a-d)** Section-b, in a Claisen rearrangement by refluxing N,N-diethylaniline at 220 °C.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Chromones and isoflavones constitute an important class of oxygen heterocyclics. Substituted as well as heterocyclic ring fused chromones and isoflavones have a wide range of pharmacological activity. Chromones and isoflavones with medicinal use are Khellin a coronary vasodilator [1-5]. Chromones-2-carboxylate spasnolitic agent and disodium chromo glycate and anti elergitic drug [6-8]. Genstein having estrogen hormonal activity, and 7-isopropoxy flavones for treatment of postmenopausal and senile osteoporosis.

Experimental Section (3a-d) and (5a-d):

General: - Melting points were determined in a sulfuric acid-bath and are uncorrected. IR spectra were recorded in KBr on a Shimadzu 435 spectrometer, ^{1}H NMR spectra on a Varian Gemini 200 MHz spectrometer with TMS as an internal standard and mass spectra on a Perkin Elmer Hitachi RDO-62 and MS-30 instrument.

Section-A

General procedure for the synthesis of 8-methyl2 [(E)-2-phenyl-i-ethenylj-4H-furo [2,3-h] chromen-4-ones (3a-d)

1. 3,8-Dirnethyl-2[(E)-2-phenyl-1-ethenyl]-4H-furo[2,3-h]chromen-4-one (3a):

A suspension of sodium salt of 7-hydroxy-8-allyl-3-methyl-2-styrylchromone **(1a)** (1.7 g, 5 mmol) in benzene (200 mL) containing $PdC1_2(PhCN)_2$ (2.25 g) of was stirred at room temperature for 30 minutes The suspension became clear and developed intense red colour during stirring. The clear solution was refluxed for 2 h when black metallic palladium separated out and the solution turned colorless. Palladium was filtered, and the filtrate concentrated to yield the crude product. The product was purified by column chromatography using silica gel (50 g, 200 mesh). Elution with benzene (200 ml) gave benzonitrile and subsequent elution with chloroform gave 3,8-dimethyl-2[(E)-2-phenyl-1ethyl]-414-furo[2,3-h] chromen-4-one **(3a).** It was recrystallized from chloroform as yellow crystals, yield 1.4g, m.p. 120 °C.

UV (MeOH): 214, 262, 346 nm.

IR (KUr, cm^{-1}): 1246, 1609, 2092, and 3093.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.20 (s, CH_3-3), 2.55 (s, CH_3-8), 6.77 (s, H-9), 6.53 (d, J=10 Hz, H-6), 7.15 (d, J=16 Hz, H-β), 7.38 - 7.50 (m, H-2', 3', 41, 51, 6'), 7.55 (d, J=16 Hz, H-α), 8.04 (d, J=l0 Hz, H-5).

ISSN: 0975-8585

^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 9.6 (CH_3-3), 14.1 (CH_3-8), 100.1 (C-9), 108.9 (C-4a, C-6), 117.5 (C-1, 9a), 117.8 (C-3), 117.9 (C-α), 121.0 (C-4'),126.7 (C-2', 6'), 127.5 (C-3',5'), 129.4 (C-5), 135.6 (C-β)), 149.0 (C-8), 156.2 (C-6a,2),,158.0 (C-9b), 178.2 (C-4).

MS: 316 (M^+, 38%), 315 (1001/o), 301 (30%), 239 (100%), 174 (55%), 146

Similarly **3b-d** were obtained from **1b-d** yield is 70-75% respectively.

2. 3-Ethyl-8-rnethyl-2[(E)-2-phenyl-1-ethenyl]-4H-furo [2,3-h] chromen-4-one (3b):

It is recrystallized from chloroform as yellow crystals, mp. 119 °C.

IR (KBr, cm^{-1}): 1245, 1585, 1608, 2092, and 3095.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.20 (t, CH_2-CH_3-3), 2.53 (s, CH_3-8), 2.79 (q, CH_2-CH_3-3), 6.80 (s, H-9), 6.95 (d, J=10 Hz, H-6), 7.15 (d, J=16 Hz, H-α), 7.50 (d, J=16 Hz, H-β), 7.35-7.45 (m, H-2',3',4',5',6'), 8.05 (d, J=10 Hz, H-5).

3. 3-Phenyl-8-rncthyl-2[(E)-2-phenyl- 1-ethenylJ-4H-furof2, 3-/tic hromen-4-one (3c):

It is recrystallized from chloroform as yellow crystals, mp 124 °C.

