Studies on Electrolytic Substitution Reactions. XVIII.* Attempted Methoxylation of *N*-Acetylaziridine and *N*-Formylazetidine

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We have earlier reported on the anodic oxidation of *N*,*N*-dialkylamides in methanolic solution, giving *N*-α methoxylated amides in high yields (eqn. 1).[1-4]

$$RCH_2N(R^1)CHO \xrightarrow{-2e^-,\ -H^+} RC^+H-N(R^1)CHO \xrightarrow{CH_3OH} RCH(OCH_3)N(R^1)CHO + H^+ \quad (1)$$

The reaction proceeds smoothly with both cyclic and acyclic amides and has been investigated also by other workers.[4,5] Our major interest has been focussed on cyclic methoxylated amides, obtained from the oxidation of cyclic *N*-formylamines. These compounds, capable of acylimmonium ion formation in the presence of an acidic catalyst, have been successfully utilized for the amidoalkylation of aromatics and active methylene compounds.[5-8] Together these methods serve as a simple and convenient route to 2-substituted heterocyclic compounds.

The content of this paper was aimed at demonstrating the same methods as applied to aziridine and azetidine compounds. Previously, *N*-formyl-2-methoxy-4,4-dimethylazetidine has been prepared by anodic oxidation of *N*-formyl-2,2-dimethylazetidine in methanol solution using tetramethylammonium tetrafluoroborate as supporting electrolyte.[4]

Results and discussion. *N*-Formylazetidine was oxidized in methanol in an undivided cell using platinum as anode and Bu_4NBF_4 as supporting electrolyte. After 2.1 F/mol had been passed, the starting material was totally consumed and GLC analysis showed a single product. According to NMR and MS analysis of the isolated product this was, however, not the expected *N*-formyl-2-methoxyazetidine, but instead *N*-(3,3-dimethoxypropyl)formamide.

Evidently initially formed *N*-formyl-2-methoxyazetidine undergoes rapid acid-catalyzed ring-opening involving addition of methanol. No trace of *N*-formyl-2-methoxyazetidine could be detected (GLC) during the electrolysis. Acid-catalyzed ring-opening reactions are well established for azetidine compounds, and *N*-formyl-2-methoxyazetidine, possessing a methoxy group in the 2-position capable of stabilizing an intermediate cation would not be expected to deviate from this behaviour. A possible source of protons are the reactions of eqn. 1. In order to suppress the undesired acid-catalyzed ring-opening a different set of experiments was designed. To the electrolyte was added 10 mol % (*vs.* substrate) of 4-methyl-2,6-di-*tert*-butylpyridine or sodium methoxide.

The addition of base did not alter the outcome of the oxidation, neither did the exchange of Bu_4NBF_4 for Me_4NBF_4. The difference in behaviour between *N*-formylazetidine and *N*-formyl-2,2-dimethylazetidine is best explained in terms of the *gem*-dimethyl effect.[9a,b]

N-Acetylaziridine (the acetyl compound was used due to the inaccessibility of the *N*-formyl analogue)[10] was oxidized according to the procedure described above for *N*-formylazetidine. After 0.5 F/mol of charge had been passed GLC analysis showed complete disappearance of the starting material and formation of a single product.

MS and NMR analysis showed it to be *N*-(2-methoxyethyl)acetamide. This compound, being a non-oxidized derivative of the starting material, evidently was formed *via* solvolysis. The possibility of acid-catalyzed solvolysis was easily demonstrated by the treatment of a methanolic solution of *N*-acetylaziridine with the strongly acidic resin Amberlyst 15. GLC and MS analysis showed complete conversion to *N*-(2-methoxyethyl)-acetamide. Catalysis by acidic impurities possibly present in the starting materials was ruled out by checking the stability of the electrolyte – substrate system under non-electrochemical conditions. (Apparently the higher strain introduced in the 3-membered ring as compared to the 4-membered one provides the reactivity needed to undergo solvolysis without the necessity of forming cation stabilizing intermediates.) Addition of 4-methyl-2,6-di-*tert*-butylpyridine dramatically altered the course of the reaction so as to almost completely suppress the formation of the solvolysis product. Nevertheless, we observed merely decomposition of the starting material and no formation of the desired 2-

* Part XVII, see Eberson, L. and Oberrauch, E. *Acta Chem. Scand. B 35* (1981) 193.

