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Electrochemical carboxylation of fluorocontaining imines with preparation of fluorinated *N*-phenylphenylglycines

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ABSTRACT

A possibility of obtaining fluorine-containing *N*-phenylphenylglycine derivatives at yields of up to 85% via the electrochemical carboxylation of corresponding benzalanilines was shown. The influence of imine's electron structure, the nature of supporting electrolyte and cathodic material on such processes is examined. It was found, that increasing electron accepting ability of the substituents in benzylidene and aniline fragments of the imine molecule lead to decrease of amino acid yields. The dependence of the *N*-phenyl-*p*-fluorophenylglycine yield on the cathode material (Zn, GC, Cu, Ag, Pt) and on the nature of the supporting electrolytes (Bu_4NBr, Et_4NBr, Et_4NClO_4, $PhCH_2Me_3NClO_4$, $LiBF_4$, $LiClO_4$, $NaBF_4$ and KBF_4) was investigated. The highest amino acid yields were obtained at cathodes (GC and Zn) that do not exhibit specific adsorption of fluorine-containing imines, as well as in the presence of background salts (Alk_4NBr) whose cations do not show tendency to strong ion pairing with anion radicals formed by the electrochemical activation of the imines.

1. Introduction

Fluorocontaining amino acids and their derivatives already found widespread application in medicine, pharmacology, etc. [1]. Fluorine atoms appreciably influence on the acid–base properties of functional groups of amino acids, lend them the ability to form hydrogen bonds F···H and increase the lipophilicity of amino acid molecules [2,3]. Owing to this features fluorocontaining amino acids show various types of biological activity, different from natural amino acids. Also it makes possible to study their conversion routes in the organism by ^{19}F NMR spectroscopy.

Among amino acids and their derivatives *N*-phenylphenylglycine derivatives that are structural analogues of glycine's natural amino acid are of considerable interest to researchers [4–7]. However fluorine-containing *N*-phenylphenylglycine derivatives are still practically unexplored [7], due to the synthetic difficulties [4,5,7], particularly via a multi-step process, frequently involving the use of expensive and toxic reactants (cyanides, bromine).

As is known, electrochemically activated insertion of carbon dioxide into various organic substrates [8–12] opens up broad possibilities for preparation of various carboxylic acids, that, in some cases, enable to carry out synthesis via a simpler route and use more available and cheaper reactants. In particular, electrochemically activated introduction of CO_2 to the C=N bond can result in α-amino acids [13,14].

In this paper the possibility to produce fluorocontaining *N*-phenylphenylglycine derivatives through electrochemical carboxylation of corresponding imines with the fluorine atom (or fluorine-containing group) retained to give fluorine-containing amino acids. As is known [15,16], electrochemical activation of some fluorine-containing organic substrates may proceed with the elimination of the fluorine. Taking this into consideration, in the case of fluorine-containing imines one could expect at least three ways for the process to unfold in the course of the imines' cathodic activation in the presence of CO_2: carboxylation at fluorine atom with its replacement by carboxy group as in the case of trifluoromethylarenes [15]; detachment of the fluorine as fluoride ion and follow-on carboxylation at the carbon atom of the imine's C=N bond to give defluorinated amino acid; carboxylation at the C=N bond's carbon atom to retain the fluorine atom (or fluorine-containing group), which would open up a possibility of obtaining fluorine-containing amino acids.

2. Results and discussion

Used as the objects have been the following imines containing the fluorine atoms in different positions in the benzylidene fragment (**1**–**3**), and imines with fluorine atom in the para-position of the benzylidene fragment and electron-donor (**4**, **5**) or electron–acceptor (**6**–**10**) substituents in the aniline fragment.

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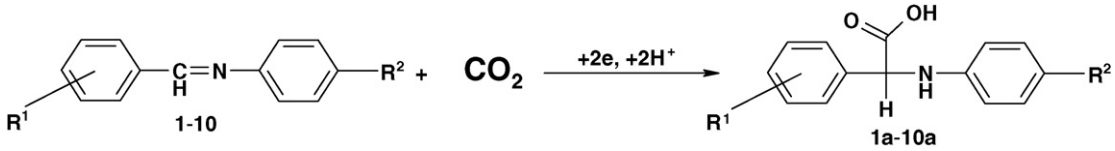


Scheme 1. **1**, R^1 = *para*-F, R^2 = H; **2**, R^1 = *meta*-F, R^2 = H; **3**, R^1 = *ortho*-F, R^2 = H; **4**, R^1 = *para*-F; R^2 = OCH_3; **5**, R^1 = *para*-F; R^2 = CH_3; **6**, R^1 = *para*-F, R^2 = F; **7**, R^1 = *para*-F, R^2 = Cl; **8**, R^1 = *para*-F, R^2 = Br; **9**, R^1 = *para*-F, R^2 = CF_3; **10**, R^1 = *para*-F, R^2 = COOEt.

2.1. Electrochemical activation of fluorocontaining imines

As a result of preliminary study we have found that the employed fluorine-containing imines **1**–**10** undergo electrochemical reduction at less negative potentials (E_{pc} = −1.53V to −1.98 V) than carbon dioxide does ($E_{pc} < -2.2$ V) under comparable conditions. Hence, the imines activation can be the key step in carboxylation process via the assumed route as represented by Scheme 1. Therefore we studied the electrochemical behaviour of the imines **1**–**10** in the absence and in the presence of carbon dioxide.

