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HYDROLYSIS OF CARTHAMIN

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2,5-Bis(p-methoxycinnamoyl)-1,3,4,6,7,8-, and 2,7-bis(p-methoxycinnamoyl)-1,3,4,5,6,8- or 4,5-bis(p-methoxycinnamoyl)-1,2,3,6,7,8-hexamethoxyxanthen (8, and 9 or 10) were obtained by the methylation of the hydrolysis products of carthamin. The structure of 8 was confirmed by the direct comparison with a synthetic sample. The formation process of 8, and 9 or 10 is discussed.

In a previous communication,[1] we have proposed the structure 1 for carthamin, the red coloring matter of the flowers of Safflower (Carthamus tinctorius L.), on the basis of its spectroscopic evidence and hydrolytic behavior. It has so far been known that carthamin is hydrolyzed with 10% phosphoric acid to give two flavanones, carthamidin and isocarthamidin,[2] glucose, and formic acid.[1] However, the aglycon (2) has not been isolated yet. Now, we wish to report the hydrolysis of carthamin (1) in a large amount of ethanol containing 6 M hydrochloric acid instead of phosphoric acid.[3]

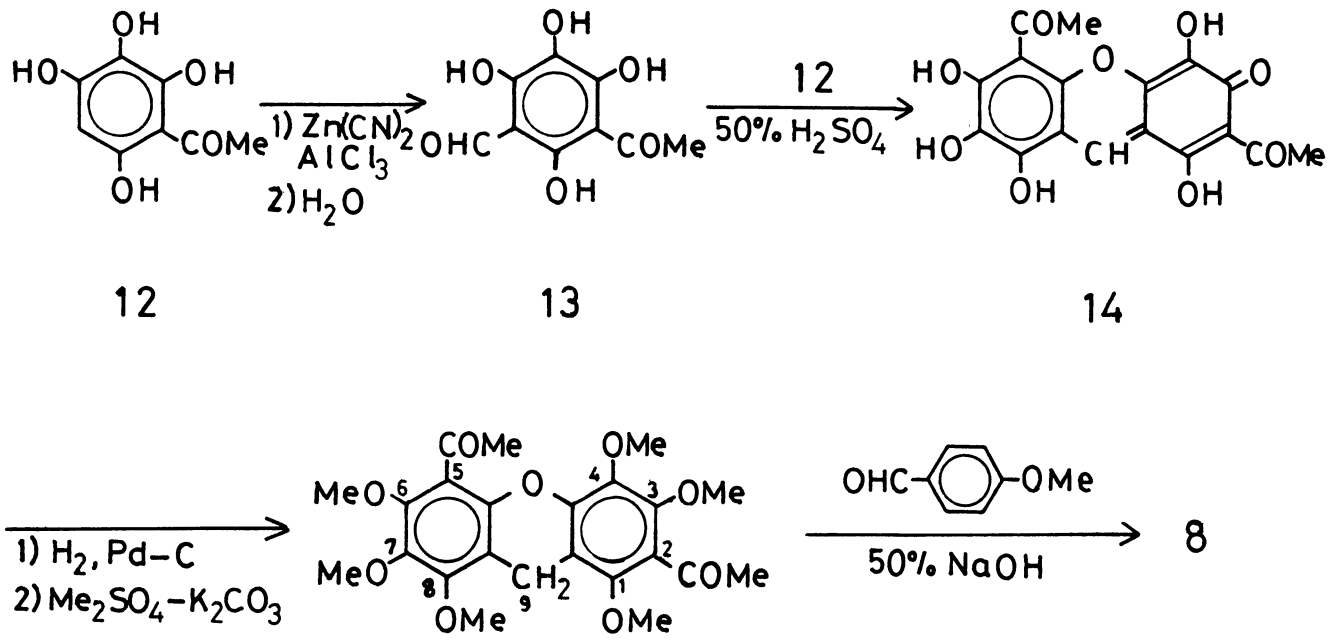
A solution of 300 mg of carthamin (pyridine salt)[4] in 240 ml of ethanol containing 60 ml of 6 M hydrochloric acid was refluxed for 10 h to yield 180 mg of an isomeric mixture, which was unable to be purified.

