CHEMISTRY LETTERS, pp. 1469-1472, 1987.

Conversion of Cyclic Aziridines and 2-Amino-1-cycloalkanols to Keto Nitriles by Using Electrogenerated Reactive Halogen Species(1)

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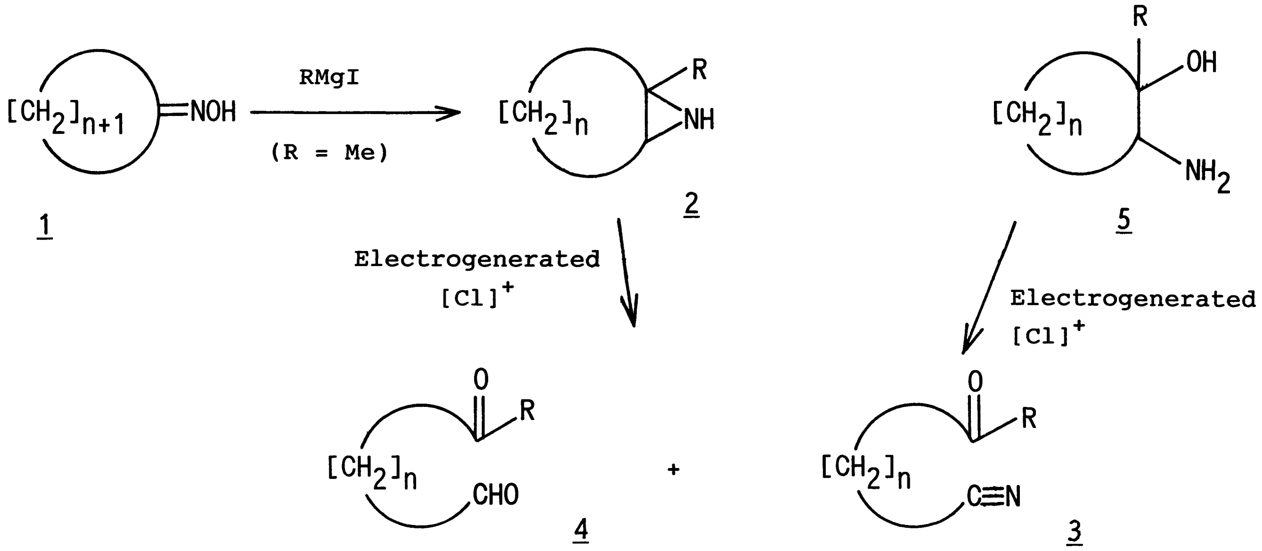
Oxidative cleavage of C(1)-C(2) bond of aziridines and 2-amino-1-cycloalkanols, giving the corresponding keto nitriles, exclusively, have been performed by oxidation with electrogenerated reactive halogen species (e.g., $[Cl]^+$).

Keto nitriles are valuable intermediates for a variety of synthetic transformations and any quick and reliable route to this grouping with increased yields would therefore be useful.(2) In contrast to the method for the preparation of ω-cyano acids,(3) there are few convenient and general access to these compounds. In the course of our synthetic studies dealing with the oxidation of nitrogen containing compounds,(4) we became interested in the fragmentation of nitrenium ion(5) derived from strained amines such as aziridines and their analogues. Oxidation of aziridines **2** with lead tetraacetate has been reported to give the corresponding keto nitriles by the cleavage of carbon-carbon bond.(6) N-Ethoxycarbonyl derivatives of **2** can be converted into 2-amino ketones by C-N fission on treatment with dimethylsulfoxide.(7) Another carbon-carbon bond



cleavage occurs by direct electrooxidation of 2-phenyl-2-ethylaziridine, giving the corresponding carbonyl compounds.[8)] In this paper, we report an indirect electrooxidation of **2** and 2-amino-1-cycloalkanol **5**, leading to keto nitriles **3**, by the aid of electrochemically generated reactive halogen species such as $[Cl]^+$ and $[Br]^+$.[9, 10)]