The cyclic voltammogram (CV) of reduction of **1** shows two cathodic peaks with E_{p1} = −1.86 V and E_{p2} = −2.41 V (Fig. 1a), with the intensity of the first peak being noticeably higher than that of the second one. The evaluation of the number of electrons involved in the first step of the imine reduction (E_{p1} = −1.86 V) by coulometric and computational methods [17–19], points to the value being close to unity. Consequently, this peak corresponds to one electron reduction of imine to corresponding anion radical. The second peak on CV of imine **1** reduction may be relevant to the transfer of the second electron, resulting in imine dianion formation (Scheme 2).

Studying the electrochemical activation of imine **1** at different scan rates showed, that an increase of potential scan rate from 0.2 V/s to 2.0 V/s leads to the increase of both cathodic peaks intensity and to the appearance of an anodic peak, which can be attributed to the oxidation of the imine anion radical formed in primary step of the process (Fig. 1b; Scheme 2). Similar CVs are observed also in the case of electrochemical activation of other studied imines. However for imines **2** and **3** the anodic peaks were observed already at low potential scan rates (v = 0.2 V/s), whereas for imines **8**–**10** it does not appear even at comparatively high scan rates (100.0 V/s). This may be relevant to the fact that their anion radicals are less stable, and faster undergo further conversions in the solution. On the base of CVs of imines we estimated the stability of forming anion radicals. They can be dispose in following consecution: $(i_a/i_k) = 3(0.46) > 2(0.11) > 5(0.09) > 1(0.05) > 4(0.04) = 6(0.04) > 7(0.01) \gg 8(0) = 9(0) = 10(0)$ (v = 1.0 V/s) in accordance with i_a/i_k value diminution.

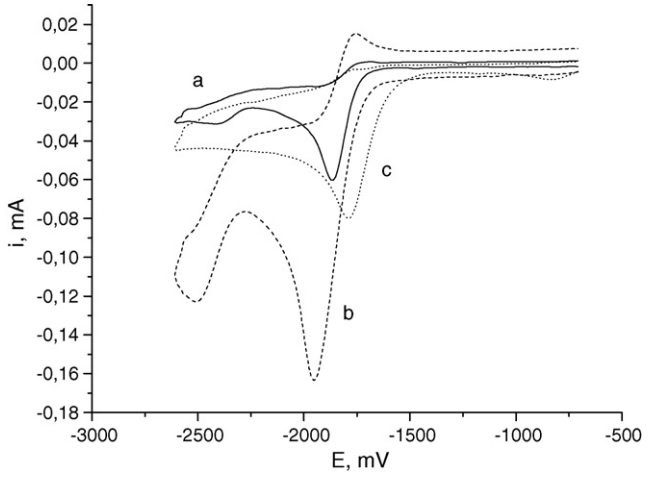
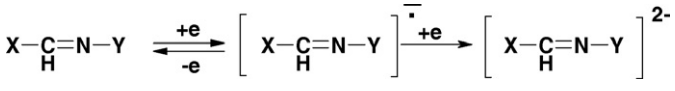


Fig. 1. CV of electrochemical reduction of imine **1** (a) without CO_2 at v = 0.2 V/s, (b) without CO_2 at v = 2.0 V/s, (c) saturated with CO_2 at v = 0.2 V/s (dimethylformamide (DMF) + 0.1 M tetrabutylammonium bromide (Bu_4NBr), cathode, glassy carbon (GC); anode, Pt; reference electrode Ag/AgCl, C(**1**) = 5×10^{-3} M).



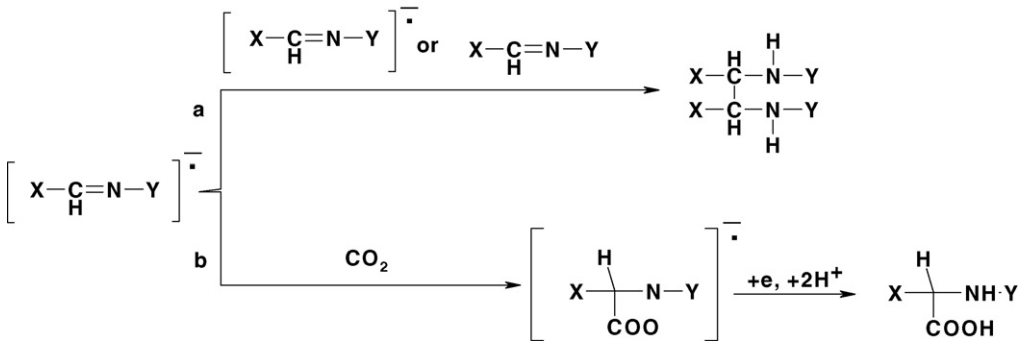
Scheme 2.

Unlike other studied imines, in the case of bromocontaining imine **8** the first and second cathodic peaks partially overlap and the later has current intensity higher than the former, which may be due to the C–Br bond cleavage in the electrochemical reduction of the imine.

The imines anion radicals can undergo different conversions, in particular they can interact with the starting imines and/or with themselves to produce dimers (Scheme 3a). The possibility of forming similar dimers has been shown in Refs. [13,14] in the case of some imines, that does not contain fluorine atoms. The similar dimers can be formed in the case of electrochemical reduction of fluorocontaining imines that confirm with results of chromatography–mass spectrometry study of the products of preparative electrolysis of imine **1** (cathode, GC; anode, Al; Bu_4NBr, DMF). At that there is intensive signal of the main product with m/z = 401 in mass-spectra which corresponds to the dimer of starting imine.

To size up the probability of the dimer formation process preferentially proceeding via anion radical—starting imine interaction or dimerisation of two anion radicals we have computed the rate constants of these reactions, using Digielch.2.0 software [17–19]. The first reaction has been found to be likely to proceed at a much higher rate (for the explored imines the rate constants of the reaction of the anion radical with the starting imine are in the range of 10^2 l/mol s to 10^5 l/mol s than the second one 10 l/mol s to 10^4 l/mol s, due to the Coulomb repulsion of similarly charged species in the case of dimerisation of two anion radicals.

