ACTA CHEMICA SCANDINAVICA 8 (1954) 734—737

Synthesis of Some 3-Benzalcoumaran-2-ones

JARL GRIPENBERG and BÖRJE JUSELIUS

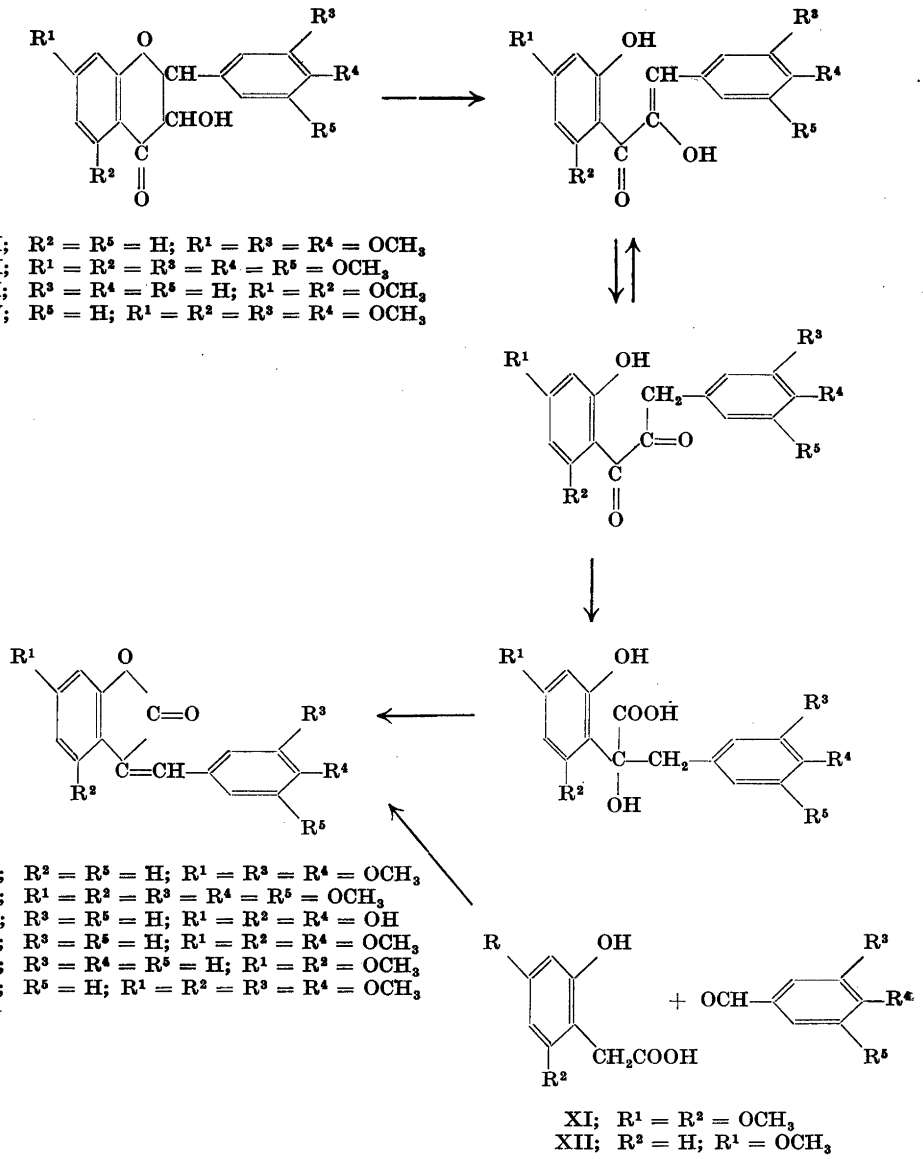
Department of Chemistry, Institute of Technology, Helsingfors, Finland

3-Hydroxyflavanones have been found to be very unstable towards alkali. They are partly dehydrogenated to 3-hydroxyflavones and partly rearranged. It has recently been shown [1] that this rearrangement in some cases gives 2-hydroxy-2-benzylcoumaran-3-ones, but it is reported in the literature that in other cases the reaction can go further, giving acids, which easily yield anhydrolactones. The formation of these acids has been assumed to take place through a benzilic acid rearrangement. Thus fustintrimethylether (3-hydroxy-3′,4′,7-trimethoxyflavanone) (I) and ampeloptinpentamethylether (3-hydroxy-3′,4′,5,5′,7-pentamethoxyflavanone) (II) give anhydrotrimethylhazeyl lactone [2] (V) and anhydropentamethylampeloptin lactone [3] (VI) respectively.

A third lactone is garcinol [4] (VII) obtained from fukugetin by treatment with alkali [5]. Because the structure of fukugetin is not known with certainty, it is impossible to say whether the formation of garcinol is quite analogous to the formation of the two other lactones.

