Electrochemical Deacetylation of 1,3-Dicarbonyl Compounds

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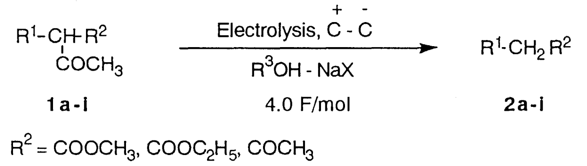
Mild deacetylation of 1,3-dicarbonyl compounds was achieved by halonium-ion mediated electrolysis. In this reaction, the supporting electrolyte including sodium halide NaX (X = Cl or Br) was essential since the reaction proceeded through substitution by a halonium ion, generated electrochemically at anode, on active methine carbons followed by base-catalyzed deacetylation, and was terminated by reductive dehalogenation of the formed α-halo carbonyl compounds at cathode.

In our continuing studies on halonium ion-mediated electrolysis of carbonyl compounds, electrochemical haloform reaction was found to take place when a variety of methyl ketones were subjected to electrolysis in a NaBr-MeOH system.[1]

In this study, the electrolysis of 1,3-diketones and β-ketoesters was carried out under the similar conditions to give quite different compounds, deacetylated products. Although it is well-known that hydrolysis of β-ketoesters easily accompany with decarboxylation,[2] efficient removal of an acetyl group is rare, and is considerably useful in organic synthesis.

On the other hand, it was reported by Torii et al.[3] that electrolysis of 1, 3-dicarbonyl compounds in CH_2Cl_2 containing Et_4NBr and MeONa gave only α-brominated products at active methylene carbons. In this electrochemical reaction, however, a halide ion was reproduced by cathodic reduction of deacetylated mono-halogenated compounds generated in situ., and was electrochemically re-oxidized to a halonium ion which played an important role as a mediator.



$$\underset{\textbf{1a-i}}{R^1\text{-}\underset{COCH_3}{CH}\text{-}R^2} \xrightarrow[R^3OH\text{ - }NaX,\ 4.0\ F/mol]{\text{Electrolysis, }\overset{+}{C}\text{ - }\overset{-}{C}} \underset{\textbf{2a-i}}{R^1\text{-}CH_2R^2}$$

$R^2 = COOCH_3, COOC_2H_5, COCH_3$

It is sufficient to pass 4.0F/mol of electricity in the presence of 1.0 eq. of NaBr as a mediator to complete the reaction.[4] Use of $NaBF_4$ instead of NaBr as a supporting electrolyte resulted in the almost quantitative recovery of the starting compound.[5]

Table 1. Deacetylation of acetoacetates and acetylacetones

Entry	R^1	R^2	NaX (eq)	Yield (%)
a	$C_6H_5CH_2$	$COOCH_3$	NaBr (1.0)	89
b	$C_6H_5CH_2$	$COOC_2H_5$	NaBr (1.0)	92
c	C_6H_{13}	$COOCH_3$	NaBr (1.0)	88
d	cycloC_6H_{11}	$COOCH_3$	NaBr (1.0)	91
e	cycloC_6H_{11}	$COOC_2H_5$	NaBr (1.0)	94
f	C_4H_9	$COOCH_3$	NaBr (1.0)	85
g	$C_6H_5CH_2$	$COCH_3$	NaCl (0.5)	89
h	n-C_4H_9	$COCH_3$	NaCl (0.5)	85
i	n-C_6H_{13}	$COCH_3$	NaCl (0.5)	81

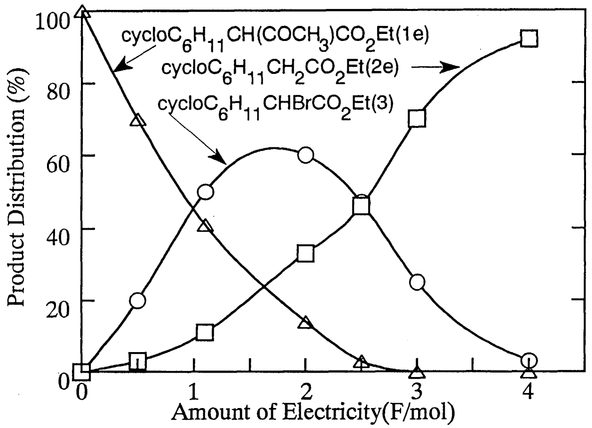
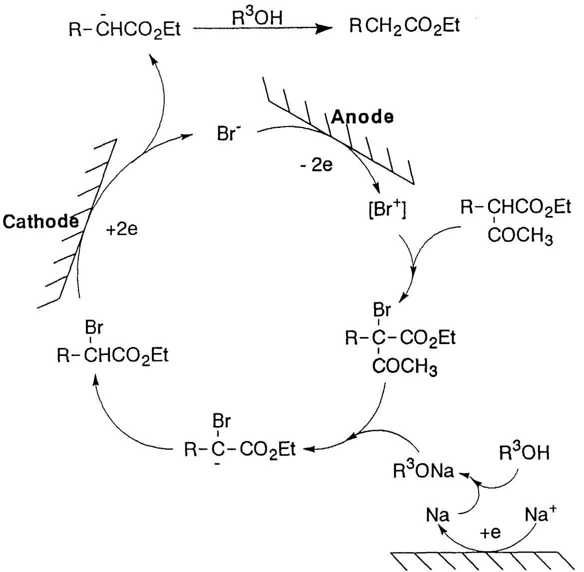


Figure 1. Relationship of passed electricity and products.