IR (KBr, cm^{-1}): 1245, 1585, 1612, 2928, and 3070.

^{1}H NMR ($CDC1_3$, 200 MHz): δ 2.55 (s, CH_3-8), 6.80 (s, H-9), 6.90 (d, J=16 Hz, H-a), 6.94 (d, J=10 Hz, H-6), 7.10 (d, J=16 Hz, H-α), 7.30-7.45 (m, 10H Ar-H), 7.50 (d, J=16 Hz, H-β), 8.05 (d, J=10 Hz, H-5).

4. 8-methyl-2[(E)-2-phenyl-1-etheny11-4H-furog3-hj-chromen-4-one (3d):

It is recrystallized from chloroform as yellow crystals, mp 120 °C.

IR (KBr, cm^{-1}): 1246, 1617, 3024, and 3076.

^{1}H NMR ($CDC1_3$, 200 MHz): δ 2.53 (s, CH_3-8), 6.25 (s, H-3), 6.70 (d, J=16

Hz, H-α), 6.75 (s, H-9), 6.92 (d, J=9 Hz, H-6), 7.58 (d, J=16 Hz, H-β), 7.37 -

7.50 (m, H-2', 3', 4', 5', 6'), 8.05 (d, J=10 Hz, H-5).

Section-B

General procedure for the synthesis of 2[(E)-2-phenyl-1-ethenyl-4H, 8H-pyrono [2,3-f] chromen-4,8-diones (6a-d):

1.3-Methyl-4(E)-2-phenyl-1-ethenyl-4H, 8H-pyrono [2,3-f] chromen-4,8-dione (6a):

A solution of 7-hydroxy-8-ally1-3-methyl-2-styrylchromone **(5a)** (3.18 g, 10 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinontetr(DDQ) (6.81 g, 30 mmol) in benzene (100 mL) containing few drops of water was refluxed for 12 h on steam bath. 2,3-Ddichloro-5,6-dicyano-

1,4-hydroquinone that separated was filtered off and benzene solution was washed with saturated sodium bisulphite, solution (200 mL) followed by water. Benzene layer was dried and concentrated under vacuum. The crude product thus obtained was chromatographed over silica gel (ACME, 200 mesh, 100 g). Elution with chloroform gave 3-methyl-2[(E)-2-phenyl-1-etheny1]-4H, 8H-pyrono [2,3-f] chromen-4,8-dione **(6a).** It was recrystallized from chloroform gave as yellow crystals, yield 2.6 g, mp. 198 °C.

UV (Me0H): 218, 267, 332 nm.

IR (KBr, cm^{-1}): 1287, 1369, 1410, 1626 (C=0), 1738 (C=0), 2919, 3055.

^{1}H NMR ($CDC1_3$, 200 MHz): 5 2.25 (s, CH_3-3), 6.58 (d, J=10 Hz, H-6), 7.17 (d, J=16 Hz, H-a), 7.28 (d, J=9 Hz, H-9), 7.40 (d, J=16 Hz, H-13), 7.45 and 7.60 (m, H-3',4',5') and H-2',6'), 7.95 (d, J=9 Hz, H-5), 8.32 (d, J=9 Hz, H-10).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 9.5 (CH_3-3), 114.1 (C-10a), 117.9 (C-a),

6a), 159.4 (C-8), 176.8 (C-4).

MS: 330 (M^+. 13%), 329 (12%), 315 (44%), 301 (16%), 253 (12%), 115

Similarly **6b-d** were obtained from **5b-d** yield is 70-75% respectively.

2.3-Ethyl-2[(E)-2-phenyl-1-etheny1-4H, 8H-pyrono [2,3-f]chromen-4,8-dione (6b):

It is recrystallized from chloroform as yellow crystals, mp 237 °C.

IR (KBr, cm^{-1}): 1286, 1573, 1624, 1730, 2916, and 3052.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.20 (t, CH_2-CH_3-3), 2.80 (q, CH_2-CH_3-3), 6.62 (d, J=10 Hz, H-6), 7.16 (d, J=16 Hz, H-α), 7.32 (d, J9 Hz, H-9), 7.65 (d, J=16 Hz-β), 7.45-7.60 (m, H-2', 3',4',5',6'), 8.10 (d, J=9 Hz, H-5), 8.43 (d, J9 Hz,H-10).

