

Electrochemical Reduction of 2-Bromo-carboxamides. Self-protonation Mechanism and Reaction with Dimethylformamide

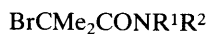
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Electrochemical reduction of 2-bromo-carboxamides involves self-protonation of the electrogenerated bases and affords, among other products, cyclo-adducts incorporating a dimethylformamide unit.

Base-promoted self- and cross-cyclocondensation of 2-bromo-carboxamides $\text{BrCR}^3\text{R}^4\text{CONR}^1\text{R}^2$ occur with useful regioselectivity, affording various heterocyclic products.¹ Some mechanistic pathways are being investigated through *ab initio* calculations,² but we thought it would also be of interest to study the electrochemical behaviour of this type of compound in anhydrous dipolar aprotic solvents. In these media, the anionic intermediates formed during the electroreduction of bromo-amides (electrogenerated bases) are likely to abstract protons from the parent compound through a self-protonation mechanism.³ To shed more light on the mechanisms of α -halogenoamide reactions and to ascertain to what extent the electrogenerated-base-promoted reactions overlap with the processes promoted by an exogenous base, we have been examining the electrochemical reduction of a series of 2-bromo-carboxamides. We report here preliminary results obtained with the carboxamides (1) and the aprotic *N*-methyl analogues (2).



(1) $\text{R}^2 = \text{H}$

(2) $\text{R}^2 = \text{Me}$



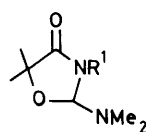
(3) $\text{R}^2 = \text{H}$

(4) $\text{R}^2 = \text{Me}$



(5) $\text{R}^2 = \text{H}$

(6) $\text{R}^2 = \text{Me}$

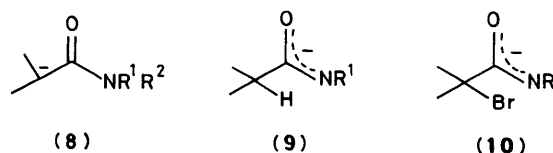


(7)

a; $\text{R}^1 = \text{Ph}$

b; $\text{R}^1 = \text{CH}_2\text{Ph}$

The electrochemical reduction of (1) and (2) was carried out at mercury cathodes in a three-electrode cell containing 0.1 M Et_4NClO_4 or Bu_4NBr in dimethylformamide (DMF) or MeCN. The voltammogram exhibits two cathodic peaks which are strongly dependent on the sweep rate and the nature of both the substrate and the electrolyte. At 0.2 V/s, the first peak is located in the range -1.0 to -1.4 V vs. saturated calomel electrode (s.c.e.), while the second one is observed below -2.0 V. Controlled potential electrolyses were carried out at -1.4 or -1.7 V at a stirred mercury pool. Coulometry indicated that after exhaustive reduction, as shown by the disappearance of the first voltammetric peak, one electron per molecule had been formally consumed. Product analysis (^1H n.m.r., mass spectra, and comparison with authentic samples) indicated that the electrochemical reduction had involved the halide moiety. The amides (3) and (4), in which the bromine in (1) or (2) had been replaced by hydrogen, were formed in yields of ca. 50%. In each electrolysis, the coproduct was identical to the product of base-promoted reactions. Its nature depended strongly upon the substrate and the dipolar aprotic



solvent employed. Methacrylamides (5) and (6) arose upon controlled potential electrolysis of (1) in MeCN and of (2) in both DMF or MeCN. Electrochemical reduction of compounds (1) under otherwise identical conditions, affords adducts with the solvent itself in which DMF is incorporated into a five-membered heterocycle, to give the oxazolidinones (7a and b).[†] This unusual behaviour of DMF, a solvent commonly employed in organic electrosynthesis because of its low reactivity, must be emphasized.

The results obtained can be rationalized by assuming that a carbanion such as (8) is formed as a result of 2-electron C–Br bond cleavage in (1) or (2). We believe that the aprotic methacrylamides (6a and b) may arise through 1,2-elimination from the parent (2) promoted by the electrochemically generated carbanion (8). On the other hand, the formation of the methacrylamides (5a and b) and the heterocyclic adducts (7a and b) are subject to a more complex dependence on acid-base equilibria. The carbanion (8, $\text{R}^2 = \text{H}$) may isomerize to give the anion (9) through intramolecular proton transfer. The parent protic bromoamide (1) may behave in turn as a proton donor, so that the amide (3) is formed along with the anion (10). We are currently investigating the decay of the anion (10) to give the unsaturated amides (5) or the DMF adducts (7). The coulometric results, *i.e.* the apparent consumption of one electron per molecule, are consistent with the self-protonation scheme. According to this scheme, half of the starting material undergoes 2-electron reduction to give the carbanion (8) and half acts as proton donor.

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References

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[†] (7a): colourless prisms, m.p. 98–99 °C: ^1H n.m.r. δ (CDCl_3), 1.42 and 1.5 (6H, 2 s, Me_2C), 2.32 (6H, s, Me_2N), 6.2 (1H, s, 2-H), and 7.2–7.6 (5H, m, Ph). Satisfactory elemental analyses were obtained. (7b) and another analogue ($\text{R}^1 = \text{Me}$) were obtained from the α -bromo-isobutyramides and DMF in the presence of NaH.^{1c}