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ELECTROCHEMICAL ACYLATION AND ALKYLAMINOCARBONYLATION OF AMINES AND ALCOHOLS

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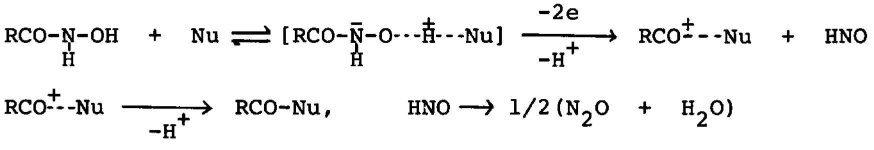
Abstract: Electrochemical acylation and ethylaminocarbonylation of amines and alcohols are performed by anodic oxidation of the hydroxamic acids and N-ethyl-N'-hydroxyurea, respectively, in acetonitrile at a glassy-carbon electrode.

Mild and efficient method for effecting transacylation are desired in many fields, and electrochemical transacylation to five to ten fold excess of alcohols has been reported by Johnson and others.[1] Their method requires a relatively high voltage to oxidize their reagents, hydroquinone monoesters, the acylation of amines, therefore, is not possible.

In the mechanistic investigation for the anodic oxidation of hydroxamic acids [2] and hydroxyureas,[3] we found that RCO^+ and $RNHCO^+$ were produced as the intermediate respectively, and those cations reacted with nucleophiles present in the solution. Since oxidation potential of a compound having acidic proton can be shifted to a less positive potential in the presence of base and the magnitude of the shift is larger the stronger the base,[4] hydroxamic acids and hydroxyureas are thought to be useful for transacylation and carbamoylation by an electrochemical method with relatively low oxidation potential.

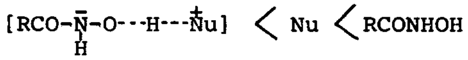
In the present work, we investigated the oxidative benzoylation, acetylation and ethylaminocarbonylation of amines and alcohols by anodic oxidation of benzohydroxamic acid (BHA), acetohydroxamic acid (AHA) and N-ethyl-N'-hydroxyurea (EHU), respectively, according to the scheme as below:[3,4]



$$\mathrm{RCO\text{-}\underset{H}{N}\text{-}OH} + \mathrm{Nu} \rightleftharpoons [\mathrm{RCO\text{-}\underset{H}{\bar{N}}\text{-}O\cdots\overset{+}{H}\cdots Nu}] \xrightarrow[-H^+]{-2e} \mathrm{RCO\overset{+}{-}\text{-}Nu} + \mathrm{HNO}$$

$$\mathrm{RCO\overset{+}{-}\text{-}Nu} \xrightarrow[-H^+]{} \mathrm{RCO\text{-}Nu}, \qquad \mathrm{HNO} \longrightarrow 1/2(N_2O + H_2O)$$

where $R=C_6H_5$, CH_3, EtNH, and the oxidation potential for the compounds increases in the order;

a) 

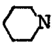
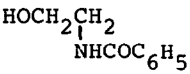
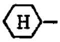
$[\mathrm{RCO\text{-}\underset{H}{\bar{N}}\text{-}O\cdots H\cdots\overset{+}{N}u}] < \mathrm{Nu} < \mathrm{RCONHOH}$ (Nu:amine)

b) $\mathrm{RCONHOH} < \mathrm{Nu}$ (Nu:alcohol)

Electrolysis of BHA (AHA) or EHU was performed potentiostatically with about 10^{-2}M of the substrate and four fold excess of nucleophile in acetonitrile containing 0.1M of sodium perchlorate at a glassy-carbon in undivided cell. The results of the electrolysis are summarized in Tables I and II .