We have studied the electrochemical behavior of imines in the presence of CO_2. With carbon dioxide added into a solution of imine **1** in the course of electrochemical reduction there is observed growth the first cathodic peak and its shift into more anodic region as well as the complete disappearance of the second cathodic peak attributed to the imine dianion formation, and of the anodic peak (Fig. 1c). This is also the case for the other explored imines being electrochemically activated in the presence of CO_2. The observed changes may be relevant to the interaction of the imine anion radical with the CO_2 molecule. As CO_2 is stronger electrophile, than imine, the carboxylation reaction (Scheme 3, route b) must dominate the dimer formation (Scheme 3, route a). The first cathodic peak shift into the less negative potential region may be caused by both subsequent chemical reactions of the anion radicals with the carbon dioxide and by the formation of imine complexes with the CO_2 molecule. Similar association of CO_2 with ketones has been revealed recently [20].



Scheme 3.

2.2. Electrocarboxylation of imines in preparative scale

To confirm the possibility of imine anion radical–CO_2 interaction to form carboxylation products we have carried out preparative electrolysis of imines in the presence of CO_2. The preparative carboxylation was made in a DMF solution, under a constant CO_2 flow, in an undivided cell using the different cathodes and a soluble aluminium anode. After electrolysis DMF was distilled off and the carboxylation product was isolated via acidification of the residue followed by extraction with diethyl ether, purified and analysed by ^{1}H, ^{13}C, ^{19}F NMR and IR spectroscopy, mass spectrometry and elemental analysis. The conditions for preparative electrosyntheses and analytical data of the products are given in detail in Section 4. We found, that electrochemical activation of imines **1**–**10** in the presence of carbon dioxide leads to carboxylation products with the fluorine atoms retained in the molecule, which enables the fluorocontaining amino acids **1a**–**10a** to be obtained at sufficiently high yields (Table 1).

2.2.1. Effect of the electron structure of imines on the N-phenylphenylglycine derivatives yields

It was of interest to elucidate the influence of the nature of different substituents in the imines' benzylidene and aniline fragments on the yields of the corresponding fluorocontaining *N*-phenylphenylglycine derivatives (**1a**–**10a**). The results of preparative carboxylation of the various imines are present in Table 1. As follows from listed data, the amino acid derivative yields are critically dependent on the electron structure of the imines. In general, there can be discerned a trend for decreasing amino acids yields with introduction of electron–acceptor substituents in of both the benzylidene and aniline fragments of the imines molecules, which are conjugated with the reaction center (the carbon atom of the C=N bond) where the carboxylation occurs. The observed yields' decreasing may be related to the decrease in electron density on the carbon atom, that diminishes nucleophilic properties and as a consequence—the reactivity of imine anion radical towards CO_2. In particular, unsubstituted acid yield ($R^1 = R^2 = H$) under conditions implied is 84%, whereas introduction of fluorine atom into para- (imine **1**) and ortho- (imine **3**) positions of the imines' benzylidene fragment falls the amino acid **1a** and **3a** yields to 47% and 44%, respectively. On the contrary, fluorine atom in meta-position (imine **2**) that is not conjugated to the reaction site, does not impact on the amino acid yield so very critically. The lower amino acid yield in the carboxylation of imines **4** and **8** is evidently linked to various side reactions. In particular, for imine **8**, there can occur electrochemical reduction and carboxylation at the C-Br bond (the corresponding diacid has been found among the electrosynthesis products; its formation is attested to by ^{13}C NMR data and the peak with *m*/*z* 289 in the mass spectrum).

Table 1
Results of electrochemical carboxylation of fluorocontaining imines (DMF, Bu_4NBr (0.1 M), C (**1**–**10**) = 0.1 M; cathode, Zn; anode, Al)

Imine	*N*-Phenylphenylglycine	*N*-Phenylphenylglycine	
		Yield (%)	Current efficiency (%)
1	**1a**	47	56
2	**2a**	85	87
3	**3a**	44	58
4	**4a**	28	20
5	**5a**	54	85
6	**6a**	46	70
7	**7a**	39	42
8	**8a**	15	11
9	**9a**	30	42
10	**10a**	27	29

Our comparative study of electrochemical study and preparative electrolysis data shows that the amino acid yield significantly depends on the stability of the imines' anion radicals, which is defined by their electron structure. An increase in the stability of the imine's anion radical decreases the probability of its dimerisation, promoting to the process preferentially running via carboxylation (Scheme 3b). More specifically, for imines **1**–**3**, **5** and **6** their anion radicals possess a higher stability, that is confirmed by the higher anodic peak currents in CVs of the corresponding imines at a low potential scan rate (0.2 V/s), and the corresponding acids yields are. In the case of imines that do not display anodic peak in CVs at a potential scan rate of 0.2 V/s (and for imines **8**–**10** upto 100 V/s), corresponding anion radicals are less stable under these conditions, with amino acid derivatives (**4a**, **7a**–**10a**) forming at low yields (39–15%).

The current efficiency is higher than yield almost in all cases. This can be connected with one-electron competing reaction of dimer formation in contrast to two-electron process of cathodic carboxylation of imines (Scheme 3b). The imines **4** and **8** are exceptions. For them the current efficiency is lesser than yield that may be due to the mentioned earlier two-electron side reactions.

