DOI: 10.55522/jmpas.v2i1.0013 ISSN NO. 2320 – 7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Design, synthesis and antiinflammatory activity of substituted chromones

Vishal Gupta[1], S K Yadav*[2]

[1] Millennium College of Pharmacy, Bhopal, Madhya Pradesh, India

[2] Ravishankar College of Pharmacy, Bhopal, Madhya Pradesh, India

Corresponding author: S K Yadav ✉ vishalpharmacy@rediffmail.com,

Ravishankar College of Pharmacy, Bhopal, Madhya Pradesh, India

Received - 30 February 2013**, Revised -** 12 March 2013, **Accepted** – 23 April 2013 **(DD-MM-YYYY)**

Refer This Article

Vishal Gupta, S K Yadav, 2013. Design, synthesis and antiinflammatory activity of substituted chromones. Journal of medical pharmaceutical and allied sciences, V 2 - I 2, Pages -44 – 45. Doi: https://doi.org/10.55522/jmpas.V2I2.0013.

ABSTRACT

The Chromones and other related ring systems have several interesting biological activities such as anti-inflammatory effects. Chromones also having anti-bacterial and antifungal activities from heterocyclic substituent's at 2- position and exhibit good phosphodiesterase-IV inhibition activity and some chromones have potential HIV- inhibition activity as well as Spiro amine derivatives having anti-arrhythmic activity. performed reaction having catalyzed Claisen rearrangement SnCl4 of allyl aryl ethers followed by cyclization gives oxygen hetrocycles. By utilizing SnCl4 as lewis acid the rearragment reaction is affected under mild condition. The anti-inflammatory activity of the synthesized compounds was determined by rat paw edema method. Some of the compounds were found to be potent.

Keywords: Chromones, Inflammation, Melting points, NMR, IR.

INTRODUCTION

Non-steriodal anti-inflammatory drugs (NSAID's) are widely used to treat pain, fever and inflammatory condition including osteoarthritis. Several research studies exhibits the antiinflammatory properties of chromones. Chromones are also reported as anti-microbial anti-cancer anti-allergic and coronary vasodilator. Claisen rearrangement is generally affected by prolong heating of an aryl allyl ether or by heating in vacuum at high temperature. Lewis acids are known to cause the Claisen rearrangement under mild conditions. The use of $SnCl_4$ as lewis acid act as a catalyst for Claisen rearrangement is not reported. We propose the SnCl4 catalysed Claisen rearrangement of 7-allyloxy chromones to afford 7 hydroxy 6/8 allylchromones and 2'-methyl-2', 3'-dihydrofuronochromone [1].

7- Hydroxyl chromones(2a-d) and 7-allyloxychromones(3a-d) were synthesized as per the reported methods(9,10).

7hydrooxy-6/8-allylchromone (4a-d) and 2'-methyl-2',3'-dihydrofurano chromones (5a-d) were synthesized by the treatment of 7-allyloxychromones(3a-d) with SnCl4 in dry THF (Scheme-1) [2].

MATERIAL AND METHOD

Synthesis of 7- Hydroxyl chromones (2a-d) and 7-allyloxychromones (3a-d)

10 mmol's of 1(a-d) and acetic anhydride were refluxed with 5% hydrochloric acid, methanol and sodium acetate at 180ºC for 6h. The solution was filtered and the products (2a-d) were recovered. 10mmols of 2(a-d) and 20ml of propylene bromide were refluxed with acetone and potassium carbonate for 5h to obtain compounds 3(a-d).

Synthesis of 7-hydroxy-6/8-allylchromone (4a-d) and 2'-methyl-2', 3'-dihydrofurano chromones (5a-d):

10 mmol's of 3(a-d) and SnCl4 in dry THF (10ml) were stirred for 14 h under N_2 atmosphere at 0-5ºC. The solution was filtered and solvent is removed under reduced pressure. The resulting mixture was chromotographed over silica gel. Elution with benzene-ethyl acetate (1:1, v/v) mixture gave two products 4 and 5. These compounds were crystallized from benzene. The compounds were subjected for NMR studies. **4a** δ 1.95 (s, CH_{3-3}), 2.35(s, CH_{3-2}), 7.65(ar, H-5, J=10H-2), 3.52(m, H-1'), 5.05(dd, H-3', J=10, 1H-2), 9.95(dd, H-3', J=16, 1H-2), 5.90(m-H-2'), 10.20(s, 7-OH). **4b** δ 1.96 (s, CH_{3-3}), 2.38(s, CH_{3-2}), 7.62(s, H-5), 3.59(m, H-1'), 5.91(m-H-2), 5.10(dd, H-3', J=10, 1H-2), 4.99(dd, H-3', J=16, 1H-2). **4c.** δ 1.97 (s, CH_{3-3}), 2.39(s, CH_{3-2}), 7.64(s, H-5), 3.49(m, H-1'), 5.90(m-H-1'), 5.12(dd, H-3', J=10, 1H-2), 4.99(dd, H-3', J=16, 1H-2). **4d** δ 2.10 (s, CH_{3-3}), 2.46(s, CH_{3-2}), 7.80(s,

