Tetrahedron 62 (2006) 8021–8028

Tetrahedron

Indirect electrochemical oxidation of piperidin-4-ones mediated by sodium halide-base system

Michail N. Elinson,* Alexander S. Dorofeev, Sergey K. Feducovich, Ruslan F. Nasybullin, Evgeny F. Litvin, Mikhail V. Kopyshev and Gennady I. Nikishin

N. D. Zelinsky Institute of Organic Chemistry, Leninsky prospect 47, 119991 Moscow, Russia

Received 23 March 2006; revised 29 May 2006; accepted 8 June 2006

Abstract—Indirect electrochemical oxidation of 1-*N*-subsituted piperidin-4-ones in methanol in an undivided cell in the presence of sodium iodide/sodium methoxide system leads to the corresponding α-hydroxyketals in 50–80% substance yield (50–65% current yield). 2,2,6,6-Tetramethylpiperidin-4-one under the same conditions forms a mixture of methyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate and methyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate in 70% substance yield (60–70% current yield) via electrochemically induced Favorskii rearrangement.

1. Introduction

The oxidation of ketones is a known method for preparing carboxylic acids and their derivatives, bifunctional compounds such as α-hydroxyketones, diketones and other useful intermediates in organic synthesis.[1] The formation of adipic acid from cyclohexanone is an important industrial process. α-Hydroxyketones are significant 'building blocks' in the construction of natural products and fine chemicals.[2,3] In the case of aryl alkyl ketones, the corresponding α-hydroxyketones and α-hydroxyketals are convenient compounds for synthesis of the pharmacologically active 2-arylalkanoic acids.[4,5]

Due to the considerable progress in the electrochemistry of organic compounds in the last decades, the electrosynthesis became a highly competitive method in modern organic chemistry.[6,7] However, in the case of the electrochemical oxidation of ketones, only some examples of the procedures, which could ensure product-selectivity are known.

The direct electrochemical oxidation of ketones led to the formation of a mixture of acids, saturated and unsaturated hydrocarbons, carbon monoxide and dioxide.[8–11] Remote non selective oxidative functionalization of aliphatic ketones was observed when electrooxidation was carried out in acetonitrile or trifluoroacetic acid as a result of the subsequent transformation of the initially produced cation radical $R^1R^2C{=}O^{+\bullet}$.[12,13]

In some oxidative transformations of ketones, such as in the haloform reaction, the α-halogenation of ketones is an important step.[14] So for certain cases, the selective indirect electrooxidation of ketones with the electrochemically generated halides is also possible. Thus, the electrocatalytic variant of the haloform reaction–the procedure to prepare carboxylic acid esters by the electrooxidation of methyl alkyl and methyl aryl ketones in methanol in the presence of alkali metal bromides is well known.[15]

The NaI/NaOH mediatory system is also known for the effective indirect electrochemical oxidation of carbonyl compounds. Using this mediatory system aryl alkyl ketones are oxidized into the corresponding α-hydroxyketals.[16] Electrolysis of alkyl benzyl ketones in methanol in an undivided cell in the presence of the NaI/NaOH system induces a process similar to the Favorskii rearrangement of α-haloalkyl benzyl ketones to produce methyl arylalkanecarboxylates.[17] Electrolysis of dialkyl ketones under the same conditions involves a process analogous to the Favorskii rearrangement of α,α-dihalodialkyl ketones giving rise to methyl esters of α,β-unsaturated carboxylic acids.[18,19]

It has been found that the result of the indirect electrochemical oxidation of cyclic ketones in methanol in an undivided cell in the presence of sodium halide or sodium halide-base system depends on the ring size of ketone. Cyclopentanone affords 2,2-dimethoxycyclopentanone, while cyclohexanone gives rise to 2,2-dimethoxycyclohexanol. Cyclic

---

Keywords: Electrochemical reactions; Mediators; 4-Piperidinones; α-Hydroxyketals; Favorskii rearrangement.

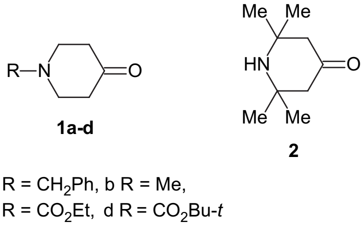
* Corresponding author. Tel.: +7 495 137 38 42; fax: +7 495 135 53 28; e-mail: elinson@ioc.ac.ru

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.06.031

ketones with higher ring size after α,α-dihalogenation undergo the electrochemically induced Favorskii rearrangement with the formation of methyl cycloalkenecarboxylates containing in the ring one carbon less than starting ketone. So the simple electrocatalytic system can distinguish the ring size of cyclic ketones.[20,21]

Recently we have found that electrolysis of 4-substituted cyclohexanones in methanol in the presence of sodium halides in an undivided cell results in the stereoselective formation of *cis*-5-substituted-2,2-dimethoxycyclohexanols.[22]

Continuing our studies on the electrocatalytic and indirect electrooxidation of ketones[15–22] we have accomplished indirect electrochemical oxidation of substituted piperidin-4-ones **1a–d** and **2** in the presence of sodium halides as mediators and in the presence of mediatory systems sodium halide-base (Scheme 1).



Scheme 1.

2. Results and discussion

In the present study we report our results on the indirect electrochemical oxidation of substituted piperidin-4-ones **1a–d** and **2** (Tables 1–4). It has been found that electrooxidation of *N*-substituted 4-piperidinones **1a–d** in methanol in the presence of sodium halides as mediators led to the formation of 1-substituted 4,4-dimethoxypiperidine-3-ols **3a–d** (Scheme 2) (Table 1).

Thus the general result of the indirect electrochemical oxidation of *N*-substituted piperidin-4-ones **1a–d** is similar to the result of indirect electrochemical oxidation of cyclohexanone **4**[20,21] and 4-substituted cyclohexanones[22] (Scheme 3).