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methoxyaziridine was achieved. Disappearance of the starting material was monitored by GLC and displayed a rate normally encountered for two-electron processes, thus suggesting the formation of a highly reactive intermediate, which was then rapidly consumed. If the mechanism is the same as the one generally accepted for amide oxidations (eqn. 1) one can envisage the formation of a cation which bears close resemblance to a cyclopropyl cation. This can well explain the inability of the intermediate to discriminate among the multitude of reaction modes.

Experimental. GLC analyses were performed on a Hewlett-Packard HP-5830 instrument fitted with a 3 m × 3 mm 5 % OV 17 on Chromosorb W column. ^{1}H NMR spectra were recorded on a Jeol MH 100 instrument, using $CDCl_3$ as solvent. GLC/MS analyses were performed on a Finnegan 4021 spectrometer at 70 eV. Methanol and tetramethylammonium tetrafluoroborate were of highest available commercial quality and were used as received. *Azetidine*,[11,12] *N-acetylaziridine*,[13] *4-methyl-2,6-di-tert-butylpyridine*[14] and *tetrabutylammonium tetrafluoroborate*[15] were prepared according to published methods. *N-Formylazetidine*[16] was prepared by treating azetidine with excess ethylformate.

Electrolyses were carried out in 50 – 200 ml water-jacketed cells and the solutions were stirred by means of a magnetic stirrer. Electrolytes were either 0.5 M or 1.0 M in substrate and 0.04 – 0.1 M in supporting electrolyte. Platinum foil was used as anode and platinum or stainless steel as cathode. Current was passed at 15 °C by means of a PAR 373 potentiostat/galvanostat in the galvanostatic mode and was monitored by an electronic integrator. The current density was maintained at 25 – 40 mA/cm^2.

N-(3,3-Dimethoxypropyl)formamide. *N*-Formylazetidine (0.112 mol) was dissolved in 130 ml of a 0.04 M solution of tetrabutylammonium tetrafluoroborate in methanol. The electrolysis was performed in a 200 ml water-jacked cell fitted with a 50 cm^2 platinum foil as anode and a platinum wire as cathode. The current was kept constant at 2 A until complete conversion of the starting material was achieved at 2.1 F/mol. The solvent was removed by evaporation *in vacuo* and the product distilled under reduced pressure. Yield 83 %, b.p. 106 – 109 °C/0.7 mm Hg. MS *m/e* (% rel. int.): 116 (15, M – CH_3O), 115 (20, M – CH_4O), 100 (17), 86 (27), 84 (28), 75 (100, M – C_3H_6NO), 71 (77), 58 (53, M – $C_4H_9O_2$). ^{1}H NMR: 1.72 – 1.87 and 1.78 – 1.94 (2 H, 2 t, *J* 6.6 Hz), 3.36 (6 H, s), 3.30 – 3.47 (2 H, t, obscured by the singlet), 4.37 – 4.51 (1 H, t, *J* 5.4 Hz), 7.00 – 7.39 (1 H, br. s), 8.14 (1 H, s).

Attempted oxidation of N-*acetylaziridine.* *N*-Acetylaziridine (0.025 mol) was dissolved in 50 ml of methanol. Bu_4NBF_4 (0.005 mol) was added and the resulting solution was transferred to a 50 ml electrolysis cell. A platinum foil anode and a stainless steel cathode were immersed and current equalling 25 mA/cm^2 was passed. When GLC analysis showed the complete disappearance of starting material (0.5 F/mol of charge) electrolysis was discontinued and the electrolyte was further analyzed.

N-(2-Methoxyethyl)acetamide[17] was prepared by treating a methanolic solution of *N*-acetylaziridine with Amberlyst 15. The solvent was removed giving a quantitative yield of the pure (GLC and NMR) acetamide. MS: *m/e* (% rel. int.): 118 (8, M + 1), 85 (108, M – CH_3OH), 58 (54, M – CH_3CONH_2). ^{1}H NMR: 1.95 (3 H, s), 3.30 (3 H, s), 3.31 – 3.48 (4 H, m), 6.98 (1 H, br. s).

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