It was at one time thought that the rearrangement of pinobanksindimethylether [6] (3-hydroxy-5,7-dimethoxyflavanone) (III) might be analogous to the above rearrangement and that the product obtained, which is now regarded as 2-hydroxy-2-benzyl-4,6-dimethoxycoumaran-3-one [1] was possibly the acid corresponding to (IX). It was therefore decided to synthesise this acid and the corresponding lactone (IX) and at the same time to synthesise the lactones (V) and (VI) and the trimethylether of (VII). The lactone (X), which should be produced by the benzilic acid rearrangement of taxifolintetramethylether (3-hydroxy-3′,4′,5,7-tetramethoxyflavanone) (IV) was also synthesised. None of these lactones, which can also be regarded as substituted 3-benzalcoumaran-2-ones, has previously been synthesised, although the methylester-methylether of the free acid corresponding to (VIII) has been synthesised [4].

The route followed in these syntheses was essentially that given by Czaplicki, v. Kostanecki and Lampe [7], *viz.* condensation of the appropriate 2-hydroxyphenylacetic acid with benzaldehyde or a substituted benzaldehyde. The 2-hydroxyphenylacetic acids (XI) and (XII) were prepared by the Willgerodt reaction, as modified by Schwenk and Bloch [8], from the corresponding 2-hydroxyacetophenones. According to Schwenk and Bloch their method is



I; $R^2 = R^5 = H$; $R^1 = R^3 = R^4 = OCH_3$
II; $R^1 = R^2 = R^3 = R^4 = R^5 = OCH_3$
III; $R^3 = R^4 = R^5 = H$; $R^1 = R^2 = OCH_3$
IV; $R^5 = H$; $R^1 = R^2 = R^3 = R^4 = OCH_3$

V; $R^2 = R^5 = H$; $R^1 = R^3 = R^4 = OCH_3$
VI; $R^1 = R^2 = R^3 = R^4 = R^5 = OCH_3$
VII; $R^3 = R^5 = H$; $R^1 = R^2 = R^4 = OH$
VIII; $R^3 = R^5 = H$; $R^1 = R^2 = R^4 = OCH_3$
IX; $R^3 = R^4 = R^5 = H$; $R^1 = R^2 = OCH_3$
X; $R^5 = H$; $R^1 = R^2 = R^3 = R^4 = OCH_3$

XI; $R^1 = R^2 = OCH_3$
XII; $R^2 = H$; $R^1 = OCH_3$

not adaptable to the preparation of acids with a free hydroxyl group, whereas such acids have been prepared by the usual Willgerodt-Kindler reaction [9]. We find however that the method of Schwenk and Bloch can be used, although the yields are low. As the starting materials were easily available the method was, in spite of the low yield, convenient for the preparation of the small amounts of acids necessary for our purposes.

The condensation with the aldehyde was carried out in the presence of acetic anhydride and triethylamine [10].

As can be seen from Table 1 the m.p:s of the synthetic 3-benzalcoumaran-2-ones are in good agreement with the values given for the compounds obtained through rearrangement from natural products. Although no mixed m.p. determinations could be carried out, owing to lack of authentic material, these syntheses are however additional evidence in support of the structures given to anhydrotrimethylhazeyl lactone, anhydropentamethylampeloptin lactone and garcinoltrimethylether respectively.

Table 1.

(V)	m.p. 183—184°	Anhydrotrimethylhazeyl lactone	m.p. 184—185° [2]
(VI)	m.p. 159—160°	Anhydropentamethylampeloptin lactone	m.p. 159—160° [3]
(VIII)	m.p. 167°	Garcinoltrimethylether	m.p. 167° [4]
(IX)	m.p. 169.5—170.5°		
(X)	m.p. 173—174°		

3-Benzal-4,6-dimethoxycoumaran-2-one (IX) was converted by hydrolysis into the free acid, the m.p. of which cannot be determined as upon heating it is converted back into the lactone thus exhibiting its m.p. Although this m.p. coincides with the m.p. of the rearrangement product of pinobanksindimethylether [6], mixed m.p. determination shows that they are definitely different compounds.

EXPERIMENTAL

2-Hydroxy-4,6-dimethoxyphenylacetic acid (XI). 2-Hydroxy-4,6-dimethoxyacetophenone (5 g) was heated with sulphur (2 g) and morpholine (4.35 g) in an oil-bath at 150—160° for 5 hours. The mixture was then dissolved in chloroform and the chloroform solution was washed with water and hydrochloric acid. The chloroform was removed in vacuum and the residue crystallised from alcohol. The thiomorpholide thus obtained was hydrolysed by boiling with 30 % potassium hydroxide (20 ml). The alkaline solution was diluted with water, extracted with ether and then acidified, whereupon 2-hydroxy-4,6-dimethoxyphenylacetic acid was precipitated as an oil. It was taken up in ether, the acid extracted in sodium hydrogen carbonate and precipitated once again. Extraction with ether and removal of the ether in vacuum gave a yellow oil which crystallised. Crystallisation from ether-light petroleum gave colourless crystals, m.p. 140—140.5°. Yield 0.8 g (15 %). (Found: C 56.7; H 5.6. $C_{10}H_{12}O_5$ requires: C 56.6; H 5.7.)