But there is a difference in the conditions of the electrooxidation. In the indirect electrooxidation of cyclohexanone[21]

Table 2. Electrooxidation of 2,2,6,6-tetramethylpiperidin-4-one **2** in methanol[a]

No.	Ketone	Mediator	Base equivalent	Product, yield %[b]	Current yield %[c]
1	**2**	NaBr	—	**6a**, 18; **7a**, 28	37
2	**2**	NaBr	0.1 MeONa	**6a**, 29; **7a**, 42	57
3	**2**	NaBr	0.3 MeONa	**6a**, 42; **7a**, 34 (59)	55
4	**2**	NaBr	0.5 MeONa	**6a**, 36; **7a**, 29 (57)	50
5	**2**	NaBr	0.8 NaONa	**6a**, 32; **7a**, 21	37
6	**2**	NaBr	1.0 MeONa	**6a**, 28; **7a**, 15	29
7	**2**	NaI	—	**6a**, 23; **7a**, 5	17
8	**2**	NaI	0.1 MeONa	**6a**, 43; **7a**, 8	30
9	**2**	NaI	0.3 MeONa	**6a**, 52; **7a**, 14	40
10	**2**	NaI	0.5 MeONa	**6a**, 59; **7a**, 26 (71)	56
11	**2**	NaI	0.8 MeONa	**6a**, 53; **7a**, 29 (68)	56
12	**2**	NaI	1.0 MeONa	**6a**, 38; **7a**, 45 (69)	64
13	**2**	NaI	3.0 MeONa	**6a**, 29; **7a**, 58 (73)	73

[a] Ketone (10 mmol), 10 mmol of mediator, 20 ml of MeOH, Fe-cathode, C-anode, current density 200 mA/cm^2, 4 F/mol electricity passed, 30 °C, conversion of **2** (95–100%).
[b] Determined by gas chromatography and NMR spectra, in parenthesis–isolated yields for the mixture of **6a** and **7a**.
[c] For the mixture of **6a** and **7a**.

Table 3. Electrooxidation of 2,2,6,6-tetramethylpiperidin-4-one **2** in ethanol[a]

No.	Ketone	Mediator	Base equivalent	Product, yield %[b]	Current, yield %[c]
1	**2**	NaI	—	**6b**, 36	18
2	**2**	NaI	0.1 EtONa	**6b**, 53 (40)	27
3	**2**	NaI	0.3 EtONa	**6b**, 65 (51); **7b**, 2	35
4	**2**	NaI	0.5 EtONa	**6b**, 44; **7b**, 11	33

[a] Ketone (10 mmol), 10 mmol of NaI, 20 ml of EtOH, Fe-cathode, C-anode, current density 200 mA/cm^2, 4 F/mol electricity passed, 30 °C, conversion of **2** (95–100%).
[b] Determined by gas chromatography and NMR spectra, in parenthesis–isolated yields for **6b**.
[c] For **6b** or the mixture of **6b** and **7b**.

Table 4. Electrooxidation of 3,3,5,5-tetramethylcyclohexanone **8** in methanol[a]

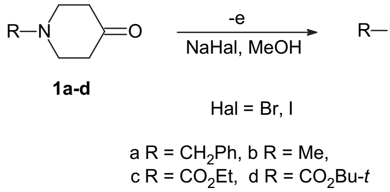
No.	Ketone	Base equivalent	Product, yield %[b]	Current yield %[c]
1	**8**	—	**9** 7; **10** 53 (38); **11** 15	72
2	**8**	0.5 MeONa	**9** 12; **10** 34 (18); **11** 29 (17)	69
3	**8**	1 MeONa	**9** 17 (11); **10** 13; **11** 46 (31)	68

[a] Ketone (10 mmol), 10 mmol of NaI, 20 ml of MeOH, Fe-cathode, C-anode, current density 200 mA/cm^2, electricity passed 4 F/mol, 30 °C, conversion of **8** (95–100%).
[b] Determined by gas chromatography and NMR spectra, in parenthesis–isolated yields.
[c] For the mixture of **9**, **10** and **11**.

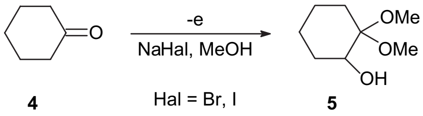
Table 1. Electrooxidation of *N*-substituted piperidin-4-ones **1a–d**[a]

No.	Ketone	R	Mediator	Base equivalent	Electricity passed, F/mol	Product, yield %[b]	Current yield %
1	**1a**	CH$_2$Ph	NaBr	—	6	**3a**, 45	15
2	**1a**	CH$_2$Ph	NaI	—	4.5	**3a**, 56	25
3	**1a**	CH$_2$Ph	NaI	0.3 NaOH	4	**3a**, 67	34
4	**1a**	CH$_2$Ph	NaI	0.5 NaOH	4	**3a**, 74 (59)	37
5	**1a**	CH$_2$Ph	NaI	1.0 NaOH	4	**3a**, 61	31
6	**1a**	CH$_2$Ph	NaI	0.5 MeONa	3	**3a**, 86 (71)	57
7	**1a**	CH$_2$Ph	NaBr	0.5 MeONa	3	**3a**, 66	44
8	**1b**	Me	NaI	0.5 MeONa	3	**3b**, 94 (81)	65
9	**1c**	CO$_2$Et	NaI	0.5 MeONa	3	**3c**, 69 (55)	46
10	**1d**	CO$_2$Bu-*t*	NaI	0.5 MeONa	3	**3d**, 67 (52)	45

[a] Ketone (10 mmol), 10 mmol of mediator, 20 ml of MeOH, Fe-cathode, C-anode, current density 200 mA/cm^2, 30 °C, conversion of **1a–d** (98–100%).
[b] Determined by gas chromatography and NMR spectra, in parenthesis–isolated yields.



