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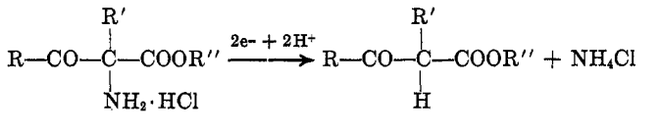
A Novel Electrolytic Deamination. Synthesis of β-Keto Esters[1]

Summary: An electrolytic deamination of the α-acylamino acid esters afforded the corresponding β-keto esters in good yields.

Sir: In the course of electrochemical studies of amino acids, we have reported the electrolytic cleavage of the N–S bond of *N*-tosyl amino acids and peptides,[2] the C–S bond of *S*-benzylcysteine,[3] and the C–S bond of *S*-methylmethionine.[4]

In this communication, an electrolytic reductive cleavage of the C–N bond of α-acylamino acid derivatives is described. We have carried out the electrolysis of α-acylamino acid esters[5] to produce the corresponding β-hydroxy amino acid esters. However, the yield of the resulting amino acids was too low for a practical preparation, but the β-keto esters due to the deamination were obtained in good yields. The electrolytic reduction proceeds *via* a two-electron change resulting in C–NH_2 bond cleavage according to the following scheme.



The electrolysis was carried out as follows. For example, α-benzoylglycine ethyl ester hydrochloride (1 g, 4.1 mmol) dissolved in a mixture of 50% aqueous methanol (20 ml) and concentrated hydrochloric acid (0.5 ml) was placed in a cathodic compartment using a mercury pool electrode (15 cm^2). The anodic compartment consisted of 50% aqueous methanol, a few drops of concentrated hydrochloric acid, and a platinum electrode. The anode and cathode compartments were separated by a pottery membrane. A dc voltage of about 10 V was applied until a current of 0.45 A flowed. The current was held constant, and the electrolysis was continued for 31 min at 7° with stirring (the current density being 0.03 A/cm^2 at the cathode). Reaction was complete with 87% current efficiency. The cathodic mixture was evaporated *in vacuo*, and the resulting products were extracted with chloroform. The chloroform solution was washed with water, dried, and evaporated under reduced pressure. Ethyl benzoylacetate was obtained by the vacuum distillation, yield 0.75 g (90%). The compound obtained was homogeneous by glc criterion and was identified by ir and nmr spectra, in which the amino group disappeared, and with an authentic specimen. On the other hand, the aqueous solution separated from the keto ester was neutralized with sodium bicarbonate solution and extracted with ethyl acetate. To the dried ethyl acetate solution was added HCl–ether to precipitate the amino acid ester hydrochloride. The resulting β-hydroxyphenylalanine ethyl ester hydrochloride was obtained in 9% yield and agreed with an authentic specimen.

In the same process, various β-keto esters which are of interest and useful as intermediates were easily obtained from the corresponding α-acylamino acid esters. These results are summarized in Table I.

Table I

Formation of β-Keto Esters by Electrolytic Deamination

R	R′	R″	Current density, A/cm^2	Yield, %	Current efficiency, %
Ph	H	Et	0.03	90	87
Ph	Et	Me	0.03	80	80
3,4-Methylenedioxyphenyl	Me	Me	0.02	82	80
$PhCH_2$	H	Et	0.03	85	60
CH_3	H	Et	0.03	35	25
$CH_3CH_2CH_2$	H	Et	0.03	40	40

Aromatic β-keto esters were generally obtained in high yields. In aliphatic compounds, however, the yield of the β-keto esters was low, and the β-hydroxyamino acid esters were afforded in considerable yields (*ca.* 50%).

Although the same process as described above was carried out using other electrodes, the yield was unsatisfactory. With zinc and nickel cathodes, methyl benzoylacetate was obtained from α-benzoylglycine methyl ester hydrochloride in 40 and 25% yields respectively.

The deamination occurred also in the case of α-amino ketones.[5] For example, acetophenone was obtained from phenacylamine hydrochloride by reduction with a mercury cathode in 75% yield.

Thus, the deamination proceeds easily under mild conditions, and this method is a new synthetic methode for β-keto esters. The study is currently in progress and will be reported elsewhere in the near future.

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