2.2.2. Effect of the nature of the supporting electrolyte on the N-phenylphenylglycine derivatives yields

To study the influence of the nature of supporting electrolyte on carboxylation process we carried out preparative electrochemical carboxylation of imine **1** as a model compound (it has the simplest structure and is prevented from steric effects) using different background salts. The results of the conducted research are shown in Table 2. As it follows from the listed data, varying the supporting electrolyte anion does not lead to an appreciable change in the amino acid **1a** yield (entries 2 and 3), owing to negligible effect of the anion on the similarly charged reaction intermediates (anion

Table 2
The results of electrochemical carboxylation of imine **1** using the different supporting electrolytes (DMF; background salt (0.1 M); C (**1**) = 0.1 M; cathode, Zn; anode, Al)

Entry	Supporting electrolyte	**1a**	
		Yield (%)	Current efficiency (%)
1	Bu_4NBr	47	56
2	Et_4NBr	35	36
3	Et_4NClO_4	34	38
4	$PhCH_2Me_3NClO_4$	24	31
5	$LiBF_4$	0	0
6	$LiClO_4$	0	0
7	$NaBF_4$	0	0
8	KBF_4	0	0

Table 3
Results of the electrochemical carboxylation of imine **1** using different cathodes (DMF; Bu_4NBr (0.1 M); C (**1**) = 0.1 M; anode, Al)

Entry	Cathode	**1a**	
		Yield (%)	Current efficiency (%)
1	Zn	47	56
2	GC	45	49
3	Cu	18	22
4	Pt	17	34
5	Ag	13	22
6	Mg	31	37
7	Al	35	40

radicals). On the contrary, the nature of cation effects crucial on the carboxylation of imines. Unlike the background salts with tetraalkylammonia cations (entries 1–4), when using salts with cations of metals (entries 5–8) as supporting electrolytes in the electrochemical activation of the imine in the presence of CO_2 no amino acid was formed. No oxidation peaks of the imines anion radicals in CVs of imines reduction appear in the absence of carbon dioxide even at a high scan rate (100 V/s), which indicates the low stability of these species in the presence of alkali metals cations. As is known [21], alkali metal cations have tendency to strong ion pairing with organic anion radicals in aprotic solvents. Formation of the close ion pairs leads to compensation of negative charge on the imine's anion radical, which decreases its nucleophilicity and lowers its reactivity toward CO_2. Moreover, increasing the extent of ion paring can raise the rate of anion radical dimerisation (by decreasing of repulsion of equally charged species) (Scheme 3, route a), which decreases the efficiency of electrochemical carboxylation of imines.

For the background salts with organic cations the amino acid yields decrease in following order $Bu_4NBr > Et_4NBr \approx Et_4NClO_4 > PhCH_2Me_3NClO_4$. Perhaps, in the case of organic cations there are formed loose ion pairs with anion radicals or there occurs no ion pairs formation at all. The largest radius may cause the highest yields 1a in the case of Bu4NBr and, consequently, the lowest charge density of cation Bu_4N^+ among the other salts with organic cations employed. Therefore, compared with the other salts, it is less inclined to forming tight ion pairs, which does not decrease in the nucleophilicity of anion radicals and a rise in the rate of their dimerisation to result in by-products. The somewhat lower product yields in the case of trimethylbenzylammonium perchlorate (entry 4) may be accounted for substantial decomposition of the latter under preparative electrolysis conditions.

2.2.3. Effect of the cathode material on the N-phenylphenylglycine derivatives yields

Taking imine **1** as a model compound, we studied the effect of the cathode material on the corresponding amino acid yields with Zn, Cu, Pt, Ag and GC used as the cathodes. The data obtained are presented in Table 3, from which it follows that the highest amino acid yields were obtained on zinc and glassy carbon among the cathodes employed when conducting preparative electrolysis. Similar results were obtained by Silvestri et al. [14] in the electrochemical carboxylation of unsubstituted benzalaniline on Zn and GC electrodes. One reason for the varying amino acid yields on cathodes of the different materials could be the singularities of the imines' adsorption on them which effects on subsequent electrochemical and chemical processes. It was reported [22], that glassy carbon does not exhibit specific adsorption toward halogenated compounds. In the absence of specific adsorption, with other conditions being equal, the concentration of fluorocontaining imines on the GC surface may be lower than that on the other electrodes. This should decrease the possibility of any competitive side process of consumption of anion radical via dimerisation (Scheme 3, route a) and should contribute to carboxylation route (Scheme 3, route b). A different scenario can take place on a silver cathode, which display pronounced specific adsorption toward halogen-containing compounds (RHal) [23,24], owing to the formation of complexes of RHal with the silver atoms on the electrode surface RHal···Ag, which generally causes a RHal reduction potential shifts to a less cathodic field, compared to those obtained at a GC cathode. There is the same effect in the case of reduction of imine **1**: $E_p = -1.86$ V on GC and -1.77 V at Ag. Specific adsorption can lead to an increase in the imines concentration on the electrode surface and to raise the dimers formation rates, which diminishes the carboxylation product yields.

3. Conclusions

A possibility was shown of obtaining fluorocontaining *N*-phenylphenylglycine derivatives at yields up to 85% via the electrochemical carboxylation of corresponding benzalanilines. The influence of electron structure of imines was studied. The enhanced stability of the imines' anion radicals can lead to a decrease in the probability of anion radical dimerisation and to an increase in the amino acid derivative yields. The influence of nature of supporting electrolyte (Bu_4NBr, Et_4NBr, $PhCH_2Me_3NClO_4$, $LiBF_4$, $NaBF_4$ and KBF_4) on these processes is examined. The amino acid yields decrease in following row of organic supporting electrolytes: $Bu_4NBr > Et_4NBr \approx Et_4NClO_4 > PhCH_2Me_3NClO_4$ with no carboxylation products being formed at all, when the background salt includes a metal cation. Analysis of CVs of reduction of the imines enables to evaluate the *N*-phenylphenylglycine yields prior to preparative carboxylation. The high acids yields can be expected in the case of imines, those CVs show anodic peaks at low potential scan rates.