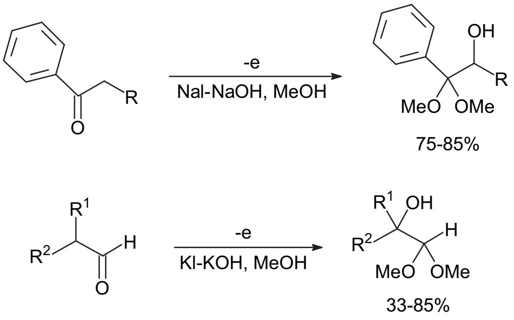
Scheme 2.



Scheme 3.

or 4-substituted cyclohexanones[22] into α-hydroxyketals of type **5**, there is no significant difference between the use of NaI or NaBr as a mediator and it is not necessary to use base additive to ensure good current efficiency.

As it follows from the data of Table 1, NaI is more efficient as mediator when compared with NaBr for the indirect electrooxidation of **1a–d** into α-hydroxyketals **3a–d**. In the case of NaOH as additive the best results were obtained with 0.5 equiv of NaOH. The next improvement of the conditions for the indirect electrochemical oxidation of **1a** was achieved using 0.5 equiv of MeONa. Under these optimal conditions **3a** was obtained in 86% substance and 57% current yields. Earlier only NaOH was used as additive for the electrooxidation of carbonyl compounds into corresponding α-hydroxyketals. Aryl alkyl ketones were successfully electrooxidized in the presence of NaI as mediator and 0.1 equiv of NaOH;[16] analogous transformation of aliphatic aldehydes was performed in the presence of NaI and 0.4 equiv of NaOH[23](Scheme 4):



Scheme 4.

Earlier oxidation of **1a** by iodine/KOH (0 °C, 2.5 h)[24] resulted in **3a** formation in 50% yield and **3b** was obtained by oxidation of **1b** with iodobenzenediacetate[25] in MeOH/KOH (36 h) in 32% yield.

Taking into consideration the above results and the data on the mechanism of the electrocatalytic oxidation of cyclohexanone and 4-substituted cyclohexanones with sodium halide as mediator the following mechanism of the electrochemical oxidation of *N*-substituted piperidin-4-ones **1a–d** into α-hydroxyketals **3a–d** in the presence of sodium halide/NaOMe system is suggested.

The reactions at the electrodes, which take place during the process, are shown below (Scheme 5):

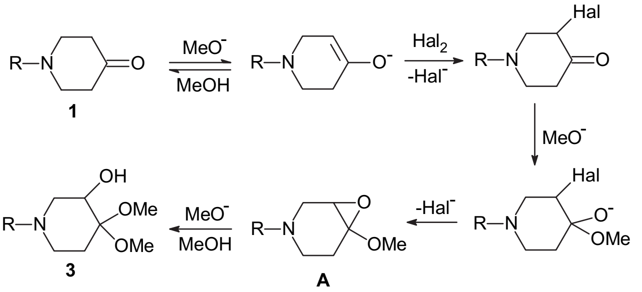
$$\text{anode:}\quad 2\,\text{Hal}^- - 2e \longrightarrow \text{Hal}_2 \qquad \text{Hal} = \text{Br, I}$$

$$\text{cathode:}\quad 2\,\text{MeOH} + 2e \longrightarrow 2\,\text{MeO}^- + \text{H}_2$$

Scheme 5.

The formation of iodine or bromine at the anode is a well-known process and the corresponding colour was observed when the electrolysis was conducted without stirring the reaction mixture, as well as evolution of hydrogen at the cathode.

Further bromination of enolate anion of **1** takes place in solution with following addition of methoxide anion to the carbonyl group and intramolecular substitution of halogen with the formation of intermediate epoxide (**A**). Then the attack of another methoxide anion leads to epoxide ring opening, and finally to formation of **3** (Scheme 6).

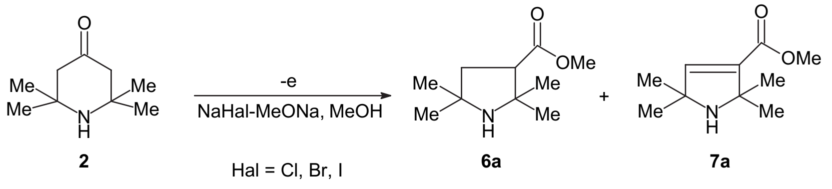


Scheme 6.

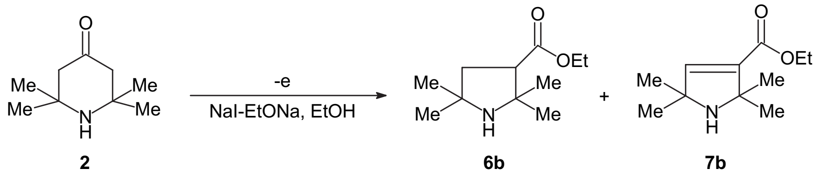
Sodium iodide gives better results for the indirect electrochemical oxidation of ketone **1** into α-hydroxyketal **3** compared to sodium bromide as bromine generated at anode is more effective for competitive oxidation of methoxide anions.

Taking into consideration that the indirect electrochemical oxidation of *N*-substituted piperidin-4-ones **1a–d** is similar to the result of indirect electrochemical oxidation of cyclohexanone **4** and leads to *N*-substituted 4,4-dimethoxypiperidine-3-ols **3a–d**, it was strange for us to find in recent preliminary communication that 2,2,6,6-tetramethylpiperidin-4-one **2** under conditions of the indirect electrochemical oxidation in methanol in the presence of sodium halides and 2.5 equiv of MeONa undergoes the electrochemically induced Favorskii rearrangement with the formation of mixtures of methyl 2,2,5,5-tetramethylpyrrolidine-3-carboxylate **6a** and methyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate **7a**[26] (Scheme 7).

Indirect electrochemical oxidation of **2** in the presence of NaCl under our conditions without base or in the presence of 0.5 equiv of MeONa resulted in the formation of a complex mixture of compounds. The combined yields of esters **6** and **7** were less than 10% by GC and NMR data. The results of the electrochemical oxidation of **2** in the presence of NaI and NaBr in methanol are given in the Table 2.



Scheme 7.



