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Short Communication

Synthesis of 2,2-Dimethylchromans by the Hydrogenation of 2,2-Dimethyl-2 *H*-chromenes*

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Summary. 2,2-Dimethylchromans **19** – **36** have been synthesized by the hydrogenation of 2,2-dimethyl-2 *H*-chromenes **1** – **18** in acetic acid solution in the presence of 10% Pd-C catalyst.

Keywords. 2,2-Dimethyl-2 *H*-chromenes; 2,2-Dimethylchromans; Hydrogenation.

Darstellung von 2,2-Dimethylchromanen durch Hydrierung von 2,2-Dimethyl-2 *H*-chromenen (Kurze Mitt.)

Zusammenfassung. Die 2,2-Dimethylchromane **19** bis **36** wurden durch Hydrierung von 2,2-Dimethyl-2 *H*-chromenen **1** bis **18** in Essigsäure in Gegenwart von 10% Pd/C-Katalysator gewonnen.

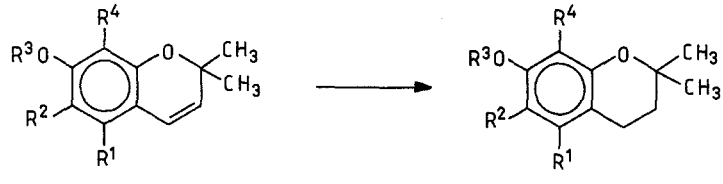
2,2-Dimethylchromans were found to exhibit various bioactivities. This stimulated the endeavour to develop different procedures for their synthesis. The most frequently used method is based on the reaction of phenols with isoprene affording 2,2-dimethylchromans [1 – 5]. A similar procedure [6, 7] utilizes the reaction of phenols with 1,3-dichloro-3-methylbutane. Since these methods afford 2,2-dimethylchromans only in low or moderate yields, new procedures would be of interest. Formerly we developed an efficient method providing 2,2-dimethylchromans by the hydrogenation of 2,2-dimethyl-4-methoxychromans [8].

Recently we were engaged in the synthesis of 2,2-dimethyl-2 *H*-chromenes possessing either a benzyloxy or carboxamide containing side chain [9, 10]. Some of these chromenes were shown to have analgetic activity. On this basis it seemed expedient to prepare and to investigate the related 2,2-dimethylchromans as well. The appropriate 2,2-dimethyl-2 *H*-chromenes **1** – **18** have been hydrogenated in acetic acid solution at ambient temperature and pressure in the presence of 10% Pd-C catalyst to obtain 2,2-dimethylchromans **19** – **36**. In the case of compound

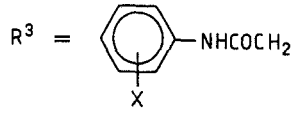
** Dedicated to Prof. Dr. W. Fleischhacker on the occasion of his 60th birthday

18 the benzyl group was eliminated together with the saturation of the double bond of the hetero ring to afford 2,2-dimethyl-7-hydroxy-6-methoxychroman **36**. While the 4-bromobenzyloxy group was not split in the course of the conversion of the 2,2-dimethyl-2 *H*-chromenes **16** and **17** into 2,2-dimethylchromans **34** and **35**.

The structure of the new compounds has been elucidated by ^{1}H-NMR spectroscopy and the relevant data are summarized in Table 1. On the basis of our results it can be concluded that the hydrogenation of the 2,2-dimethyl-2 *H*-chromenes is a simple and convenient procedure for the preparation of 2,2-dimethylchromans.



1 - 18 19 - 36



1, 19: $R^1 = R^2 = R^4 = H$, R^3 (X=2-CH_3, 6-C_2H_5)

2, 20: $R^1 = R^2 = R^4 = H$, R^3 (X=2,6-$(C_2H_5)_2$)

3, 21: $R^1 = CH_3$, $R^2 = R^4 = H$, R^3 (X=2-CH_3)

4, 22: $R^1 = CH_3$, $R^2 = R^4 = H$, R^3 (X=4-CH_3)

5, 23: $R^1 = CH_3$, $R^2 = R^4 = H$, R^3 (X=2,6-$(C_2H_5)_2$)