4. Experimental

DMF was purified according to Ref. [25]. Supporting electrolytes Bu_4NBr (Fluka), Et_4NBr, $PhCH_2Me_3NClO_4$, $LiBF_4$, $NaBF_4$ and KBF_4 before experiments were dried in vacuo during 24 h at 100 °C. Tetraethylammonium perchlorate Et_4NClO_4 (Fluka) was crystallized twice from ethanol and dried in a vacuum oven at 60 °C. For all experiments supporting electrolytes concentration was 0.1 mol/l. Fluorocontaining imines were prepared similarly to Ref. [26] via reaction of equimolar amounts of corresponding aldehydes and amines in ethanol solution and were purified via double crystallization from ethanol (imine's yields after purification were ≈80–90%). The ^1H NMR spectra for imines **1** [27] and **4** [28] were consistent with literature data and the elemental analysis results were in agreement with calculated. The ^1H and ^{19}F NMR spectra and the elemental analysis data for other imines are

given below. Before experiments imines were dried for several hours in vacuo at room temperature.

Cyclic voltammetry experiments were carried out in DMF with different background salts in a three-electrode cell using a glassy carbon disc $S = 0.0314\ cm^2$ as a working electrode. The counter electrode and the reference electrode were a Pt foil and Ag/AgCl, respectively. Imine's concentration was 5×10^{-3} M. All solutions were deaerated with high-purity argon before electrochemical experiments.

Preparative-scale carboxylation reactions were performed in an undivided three-electrode 50 cm^3 cell using GC, Zn, Ag, Pt or Cu as cathode ($S = 10\ cm^2$) and a sacrificial Al anode ($S = 10\ cm^2$) and Pt wire as reference electrode (0.31V vs. Ag/AgCl). Starting concentration of imines was 0.1 mol/l. Before electrolysis metallic electrodes (Zn, Pt, Ag, Cu) were immersed in 10% hydrochloric acid solution for several minutes, and then rinsed with distilled water and acetone, and several times with DMF. Carbon dioxide was bubbled into electrolytic cell after pre-drying over P_2O_5. For imines **1**–**7**, **9** and **10** process was carried out in potentiostatic conditions at a cathode potential of −1.80 V, with the initial values of current constituting 2×10^{-2} A to 3×10^{-2} A. Electrolysis was stopped when current fell to 2×10^{-3} A. For imine **8** controlled potential electrolysis was run potentiostatically at a potential of the first cathodic peak −1.38 V ($I_{start} = 8 \times 10^{-3}$ A), until current fall to 1×10^{-3} A.

To isolate the electrolysis products DMF was distilled off in vacuo, the residue was acidified with 8 ml of 3% solution hydrochloric acid and extracted three times with 50 ml of ether. Ether extracts were collected and after evaporation of ether the residue was treated with 25–30 ml of 3% water solution of $NaHCO_3$. The suspension was extracted three times with 50 ml of diethyl ether for removing of organic contaminants. Water solution was acidified with 4% hydrochloric acid to pH 5–6 with precipitated amino acid being filtered off. For final purification products were recrystallized from ethanol/water mixture.

^{1}H NMR spectra were measured using "Varian XL-300" or "Bruker-CXP-90", ^{19}F NMR using "Gemini VXR-200" or "Bruker-CXP-90" and ^{13}C NMR using "Bruker AVANCE 400" spectrometers. Chemical shifts were measured relative to TMS (internal standard) and trichlorofluoromethane (internal standard). Mass-spectra were recorded using "Autoflex II Bruker Daltonics" spectrometer and chromatomass study was performed with LC/MSD agilent 1100 Series.

3-Fluorobenzylideneaniline (**2**), CAS 58606-65-8; mp: 33–34 °C (lit. 30–30.5 °C [29]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.1–7.7 (9H, m), 8.43 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −113.7 (s).

2-Fluorobenzylideneaniline (**3**), CAS 39087-92-8, 135663-15-9; mp: 13–14 °C. ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.05–7.45 (8H, m), 8.19 (1H, t), 8.74 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −122.3 (s).

4-Fluorobenzylidene-4-methylaniline (**5**), CAS 397-69-11-4; mp: 60–61 °C (lit. 58 °C [30]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.37 (3H, s), 7.17 (6H, t), 7.89 (2H, dd), 8.43 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −109.7 (s).

4-Fluorobenzylidene-4-fluoroaniline (**6**), CAS 39769-09-0; mp: 51–53 °C (lit. 65 °C [26], 58 °C [30]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.14 (6H, m), 7.88 (2H, dd), 8.41 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −118.3 (s), −109.2 (s).

4-Fluorobenzylidene-4-chloroaniline (**7**), CAS 39769-10-3, 103749-63-9; mp: 72–73 °C (lit. 74–75 °C [30]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.19 (4H, m), 7.36 (2H, d), 7.92 (2H, dd), 8.39 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −108.8 (s).

4-Fluorobenzylidene-4-bromoaniline (**8**), CAS 64222-86-2; mp: 60 °C. ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.15 (4H, m), 7.51 (2H, d), 7.91 (2H, dd), 8.39 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −108.8 (s).

4-Fluorobenzylidene-4-trifluoromethylaniline (**9**), CAS 39769-13-6; mp: 47 °C (lit. oil [26,30]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.21 (4H, m), 7.63 (2H, d), 7.91 (2H, dd), 8.36 (1H, s). ^{19}F NMR (90 MHz, $CDCl_3$) δ −63.3 (3F, s), −108.2 (1F, s).