Scheme 8.

As it follows from the data of Table 2, NaI is more efficient mediator when compared with NaBr for the indirect electrooxidation of cyclic ketone **2** into the mixture of the cyclic esters **6a** and **7a**. Nevertheless, NaBr as mediator with 0.3 or 0.5 equiv of MeONa also led to good results. The best yields for the mixture of cyclic esters **6a** and **7a** were obtained using NaI–0.5 and more equivalents of MeONa mediatory system. Under these conditions cyclic esters **6a** and **7a** were isolated in 70% yield. The ratio of **6a** and **7a** changes from 2:1 to 1:2 with the increase of MeONa quantity from 0.5 to 3.0 equiv. Hydrogenation of the mixture of **6a** and **7a** in autoclave on Pd/C catalyst (5% Pd) in methanol resulted in formation of **6a** in quantitative yield.

What are the main differences of the electrooxidation **2** in MeOH under our conditions from those published earlier?[26] (**1**) The electrooxidation of **2** in the presence of NaCl in our case has no selectivity. (**2**) In the electrooxidation of **2** in the presence of NaBr under our conditions, the optimal quantity of MeONa is 0.3–0.5 equiv (ratio **6a**/**7a**, 4:3); earlier 2.6 equiv of MeONa (ratio **6a**/**7a**, 2:3). (**3**) In the electrooxidation of **2** in the presence of NaI under our conditions, the optimal quantity of MeONa is 0.5–3.0 equiv (whereas ratio **6a**/**7a** changes from 2:1 to 1:2), earlier 2.6 equiv of MeONa (ratio **6a**/**7a**, 1:1). (**4**) And the last but not least, current yields for the mixture of **6a** and **7a** in our case comprise 50–70%, the twice improvement on the earlier reported 30% yields.[26]

Indirect electrochemical oxidation of **2** in the presence of NaI in ethanol was found to be more selective process, in this case **6b** was isolated from the reaction mixture directly after electrolysis (Scheme 8) (Table 3).

Taking into consideration the results of the electrocatalytic oxidation of **2** and the data on the mechanism of the electrocatalytic oxidation of cyclic ketones with sodium halide as mediator,[12] the following mechanism of the indirect electrochemical oxidation of **2** in the presence of sodium halide/NaOR system is suggested.

The reactions at the electrodes, which take place during the process, are shown below (Scheme 9):

anode: $2\ \mathrm{Hal}^- - 2e \longrightarrow \mathrm{Hal}_2$ Hal = Br, I

cathode: $2\ \mathrm{ROH} + 2e \longrightarrow 2\ \mathrm{RO}^- + \mathrm{H}_2$ R= Me, Et

Scheme 9.

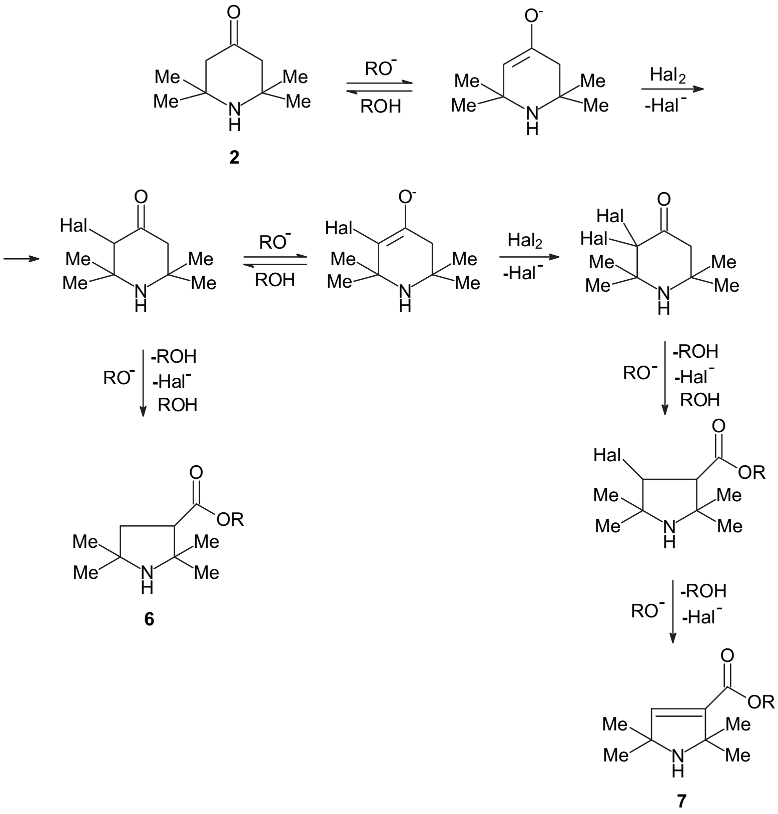
Further bromination and dibromination of enolate anion of **2** take place in solution, followed by proton abstraction with methoxide anion and Favorskii rearrangement[27] while the attack of methoxide anion on the carbonyl group is blocked by steric hindrance of the four methyl substituents (Scheme 10).

To determine an influence of tetramethyl substitution on the result of the electrocatalytic oxidation of the 6-membered cyclic ketones, the electrocatalytic oxidation of 3,3,5,5-tetramethylcyclohexanone has been studied (Table 4).