3. 3-Phenyl-2[(E)-2-phenyl-1-ethenyl-4H, 8H-pyrono [2,3–f]chromen-4, 8- dione (6c):

It is recrystallised from chloroform as yellow crystals, mp 242°C.

IR (KBr, cm^{-1}): 1240, 1624, 1732, 2931, and 3067.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.85 (d, J=10 Hz, H-6), 7.10 (d, J=16 Hz, Hα), 7.25 (d, J= 9 Hz, H-9), 7.30-7.45 (m, 10-H, Ar-H), 7.50 (d, J=16 Hz, H-β), 8.10 (d, J=10 Hz, H-5).

4. 3-Methyl-2[(E)-2-phenyl-1-ethenyl-4H, 8H-pyrono [2, 3-f] chromen-4, 8dione (6d):

It is recrystallized from chloroform as yellow crystals, mp 204 °C.

IR (KBr, cm^{-1}): 826, 1287, 1624, 1735, 2920, and 3055.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.28 (s, H-3), 6.60 (d, J=10 Hz, H-6), 7.14 (d,

J=16 Hz, H-a), 7.30 (d, J=9 Hz, H-9), 7.40 (m, H-3',4',5'), 7.60 (m, H-β,2',6'), 8.05 (d, J=9 Hz, H-5), 8.45 (d, J=10 Hz, H-10).

RESULTS AND DISCUSSION

Synthesis of 8-methyl-2- [(E)-2-phenyl-1-ethenyli-411furo [2,3-h] chromen-4-ones (3a-d) [10-16]

Equimolar quantities of 8-allyl-7-hydroxy-3- methyl-2-styrylchromone **(1a)** and dichlorobis(benzonitrile)palladium [$PdCl_2(PhCN)_2$] was taken in benzene and stirred for 30 min at room temperature to gave 3,8-dimethyl-2[(E)-2-phenyl-1-ethenyl]-4H-furo[2,3-h]chromen-4-one **(3a).** It is characterized from its analytical and spectral data in the IR spectrum 3,8-dimethyl-2 [(E)-2-phenyl-ethenyl]-4h-furo[2,3-h]chromen-4-one**(3a)** showed the carbonyl peak at 1609 cm^{-1}. Its UV spectrum recorded in methanol showed absorption maxima at 262 nm and 345 nm. In its ^1H NMR the signals due to the 2-methylfuran system (CH_3-C=C-H) as part of a new ring systems fused to 7,8- positions of 2-styrylchromone. The furan proton (H-9) and methyl protons (CH_3-8) appeared as singlet at δ 6.77 and 2.55 respectively. H-5 and H-6 appeared as doublets with J=10.0 Hz at δ 8.04 and 6.53 respectively. The α- proton resonated as doublet at δ 5 7.15 (J=16.0 Hz) while β-proton appeared at δ 7.60 (J=16.0 Hz) and overlapped with other protons i.e. H-2', 6'. The aromatic protons H-2' and H-6' resonated as a complex multiplet at δ 7.60 while 3',4',5' resonated as multiplet at δ 6 7.35. The C-3 methyl protons appeared as singlet at δ 2.20.

