

Synthesis of Some Novel $\Delta^{\alpha, \beta}$ -Butenolides

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β -benzoylacrylic acid, a γ -keto acid, has been condensed with various phenolic compounds using concentrated sulphuric acid as condensing agent. The condensation products are $\Delta^{\alpha, \beta}$ -butenolides in which γ -carbon atom is attached to two different phenyl rings. Their structures have been established by elemental analysis, chemical reactions and spectral studies.

INTRODUCTION

$\Delta^{\alpha, \beta}$ -Butenolides are five-membered unsaturated γ -lactones and some of them are reported to exhibit antibacterial^{1,2}, antifungal^{3,4}, and tumour-inhibitory^{5,6} activities. Besides this, they find applications as insecticides⁷, herbicides⁸, and seed and plant growth regulators^{8,10} also. In this communication, we report synthesis of some new unsymmetrically substituted $\Delta^{\alpha, \beta}$ -butenolides from a γ -keto acid, β -benzoylacrylic acid.

The chemistry of γ -keto acids and their derivatives has received a wide attention due to their interesting ring-chain tautomeric behaviour¹¹⁻¹³. It has been observed that generally γ -keto acids exist as lactol or as an equilibrium mixture of keto-acid and lactol tautomeric forms^{14,15}. The keto-lactol tautomerism is further exalted when hydrogen atoms on α -carbon atom are replaced by alkyl or aryl groups or α, β -ethylenic double bond^{16,17}. The conversion of open keto-acid form into cyclic lactol form or vice-versa is effected by the action of acid or basic catalysts, by specific reagents, and on heating¹². The lactols of γ -keto acids form crystalline acetyl derivatives¹⁷⁻¹⁹ possessing the cyclic lactonic structures. Formation of cyclic derivatives such as pseudo-chlorides²⁰ and pseudo-esters²¹⁻²³ takes place through the cyclic lactol form. There are many chemical reactions of γ -keto acids which take place due to their cyclisation to lactol form²⁴⁻²⁶. Instrumental methods, viz., IR^{22, 27}, Raman²³ and NMR²⁸ spectroscopy also support the formation of cyclic isomers. In recent years, we have reported the synthesis of some mixed phthaleins and succineins²⁹⁻³⁷ by condensing γ -keto acids with phenols. It has been proposed that the γ -keto acids undergo condensation through their lactol tautomeric form and hence the products possess cyclic lactonic structures.

EXPERIMENTAL

Melting points of the synthesised products were determined in open capillary tubes and are uncorrected. Compounds were routine checked for their homogeneity by TLC using silica gel-G as adsorbant and ethyl acetate-methanol-5N ammonia (60 : 30 : 10) as solvent system. IR spectra

were taken on a Perkin-Elmer spectrophotometer model 157 as potassium bromide pellets. Electronic spectra were recorded on a Perkin-Elmer-402 instrument in methanol.

The γ -keto acid, β -benzoylacrylic acid (I), was prepared by Friedel-Crafts reaction between benzene and maleic anhydride in presence of anhydrous aluminium chloride following the reported procedure³⁸. The phenols (III) used were phenol, resorcinol, cathechol, quinol, phloroglucinol and pyrogallol.

General Procedure for the Synthesis of $\Delta^{\alpha,\beta}$ -butenolides (IV-IX)

An intimate mixture of the acid (I) (0.02 mole) and the appropriate phenolic compound (III) (0.025 mole) was taken in a hard glass boiling tube and heated at temperature ranging from 100° to 120° to get a homogeneous solution. Then conc. H₂SO₄ (4-5 drops) was added cautiously with stirring, and heating temperature was raised by 10°. At the elevated temperature, heating was continued for 1.5 to 6 hr. to give a hard and brittle mass on cooling. The condensed mass so obtained was crushed, washed thoroughly with water to remove excess of phenols, extracted with 2% aq. NaOH solution and filtered. Acidification of the filtrate afforded the precipitate of γ -phenyl- γ -(*p*-hydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (IV); γ -phenyl- γ -(2,4-dihydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (V); γ -phenyl- γ -(3,4-dihydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (VI); γ -phenyl- γ -(2,5-dihydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (VII); γ -phenyl- γ -(2,4,6-trihydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (VIII) and γ -phenyl- γ -(2,3,4-trihydroxyphenyl) $\Delta^{\alpha,\beta}$ -butenolide (IX).