Electrolysis of a variety of α-substituted acetoacetates and acetylacetones under the similar conditions gave the corresponding deacetylation products in excellent yields as shown in Table 1. In the case of acetylacetones, use of NaCl as a supporting electrolyte in methanol brought about selective electrochemical deacetylation, while rearranged products were also obtained in some amounts as the by-products in a NaBr-MeOH system.[6]

Product distribution as a function of amount of passed electricity clearly showed formation of deacetylated α-bromoesters as intermediates,[7] suggesting the fact that this reaction was a halonium-mediated paired electrolysis.[8]

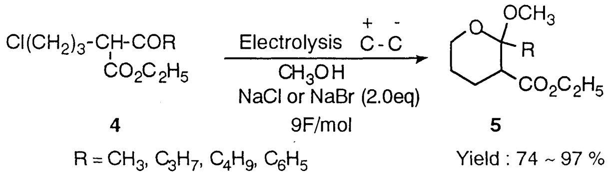
The following reaction mechanism would be proposed as shown below.



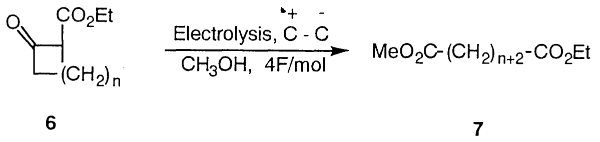
Scheme.

The reaction was initiated by substitution of a methine proton by a bromonium ion, generated electrochemically at anode, on active methine carbons, followed by deacetylation catalyzed by sodium methoxide formed from electrogenerated sodium. The formed deacetylated α-bromo esters were then subjected to electro-reductive dehalogenation at cathode to give the final products.

α-Substituted acyl acetates (**4**) possessing a chlorine atom as a leaving group within the same molecule were selectively transformed to the corresponding cyclization products (**5**) in a good yield.



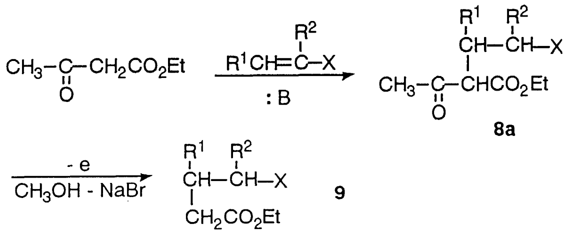
The present anodic deacetylation is useful in organic synthesis. Thus, the electrolysis of α-carboethoxycycloalkanones, prepared readily by carboethoxylation of cyclic ketones,[9] under the similar conditions led to facile ring opening to give α, ω-dicarboxylates in satisfactory yields. Retro-Dieckmann condensation was reported to take place for only tetrasubstituted 1, 3-dicarbonyl compounds such as α-alkyl-α-carboalkoxy-cyclopentanones.[10]



Furthermore, efficient synthesis of a variety of glutamate derivatives (**9a-d**) was accomplished by the present anodic deacetylation of the α-substituted acetoacetates (**8a-d**), prepared readily by base-catalyzed conjugate addition of ethyl acetoacetate to α, β-unsaturated olefins.[11]

Table 2. Electrolysis of cyclic β-ketoesters

n	Supporting Electrolyte	Yield (%)	n	Supporting Electrolyte	Yield (%)
2	NaCl	52	5	NaBr	59
3	NaBr	67	9	NaBr	69
3	NaCl	64	9	NaCl	66
4	NaBr	54			



9a : $R^1 = R^2 = H, X = CO_2Et$ (Yield = 91 %)
9b : $R^1 = CH_3, R^2 = H, X = CO_2Et$ (Yield = 56 %)
9c : $R^1 = H, R^2 = CH_3, X = CO_2Et$ (Yield = 74 %)
9d : $R^1 = R^2 = H, X = CN$ (Yield = 50 %)

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References and Notes

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4 Typical procedure is as follows. : Methyl 2-acetyl-3-phenylpropionate (10 mmol) was dissolved in methanol (30 ml) containing NaBr (10 mmol) as a supporting electrolyte in an undivided cell equipped with carbon rod electrodes and was electrolyzed under the constant current conditions (Current density 22.8mA•cm^{-2}). After 4F/mol electricity was passed, the product was isolated by distillation.

5 Almost recovery of methyl benzylacetoacetates (**1a**) on treatment of **1a** with EtOH/EtONa denied the possibility of base-catalyzed deacetylation.

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