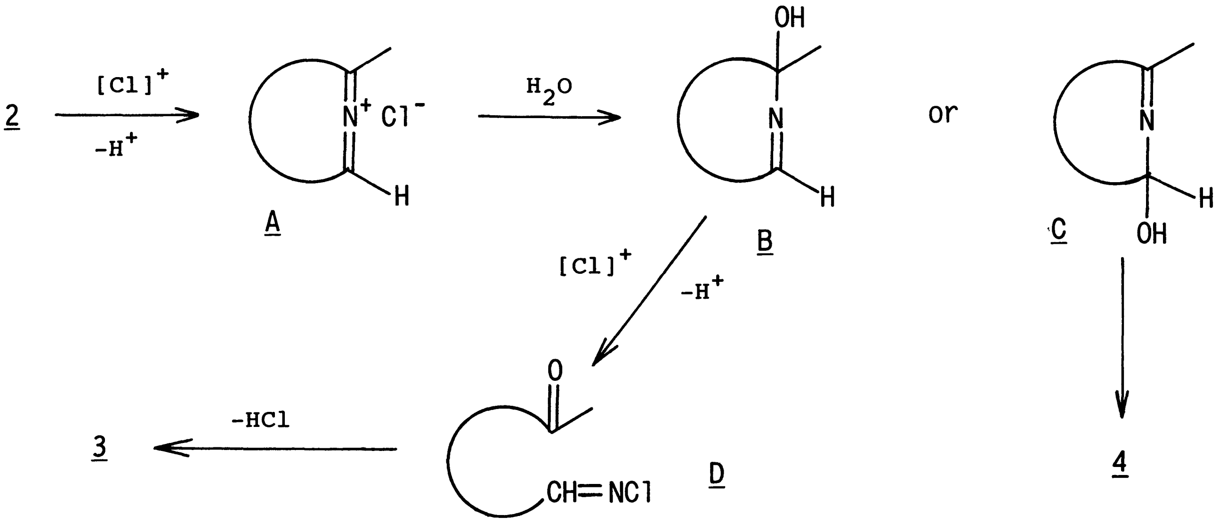
According to the procedure reported,[11)] starting aziridines **2** were prepared from cyclic ketoximes **1** by the reaction with methylmagnesium iodide. The electrooxidations of **2** were carried out in a mixed solution of MeCN-saturated NaCl buffered at pH 4 (1:2 V/V).[12)] As shown in Table 1, entry 1, the compound **2a** (n = 10, R = Me) was electrolyzed by passing 5.4 F/mol of electricity (current: 20 mA/cm^2) with two platinum electrodes immersed to an aqueous layer in an undivided cell, affording the desired keto nitrile **3a** (n = 10, R = Me) in 80% yield along with a small amount of keto aldehyde **4a** (n = 10, R = Me, 13% yield). Similar results were obtained by the electrolysis of **2a** (n = 10, R = Me) in an MeCN-saturated NaBr system (entry 2), but the electrolysis in an MeCN-saturated NaI system resulted in the recovery of the starting **2a**. Results and reaction conditions are shown in Table 1.

Table 1. Electrooxidative Cleavage of Aziridines **2** and 2-Amino-1-alkanols **5**[a)]

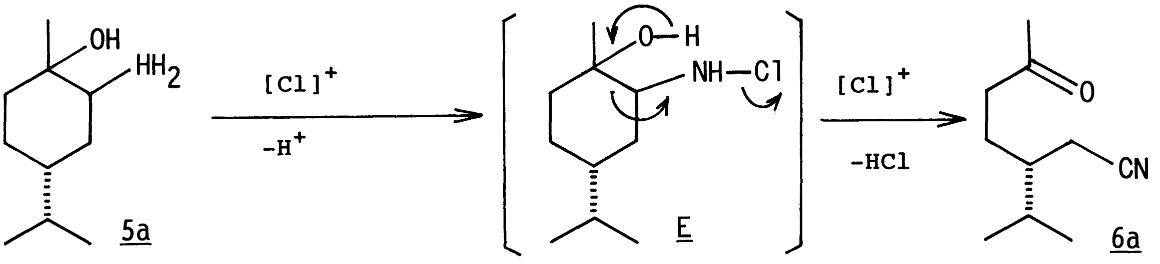
Entry	Substrate	R	Solvent-Electrolyte	Electricity F/mol	Product (Yield/%)[b)] **3**	**4**	**6**
1	**2a** (n=10)	Me	MeCN-aq NaCl	5.4	80	13	
2	**2a** (n=10)	Me	MeCN-aq NaBr	6.7	73	18	
3	**2a** (n=10)	Me	MeCN-aq NaCl	6.8	80	7	
4	**2b** (n=14)	Me	MeCN-aq NaCl	6.8	80	7	
5	**5a**		MeCN-aq NaCl	4.0		-	62
6	**5b**		MeCN-aq NaCl	5.0		-	50

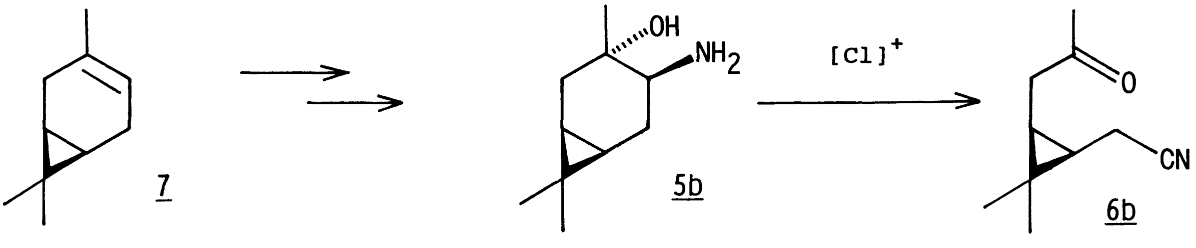
a) Electrolyses were carried out by using 0.2-1.0 mmol of the substrate in MeCN (5 ml)-aq NaCl (saturated,10 ml) buffered at pH 4 under a constant current of 20 mA cm^{-2} with two platinum electrodes in an undivided cell. b) Yields based on isolated products.