6, 24: $R^1 = R^2 = H$, R^3 (X=H), $R^4 = CH_3$

7, 25: $R^1 = R^2 = H$, R^3 (X=2-Cl), $R^4 = CH_3$

8, 26: $R^1 = R^2 = H$, R^3 (X=2-CH_3), $R^4 = CH_3$

9, 27: $R^1 = R^2 = H$, R^3 (X=4-CH_3), $R^4 = CH_3$

10, 28: $R^1 = R^2 = H$, R^3 (X=2-CH_3, 6-C_2H_5), $R^4 = CH_3$

11, 29: $R^1 = R^2 = H$, R^3 (X=2,6-$(C_2H_5)_2$), $R^4 = CH_3$

12, 30: $R^1 = R^4 = H$, $R^2 = OCH_3$, R^3 (X=H)

13, 31: $R^1 = R^4 = H$, $R^2 = OCH_3$, R^3 (X=2-Br)

14, 32: $R^1 = R^4 = H$, $R^2 = OCH_3$, R^3 (X=2-CH_3, 6-C_2H_5)

15, 33: $R^1 = R^4 = H$, $R^2 = OCH_3$, R^3 (X=2,6-$(C_2H_5)_2$)

16, 34: $R^1 = R^2 = R^4 = H$, R^3 = 4-Br-$C_6H_4CH_2$

17, 35: $R^1 = R^2 = H$, R^3 = 4-Br-$C_6H_4CH_2$, $R^4 = CH_3$

18 : $R^1 = R^4 = H$, $R^2 = OCH_3$, $R^3 = C_6H_5CH_2$

36 : $R^1 = R^3 = R^4 = H$, $R^2 = OCH_3$

Table 1. Physical constants and ^{1}H-NMR spectral data of compounds **19–36**

Compound	M. p. °C	Yield %	Molecular Formula[a]	^{1}H-NMR δ (ppm)
19	105–106	74.8	$C_{22}H_{27}NO_3$	1.14 (t, 3H), 1.38 (s, 6H), 1.82 (t, 2H), 2.54 (dd, 2H), 2.76 (t, 2H), 4.67 (s, 2H), 6.47–7.46 (m, 6 aromat. H), 7.82 (s, NH)
20	104–105	86.5	$C_{23}H_{29}NO_3$	1.17 (t, 6H), 1.36 (s, 6H), 1.81 (t, 2H), 2.57 (dd, 4H), 2.74 (t, 2H), 4.65 (s, 2H), 6.45–7.27 (m, 6 aromat. H), 7.80 (s, NH)
21	109–110	82.6	$C_{21}H_{25}NO_3$	1.34 (s, 6H), 1.84 (t, 2H), 2.20 (s, 3H), 2.22 (s, 3H), 2.56 (t, 2H), 4.62 (s, 2H), 6.33–8.02 (m, 6 aromat. H), 8.25 (s, NH)
22	114–115	87.9	$C_{21}H_{25}NO_3$	1.36 (s, 6H), 1.83 (t, 2H), 2.20 (s, 3H), 2.34 (s, 3H), 2.57 (t, 2H), 4.54 (s, 2H), 6.30–7.47 (m, 6 aromat. H), 8.21 (s, NH)
23	117–118	89.8	$C_{24}H_{31}NO_3$	1.18 (t, 6H), 1.34 (s, 6H), 1.82 (t, 2H), 2.23 (s, 3H), 2.55 (dd, 4H), 2.62 (t, 2H), 4.66 (s, 2H), 6.34–7.27 (m, 5 aromat. H), 7.76 (s, NH)
24	99–100	83.9	$C_{20}H_{23}NO_3$	1.34 (s, 6H), 1.78 (t, 2H), 2.18 (s, 3H), 2.74 (t, 2H), 4.55 (s, 2H), 6.38–7.62 (m, 7 aromat. H), 8.55 (s, NH)
25	98–99	72.7	$C_{20}H_{22}ClNO_3$	1.35 (s, 6H), 1.81 (t, 2H), 2.76 (s, 3H), 2.78 (t, 2H), 4.62 (s, 2H), 6.38–8.54 (m, 6 aromat. H), 9.12 (s, NH)
26	143–144	62.2	$C_{21}H_{25}NO_3$	1.35 (s, 6H), 1.80 (t, 2H), 2.19 (s, 3H), 2.27 (s, 3H), 2.76 (t, 2H), 4.62 (s, 2H), 6.40–8.12 (m, 6 aromat. H), 8.36 (s, NH)
27	125–126	87.5	$C_{21}H_{25}NO_3$	1.36 (s, 6H), 1.78 (t, 2H), 2.18 (s, 3H), 2.30 (s, 3H), 2.44 (t, 2H), 4.54 (s, 2H), 6.38–7.50 (m, 6 aromat. H), 8.32 (s, NH)