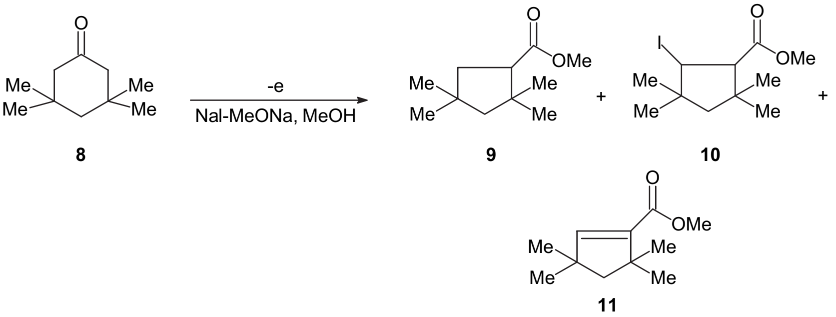
It was found that the result of electrocatalytic oxidation of 6-membered tetramethyl ketone **8** (Scheme 11) is very similar to the oxidation of 6-membered azatetramethyl ketone **2** and quite different from the electrocatalytic oxidation of cyclohexanone where only corresponding α-hydroxyketal was obtained.[21] The steric hindrance for the elimination of the iodine substituent in the ester **10** is even more stronger than in the corresponding ester formed from ketone **2** (according to the mechanism shown in Scheme 10), since only a part of iodoester **10** was converted into unsaturated ester **11** under conditions studied. Thus the steric influence of four methyl substituents is the main reason for the change in route of the indirect electrochemical oxidation of tetramethylpiperidinone **2** compare to *N*-substituted piperidin-4-ones **1a**–**d**.

3. Conclusion

To summarize, we have found that electrolysis with NaI/MeONa mediatory system in an undivided cell affords under mild conditions in methanol electrochemical oxidation of 1-*N*-substituted piperidin-4-ones into corresponding α-hydroxyketals in 50–80% yields. Under the similar conditions 2,2,6,6-tetramethylpiperidin-4-one in methanol was



Scheme 10.



Scheme 11.

transformed into the mixture of methyl 2,2,5,5-tetramethylpyrrolidine-3-carboxylate and methyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate in 70% overall yield or in ethanol directly into ethyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate in 40–50% yields as the result of the electrochemically induced Favorskii rearrangement. The simple two-step procedure, i.e., electrolysis and further hydrogenation affords methyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate in 70% yield. These methods require the use of common and commercially available reagents, inexpensive apparatus and an undivided cell. The techniques for electrolysis and isolation of the reaction products are simple and convenient to use both under laboratory conditions and in large-scale apparatus.

4. Experimental

4.1. General

All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. GC analysis was carried out on LKhM-80 chromatograph with a flame-ionization detector. Columns: (1) fused-silica capillary column HP-1 (5 m×0.53 mm×2.65 μm) and (2) glass column 3 m×3 mm with 10% FFAP on Chromaton N-Super (0.13–0.16 mm). ^{1}H NMR spectra were run for solutions in $CDCl_3$ and recorded with Bruker AM-300 and Bruker DRX-500 spectrometers. Chemical shifts are presented in δ scale with tetramethylsilane (TMS) used as an internal standard.

4.2. General electrolysis procedure

A solution of ketone (10 mmol), sodium halide (10 mmol) and base (type of the base and amount used are specified in the corresponding Tables 1–4) in methanol or ethanol (20 ml) was electrolyzed in an undivided cell equipped with C-anode and Fe-cathode at 30 °C under constant current density 200 mA/cm^2 until the quantity of the electricity indicated in tables was passed. The reaction mixture was neutralized by dilute HCl, the solvent was then removed, and the reaction mixture was extracted with ether, washed with solution of $Na_2S_2O_3$ in water, then with water, and dried over Na_2SO_4. Solvent was removed and then products were isolated by sublimation (**3a** and **3b**), vacuum distillation (mixture of **6a** and **7a**, **6b**) or column chromatography on silica gel (eluent: hexane/ethyl acetate 1:1–10:1) (**3c**, **3d**, **9**, **10** and **11**). Mixtures of **6a** and **7a** were converted into **6a** by hydrogenation.

4.3. General hydrogenation procedure

Mixtures of **6a** and **7a** (0.5 g–2.0 g) in 20 ml of MeOH in the presence of 0.12 g, 5% Pd/C catalyst was hydrogenated in steel autoclave equipped with magnetic stirrer (500 rounds per minute) under 20 bar of hydrogen pressure during 5 h. Conversion of **7a** into **6a** was controlled by GC analysis on 11 m×0.25 mm Supelco SP™ 2380 capillary column (column temperature 120 °C). After 5 h compound **7a** was fully converted into **6a** with quantitative yield. The catalyst was filtered off, and after solvent removing **6a** was isolated.

4.3.1. 1-Benzyl-4,4-dimethoxypiperidine-3-ol (3a).[23,28] Yield 1.78 g (71%) [exp. 6, Table 1], white solid, mp 89–90 °C, ^1H NMR ($CDCl_3$): δ 1.75–2.0 (m, 2H), 2.12–2.25 (m, 1H), 2.50–2.56 (m, 1H), 2.65–2.75 (m, 1H), 2.74 (s, 1H, OH), 2.83–2.90 (m, 1H), 3.22 (s, 3H, OCH_3), 3.28 (s, 3H, OCH_3), 3.57 (s, 2H, CH_2Ph), 3.70–3.74 (m, 1H, CH–O), 7.25–7.38 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$): δ 27.8 (CH_2), 47.5 (OCH_3), 47.6 (OCH_3), 49.2 (CH_2), 56.1 (CH_2), 61.9 (CH_2), 66.8 (OCH), 98.9 [$C(OCH_3)_2$], 127.0, 128.2, 128.8, 137.8 (Ph). MS (70 eV) m/z (relative intensity %): 251 (M^+, 12), 236 (14), 220 (23), 202 (15), 188 (10), 142 (6), 120 (21), 91 (100), 65 (15), 42 (17). IR (KBr): ν_{max} 3450, 2912, 2832, 1584, 1452, 1340, 1212, 1132, 1076, 948.

