Reactions of 4-Hydroxy-6-methyl-2-pyrone with αβ-Unsaturated Acyl Chlorides

By K. KATO, Y. SHIZURI, and Y. HIRATA
(*Chemical Institute, Nagoya University, Nagoya, Japan*)
and S. YAMAMURA*
(*Pharmaceutical Institute, Meijo University, Yagotourayama, Showa-ku, Nagoya, Japan*)

IN the course of our synthetic studies we have found some interesting cyclization reactions.[1]

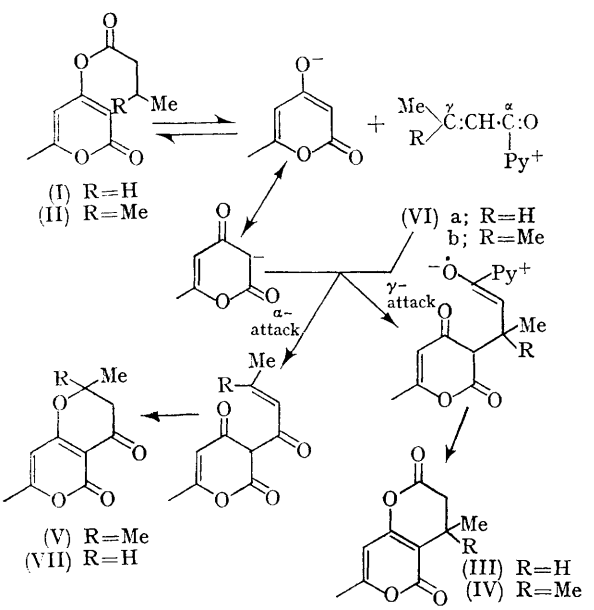
When heated with two equivalents of butyryl chloride in pyridine on a steam bath for 3 hr., 4-hydroxy-6-methyl-2-pyrone (triacetic acid lactone) is known to afford a 3-butyryl-4-hydroxy-6-methyl-2-pyrone.[2] The reactions of triacetic acid lactone with αβ-unsaturated acyl chlorides in pyridine gave esters (I) m.p. 41°, in 40% yield, and (II) m.p. 46°, in 60% yield. However, triacetic acid lactone reacted with crotonyl chloride to afford only a lactone (III) m.p. 100°, in 60% yield (on a steam bath for 3 hr.), or a mixture of (I) and (III) in 23 and 40% yields,

TABLE

Starting material	Acyl chloride	Amount (equiv.)	Product	Yield (%)
(I)[a]	3,3-Dimethyl-acrylyl chloride	2	(III)	36
			(V)	18
(I)[a]	Butyryl chloride	2	BHMP[c]	30
			(III)	14
(II)[b]	Crotonyl chloride	1	(III)	25
			(V)	20
(II)[b]	Crotonyl chloride	2	(III)	45
			(IV)	2
			(V)	12

[a] Heated at 100° for 3 hr.; [b] Reflux for 12 hr.; [c] 3-Butyryl-4-hydroxy-6-methyl-2-pyrone.

respectively (at room temp. for 12 hr.). On the other hand, the reaction of triacetic acid lactone with 3,3-dimethylacrylyl chloride did not afford any cyclization product, but gave the ester (II) in 60% yield (at room temp. for 12 hr.). However, when the reaction solution was heated under reflux for 12 hr., a mixture of two isomers (IV) m.p. 81°, and (V) m.p. 180°, in 12 and 60% yields, respectively, was obtained. Cyclization reactions probably take place, as shown below.



In the above mechanism,[3] it is plausible to suggest the formation of an $\alpha\beta$-unsaturated acylpyridinium chloride (VI) which has two positions (α and γ) that can be attacked by an anion of triacetic acid lactone. It seems reasonable that the anion reacts with (VIa) at the γ-position whereas in the case of (VIb), which has two methyl groups at the γ-position, the anion attacks the α-position.

The formation of an $\alpha\beta$-unsaturated acylpyridinium chloride is confirmed by the following. Treatment of (I) (or II) with 3,3-dimethylacrylyl chloride (or crotonyl chloride) under various conditions gave a mixture of cyclization products, as described in the Table, which indicated the order of relative reactivity: butyrylpyridinium chloride > crotonylpyridinium chloride > 3,3-dimethylacrylylpyridinium chloride. Furthermore, yields of cyclization products depend on the amount of acyl chlorides added. This indicates that the first step must be a rapid reversible reaction, rather than the second one which leads to a cyclization product.†

Finally, the high reactivity of a saturated acylpyridinium chloride led to the formation of an α-pyrone (VII),‡ m.p. 154°, in 11% yield by treatment of triacetic acid lactone with β-chlorobutyryl chloride under the abovementioned conditions.[2] Physical data for all compounds described are satisfactory.

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† A straightforward cyclisation from (I) (or II) to (III) [or (IV), (V)] is not necessarily ruled out [especially, in the case of (I)], but a stepwise mechanism seems to be more reasonable. However, it seems premature to decide which of the above mechanisms is correct.

‡ (VII) has the same pyranopyran nucleus as that of radicinin (see ref. 1).

[1] (a) J. F. Grove, *J. Chem. Soc.*, 1964, 3234; (b) The synthesis of dihydroradicinin will be reported soon.
[2] S. Iguchi and K. Hisatsune, *J. Pharm. Soc. Japan*, 1957, 77, 94.
[3] H. Eisenhauer and K. P. Link, *J. Amer. Chem. Soc.*, 1953, 75, 2044; 2046.