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Altenin. V. Pathogenic Activity of Reductones to the Pear

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The three reductones, 3-hydroxy-2, 4-dioxopentane, ethyl 2-hydroxy-1, 3-dioxovalerate and ethyl 2-hydroxy-3-oxobutyrate, were synthesized. These compounds were examined for the pathogenic activities to the pear. The pathogenic activities of reductones have some relations with the endiol contents. The center of pathogenic activity in altenin is shown to be the endiol carbonyl grouping.

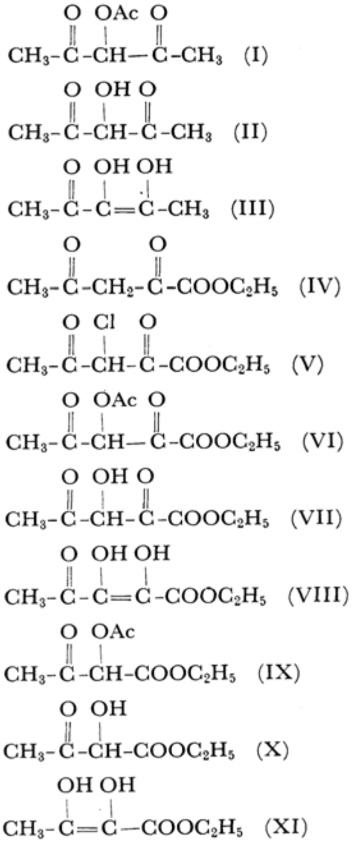
It was suggested in the preceding paper that the altenin molecule is responsible for the phytopathogenic activity.[1-3] Reductone is generally a tautomeric mixture consisting of hydroxy dicarbonyl isomers and the endiol carbonyl isomer, This sort of isomerism is effected by prototropic mobility.[4] The prototropic mobility of grouping –CO–CH(OH)–CO–R will depend on the nature of R. Considering the electron releasing effect of R, the prototropic mobility would decrease in the following order:[5,6]

$$R{=}COOC_2H_5 > CH_3 > O{-}C_2H_5$$

Three analogous compounds, 3-hydroxy-2, 4-dioxopentane (II), ethyl 2-hydroxy-1, 3-dioxovalerate (VII), and ethyl 2-hydroxy-3-oxobutyrate (X), are expected to exhibit some difference in the endiol carbonyl isomer content, and the pathogenic activity to the pear. This paper is concerned with the syntheses of these three compounds and the results of examination of their pathogenic activities to the pear.

Results and Discussion

II was obtained by the hydrolysis of 3-acetoxy-2, 4-dioxopentane (I).[7,8]



$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OAc}{|}}{CH}\text{—}\overset{\overset{O}{\|}}{C}\text{-}CH_3$ (I)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OH}{|}}{CH}\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_3$ (II)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OH}{|}}{C}{=}\overset{\overset{OH}{|}}{C}\text{-}CH_3$ (III)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_2\text{-}\overset{\overset{O}{\|}}{C}\text{-}COOC_2H_5$ (IV)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{Cl}{|}}{CH}\text{-}\overset{\overset{O}{\|}}{C}\text{-}COOC_2H_5$ (V)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OAc}{|}}{CH}\text{—}\overset{\overset{O}{\|}}{C}\text{-}COOC_2H_5$ (VI)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OH}{|}}{CH}\text{-}\overset{\overset{O}{\|}}{C}\text{-}COOC_2H_5$ (VII)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OH}{|}}{C}{=}\overset{\overset{OH}{|}}{C}\text{-}COOC_2H_5$ (VIII)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OAc}{|}}{CH}\text{-}COOC_2H_5$ (IX)

$CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{OH}{|}}{CH}\text{-}COOC_2H_5$ (X)

$CH_3\text{-}\overset{\overset{OH}{|}}{C}{=}\overset{\overset{OH}{|}}{C}\text{—}COOC_2H_5$ (XI)

Fig. 1.

VII was synthesized from ethyl 1,3-dioxovalerate (IV).[9] IV was chlorinated by sulfuryl chloride to ethyl 2-chloro-1, 3-dioxovalerate (V),[10] which

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[2] N. Sugiyama, C. Kashima, M. Yamamoto and R. Mohri, *ibid.*, **40**, 345 (1967).

[3] N. Sugiyama, C. Kashima, M. Yamamoto and R. Mohri, *ibid.*, **40**, 2591 (1967).