4-Fluorobenzylidene-4-ethylcarboxyaniline (**10**); mp: 98 °C (lit. 97 °C [26]). ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.42 (3H, t), 4.38 (2H, q), 7.22 (4H, m), 8.18–7.81 (4H, m), 8.41 (1H, s). ^{19}F NMR (200 MHz, $CDCl_3$) δ −108.3 (s).

(4-Fluoro-phenyl)-phenylamino-acetic acid (**1a**), CAS 124573-81-5, white solid; mp 191–193 °C (lit. 186–189 °C [7]). ^{1}H NMR (300 MHz, d-Me_2SO) δ 5.13 (1H, s, α-CH), 6.56 (1H, t, J = 7.16 Hz, H-4′), 6.66 (2H, d, J = 8.10 Hz, H-2′and H-6′), 7.05 (2H, t, J = 7.78 Hz, H-3′ and H-5′), 7.20 (2H, dd, J = 8.72 Hz, H-3 and H-5), 7.56 (2H, dd, J_1 = 5.60 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (300 MHz, d-Me_2SO) δ 58.9 (s, α-CH), 113.1 (s, C-2′, C-6′), 115.3 (d, J = 21.27 Hz, C-3, C-5), 116.7 (s, C-4′), 128.8 (s, C-3′, C-5′), 129.5 (d, J = 8.44 Hz, C-2, C-6), 134.8 (d, J = 2.94, C-1), 146.9 (s, C-1′), 161.7 (d, J = 243.93 Hz, C-4), 172.9 (s, COOH). ^{19}F NMR (90 MHz, d-Me_2SO) δ −115.3 (s). Anal. Calcd for $C_{14}H_{12}O_2NF$: C, 68.57; H, 4.90; N, 5.71. Found: C, 69.29; H, 4.74; N, 5.75. MS TOF LDI, 3.3×10^{14} eV, m/z (rel. int.): 245 $[M]^+$ (100), 246 $[MH]^+$ (90).

(3-Fluoro-phenyl)-phenylamino-acetic acid (**2a**), white solid; mp: 184–185 °C. ^{1}H NMR (400 MHz, d-Me_2SO) δ 5.18 (1H, s, α-CH), 6.56 (1H, t, J = 7.26 Hz, H-4′), 6.67 (2H, d, J = 7.80 Hz, H-2′ and H-6′), 7.04 (2H, t, J = 7.48 Hz, H-3′ and H-5′), 7.13 (1H, t, J = 8.12 Hz, H-4), 7.39 (3H, m, $W_{1/2}$ = 24 Hz, H-2, H-5, H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 59.0 (s, α-CH), 113.0 (s, C-2′, C-6′), 114.1 (d, J = 22.01 Hz, C-2), 114.5 (d, J = 21.27 Hz, C-4), 116.7 (s, C-4′), 123.7 (d, J = 2.93 Hz, C-6), 128.7 (s, C-3′, C-5′), 130.4 (d, J = 8.07, C-5), 141.5 (d, J = 6.60, C-1), 146.7 (s, C-1′), 162.2 (d, J = 243.56 Hz, C-3), 172.5 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −113.4 (s). Anal. Calcd for $C_{14}H_{12}O_2NF$: C, 68.57; H, 4.90; N, 5.71. Found: C, 68.66; H, 5.05; N, 5.74. MS TOF LDI, 3.8×10^{14} eV, m/z (rel. int.): 245 $[M]^+$ (100), 199 $[M-H-COOH]^+$ (23); 245 $[M]^-$ (100), 199 $[M-H-COOH]^-$ (25).

(2-Fluoro-phenyl)-phenylamino-acetic acid (**3a**), white solid; mp: 127–128 °C. ^{1}H NMR (400 MHz, d-Me_2SO) δ 5.32 (1H, s, α-CH), 6.56 (1H, t, J = 7.26 Hz, H-4′), 6.65 (2H, d, J = 8.23 Hz, H-2′ and H-6′), 7.05 (2H, t, J = 7.48 Hz, H-3′ and H-5′), 7.21 (2H, m, $W_{1/2}$ = 16 Hz, H-4 and H-5), 7.35 (1H, q, J = 7.16 Hz, H-3), 7.51 (1H, t, J = 7.48 Hz, H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 53.0 (d, J = 2.20, α-CH), 112.8 (s, C-2′, C-6′), 115.2 (d, J = 22.01 Hz, C-3), 116.8 (s, C-4′), 124.7 (d, J = 2.93 Hz, C-5), 125.9 (d, J = 14.68 Hz, C-1), 128.8 (d, J = 3.67, C-6), 128.9 (s, C-3′, C-5′), 129.9 (d, J = 8.07, C-4), 146.7 (s, C-1′), 160.3 (d, J = 245.03 Hz, C-2), 172.1 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −119.1 (s). Anal. Calcd for $C_{14}H_{12}O_2NF$: C, 68.57; H, 4.90; N, 5.71. Found: C, 68.79; H, 4.85; N, 5.94. MS TOF LDI, 3.8×10^{14} eV, m/z (rel. int.): 245 $[M]^+$ (90), 244 $[M-H]^+$ (45), 200 $[M-COOH]^+$ (10), 199 $[M-H-COOH]^+$ (100); 244 $[M-H]^-$ (45), 200 $[M-COOH]^-$ (100).