4.3.2. 1-Methyl-4,4-dimethoxypiperidine-3-ol (3b). Yield 1.41 g (81%), white solid, mp 108–109 °C [lits.[29,30] 109–110 °C], ^1H NMR ($CDCl_3$): δ 1.80–1.94 (m, 2H), 2.05–2.13 (m, 1H), 2.25 (s, 3H, CH_3), 2.38–2.43 (m, 1H), 2.58–2.65 (m, 1H), 2.76–2.81 (m, 1H), 2.85 (s, 1H, OH), 3.19 (s, 3H, OCH_3), 3.25 (s, 3H, OCH_3), 3.71–3.75 (m, 1H, CH–O). ^{13}C NMR ($CDCl_3$): δ 27.5 (CH_2), 45.5 (CH_3), 47.5 (OCH_3), 47.6 (OCH_3), 51.6 (CH_2), 58.2 (CH_2), 66.9 (OCH), 98.5 [$C(OCH_3)_2$]. MS (70 eV) m/z (relative intensity %): 175 (M^+, 24), 160 (23), 144 (29), 126 (31), 112 (20), 100 (7), 87 (45), 70 (11), 58 (49), 44 (100). IR (KBr): ν_{max} 3136, 2944, 2772, 1468, 1360, 1292, 1152, 1116, 1068, 948.

4.3.3. Ethyl 3-hydroxy-4,4-dimethoxypiperidine-1-carboxylate (3c).[28] Compound **3c** was isolated by column chromatography (eluent: hexane/ethyl acetate 1:1), yield 1.28 g (55%), colourless oil, ^1H NMR ($CDCl_3$): δ 1.22 (t, 3H, J=7.1 Hz), 1.65–1.88 (m, 2H), 2.65 (s, 1H, OH), 2.94–3.18 (m, 2H), 3.20 (s, 3H, OCH_3), 3.22 (s, 3H, OCH_3), 3.72–3.90 (m, 3H), 4.18 (q, 2H, J=7.1 Hz). ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_3), 27.0 (CH_2), 40.2 (CH_2), 46.3 (CH_2), 47.4 (OCH_3), 47.6 (OCH_3), 61.1 (OCH_2), 66.33 (OCH), 98.84 [$C(OCH_3)_2$], 156.10 (C=O). MS (70 eV) m/z (relative intensity %): 233 (M^+, 20), 218 (8), 204 (16), 202 (11), 173 (15), 160 (18), 156 (21), 144 (43), 101 (57), 88 (100), 56 (67), 42 (98). IR (KBr): ν_{max} 3460, 2944, 2832, 1685, 1436, 1272, 1228, 1120, 1076, 940.

4.3.4. *tert*-Butyl 3-hydroxy-4,4-dimethoxypiperidine-1-carboxylate (3d).[23] Compound **3d** was isolated by column chromatography (eluent: hexane/ethyl acetate 1:1), yield 1.35 g (52%), colourless oil, ^1H NMR ($CDCl_3$): δ 1.40 (s, 9H), 1.71–1.86 (m, 2H), 2.65 (s, 1H, OH), 2.95 (m, 1H), 3.15 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 3.29 (m, 1H), 3.61–3.73 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 28.1 (CH_3), 28.4 (CH_2), 42.2 (CH_2), 47.5 (OCH_3), 47.6 (OCH_3), 48.47 (CH_2), 65.86 (OCH), 79.12 (C–O), 99.92 [$C(OCH_3)_2$], 154.56 (C=O). MS (70 eV) m/z (relative intensity %): 261 (M^+, 2), 204 (5), 188 (2), 160 (4), 146 (14), 101 (15), 89 (24), 57 (100), 43 (66). IR (KBr): ν_{max} 3400, 2944, 2832, 1692, 1428, 1368, 1172, 1120, 1076, 940.

4.3.5. Methyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate (6a).[31,32] Yield 1.26 g (70%) [two-step procedure: electrolysis (exp.10, Table 2) and hydrogenation], colourless oil, bp 96–99 °C (14 Torr), [lit.[33] bp 86 °C (10.5 Torr)], ^1H NMR ($CDCl_3$): δ 1.10 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.91 (dd, 1H, J_1=7.3 Hz, J_2=13.1 Hz), 2.19 (dd, 1H, J_1=11.5 Hz, J_2=13.1 Hz), 2.88 (dd, 1H, J_1=7.3 Hz, J_2=11.5 Hz), 3.65 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 25.9 (CH_3), 30.8 (CH_3), 31.0 (CH_3), 31.3 (CH_3), 42.4 (CH_2), 51.2 (OCH_3), 54.7 (CH), 57.5 (C), 62.0 (C), 173.2 (C=O). MS (70 eV) m/z (relative intensity %): 185 (M^+, 4), 170 (100), 154 (11), 138 (14), 124 (10), 110 (45), 99 (33), 84 (24), 58 (98). IR (KBr): ν_{max} 2964, 2930, 2872, 1736, 1464, 1436, 1368, 1288, 1188, 1148.

4.3.6. Methyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate (7a).[26,32] Compound **7a** was obtained by method as described in Ref. 34. 70% Yield, colourless oil, bp 110–112 °C (15 Torr) [lit.[34] bp 56–58 °C (1.3 Torr)], ^1H NMR ($CDCl_3$): δ 1.29 (s, 6H), 1.40 (s, 6H), 3.71 (s, 3H, OCH_3), 6.60 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 29.7 (CH_3), 29.8 (CH_3), 51.0 (OCH_3), 63.2 (C), 65.7 (C), 139.0 (C=), 148.9 (CH=), 164.3 (C=O). MS (70 eV) m/z (relative intensity %): 183 (M^+, 25), 168 (100), 152 (18), 136 (43), 122 (30), 108 (82), 94 (49), 67 (45). IR (KBr): ν_{max} 2964, 2928, 2872, 1730, 1632, 1436, 1368, 1328, 1148, 1064.