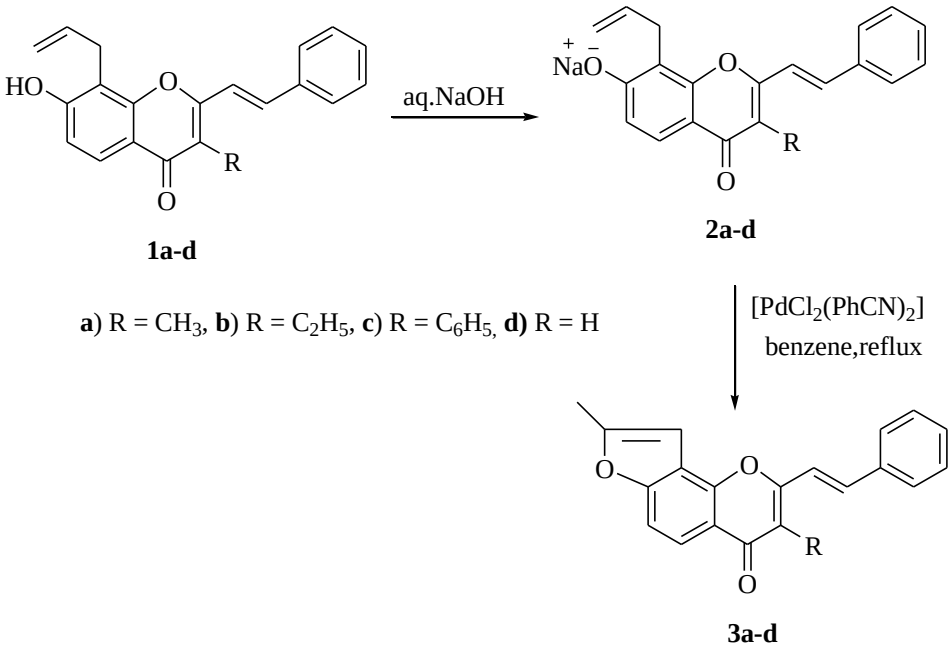
In its ^{13}C NMR spectrum showed carbons resonated at δ 149.0 (C-8), 158.0 (C-9b), 100.1 (C-9) and 14.1 (CH_3-8). The other carbons appeared at δ 178.2 (C-4), 156.2 (C-2, 6a), 135.6 (C-β)), 129.4 (C-5), 127.5 (C-3',5t), 126.7 (C-2',6), 121.0 (C-4'), 117.9 (C-a), 117.8 (C-3), 117.5 (C-1',9a), 108.9 (C-4a, 6), 9.6 (CH_3-3).

The MS of **(3a,),** showed M^+ at m/z 316. Other major ions in the spectrum appeared at mlz 315, 301, 239, 174 and 146. The fragment ions mlz 315, 301 and 239.

The mechanic pathway of the oxidative cyclisation of sodium salt of 7-hydroxy-8- ally1-2-styrylchromones **(1a-d)** with [$PdC1_2(PhCN)_2$]. Formation of dimeric it-allylic complex is the key step in this reaction". The π- allylic complex converted into unisolable monomer which gives rise to **(3a-d)** by successive elimination of NaC1, HC1 and Pd.