4,6-Dimethoxycoumaran-2-one. When the above mentioned acid is sublimed in vacuum it loses water and is converted into its lactone. M.p. after crystallisation from ether 154°. (Found: C 61.6; H 5.1. $C_{10}H_{10}O_4$ requires: C 61.8; H 5.2.)

2-Hydroxy-4-methoxyphenylacetic acid (XII) was prepared from 2-hydroxy-4-methoxyacetophenone by the same procedure as described above for the preparation of 2-hydroxy-4,6-dimethoxyacetophenone. In this case the thiomorpholide could not be obtained crystalline and was therefore hydrolysed in the crude state. Crystallisation from ether-light petroleum gave the acid, m.p. 132—133° (Lit. 133° [11]).

3-Benzal-4,6-dimethoxycoumaran-2-one (IX). 2-Hydroxy-4,6-dimethoxyphenylacetic acid (1 g), benzaldehyde (0.55 g), acetic anhydride (2 g) and triethylamine (0.5 g) were heated together on a water bath for 6 hours. Water (50 ml) was then added to the reaction mixture which was subsequently boiled for 15 minutes. The semicrystalline reaction product was separated and dried on a porous plate. It was then dissolved in acetone and filtered through aluminium oxide. Crystallisation from alcohol gave yellow plates, m.p. 169.5—170.5°. (Found: C 72.0; H 5.0. $C_{17}H_{14}O_4$ requires: C 72.3; H 5.0.)

2-Hydroxy-4,6-dimethoxystilbene-α-carboxylic acid. The 3-benzal-4,6-dimethoxycoumaran-2-one was hydrolysed by boiling with 10 % potassium hydroxide. Crystallisation from benzene, of the product obtained upon acidification of the alkaline solution gave pale yellow needles. Upon heating it turns dark yellow and melts at 169°. (Found: C 67.7; H 5.55. $C_{17}H_{16}O_5$ requires: C 68.0; H 5.4.)

3-(4-Methoxybenzal)-4,6-dimethoxycoumaran-2-one (VIII) was made as described above using anisaldehyde, except that the time of heating was 20 hours. The product was obtained as long yellow needles, m.p. 167°. (Found: C 69.1; H 5.1. $C_{18}H_{16}O_5$ requires: C 69.2; H 5.2.)

3-(3,4-Dimethoxybenzal)-4,6-dimethoxycoumaran-2-one (X) was prepared in a similar manner from veratraldehyde, giving small orange coloured needles, m.p. 173—174°. (Found: C 66.7; H 5.3. $C_{19}H_{18}O_6$ requires: C 66.5; H 5.4.)

3-(3,4,5-Trimethoxybenzal)-4,6-dimethoxycoumaran-2-one (VI) was prepared from gallaldehydetrimethylether, giving orange-red needles, m.p. 159—160° (Found: C 64.3; H 5.3. $C_{20}H_{20}O_7$ requires: C 64.5; H 5.4).

3-(3,4-Dimethoxybenzal)-6-methoxycoumaran-2-one (V) was prepared from 2-hydroxy-4-methoxyphenylacetic acid and veratraldehyde, giving bright yellow needles, m.p. 183—184°. (Found: C 68.8; H 5.3. $C_{18}H_{16}O_5$ requires: C 69.2; H 5.2.)

SUMMARY

A number of methoxysubstituted 3-benzalcoumaran-2-ones have been prepared by condensation of methoxysubstituted 2-hydroxyphenylacetic acids with benzaldehyde or methoxysubstituted benzaldehydes.

REFERENCES

1. Gripenberg, J. *Acta Chem. Scand.* **7** (1953) 1323.
2. Oyamada, T. *Ann.* **238** (1939) 44.
3. Kotake, M. and Kubota, T. *Ann.* **544** (1940) 253.
4. Murakami, M. and Irie, T. *Proc. Imp. Acad. (Tokyo)* **10** (1934) 568; *Chem. Abstr.* **29** (1935) 1818.
5. Shinoda, J. *J. Pharm. Soc. Japan* **52** (1932) 1009; *Chem. Abstr.* **27** (1933) 1883.
6. Lindstedt, G. *Acta Chem. Scand.* **4** (1950) 772.
7. Czaplicki, S., v. Kostanecki, S. and Lampe, V. *Ber.* **42** (1909) 827.
8. Schwenk, E. and Bloch, E. *J. Am. Chem. Soc.* **64** (1942) 3051.
9. Ott, A. C., Mattano, L. A. and Coleman, G. H. *J. Am. Chem. Soc.* **68** (1946) 2633.
10. Bakunin, M. and Peccerillo, D. *Gazz. chim. ital.* **65** (1935) 1145.
11. Offe, H. A. and Jatkewitz, H. *Chem. Ber.* **80** (1947) 469.

Received February 10, 1954.