In each case the precipitate was filtered, washed with water and purified by repeated crystallisation from aq. acetic acid, dried in an oven first at 60°, then at 100° and finally in a vacuum desiccator. Physical data of the prepared compounds are presented in Table 1.

TABLE I
PHYSICAL DATA OF VARIOUS BUTENOLIDES

Butenolide	m.p. (°C)	Yield (%)	Mol. formula†
IV	105-107	67.3	C ₁₆ H ₁₂ O ₃
V	220-222	64.6	C ₁₆ H ₁₂ O ₄
VI	162-164	59.7	C ₁₆ H ₁₂ O ₄
VII	210-212	65.2	C ₁₆ H ₁₂ O ₄
VIII	125-127	44.1	C ₁₆ H ₁₂ O ₅
IX	116-118	65.1	C ₁₅ H ₁₂ O ₅

†All the compounds gave satisfactory elemental analysis.

The representative butenolide (IV) was subjected to acetylation and bromination as described below.

Acetylation of Butenolide (IV)

Butenolide (IV) (1.0 g) was refluxed with acetic anhydride (15 ml) and fused sodium acetate (3.0 g) at 130–140° for 3 hr to give a pale yellow microcrystalline diacetyl compound (X) (0.7 g), m.p. 180–181° (from aq. ethanol), Found: C, 68.45%; H, 4.42%. $C_{20}H_{16}O_6$ requires C, 68.18%, H, 4.54%. IR: 1780, 1755, 1740, 1620, 1600 cm^{-1} . λ_{max} (methanol): 204, 284, 436, 490 nm.

Bromination of Butenolide (IV)

Butenolide (IV) (0.1 g) was dissolved in glacial acetic acid (10 ml) and the resulting solution was cooled. Then a solution of bromine (1 ml) in glacial acetic acid (10 ml) was added dropwise with stirring and cooling. On dilution with water a pinkish-brown dibromo compound (XI) (1.1 g), m.p. 158–160° (from aq. acetic acid). Found: C, 44.76%; H, 2.30%; Br, 37.70%. $C_{16}H_{10}O_4Br_2$ requires C, 45.07%; H, 2.34%; Br, 37.55%. IR: 3450, 1730, 1700, 1680, 1610, 1600 cm^{-1} . λ_{max} (methanol): 208, 292, 366, 498 nm.

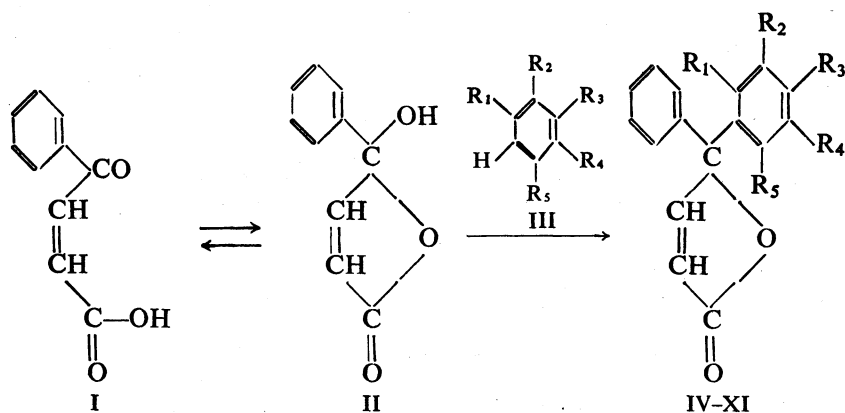
Most of the synthesised butenolides are brownish-yellow microcrystalline solids soluble in methanol, ethanol, acetic acid and acetone giving an orange-red to red-brown colour. On addition of a drop of 2% aq. NaOH solution, the colours are intensified.