The hydrolysis products, mp > 280°C, MS, m/e 570 (M^+), Mg-HCl test – purple-red, (180 mg) were methylated with dimethyl sulfate – potassium carbonate in acetone; the resulting methyl ethers were chromatographed on a column of silica gel with benzene – ethyl acetate (5:1) to afford three components, A (66 mg), B (20 mg), and C (27 mg). Two compounds, A-1 and A-2, were further separated from the main product A (mp 60 – 72°C) by a high pressure liquid chromatography with benzene – methanol (17:83) using Hitachi #3010 (8 × 500 mm) column. The formation ratio of A-1 and A-2 was 45:55.

A-1, mp 74 – 76°C (from dilute methanol); UV max (EtOH) 329 nm; IR (KBr) 1632 cm^{-1} (C=O); PMR ($CDCl_3$) δ 3.75 (2H, s, $-CH_2-$), 3.80 – 4.10 (24H, m, -OMe × 8), 6.95 – 7.60 (12H, m, p-substituted cinnamoyl × 2); Found: C, 68.36; H, 5.67%; M^+, 682. Calcd for $C_{39}H_{38}O_{11}$: C, 68.61; H, 5.61%; M, 682.

A-2, mp 190 – 191°C (from methanol); UV max (EtOH) 330 nm; IR (KBr) 1630 cm^{-1} (C=O); PMR ($CDCl_3$) δ 3.76, 3.82, 3.89, and 4.03 (each 6H, s, -OMe × 8), 3.92 (2H, s, $-CH_2-$), 6.89 and 7.49 (each 4H, d, J=8.5Hz, p-substituted phenyl × 2), 6.91 and 7.35 (each 2H, d, J=16Hz, -CH=CH- × 2); Found: C, 68.39; H, 5.58%; M^+, 682. Calcd for $C_{39}H_{38}O_{11}$: C, 68.61; H, 5.61%; M, 682.

Compound A-1 was completely identical with the synthetic sample of 2,5-bis(p-methoxycinnamoyl)-1,3,4,6,7,8-hexamethoxyxanthen (8), prepared by the following method (Scheme 1).