(4-Fluoro-phenyl)-(4-methoxy-phenylamino)-acetic acid (**4a**), CAS 124573-83-7, white solid; mp: 167–171 °C (lit. 171–174 °C [7]). ^{1}H NMR (300 MHz, d-Me_2CO) δ 3.61 (3H, s, OCH_3), 5.06 (1H, s, α-CH), 6.64 (4H, m, J = 9.03 Hz, J = 10.89 Hz, H-2′, H-3′, H-5′, H-6′), 7.18 (2H, dd, J = 8.72 Hz, H-3 and H-5), 7.54 (2H, dd, J_1 = 5.50 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 55.2 (s, OCH_3), 60.5 (s, α-CH), 114.0 (s, C-3′, C-5′), 114.4 (s, C-2′, C-6′), 114.8 (d, J = 21.28 Hz, C-3, C-5), 129.2 (d, J = 8.44 Hz, C-2, C-6), 136.3 (d, J = 2.56, C-1), 141.2 (s, C-1′), 150.9 (s, C-4′), 161.3 (d, J = 242.46 Hz, C-4), 172.7 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −114.9 (s). Anal. Calcd for $C_{15}H_{14}O_3NF$: C, 65.45; H, 5.09; N, 5.09. Found: C, 64.93; H, 5.31; N, 5.27. MS TOF LDI, 1.6×10^{14} eV, m/z (rel. int.): 243 $[M-H-OCH_3]^+$ (100); 2.6×10^{14} eV, 274 $[M-H]^-$ (30), 231 $[M-COOH]^-$ (75), 230 $[M-COOH]^-$ (100), 200 $[M-CH_3-COO]^-$ (50).

(4-Fluoro-phenyl)-(4-methyl-phenylamino)-acetic acid (**5a**), white solid; mp: 205–208 °C. ^{1}H NMR (300 MHz, d-Me_2CO) δ 2.13

(3H, s, CH_3), 5.09 (1H, s, α-CH), 6.58 (2H, d, J = 8.40 Hz, H-2′ and H-6′), 6.87 (2H, d, J = 8.09 Hz, H-3′ and H-5′), 7.11 (2H, dd, J = 8.71 Hz, H-3 and H-5), 7.59 (2H, dd, J_1 = 5.30 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (400 MHz, d-Me_2SO): δ 20.0 (s, CH_3), 59.2 (s, α-CH), 113.3 (s, C-2′, C-6′), 115.2 (d, J = 21.27 Hz, C-3, C-5), 125.1 (s, C-4′), 129.2 (s, C-3′, C-5′), 129.4 (d, J = 8.44 Hz, C-2, C-6), 134.9 (d, J = 2.93, C-1), 144.5 (s, C-1′), 161.6 (d, J = 243.20 Hz, C-4), 172.9 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −114.8 (s). Anal. Calcd for $C_{15}H_{14}O_2NF$: C, 69.50; H, 5.41; N, 5.41. Found: C, 69.63; H, 5.65; N, 5.53. MS TOF LDI, 3.8×10^{14} eV, m/z (rel. int.): 259 $[M]^+$ (55), 258 $[M-H]^+$ (100), 214 $[M-COOH]^+$ (100); 259 $[M]^-$ (35), 258 $[M-H]^-$ (95), 215 $[M-COO]^-$ (45), 214 $[M-COOH]^-$ (100), 200 $[M-CH_3-COO]^-$ (100).

(4-Fluoro-phenyl)-(4-fluoro-phenylamino)-acetic acid (**6a**), CAS 124573-82-6, white solid; mp: 184–187 °C (lit. 178–182 °C [7]). ^{1}H NMR (90 MHz, d-Me_2CO) δ 5.10 (1H, s, α-CH), 6.77 (4H, m, $W_{1/2}$ = 78 Hz, H-2, H-3′, H-5′, H-6), 7.20 (2H, s, H-3 and H-5), 7.52 (2H, d, J = 20 Hz, H-2′ and H-6′). ^{13}C NMR (400 MHz, d-Me_2SO) δ 59.3 (s, α-CH), 114.0 (d, J = 7.34 Hz, C-2′, C-6′), 115.2 (d, J = 22.01 Hz, C-3, C-5), 115.3 (d, J = 21.27 Hz, C-3′, C-5′), 129.4 (d, J = 8.43 Hz, C-2, C-6), 134.7 (d, J = 2.93, C-1), 143.5 (d, J = 1.47, C-1′), 154.7 (d, J = 232.15 Hz, C-4′), 161.7 (d, J = 243.56 Hz, C-4), 172.7 (s, COOH). ^{19}F NMR (90 MHz, d-Me_2SO) δ −115.0 (s, p-FPhCH), −128.9 (s, p-FPhNH). Anal. Calcd for $C_{14}H_{11}O_2NF_2$: C, 63.88; H, 4.18; N, 5.32. Found: C, 64.16; H, 4.39; N, 5.38. MS TOF LDI, 3.8×10^{14} eV, m/z (rel. int.): 263 $[M]^+$ (5), 244 $[M-F]^+$ (10), 243 $[M-F-H]^+$ (100), 219 $[M-COO]^+$ (90); 263 $[M]^-$ (50), 262 $[M-H]^-$ (100), 218 $[M-COOH]^-$ (90).