RESULTS AND DISCUSSION

β -Benzoylacrylic acid (I) reacted with phenols (III) in presence of conc. H_2SO_4 to give some unsymmetrically substituted $\Delta^{\alpha,\beta}$ -butenolides (IV–IX) in which γ -carbon is attached to two different phenyl rings. The reaction with phenols follows through the lactol form (II) of the acid (I) and with excess of phenols (III) the whole of acid taken reacting as lactol (Scheme 1). Structures have been proposed to the synthesised products on the basis of elemental analysis, acetylation and bromination studies. The butenolide (IV) on acetylation and bromination gave a diacetyl (X) and a dibromo (XI) derivative respectively and thus indicating the presence of only one resorcinol molecule in its structure.

IR spectra of IV to IX and XI displayed a strong and broad band in the region 3300 to 3400 cm^{-1} due to OH stretching. The broad shape and low frequency of this band revealed that OH groups are either involved in a strong hydrogen bonding or tautomeric shift. In X, hydroxyl groups are acetylated and, therefore, it gave a band at 1755 cm^{-1} due to carbonyl stretching in phenolic acetate. Presence of two peaks at 1780 cm^{-1} and 1720–1740 cm^{-1} (lactonic carbonyl stretching) supported the existence of five-membered α, β -unsaturated γ -lactone ring³⁹ in all the butenolides. All the compounds gave a sharp peak near 1620 cm^{-1} which can be assigned to $>C=C<$ stretch, of the othylenic double bond. These IR

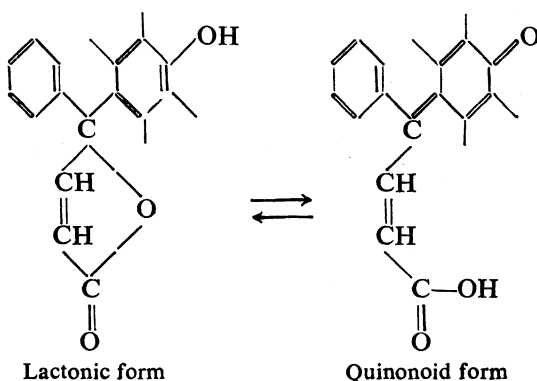
Scheme—1



- | | |
|-----------------------------------|--------------------------------------|
| (IV) $R_1=R_2=R_4=R_5=H; R_3=OH$ | (VIII) $R_2=R_4=H; R_1=R_3=R_5=OH$ |
| (V) $R_2=R_4=R_5=H; R_1=R_3=OH$ | (IX) $R_4=R_5=H; R_1=R_2=R_3=OH$ |
| (VI) $R_1=R_4=R_5=H; R_2=R_3=OH$ | (X) $R_2=R_4=R_5=H; R_1=R_3=OCOCH_3$ |
| (VII) $R_2=R_3=R_5=H; R_1=R_4=OH$ | (XI) $R_5=H; R_2=R_4=Br; R_1=R_3=OH$ |

observations fully support the proposed lactonic structures. But in the IR spectra of IV–IX and XI, two prominent bands were noticed at $1700\text{--}1710\text{ cm}^{-1}$ and $1670\text{--}1680\text{ cm}^{-1}$ also which could be assigned to carboxyl carbonyl and quinone carbonyl respectively. Hence it may be concluded that these butenolides have a tendency to acquire a quinonoid structure with the destruction of five-membered heterocyclic ring and a tautomeric shift exists in the molecules (Scheme 2)³⁹⁻⁴¹.

Scheme—2



Electronic spectra of the butenolides also support the existence of above mentioned tautomeric shift. Presence of an absorption band near $276\text{--}290\text{ nm}$ is in accordance with the lactonic structures⁴². On the other

hand, a very intense band near 204–220 nm (characteristic of α, β -unsaturated acids) and low intensity band around 436–500 nm (assignable to quinone carbonyl group) clearly indicate the existence of corresponding quinonoid tautomeric forms.

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