4.3.7. Ethyl 2,2,5,5-tetramethyl-3-pyrrolidinecarboxylate (6b).[35] Compound **6b** was isolated by reaction mixture distillation (exp. 3, Table 3), 1.01 g (51%) colourless oil, bp 114–116 °C (15 Torr) [lit.[35] bp 217 °C (748 Torr)], ^1H NMR ($CDCl_3$): δ 1.07 (s, CH_3), 1.20 (s, CH_3), 1.25 (t, 3H, J=7.1 Hz), 1.29 (s, CH_3), 1.39 (s, CH_3), 1.89 (dd, 1H, J_1=7.3 Hz, J_2=13.0 Hz), 2.15 (dd, 1H, J_1=11.6 Hz, J_2=13.0 Hz), 2.85 (dd, 1H, J_1=7.3 Hz, J_2=11.6 Hz), 4.05–4.20 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 25.9 (CH_3), 30.9 (CH_3), 31.1 (CH_3), 31.4 (CH_3), 42.4 (CH_2), 54.9 (CH), 57.5 (C), 60.0 (OCH_2), 62.0 (C), 172.73

(C=O). MS (70 eV) *m/z* (relative intensity %): 199 (M^+, 3), 184 (100), 154 (14), 138 (12), 124 (6), 110 (39), 99 (24), 84 (18), 58 (50). IR (KBr): ν_{max} 2968, 2932, 1736, 1464, 1368, 1284, 1256, 1184, 1148, 1064.

4.3.8. Ethyl 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate (7b).[36] Compound **7b** was obtained by method as described in Ref. 34. 55% Yield, colourless oil, bp 120–122 °C (12 Torr) [lit.[36] bp 212 °C (740 Torr)], ^1H NMR ($CDCl_3$): δ 1.26 (s, 6H), 1.30 (t, 3H, $J=7.2$ Hz), 1.41 (s, 6H), 4.22 (q, 2H, $J=7.2$ Hz), 6.65 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 29.9 ($2CH_3$), 30.1 ($2CH_3$), 59.9 (OCH_2), 63.2 (C), 65.9 (C), 139.4 (C=), 148.6 (CH=), 163.9 (C=O). MS (70 eV) *m/z* (relative intensity %): 197 (M^+, 2), 182 (100), 152 (21), 136 (15), 122 (10), 109 (66), 94 (18), 58 (11). IR (KBr): ν_{max} 2928, 2868, 1720, 1632, 1468, 1360, 1328, 1160, 1060.

4.3.9. Methyl 2,2,4,4-tetramethylcyclopentanecarboxylate (9). Compound **9** was isolated by column chromatography (exp. 3, Table 4) (eluent: hexane/ethyl acetate 8:1) 0.20 g (11%), colourless oil, ^1H NMR ($CDCl_3$): δ 0.85 (s, 3H), 0.95 (s, 3H), 1.04 (s, 3H), 1.13 (s, 3H), 1.41 (s, 2H), 1.65 (dd, 1H, $J_1=7.3$ Hz, $J_2=13.0$ Hz), 1.95 (dd, 1H, $J_1=11.7$ Hz, $J_2=13.0$ Hz), 2.63 (dd, 1H, $J_1=7.3$ Hz, $J_2=11.7$ Hz), 3.59 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 25.8 (q), 30.6 (q), 31.0 (q), 31.2 (q), 36.3 (s), 42.5 (s), 42.9 (t), 50.9 (q), 54.0 (t), 56.6 (d), 174.2 (s). MS (70 eV) *m/z* (relative intensity %): 184 (M^+, 7), 169 (24), 153 (8), 137 (11), 123 (61), 109 (100), 95 (92), 83 (97), 56 (30). IR (KBr): ν_{max} 2956, 2930, 2868, 1736, 1464, 1436, 1256, 1192, 1172, 1064. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.56; H, 11.05.

4.3.10. Methyl 5-iodo-2,2,4,4-tetramethylcyclopentanecarboxylate (10). Compound **10** was isolated by column chromatography (exp. 1, Table 4) (eluent: hexane/ethyl acetate 10:1) 1.17 g (38%), pink oil, ^1H NMR ($CDCl_3$): 0.91 (s, 3H), 1.05 (s, 3H), 1.13 (s, 3H), 1.27 (s, 3H), 1.52 (d, 1H, $J=13.2$ Hz), 1.71 (d, 1H, $J=13.3$ Hz), 3.11 (d, 1H, $J=12.4$ Hz), 3.72 (s, 3H, OCH_3), 4.29 (d, 1H, $J=12.4$ Hz). ^{13}C NMR ($CDCl_3$): δ 27.7 (CH_3), 28.1 (CH_3), 29.2 (CH_3), 31.6 (CH_3), 41.4 (C), 41.9 (CH), 48.1 (C), 51.3 (CH_2), 51.6 (OCH_3), 63.8 (CH), 172.1 (C=O). MS (70 eV) *m/z* (relative intensity %): 310 (M^+, 6), 279 (7), 251 (3), 237 (11), 183 (M^+-I, 43), 167 (6), 151 (26), 123 (100), 109 (16), 97 (40). IR (KBr): ν_{max} 2960, 2932, 2868, 1740, 1460, 1436, 1372, 1256, 1192, 1168. Anal. Calcd for $C_{11}H_{19}IO_2$: C, 42.60; H, 6.17; I, 40.91. Found: C, 42.46; H, 6.03; I, 40.77.

4.3.11. Methyl 3,3,5,5-tetramethyl-1-cyclopentene-1-carboxylate (11). Compound **11** was isolated by column chromatography (exp. 3, Table 4) (eluent: hexane/ethyl acetate 8:1) 0.56 g (31%), colourless oil, ^1H NMR ($CDCl_3$): 1.08 (s, 6H), 1.21 (s, 6H), 1.67 (s, 2H), 3.65 (s, 3H, OCH_3), 6.40 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 29.2 (q), 29.4 (q), 35.1 (s), 45.6 (s), 50.8 (q), 55.4 (t), 139.8 (s), 152.1 (d), 165.4 (s). MS (70 eV) *m/z* (relative intensity %): 182 (M^+, 18), 167 (33), 151 (7), 135 (15), 120 (20), 107 (100), 93 (22), 65 (25). IR (KBr): ν_{max} 2960, 2930, 2869, 1720, 1628, 1436, 1340, 1304, 1192, 1060. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.35; H, 9.81.

Acknowledgements

The authors gratefully acknowledge the financial support of the Russian Foundation for Basic Research (Project N 06-03-32181a).