Table I

Products from Electrolysis of BHA and AHA in the Presence of Amine or Alcohol

Amine or Alcohol	$E_{app.}$[a]	n[b]	Product	Yield (%)[c]
$MeNH_2$	0.40	2.2	$C_6H_5CONHMe$	59
Pr^iNH_2	0.40	2.1	$C_6H_5CONHPr^i$	59
NH	0.60	3.0	C_6H_5CO	26 [d]
$HOCH_2CH_2NH_2$	0.45	2.7 (2.5)[e]	 $HOCH_2CH_2NHCOC_6H_5$	78,[f] (56)[e]
MeOH	1.35	2.3 (2.1)[g]	C_6H_5COOMe	59, (80)[g]
–OH	——[h]	2.6	C_6H_5COO–	31 [h]
$MeNH_2$[i]	0.60	2.1	MeCONHMe	75

a) Applied potential, volt v.s. SCE.

b) Coulombs passed per mole of BHA or AHA.

c) The yields were determined by high performance liquid chromatography (HPLC), mole per cent of BHA or AHA.

d) Supporting electrolyte was $Et(nBu)_3NBF_4$.

e) Equimolar quantities of BHA and ethanolamine were used in the presence of excess pyridine.

f) Supporting electrolyte was Et_4NClO_4.

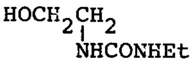
g) Performed in MeOH using a divided cell.

h) Electrolysed with constant current of 5mA/cm^2 in the presence of CF_3COOH of ca. three times of BHA.

i) Electrolysis of AHA.

Table II

Products from Electrolysis of EHU in the presence of Amine or Alcohol.

Amine or Alcohol	$E_{app.}$ [a]	n [a]	Product	Yield (%) [a]
$EtNH_2$	0.30	1.9	$(EtNH)_2CO$	100
Pr^iNH_2	0.30	1.9 (2.4)[b]	$Pr^iNHCONHEt$	97, (39)[b]
	0.60	2.1		94
	0.50 (0.70)[c]	1.84 (2.0)[c]		91, (72)[c]
MeOH	1.20	2.7 (2.0)[d]	MeOCONHEt	22, (80)[d]
$HOCH_2CH_2NH_2$	0.80	2.0	 $HOCH_2CH_2NHCONHEt$	48, 23 [e]

a) $E_{app.}$, n and Yield are used in the same sense as in Table I. Yield of ureas except for  were determined on a TLC analyser, and those of the urea and $MeCO_2NHEt$ were determined by HPLC and GLC, respectively.

b) Performed with equimolar amount of EHU and Pr^iNH_2.

c) Performed with equimolar amount of EHU and imidazole in the presence of excess of pyridine.

d) Performed in MeOH using a divided cell.

e) Performed with equimolar quantities of EHU and ethanolamine

As shown in the Tables, in our system, acylation and ethylaminocarbonylation take place in good yield without competitive oxidation of the amines, since electrolysis proceeds at lower potentials than those required for anodic oxidation of free BHA or EHU.[4] The reaction condition is very mild, and only the amino group of ethanolamine is selectively benzoylated under the condition using equimolar amount of BHA and ethanolamine. In chemical benzoylation of ethanolamine with benzoylchloride, both amino and hydroxy groups are usually subjected to benzoylation even when excess ethanolamine was used.

The following conditions for the electrolysis are found to be useful on improving the yield of the corresponding amide, urea, ester, and carbamate.

1) When equimolar quantities of BHA (or EHU) and amine are employed, the yield can be improved by the addition of excess bases such as pyridine or γ-collidine in order to make the oxidation potential lower.

2) When the added nucleophile is less reactive to RCO^+ than water, use of freshly distilled dry acetonitrile is preferable in order to avoid the reaction of RCO^+ with water.

3) When the added nucleophile is less reactive to RCO^+ than BHA or EHU, electrolysis in acidic condition, i.e., with an added acid or in a divided cell, gives better yield than that performed in neutral condition, since BHA or EHU is protonated not to react with RCO^+.

Similarly transethoxycarbonylation to isopropylamine was observed in the anodic oxidation of N-hydroxycarbamate, but the yield was very low, because the ethoxycarbonylation of the starting material proceeded mainly.[5]

References

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