H-5), 2.30(s-CH_{3-1}) 3.50(m, H-1'), 6.08(m-H-2), 5.30(dd, H-3', J=10, 1H-2), 5.09(dd, H-3', J=16, 1H-2). **5a.** δ 1.50 (d, $CH_{3-2'}$, J=6H-2), 2.05(s, CH_{3-3}), 2.45(s, CH_{3-2}), 2.90(dd, H-3', J=12, 8H-2), 3.42(dd, H-3', J=16, 6H-2), 5.10(m, H-2'), 8.20(d, H-8, J=10H-2), 6.75(d, H-9, J=10 H-2). **5b** δ 1.62(d-$CH_{3-2'}$, J=6H-2), 2.05 (s, CH_{3-3}), 2.42(s, CH_{3-2}), 3.02(dd, H-3', J=12, 8H-2), 3.56(dd, H-3', J-12, 6H-2), 5.25(m, H-2'), 8.12(s-H-5). **5c** δ 1.62 (d, $CH_{3-2'}$, J=6H-2), 2.07(s, CH_{3-3}), 2.41(s, CH_{3-2}), 5.18(m, H-2'), 3.00(dd, H-3', J=12, 8H-2), 3.56(dd, H-3', J=12, 6H-2), 8.06(s, H-5). **5d** δ 1.61(d, $CH_{3-2'}$, J=6H-2), 2.06 (s, CH_{3-3}), 2.44(s, CH_{3-2}), 2.30(s, CH_{3-8}), 3.02(dd, H-3', J=12, 8H-2), 3.52(dd, H-3', J-12, 6H-2), 5.20(m, H-2'), 8.20(s, H-8) [3].

Analytical experimental

The melting points were determined in open capillary tubes and are uncorrected. Elemental analysis was determined using Carlo Erba model 1108. IR Spectras were recorded on Perkin-Elmer 881 spectrophotometer in KBr($cm^{-1,}$) and ^{1}H NMR spectra on a Bruckers advanced DXP 200 spectrophotometer using TMS as internal reference [4].

Anti-inflammatory activity

Animals

Adult male albino rats (wistar strain) weighing between 150-250g were used for anti-inflammatory study. They were fed on commercial diet and water *ad libitum*. All the animals were acclimatized for a week before use. The room temperature was maintained at 25±1ºC. The experimental protocol was approved by institutional animal ethical committee [5].

Experimental design for anti-inflammatory activity

The anti-inflammatory activity of the synthesized compounds was carried out by the method of Winter et al. Wistar rats weighing 150-250 g were used for the edema test. Animals were divided into six rats per group. Rats were put on fast for 18 h. prior to the experiment. The standard drug ibuprofen (100mg / kg body wt.) and the drug (100mg / kg body wt.) were given orally as a suspension in 0.1% sodium carboxy methylcellulose as vehicle. One h later 0.1 ml of carageenin solution in saline was injected in the subplantar region of the right hind paw of each rats. After 3 h of carageenin injection the reduction in paw volume compared to control vehicle was measured using plethysmometer. (Table-1) [6].

Table 1: Characterization and antiinflammatory activity of synthesized compounds

Compounds	M.P(ºC)	Yield (%)	Paw Volume(% protection)
Control			2.25± 0.08
Ibuprofen			0.89± 0.13(60)
4a	134	34	1.80± 0.19(20)
4b	147	36	1.73± 0.14(23)
4c	132	57	0.77± 0.18(66)
4d	176	74	1.08± 0.02(52)
5a	145	45	1.40± 0.01(38)
5b	139	51	1.64± 0.11(27)

Statistical analysis

Values for anti-inflammatory activity were expressed as "mean increase in paw volume ±SEM". The significance of difference between means was determined by student's t-test values of $p<0.05$ were considered significant and $p<0.01$ as highly significant.

Acknowledgment

The authors are thankful to Principal and Chairman of Millennium College of Pharmacy, Bhopal for providing laboratory facilities and Central Drug Research Institute (CDRI), Lucknow for spectral analysis of the compounds.

REFERENCES

1. Wei Huang, Yu Ding, Yan Miao, et al, 2009. Synthesis and antitumor activity of novel dithiocarbamate substituted chromones. Eur J Med Chem. 44(9), Pages 3687-3696. Doi: 10.1016/j.ejmech.2009.04.004.

2. Christine Dyrager, 2012. Design and synthesis of chalcone and chromone derivatives as novel anticancer agents. Heterocyclic Chemistry. 18, Pages 796.

3. Wei Huang, Ming-Zhen Liu, Yan Li, et al, 2007. Design, syntheses, and antitumor activity of novel chromone and aurone derivatives. Bioorganic & Medicinal Chemistry. 15, Pages 5191-5197. Doi: https://doi.org/10.1016/j.bmc.2007.05.022.

4. Christine Dyrager, Linda Nilsson Möllers, Linda Karlsson Kjäll, et al, 2011. Journal of Medicinal Chemistry. 54, Pages 7427–7431. Doi: https://doi.org/10.1021/jm200818j

5. Christos A Kontogiorgis, Dimitra J Hadjipavlou-Litina, 2005. Synthesis and antiinflammatory activity of coumarin derivatives. J Med Chem. 8(20), Pages 6400-6408. Doi: 10.1021/jm0580149.

6. Noor Fathima Anjum, Abdul Aleem, Naira Nayeem, 2011. Synthesis and antibacterial activity of substituted 2-phenyl-4-chromones. J.Med.Chem. 3 (5), Pages 56-62.