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[7] A. Combes, *Compt. rend.*, **111**, 241 (1890).

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TABLE 1. THE ULTRAVIOLET ABSORPTION MAXIMA (mμ) 2, 3-UNSATURATED CARBONYL COMPOUNDS IN ETHANOL

Chromophore*	X=Y=H		X=OH, Y=H			X=Y=OH		
	Compound	λ_{max}	Compound	λ_{max}	Δ**	Compound	λ_{max}	Δ***
A	3-Pentenone-2	224	4-Hydroxy-3-pentenone-2	269	44	II (or III)	289	65
B	Ethyl crotonate	204	Ethyl 3-hydroxy 2-butenoate	245	41	X (or XI)	268	64
C	Methyl β-acetacrylate	220				VII (or VIII)	268	48

* Chromophore A: -CX=CY-CO-, B: -CX=CY-COOR, C: -CO-CX=CY-COOR.

** Δ: The bathochromic shift of hydroxyl group, $\lambda_{max}^{X=OH,\ Y=H}-\lambda_{max}^{X=Y=H}$.

*** Δ: The bathochromic shift of two hydroxyl groups, $\lambda_{max}^{X=Y=OH}-\lambda_{max}^{X=Y=H}$.

TABLE 2. THE ε VALUES AND THE PATHOGENIC ACTIVITIES OF REDUCTONES

Compound	λ_{max}^{EtOH} mμ	ε_{max}^{EtOH} mμ	λ_{max}^{buffer} mμ	$\varepsilon_{max}^{buffer}$ mμ	Activity mm²
Acetoin	—	—	—	—	1.7
II (or III)	289	1550	290	1100	7.7
VII (or VIII)	268	1100	280	240	7.1
X (or XI)	268	930	280	60	5.4
Altenin	—	—	—	—	10.1

gave ethyl 2-acetoxy-1, 3-dioxovalerate (VI) by treating with acetic acid and potassium acetate. The infrared absorption spectrum of VI showed carbonyl absorption bands at 1740, 1250 and 1190 cm⁻¹. VI showed a positive red coloration with ferric chloride. Hydrolysis of VI with hydrochloric acid in ethanol afforded a product, mp. 68°C, which showed carbonyl absorption bands at 1730 and 1250 cm⁻¹, and hydroxyl absorption bands at 3400 and 1100 cm⁻¹ in the infrared absorption spectrum. This product reduced Tillman's reagent. These data and the elemental analysis supported the structure of this product as ethyl 2-hydroxy-1, 3-dioxovalerate (VII).

X was synthesized as follows. Hydrolysis of ethyl 2-acetoxy-3-oxobutyrate (IX) afforded white needles, mp 62°C,[11,12] which showed in the infrared absorption spectrum carbonyl absorption bands at 1730 and 1250 cm⁻¹, hydroxyl absorption bands at 3450 and 1100 cm⁻¹, and reduced Tillman's reagent. These data and the elemental analysis support its structure as ethyl 2-hydroxy-3-oxobutyrate (X).

There are posibilities of the existence of tautomeric isomers in compounds II, VII and X. The characteristics of the ultraviolet absorption spectra of 4-hydroxy-3-pentenone-2,[13] ethyl 3-hydroxy-2-butenoate,[13] 3-pentenone-2,[14] ethyl crotonate,[15] methyl β-acetacryrate,[16] II (or III), VII (or VIII) and X (or XI) are listed in Table 1. Acetylacetone shows an absorption maximum at 275 mμ (ε 100),[13] but its enol isomer 4-hydroxy-3-pentenone-2 shows a high intensive absorption at 269 mμ (ε 12500), which corresponds to a 45 mμ bathochromic shift induced by the hydroxyl group at C-4 as compared with that of 3-pentenone-2 at 224 mμ (ε 9750). The absorption maximum of II at 289 mμ (ε 1550) was assigned to the endiol isomer (III), because the ε value (1550) seemed too high for II. The bathochromic shift caused by the two hydroxyl groups at C-3 and C-4 is now calculated 65 mμ. The absorption maximum of ethyl 3-hydroxy-2-butenoate, an enol isomer of ethyl acetacetate, was 245 mμ (ε 15800), which corresponds to a 41 mμ red shift due to the hydroxyl group in chromophore B, a value which is similar to that in chromophore A. Compared with the absorption maximum of ethyl crotonate at 204 mμ, the absorption maximum at 268 mμ in X can reasonably be assigned to the endiol tautomer (XI), in which the bathochromic shift due to the two hydroxyl groups at C-2 and C-3 is 64 mμ. Similarly, the absorption maximum of VII at 268 mμ was assigned to the endiol isomer (VIII). Methyl acetacryrate shows an absorption maximum at 220 mμ. The red shift caused by the two hydroxyl groups at C-2 and C-3 is 48 mμ. This shift is smaller than that of chromophore A (65 mμ) and B(64 mμ), and can be accounted for by the

