Monatshefte für Chemie 114, 123—125 (1983)

Monatshefte für Chemie
Chemical Monthly

Synthesis of 2,2-Dimethyl-5-hydroxy-3-(3-oxobutyl)-7-pentyl-4-chromone

Short Communication

R. C. Anand* and **H. Ranjan**

Department of Chemistry, Indian Institute of Technology, Hauz Khas, New Delhi-110016, India

(Received 20 September 1982. Accepted 12 October 1982)

Alkylation and deformylation of 2,2-dimethyl-3-hydroxymethylene-5-hydroxy-7-pentyl-4-chromone occurs in the same step to give the title compound.

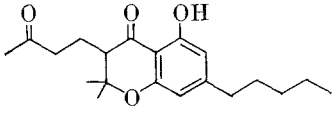
(Keywords: Chromones, synthesis; Heterocyclic compounds)

Synthese von 2,2-Dimethyl-5-hydroxy-3-(3-oxobutyl)-7-pentyl-4-chromon (Kurze Mitteilung)

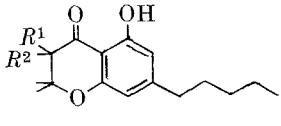
Alkylierung und Deformylierung führte in einem Schritt von 2,2-Dimethyl-3-hydroxymethylen-5-hydroxy-7-pentyl-4-chromon zur Titelverbindung.

2,2-Dimethyl-5-hydroxy-3-(3-oxobutyl)-7-pentyl-4-chromone, a cannabinoid, has been isolated from the extracts of cannabis by micro preparative GC. It has been assigned structure **1** on the basis of spectroscopic studies and microchemical reactions.

In the present paper we report a synthesis of the title compound and thus corroborate its structure.



1



2 R^1, R^2; H_2
3 R^1, R^2; =CHOH

0026-9247/83/0114/0123/$ 01.00

2,2-Dimethyl-7-pentyl-5-hydroxy-4-chromone (**2**), was prepared by the condensation of olivetol (3,5-dihydroxy-1-pentyl benzene) and 3,3-dimethylacrylic acid[2] in the presence of BF_3. Formylation of the chromone **2** with ethyl formate in the presence of sodium hydride furnished 2,2-dimethyl-3-hydroxymethylene-7-pentyl-5-hydroxy chromone (**3**). This α-hydroxymethylene-ketone (**3**) was stirred with methyl vinyl ketone in the presence of triethylamine for 48 hours at room temperature. The isolated product was found to be 2,2-dimethyl-5-hydroxy-3-(3-oxobutyl)-7-pentyl-4-chromone by comparison of its IR and NMR with the one recorded for the title compound[3]. It is interesting to note that alkylation and deformylation have taken place in the same step which seems to be without precedent.

Experimental

2,2-Dimethyl-5-hydroxy-7-pentyl chromone (**2**)

A mixture of olivetol (3,5-dihydroxy-1-pentyl benzene) (0.5 g, 2.6 mmol), 3,3-dimethyl acrylic acid (0.3 g, 3 mmol) was heated to 125 °C followed by addition of BF_3 (0.6 g). After heating for 20 h at 130° the isolated product was taken up in ether and washed with 1 *N* NaOH (8 × 20 ml). Evaporation of the solvent and purification of the residue by preparative TLC rendered 0.6 g of the chromone **2** (colourless oil). IR: 1645, 1580, 1440, 1380, 1320, 1260, 1212, 1175, 1080, 790, 760 cm^{-1}. NMR (δ, ppm): 0.88 (t, 3 H), ~ 1.32 (m, 4 H), 1.44 (s, 6 H), 2.5 (t, 2 H), 2.72 (s, 2 H), 6.24 and 6.32 (d, 2 H), 7.28 (s, 1 H).

2,2-Dimethyl-3-hydroxymethylene-5-hydroxy-7-pentyl chromone (**3**)

The chromone **2** (0.3 g, 0.0011 mol) was formylated using sodium hydride (0.528 g, 50%, 0.011 mol), dry ether (20 ml) and ethyl formate (1.25 g, 0.017 mol). Usual workup furnished the crude product (0.18 g) which was purified by preparative TLC to give the hydroxymethylene ketone (0.13 g, colourless oil, 47%). IR: 1630, 1580, 1450, 1400, 1320, 1280, 1270, 1212, 1135, 1120, 1070, 980, 965, 850, 738 cm^{-1}. NMR (δ, ppm): 0.88 (t, 3 H), 1.24–1.40 (m, 6 H), 1.48 (s, 3 H), 1.60 (s, 3 H), 6.12–6.24 (d, 2 H), 7.22–7.32 (d, 1 H).

2,2-Dimethyl-5-hydroxy-3-(3-oxobutyl)-7-pentyl-4-chromone (**1**)

To a solution of the hydroxymethylene ketone **2** (0.125 g, 0.43 mmol) in methanol (5 ml) at 0° under N_2 was added triethylamine (0.1 ml) followed by methyl vinyl ketone (0.030 g, 0.5 mmol). It was stirred for two days followed by treatment with sodium carbonate (10%, 50 ml). Extraction with ether and solvent removal afforded the crude product which on purification by preparative TLC gave the title compound (0.070 g colourless oil, 48.5%). IR: 1718, 1640, 1570, 1440, 1375, 1210, 1075, 735 cm^{-1}. NMR (δ, ppm): 0.9 (t, 3 H), 1.4 (s, 3 H), 1.45 (s, 3 H), 2.1 (s, 3 H), 6.2–6.4 (d, 2 H, $J = 1.5$ Hz).

References

[1] *Friedrich-Fiechtl J.*, *Spiteller G.*, Tetrahedron **31**, 479 (1975).
[2] *Apsimon J.*, (ed.), The Total Synthesis of Natural Products, Vol. 4, p. 204. Wiley Interscience. 1981.
[3] *Grote H.*, *Spiteller G.*, Tetrahedron **34**, 3207 (1978).

Verleger: Springer-Verlag, Mölkerbastei 5, A-1010 Wien. — Herausgeber: Österreichische Akademie der Wissenschaften, Dr. Ignaz Seipel-Platz 2, A-1010 Wien, und Verein Österreichischer Chemiker, Eschenbachgasse 9, A-1010 Wien. — Redaktion: Währinger Straße 38, A-1090 Wien. — Hersteller: Adolf Holzhausens Nachfolger, Kandlgasse 19-21, A-1070 Wien. — Verlagsort: Wien. — Herstellungsort: Wien. — Printed in Austria.

Offenlegung gem. § 25 Abs. 1 bis 3 Mediengesetz: Unternehmensgegenstand: Verlag von wissenschaftlichen Büchern und Zeitschriften.

An den Springer-Verlag GmbH&Co. KG sind beteiligt: Prof. Dr. Georg F. Springer als Kommanditist zu 39,8%, Dr. Konrad F. Springer als Kommanditist zu 39,8%, beide Mölkerbastei 5, A-1010 Wien. Geschäftsführer: Dr. Konrad F. Springer, Ing. Wolfram F. Joos und Dr. Wilhelm Schwabl, alle Mölkerbastei 5, A-1010 Wien.