28	97–98	83.0	$C_{23}H_{29}NO_3$	1.18 (t, 3H), 1.34 (s, 6H), 1.80 (t, 2H), 2.18 (s, 3H), 2.26 (s, 3H), 2.57 (dd, 2H), 2.78 (t, 2H), 4.67 (s, 2H), 6.45–7.23 (m, 5 aromat. H), 7.92 (s, NH)
29	83–84	77.9	$C_{24}H_{31}NO_3$	1.26 (t, 6H), 1.34 (s, 6H), 1.79 (t, 2H), 2.17 (s, 3H), 2.60 (dd, 4H), 2.28 (t, 2H), 4.68 (s, 2H), 6.46–7.27 (m, 5 aromat. H), 7.90 (s NH)
30	81–82	89.8	$C_{20}H_{23}NO_4$	1.33 (s, 6H), 1.80 (t, 2H), 2.72 (t, 2H), 3.87 (s, 3H), 4.60 (s, 2H), 6.47–7.62 (m, 7 aromat. H), 9.00 (s, NH)
31	85–86	71.4	$C_{20}H_{22}BrNO_4$	1.38 (s, 6H), 1.81 (t, 2H), 2.71 (t, 2H), 3.82 (s, 3H), 4.62 (s, 2H), 6.46–8.43 (m, 6 aromat. H), 9.29 (s, NH)
32	66–67	89.7	$C_{23}H_{29}NO_4$	1.17 (t, 3H), 1.35 (s, 6H), 2.11 (s, 3H), 2.22 (s, 3H), 2.55 (dd, 2H), 2.74 (t, 2H), 3.82 (s, 3H), 4.71 (s, 2H), 6.50–7.20 (m, 5 aromat. H), 8.30 (s, NH)
33	77–78	97.6	$C_{24}H_{31}NO_4$	1.17 (t, 6H), 1.33 (s, 6H), 1.82 (t, 2H), 2.10 (s, 3H), 2.57 (dd, 4H), 2.74 (t, 2H), 3.80 (s, 3H), 4.70 (s, 2H), 6.51–7.28 (m, 5 aromat. H), 8.28 (s, NH)
34	64–65	69.7	$C_{18}H_{19}BrO_2$	1.32 (s, 6H), 1.76 (t, 2H), 2.70 (t, 2H), 4.94 (s, 2H), 6.25–7.50 (m, 7 aromat. H)
35	73–74	76.2	$C_{19}H_{21}BrO_2$	1.30 (s, 6H), 1.74 (t, 2H), 2.09 (s, 3H), 2.70 (t, 2H), 4.97 (s, 2H), 6.38–7.50 (m, 6 aromat. H)
36	125–126	81.8	$C_{12}H_{14}O_3$	1.34 (s, 6H), 1.72 (t, 2H), 2.64 (t, 2H), 3.73 (s, 3H), 5.60 (s, OH), 6.36 (s, 1H), 6.47 (s, 1H)

[a] Elemental analyses (C, H) were in good agreement with the calculated values

Experimental Part

The NMR spectra were recorded on a Bruker WP 200 SY spectrometer in $CDCl_3$ (internal standard *TMS*, $\delta = 0.0$ ppm) at room temperature. *TLC* was performed on Kieselgel 60 F_{254} (Merck) layer using hexane:acetone (7 : 3 *v/v*) as eluant. Starting materials **1 – 18** were prepared as described earlier [9, 10].

General Procedure for the Preparation of Compounds **19 – 36**

A solution of the appropriate 2,2-dimethyl-2*H*-chromene **1 – 18** (1.0 g) in acetic acid (50 ml) was hydrogenated at ambient temperature and pressure in the presence of 10% Pd-C (0.5 g) until no more hydrogen was taken up (approx. 2 h). The catalyst was then filtered off, the solvent evaporated, and the residue triturated with hexane to afford compounds **19 – 36**. For properties see Table 1.

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