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cross conjugation is chromophore C. The ε values of these compounds are listed in Table 2.

From the data of the phytopathogenic activities of II, VII, X acetoin and altenin (Table 2), it is seen that the reductones are active to a certain extent but the activity of acetoin is very weak. The order of activities of reductones, II>VII>X, roughly parallels the ε values at the absorption maxima of the endiol carbonyl chromophore. These data suggest that the enol tautomer of reductones, the endiol carbonyl grouping, may be related to the pathogenic activity to the pear.

This grouping is readily oxidized to tricarbonyl compounds. The oxidation of altenin will be discussed in the elsewhere.

Experimental

Ethyl 2-Hydroxy-1, 3-dioxovalerate (VII). The mixture of 200 g of ethyl 2-chloro-1, 3-dioxovalerate (V), 275 g of anhydrous potassium acetate and 750 m*l* of glacial acetic acid was stirred for 4.5 hr at 120°C. The mixture became dark brown with white precipitate, which was filtered off after cooling. Distillation of the acetic acid from the filtrate under reduced pressure afforded an oily substance, which was poured into water and was extracted with methylene chloride. The methylene chloride extract was dried over anhydrous sodium sulfate, and distilled, giving 39 g of yellow liquid, bp 85—91°C/20 mmHg.

Four grams of yellow distillate was dissolved in the mixture of 20 m*l* of ethanol and 0.7 m*l* of hydrochloric acid. The solution was stirred for 8 hr at 50°C under nitrogen stream, and stood over night at room temperature. After removal of ethanol under reduced pressure, the residue was passed through silica gel (Merck 7729) column with benzene-acetone (19 : 1 v/v) mixture. On evaporation of the solvent from the eluted solution, which reduced the Tillman's reagent, the colorless needles was obtained, recrystallization from petroleum ether yielded 200 mg, colorless needles, mp 68°C.

Found: C, 48.07; H, 6.46%. Calcd for $C_7H_{10}O_5$: C, 48.27; H, 5.79%.

IR (liquid film): 3400, 2950, 1730, 1440, 1360, 1250, 1190, 1100, 1010 cm^{-1}.

UV (in ethanol): 268 mμ (ε 1100).

Ethyl 2-Hydroxy-3-oxobutyrate (X). Ethyl 2-acetoxy-3-oxobutyrate (IX), which was synthesized from ethyl acetacetate and lead tetraacetate, was dissolved in a mixture of 30 m*l* of ethanol and 1 m*l* of hydrochloric acid. This solution was stirred for 10 hr at 45°C under nitrogen stream, and stood over night at room temperature. After removal of the solvent, the residue was passed through silica gel (merck 7729) column chromatography with benzene-acetone (9 : 1 v/v) mixture. On evaporation of the solvent from the eluted solution, which reduced the Tillman's reagent, the colorless needles, recrystallized from petroleum ether, was obtained, mp 62°C.

Found: C, 49.28; H, 6.38%. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.90%.

IR (liquid film): 3450, 2950, 1730, 1360, 1250, 1100, 1010 cm^{-1}.

UV (in ethanol): 268 mμ (ε 930).

Ultraviolet Absorption Spectra. The ultraviolet absorption spectra were measured in ethanol and in ammonium acetate buffer (pH 7.8) solution with the concentration of about 10^{-3} mol/*l*.

The Pathogenic Activities of II, VII, X, Acetoin and Altenin to the Pear. The solution of II, VII, X, acetoin and altenin in ammonium acetate buffered solution (pH 7.8) were adjusted to the concentration of 10^{-2} mol/*l*. Acetoin was employed the commercial product from Tokyo Chemical Industry Co., Ltd. The black spot test[17] to the pear at 28°C of these five solutions were examined. By the test on the same leaf, the pathogenic activities were compared as shown in Table 2.

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