PREPARATION OF 2-$^{14}CH_3$-3-METHYL-5,7-DIHYDROXY-CHROMONE

An approach to the nature of its formation

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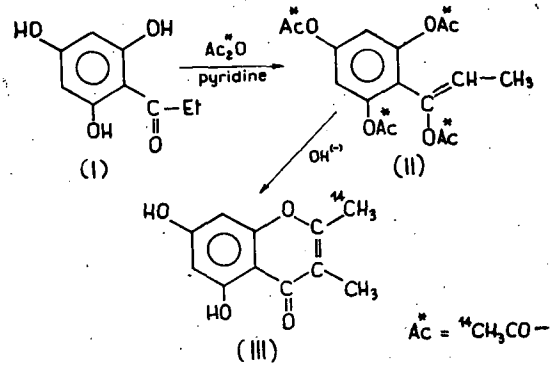
(Received June23, 1967)

2-$^{14}CH_3$-3-methyl-5,7-dihydroxy-chromone has been prepared by the base catalysed cyclization of 2, 4, 6-triacetoxy-propiophenone-enolacetate. The tetraacetate-structure of the latter has been confirmed. As to the mechanism of the ring closure a BAKER—VENKATARAMAN-like process seems to be probable though not completely proved yet.

One of us recently found a new way to synthesise 2,3-disubstituted chromones by the cyclization of acyloxy ketone enol esters [1]. The method has been now applied for the synthesis of the title compound:



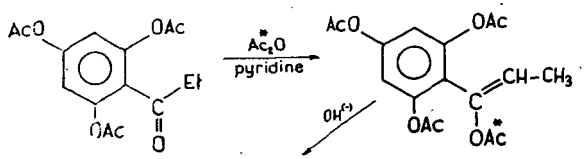
By means of the classical analytical procedure for acetyl determination including alkaline hydrolisis in compound II instead of four acetyls only three of them could be revealed. This may misindicate that in compound II only the phenolic hydroxyls have been acylated and it is therefore not an enolic-acetate. The reason for this experimental finding, however, is the fact that under the effect of alkali one of the acetyl groups is built in the γ-pyrone ring [1] so that just three of them are available for determination. The structure of the enolacetate (II) was checked by IR and NMR measurements [1], but the present experiments represent a further proof for the existence of the tetraacetate structure inasmuch as the radioactivity of compound III proved to be the quarter of that observed with compound II (Table I).

An attempt was made to approach the mechanism of the cyclization by deciding which of the two available acyl groups takes part in the ring formation. In case of the participation of the ortho-acyloxy group the mechanism would be very similar

Table I

No. of experiment	Radioactivity						
	II		IIa		III		
	imp/sec. mmol	%	imp/sec. mmol	found/expected	imp/sec. mmol	found/expected maximum	%
1	2820	100	—	—	730	1,035*	25,9
2	33180	100	—	—	8000	0,965*	24,1
3	—	—	1050	1,44	391	0,53**	—

to the BAKER—VENKATARAMAN reaction [2] while a cyclization involving the enolester would be a CLAISEN—HAASE transformation [3]. The preparation of a tetraacetate labelled with radiocarbon alone in the methyl of the enolic acetate was attempted as follows:



2,3- diMe -5,7-diOH-chromone (IIa)

In fact instead of this process considerable acyl exchange occurred (especially if the heating was prolonged) so that the radioactivity of the compound obtained was 1.5—2 times as high as the expected value (Table I). The chromone obtained from the latter compound, however, had a lower radioactivity than the chromone (III) obtained from a tetraacetate labelled at all of its acyl groups (II). This experimental result can be interpreted in terms of a BAKER—VENKATARAMAN-like mechanism, however, on the basis of these data a simultaneous competitive CLAISEN—HAASE rearrangement to a smaller extent can not be excluded either. It is impossible to state to what extent the radioactivity of the endproduct derived from IIa is the consequence of acyl exchange and to what extent the result of a CLAISEN—HAASE reaction. The fact, however, that the radioactivity of the endproduct corresponds to the difference found between the measured and expected radioactivity of IIa strongly suggests that the main reason for the radioactivity of the chromon obtained from IIa is simply acyl exchange.

Experimental

1a. *α-(2,4,6-triacetoxyphenyl)-propenyl-acetate (II).* Phlorpropiophenone (I) (1 mmole, 0,2 g), acetic anhydride (2 ml, 14 μC) and pyridine (0,2 ml) were refluxed for 3,5 hours in an air bath. After cooling to room temperature water (5 ml) was

* Expected is the quarter of the radioactivity of II.
** Expected maximum is the same as obtained for compound III at the experiment No. 1.

added when an oily phase separated which solidified on keeping overnight in a refrigerator to give 0,2 g enolacetate (75% yield). After recrystallization from 75% ethanol it melted at 98—9°. The material proved to be the same as an authentic inactive sample.

1b. *Transformation of α-(2,4,6-triacetoxyphenyl)-propenylacetate (II) to 2-$^{14}CH_3$-3-methyl-5,7-dihydroxy-chromone (III).* The enolacetate (II) (0,28 mmol, 0,1 g) was dissolved in ethanol (1 ml) and 2,5 N sodium hydroxide (5 ml) was added. The solution was kept on a waterbath for 5 minutes. After cooling the yellow solution was acidified with 5 N HCl to deposit a white crystalline product (III) (0,048 g, 82% yield) which after recrystallization from 75% ethanol and drying in vacuo melted at 216—18°. The compound did not give any m. p. depression on mixing with an authentic inactive sample.

2. *Repetition of the experiment No. 1*, however, applying an acetic anhydride having a specific radioactivity of 35μC ml^{-1} gave essentially the same result.

a) *α-(2,4,6-triacetoxyphenyl)-propenyl-$^{14}CH_3$-acetate (IIa).* 2,4,6-triacetoxy-propiophenone (0.6 mmol, 0,2 g) acetic anhydride (3,6 ml, 25,2 C) and freshly fused sodiumacetate (0,6 mmol, 0.25 g) were refluxed for 25 minutes in an air bath and after cooling it was diluted with water (10 ml). The separated oil solidified in a refrigerator to give II (0,225 g, 99% yield) which was then filtered and recrystallied from 75% ethanol. The compound melted at 98°.

b) *Conversion of α-(2,4,6-triacetoxyphenyl)-propenyl-$^{14}CH_3$-acetate (IIa) to 2,3-dimethyl-5,7-dihydroxy-chromone (III).* This reaction was carried out under the same conditions as with experiment No. 1b.

Further data can be seen in the Table I. Measurements of the radioactivity were carried out in the experiments No. 1 and 3 with GM tube (VOLVO) conected to scaler and in the experiment No. 2 with PACKARD TRI-CARB liquid scintillation counter.

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Thanks are due to Professor L. Ötvös (Central Resarch Institute of Chemistry, Hung. Acad. Sci., Budapest) for his interest in this work, and to the Ministry of Education for the grant.

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ПРИГОТОВЛЕНИЕ 2-$^{11}CH_3$-3-МЕТИЛ-ДИГИДРОКСИ-ХРОМОНА. ПРИБЛИЖЕНИЕ К ПРИПОДЕ ОБРАЗОВАНИЯ

Т. Селл и Л. Балашпири

2-$^{14}CH_3$-3-метил-5,7-дигидрокси-хромон приготовился осново-катализованной циклизацией 2,4,6-три-ацетокси-пропиофенонелацетата. Тетраацетатная структура последнего утвердилась. В отношении смыкания цикла процесс подобен тому по Бейкеру и Венкатараману является вероятным но до сих пор еще не вполне доказан.