Electro-oxidative *N*-Halogenation of 2-Azetidinone Derivatives. Reaction of *N*-Halo-2-azetidinones

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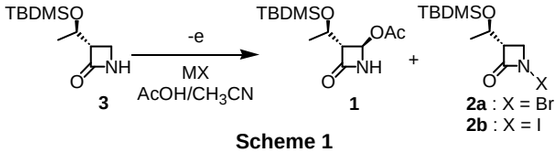
Penems and carbapenems have attracted keen interest as promising antibiotics owing to their potent and broad antimicrobial activities as well as excellent metabolic stability.[1)] 4-Acetoxy-2-azetidinone **1** and *N*-halo-2-azetidinones **2** have been reported as a key intermediates for synthesis of the important class of β-lactam antibiotics.[2)] We investigated electrolysis of 2-azetidinone **3** affording **1**, **2a** and **2b** depending on the choice of the electrolysis media and/or procedure (Scheme 1).



3 **1**

Scheme 1

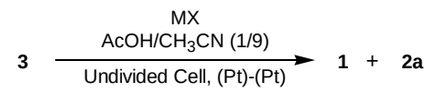
At first, electrolysis of 2-azetidinone **3** in AcOH/CH_3CN (1/9) containing Bu_4NBF_4[3)] was carried out in a beaker-type undivided cell. After passage of 10 F/mol of electricity (20 mA/cm^2), a complex mixture was obtained (Table 1, entry 1). In the presence of NaBr, *N*-bromo-2-azetidinone **2a** was obtained as an only isolable product after passage of 10-20 F/mol of electricity (entries 2-5). With 5 mol equiv. of NaBr 89% yield of **2a** was obtained (entry 5). Notably, when a similar electrolysis was carried out in a divided cell, no appreciable amount of **2a** was obtained, affording 4-acetoxy-2-azetidinone **1** (8%) together with a complex mixture (entry 6).

N-Iodo-2-azetidinone **2b** was obtained by electrolysis of **3** in NaI-AcONa-AcOH/CH_3CN (1/9) using a divided cell (Table 2, entries 1-6). With an undivided cell, only 8% yield of **2b** was obtained along with recovered **3** (86%, entry 7). The effect of the amount of NaI is significant; thus, the best yield of **2b** (79%) was attained by use of 2.5 mol equiv. of NaI (entry 3). The chemical *N*-iodination of **3** with I_2 and AcONa in AcOH/CH_3CN (1/9) afforded only 16% yield of **2b** together with recovered **3** (78%). Reaction of **2b** with NaI in AcOH/CH_3CN (1/9) gave almost same mixture (**2b**/**3** = 1/4) suggesting that the equilibrium mixture as shown in Scheme 2 would be formed. It is likely that most of I^- in the electrolysis media was converted to I_2; consequently the equilibrium (Scheme 2) would shift to the right hand side to afford **2b** in good yields.

Electrolysis of **3** in MeOH containing AcONa afforded the ring expansion product **4** in 84% yield which would be formed through the reaction with *in situ* electrogenerated CH_2=O (Scheme 3).

The conversion of *N*-halo-2-azetidinone **2** to 4-substituted-2-azetidinones **5** (Scheme 4) will be also discussed.

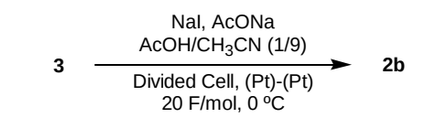
Table 1. Electro-oxidation of 2-Azetidinone



Entry	MX (eq.)	F/mol	Yield (%)[a] 1	Yield (%)[a] 2a	Recov. (%)[a] 3
1	Bu_4NBF_4 (0.2)	10	-[b]	-[b]	-[b]
2	NaBr (1)	10	-	26	71
3	NaBr (1)	20	-	31	64
4	NaBr (2)	20	-	41	50
5	NaBr (5)	20	-	89	-
6[c]	NaBr (2)	20	8	-	18

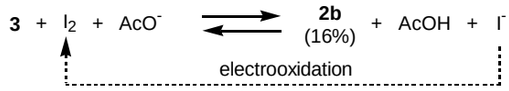
[a] Isolated yield. [b] A complex mixture. [c] Divided cell.

Table 2. Electro-oxidative *N*-Iodination

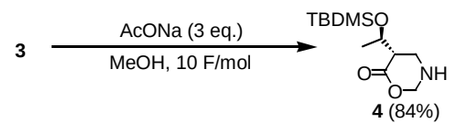


Entry	NaI (eq.)	AcONa (eq.)	Yield (%)[a] 2b	Recov. (%)[a] 3
1	1	1	10	80
2	2	1	76	10
3	2.5	1	79	17
4	3	1	70	22
5	4	1	33	49
6	2	-	47	43
7[b]	2	1	8	86

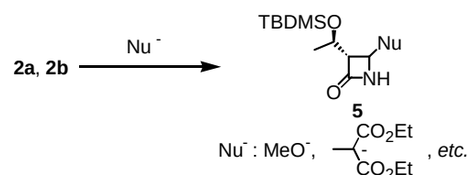
[a] Isolated Yield. [b] Undivided Cell.



Scheme 2



Scheme 3



Scheme 4

References

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