References and notes

1. Chakrabartty, S. K. *Oxidation in Organic Chemistry, Part C*; Trahanovsky, W. S., Ed.; Academic: New York, NY, 1978; pp 343–405.
2. Gala, D.; DiBenedetto, D. J.; Mergelsberg, I.; Kugelman, M. *Tetrahedron Lett.* **1996**, *37*, 8117–8120.
3. Adam, W.; Fell, R. T.; Mock-Knoblauch, C.; Saha-Moëller, C. R. *Tetrahedron Lett.* **1996**, *37*, 6531–6534.
4. Giordano, C.; Castaldi, G.; Uggeri, F. *Angew. Chem.* **1984**, *96*, 413–419.
5. Rieu, J. P.; Boucherle, A.; Cousse, H.; Mouzin, G. *Tetrahedron* **1986**, *42*, 4095–4133.
6. Shono, T. Electroorganic Chemistry as a New Tool in Organic Synthesis. *Reactivity and Structure: Concepts in Organic Chemistry*; Springer: Berlin, 1984; Vol. 20.
7. *Organic Electrochemistry*; Lund, H., Ed.; Marcel Dekker: New York, NY, 2000.
8. Bradt, W. E.; Opp, C. J. *Trans. Electrochem. Soc.* **1931**, *59*, 237–245.
9. Yokoyama, M. *Bull. Chem. Soc. Jpn.* **1933**, *8*, 71–107.
10. Pirrone, F. *Gazz. Chim. Ital.* **1936**, *66*, 244–253.
11. Shipley, J. W.; Rogers, M. T. *Can. J. Res.* **1939**, *17B*, 147–158.
12. Becker, J. Y.; Byrd, L. R.; Miller, L. L.; So, Y.-H. *J. Am. Chem. Soc.* **1975**, *97*, 853–856.
13. Campbell, C. B.; Pletcher, D. *Electrochim. Acta* **1978**, *23*, 923–927.
14. Rappe, C. *The Chemistry of the Carbon–Halogen Bond, Part 2*; Patai, S., Ed.; Wiley: New York, NY, 1973; p 1071.
15. Nikishin, G. I.; Elinson, M. N.; Makhova, I. V. *Angew. Chem. Int. Ed. Engl.* **1988**, *100*, 1716–1717.
16. Elinson, M. N.; Feducovich, S. K.; Dorofeev, A. S.; Vereshchagin, A. N.; Nikishin, G. I. *Tetrahedron* **2000**, *56*, 9999–10003.
17. Elinson, M. N.; Feducovich, S. K.; Dorofeev, A. S.; Vereshchagin, A. N.; Nikishin, G. I. *Izv. Akad. Nauk Ser. Khim.* **2003**, 216–219.
18. Barba, F.; Elinson, M. N.; Escudero, J.; Guirado, M.; Feducovich, S. K. *Electrochim. Acta* **1998**, *43*, 973–976.
19. Elinson, M. N.; Feducovich, S. K.; Zaimovskaya, T. A.; Dorofeev, A. S.; Vereshchagin, A. N.; Nikishin, G. I. *Izv. Akad. Nauk Ser. Khim.* **2003**, 946–950.
20. Barba, F.; Elinson, M. N.; Escudero, J.; Feducovich, S. K. *Tetrahedron Lett.* **1996**, *37*, 5759–5762.
21. Barba, F.; Elinson, M. N.; Escudero, J.; Feducovich, S. K. *Tetrahedron* **1997**, *53*, 4427–4436.
22. Elinson, M. N.; Feducovich, S. K.; Dmitriev, D. E.; Dorofeev, A. S.; Vereshchagin, A. N.; Nikishin, G. I. *Tetrahedron Lett.* **2001**, *42*, 5557–5559.
23. Shono, T.; Matsumura, Y.; Inoue, K.; Iwasaki, F. *J. Chem. Soc., Perkin Trans. 1* **1986**, 73–77.
24. Zacuto, M. J.; Cai, D. *Tetrahedron Lett.* **2005**, *46*, 447–450.
25. Dehmlov, E. V.; Westerheide, R. *Heterocycles* **1994**, *37*, 355–366.
26. Krivosheeva, S. N.; Zhukova, I. Yu.; Kagan, E. Sh. *Zh. Prikl. Khim.* **2002**, *75*, 1566–1568; (*Russ. J. Appl. Chem.* **2002**, *75*, 1532–1534).

27. Guijarrro, D.; Yus, M. *Curr. Org. Chem.* **2005**, *9*, 1713–1735.
28. Van Daele, G. H. P.; De Bruyn, M. F. L.; Sommen, Francois M.; Janssen, M.; Van Nueten, J. M.; Schuurkes, J. A. J.; Niemegeers, C. J. E.; Leysen, J. E. *Drug Dev. Res.* **1986**, *8*, 225–232.
29. Moriarty, R. M.; Prakash, O.; Karalis, P.; Prakash, I. *Tetrahedron Lett.* **1984**, *25*, 4745–4748.
30. Dehmlow, E. V.; Westerheide, R. *Heterocycles* **1994**, *37*, 355–366.
31. Krinitskaya, L. A.; Volodarskii, L. B. *Bull Acad. Sci. USSR, Div. Chem. Sci.* **1982**, 401–404.
32. Aneja, Davies. *Chem. Phys. Lipids* **1970**, *4*, 60–69.
33. Rozanzew, E. G.; Krinitskaya, L. A.; Neiman, M. B. *Bull Acad. Sci. USSR, Div. Chem. Sci.* **1966**, 638–640.
34. Krishna, M. C.; DeGraff, W.; Hankovszky, O. H.; Sar, C. P.; Kalai, T. I. *J. Med. Chem.* **1998**, *41*, 3477–3492.
35. Pauly, H.; Hueltenschmidt, A. *Chem. Ber.* **1903**, *36*, 3351–3370.
36. Pauly, H.; Rossbach, J. *Chem. Ber.* **1899**, *32*, 2000–2014.