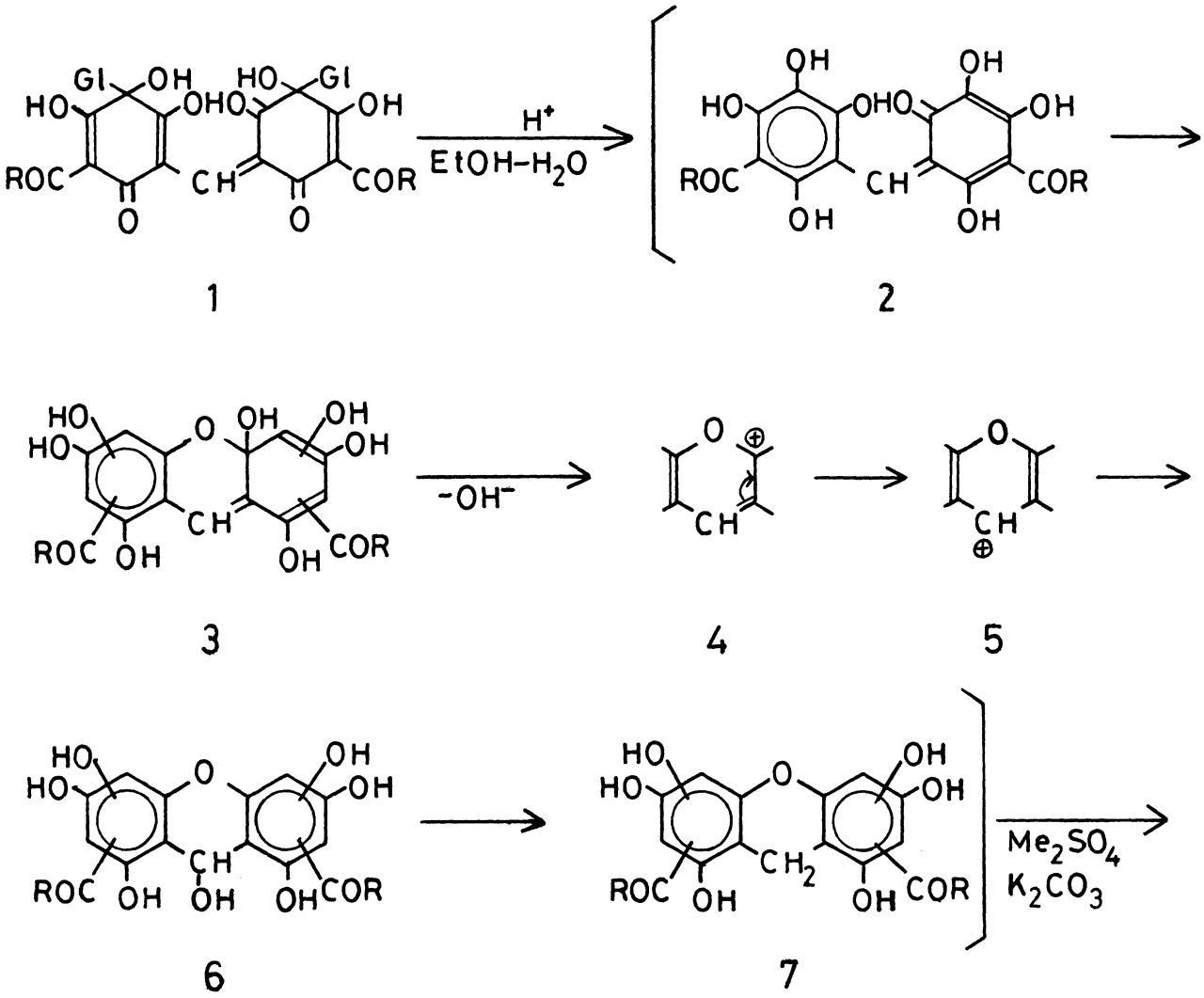
12 13 14

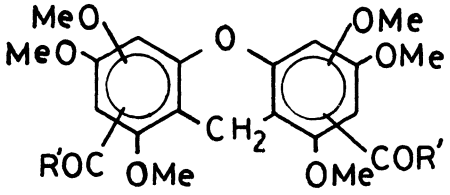
15

Scheme 1

An equimolecular mixture of 2,3,4,6-tetrahydroxyacetophenone (12) and 5-formyl-2,3,4,6-tetrahydroxyacetophenone (13), obtained by the formylation of 12, in methanol containing a small amount of 50% sulfuric acid was refluxed for 10 h to afford the condensation product (14), dark violet crystals, mp > 280°C, in a 19% yield; MS m/e 360 (M^+); IR (KBr) 1700 and 1620 cm^{-1} (C=O); PMR (DMSO-d_6) δ 2.67 and 2.82 (each 3H, s, $-COCH_3 \times 2$), 8.27 (1H, s, -CH=). Compound 14 was hydrogenated in ethanol using a 5% palladium charcoal as a catalyst; the reduction product was methylated without purification with dimethyl sulfate–potassium carbonate in acetone to yield 2,5-diacetyl-1,3,4,6,7,8-hexamethoxyxanthen (15) in a 27% yield, mp 116°C; MS m/e 446 (M^+); IR (KBr) 1647 cm^{-1} (C=O); PMR ($CDCl_3$) δ 2.49 and 2.61 (each 3H, s, $-COCH_3 \times 2$), 3.77 and 3.87 (each 3H, s, -OMe × 2), 3.84 and 3.90 (each 6H, s, -OMe × 4), 3.97 (2H, s, $-CH_2-$). The unsymmetrical structures of 14 and 15 were supported by the observation of the two separate signals of acetyl groups in their PMR spectra. Condensation of 15 with p-methoxybenzaldehyde in the presence of 50% aqueous potassium hydroxide solution in methanol afforded 2,5-bis(p-methoxycinnamoyl)-1,3,4,6,7,8-hexamethoxyxanthen (8), mp 74–76°C.