As shown below, the formation of **3** and **4** from **2** can be understood by taking into the account of intermediacy of azaallenyl cation **A**[13)] produced by the oxidation of **2** with positive chlorine species $[Cl]^+$. The hydration of **A** leads to either **B** or **C**. The intermediate **B** would be further oxidized with $[Cl]^+$ to **3** *via* **D**. Hydrolysis of **C** gives the aldehyde **4**.



Based on these findings, we next attempted the oxidation of 2-amino-1-cycloalkanol 5, easily available from cycloalkene oxide by azidation with trimethylsilyl azide followed by hydrogenation with palladium on carbon. The electrolysis of **5a** in an MeCN-aqueous saturated NaCl (buffered at pH 4)-(Pt) system yielded the desired keto nitrile **6a** in 62% yield. The formation of **6a** can be explained by fragmentaion of β-hydroxy-N-chloroimine **E** and the subsequent further oxidation with $[Cl]^+$.14) It is of interest to note that no detectable amount of keto aldehdye was isolated in this conditions. Similarly, the electrooxidation of **5b**, prepared from (+)-Δ^3-carene (**7**), produced the keto nitrile **6b**, an intermediate in chrysanthemic acid synthesis, in 50% yield.15)





The present one-step electrochemical transformation demonstrates a viable route to the ω-cyano carbonyl compounds, since the starting aziridines **2** are easily accessible from cycloalkanones through the corresponding oximes **1**.11)

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12) Typical procedure for electrooxidation of aziridine **2** is as follows. A solution of **2a** (n = 10, 54.1 mg, 0.28 mmol) in CH$_3$CN (5 ml) and aqueous saturated NaCl (10 mL) buffered with NaH$_2$PO$_4$ at pH 4 was placed into an undivided cell (2.5 cm diameter and 10 cm height) fitted with two platinum foil electrodes (3 cm^2). The mixture was electrolyzed with moderate stirring under a constant current density of 20 mA/cm^2 until 5.4 F/mol of electricity has been passed. The mixture was extracted with AcOEt and the extracts were washed with brine, dried (Na$_2$SO$_4$), and concentrated under vacuum. The crude products were purified by column chromatgraphy (SiO$_2$, hexane-AcOEt 5:1) to give **3a** (n = 10, 46.4 mg, 80%) and **4a** (n = 10, 7.7 mg, 13%). Physical properties and spectral data are as follows: **3a** (n = 10); mp 66.5 °C (from hexane); IR (Nujol) 2250 (CN), 1710 (C=O), 1465, 1380, 1160, 720 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 1.30 (brs, 16, CH$_2$), 2.03 (s, 3, COCH$_3$), 2.10-2.47 (m, 4, COCH$_2$, CH$_2$CN). **4a** (n = 10); mp 33 °C (from hexane) (lit.[16] 33 °C); IR (Nujol) 2727, 1722 (C=O), 1710 (C=O), 1490, 1400, 1290, 1240, 1180 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 1.06-1.85 (1.27 (top), 16, CH$_2$), 2.02 (s, 3, COCH$_3$), 2.13-2.58 (m, 4, COCH$_2$), 9.62 (t, J = 1.5 Hz, 1, CHO). **3b** (n = 14); mp 70 °C (from hexane); IR (Nujol) 2250 (CN), 1710 (C=O); ^{1}H-NMR (CDCl$_3$) δ 1.27 (brs, 24, CH$_2$), 2.14 (s, 3, COCH$_3$), 2.15-2.60 (m, 4, COCH$_2$, CH$_2$CN). **4b** (n = 14); mp 54 °C (from hexane); IR (Nujol) 2725, 1725 (C=O), 1710 (C=O) cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 1.27 (brs, 24, CH$_2$), 2.02 (s, 3, COCH$_3$), 2.10-2.45 (m, 4, COCH$_2$), 9.15 (t, J = 1.5 Hz, 1, CHO). **6a**; $[\alpha]_D^{23}$ -8.6° (c 1.03, CHCl$_3$); IR (neat) 2240 (CN), 1710 (CO), 1460, 1420, 1390, 1370, 1355, 1160, cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.90 (d, J = 6 Hz, 6, CH$_3$), 1.40-2.00 (m, 4, CH$_2$, CH), 2.13 (s, 3, COCH$_3$), 2.15-2.82 (m, 4, CH$_2$CO, CH$_2$CN); ^{13}C NMR (CDCl$_3$) δ 18.8, 19.0, 19.3, 24.6, 30.0, 30.2, 40.7, 41.2, 119.3, 207.9. **6b**; $[\alpha]_D^{23}$ +6.5° (c 1.5, CHCl$_3$); IR (neat) 2240 (CN), 1710 (CO), 1430, 1360, 1165, 1140 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.75-1.20 (m, 1, CH), 0.97, 1.11 (s, 6, CH$_3$), 1.20-1.90 (m, 1, CH), 2.10-2.45 (m, 4, CH$_2$CO, CH$_2$CN), 2.15 (s, 3, COCH$_3$).

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(Received May 9, 1987)