ISSN: 0975-8585

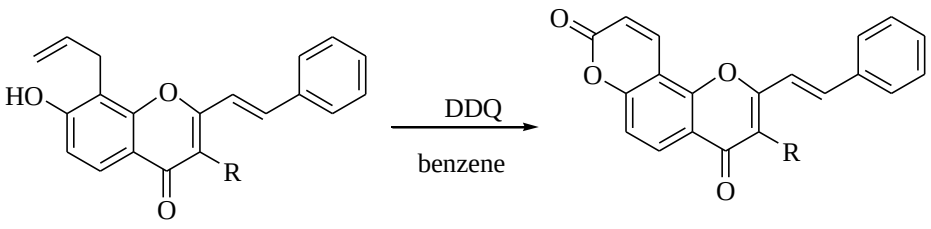
Scheme-1



1a-d **2a-d** **3a-d**

a) R = CH_3, **b**) R = C_2H_5, **c**) R = C_6H_5, **d)** R = H

Scheme-2

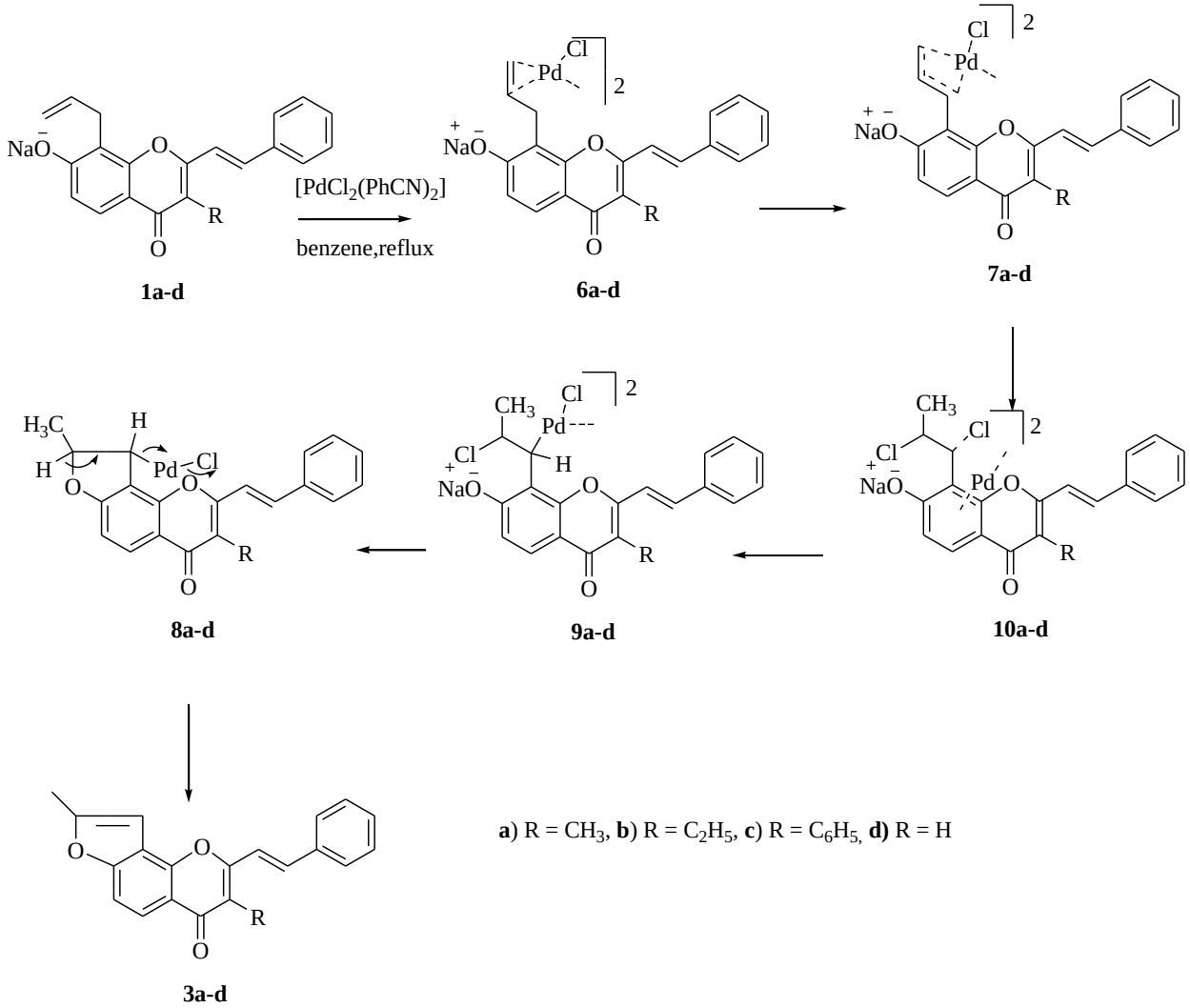


4a-d **5a-d**

a) R = CH_3, **b**) R = C_2H_5, **c**) R = C_6H_5, **d)** R = H

ISSN: 0975-8585

Scheme-3



REFERENCES

[1] Ares JJ, Outt EP, Randall LJ, Murray DP, Weisshaav SP, O Brien ML, Ems LB, Kakodakar VS, Kelm RG, Kershaw CW, Werchowski M K, Parkinson. A J Med Chem 1995; 38: 4937.

[2] Misra G, Mitra CR. Phytochemsity 1969; 8: 249.

[3] Re PD, Sagramora L, Mancini V, Valanti P, Cima P. J Med Chem 1970; 13: 527.

[4] Setniker I, Cova A, Magistretti M. J Arzeneimittal- Forsch 1975; 25: 1916.

[5] Bandopadhyay M, Pardeshi NP, Seshadri TR. Indian J Chem 1972; 10: 808.

[6] Burda S, Oleszek W. J Agric Food Chem 2001; 49: 2774.

[7] Foti M, Piatelli M, Baratta MT, Ruberto G. J Agric Food Chem 1996; 44:497.

[8] Jen-Kun L, Shu-Huei T, Shoei-yn, LS. Drugs of the Future 2001; 26:145.

[9] Naoko S, Takesh T, Takao K, Naomichi B, Mitsuyoshi M. Biol Pharm Biol Pharm Bull 2002;25: 1093.

ISSN: 0975-8585

[10] Wen-Hsin, H, Pei-Yu, C, Ching-Huey, Yu, C, Ching-Huey, Y, An-Rong, L. Chem Pharm Bull 2003; 51:339.
[11] Maitlis, P.M. "The Organic Chemistry of Palladium", 1, Metal Complexes, Academic Press, New York: 1971.
[12] Subba Raju Ky, Srimannarayana G, Subba Rao NV. Tetrahedron Lett 1977; 5: 473
[13] Zsindely VJ, and Schmid H. Chirn Acla 1968; 51: 1510.