On the other hand, the symmetrical structure, 2,7-bis(p-methoxycinnamoyl)-1,3,-4,5,6,8- or 4,5-bis(p-methoxycinnamoyl)-1,2,3,6,7,8-hexamethoxyxanthen (9 or 10) would to be given for A-2 from the above spectroscopic data. Although B and C were

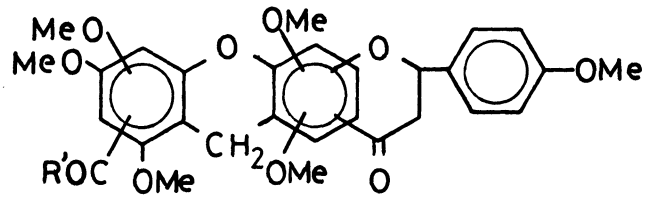




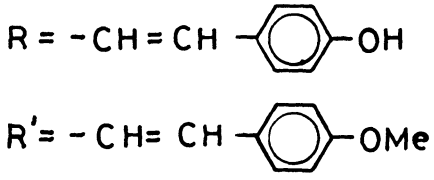
8 2-and 5-COR', 4-and 7-OMe

9 2-and 7-COR', 4-and 5-OMe

10 4-and 5-COR', 2-and 7-OMe



11



Scheme 2

not pure compounds, they gave a molecular ion peak at m/e 668 in their mass spectra, two carbonyl absorption bands at 1690 and 1630 cm^{-1} in their IR spectra, and showed a purple-red coloration with Mg−HCl test. From these properties, the isomeric structures of 11 would be assumed for both B and C.

The formation process of A-1, A-2, B, and C is pressumed as follows (Scheme 2). Hydrolysis of 1 affords the aglycon 2, which immediately forms an isomeric mixture of hemiacetal 3. Since the acetal formation proceeds via keto-enol tautomerism of 1 or 2, the three structures, one unsymmetrical and two symmetrical, are considered. The acetal 3 is converted into xanthydrol 6 via the carbonium ions 4 and 5. The reductive reaction of 6 into xanthen 7 is considered similar to that of the formation of xanthen from xanthydrol.[5] In fact, the authors have confirmed the formation of xanthen from xanthydrol by the same conditions of the hydrolysis of 1. Although the formation of three isomeric methoxyxanthens (8, 9, and 10) was predicted by the methylation of the hydrolysis products, only two compounds, 8 , and 9 or 10, were isolated in the present work. The identification of the structure of 9 or 10 will be reported elsewhere.[6]

Further, it is thought that the ring closure of the hydrolysis products into the corresponding flavanones has occurred during the hydrolysis. This fact is also supported by the formation of B and C.

As mentioned above, we have first obtained the xanthen derivatives (8, and 9 or 10), which have a carbon skeleton of carthamin 1, from the hydrolysis products. It will be difficult to obtain the aglycon 2 by usual hydrolysis.

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References and Notes

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2) C. Kuroda, Nippon Kagaku Zasshi, 51, 237 (1930); C. Kuroda, J. Chem. Soc., 1930, 752; H. Obara, J. Onodera, and F. Yamamoto, Chem. Lett., 1973, 915; H. Obara, J. Onodera, Y. Kurihara, and F. Yamamoto, Bull. Chem. Soc. Jpn., 51, 3627 (1978).
3) A large amount of solvent was used to prevent the polymerization of the hydrolysis products.
4) H. Obara and J. Onodera, Chem. Lett., 1978, 643.
5) H. E. Ungnade, E. F. Kline, and E. W. Crandall, J. Am. Chem. Soc., 75, 3333 (1953).
6) The synthesis of 9 and 10 is now in progress.

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