(4-Fluoro-phenyl)-(4-chloro-phenylamino)-acetic acid (**7a**), white solid; mp: 175–177 °C. ^{1}H NMR (300 MHz, d-Me_2CO) δ 5.13 (1H, s, α-CH), 6.66 (2H, d, J = 8.72 Hz, H-2′ and H-6′), 7.06 (2H, d, J = 8.71 Hz, H-3′ and H-5′), 7.19 (2H, dd, J = 8.72 Hz, H-3 and H-5), 7.53 (2H, dd, J_1 = 5.60 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 58.8 (s, α-CH), 114.5 (s, C-2′, C-6′), 115.3 (d, J = 21.27 Hz, C-3, C-5), 120.0 (s, C-4′), 128.4 (s, C-3′, C-5′), 129.5 (d, J = 8.07 Hz, C-2, C-6), 134.5 (d, J = 3.00, C-1), 145.8 (s, C-1′), 161.7 (d, J = 243.56 Hz, C-4), 172.6 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −115.0 (s). Anal. Calcd for $C_{14}H_{11}O_2NClF$: C, 60.11; H, 3.94; N, 5.01; Cl, 12.70. Found: C, 59.52; H, 4.01; N, 4.89; Cl, 13.67. MS TOF LDI, 3.3×10^{14} eV, m/z (rel. int.): 281 $[M^{37}Cl]^+$ (5), 279 $[M^{35}Cl]^+$ (15), 244 $[M-Cl]^+$ (60), 243 $[M-Cl-H]^+$ (100), 236 $[M-COOH]^+$ (20), 234 $[M-COOH]^+$ (50); 2.9×10^{14} eV, 281 $[M^{37}Cl]^-$ (20), 279 $[M^{35}Cl]^-$ (100).

(4-Fluoro-phenyl)-(4-bromo-phenylamino)-acetic acid (**8a**), white solid; mp: 147–151 °C. ^{1}H NMR (90 MHz, d-Me_2SO) δ 5.12 (1H, s, α-CH), 6.63 (2H, d, J = 33 Hz, H-2′, H-6′), 7.18 (4H, m, $W_{1/2}$ = 72 Hz, H-3, H-5, H-3′, H-5′), 7.54 (2H, dd, J_1 = 5.60 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 58.7 (s, α-CH), 107.4 (s, C-4′), 115.1 (s, C-2′, C-6′), 115.3 (d, J = 21.65 Hz, C-3, C-5), 129.5 (d, J = 8.07 Hz, C-2, C-6), 131.2 (s, C-3′, C-5′), 134.4 (d, J = 3.67, C-1), 146.2 (s, C-1′), 161.7 (d, J = 241.72 Hz, C-4), 172.5 (s, COOH). ^{19}F NMR (90 MHz, d-Me_2SO) δ −115.0 (s). Anal. Calcd for $C_{14}H_{11}O_2NBrF$: C, 51.85; H, 3.39; N, 4.32; Br 24.69. Found: C, 51.62; H, 3.57; N, 4.51; Br 25.21. MS TOF LDI, 2.1×10^{14} eV, m/z (rel. int.): 244 $[M-Br]^+$ (10), 243 $[M-Br-H]^+$ (100); 2.9×10^{14} eV, 325 $[M^{81}Br]^-$ (20), 324 $[M^{81}Br-H]^-$ (100), 323 $[M^{79}Br]^-$ (20), 322 $[M^{79}Br-H]^-$ (100), 280 $[M^{81}Br-COOH]^-$ (55), 278 $[M^{79}Br-COOH]^-$ (50), 244 $[M-Br]^-$ (45), 200 $[M-Br-COO]^-$ (40), 81 $[^{81}Br]^-$ (40), 79 $[^{79}Br]^-$ (40).

(4-Fluoro-phenyl)-(4-trifluoromethyl-phenylamino)-acetic acid (**9a**), white solid; mp: 137–139 °C. ^{1}H NMR (300 MHz, d-Me_2SO) δ 5.22 (1H, d, J = 6.85 Hz, α-CH), 6.77 (2H, d, J = 8.40 Hz, H-2′ and H-6′), 6.99 (1H, d, J = 7.16 Hz, NH), 7.20 (2H, dd, J = 8.72 Hz, H-3 and H-5), 7.35 (2H, d, J = 8.40 Hz, H-3′ and H-5′), 7.54 (2H, dd, J_1 = 5.50 Hz, J_2 = 8.70 Hz, H-2 and H-6). ^{13}C NMR (400 MHz, d-Me_2SO) δ 58.6 (s, α-CH), 112.5 (s, C-2′, C-6′), 115.3 (d, J = 21.61 Hz, C-3, C-5), 116.3 (q, J = 31.74 Hz, C-4′), 125.21 (q, J = 270.08 Hz, CF_3), 126.1 (s, C-3′, C-5′), 129.5 (d, J = 8.10 Hz, C-2, C-6), 134.4 (d, J = 2.70, C-1), 150.0 (s, C-1′), 161.7 (d, J = 243.75 Hz, C-4), 172.3 (s, COOH). ^{19}F NMR (90 MHz, d-Me_2SO) δ −114.9 (s, 1F), −59.4 (s, 3F, CF_3). Anal. Calcd for $C_{15}H_{11}NO_2F_4$: C, 57.51; H, 3.51; N, 4.47. Found: C, 57.42; H, 3.68; N, 4.59. MS TOF LDI, 3.3×10^{14} eV, m/z (rel. int.): 244 $[M-CF_3]^+$; 313 $[M]^-$ (80), 269 $[M-COO]^-$ (100).

(4-Fluoro-phenyl)-(4-ethoxycarbonyl-phenylamino)-acetic acid (**10a**), white solid; mp: 148–150 °C. ^{1}H NMR (300 MHz, d-Me_2SO) δ 1.30 (3H, t, CH_3), 4.24 (2H, q, J = 7.15 Hz, CH_2), 5.32 (1H, s, α-CH), 6.75 (2H, d, J = 9.03 Hz, H-2′ and H-6′), 7.15 (2H, dd, J = 8.72 Hz, H-3 and H-5), 7.63 (2H, dd, J_1 = 5.60 Hz, J_2 = 8.80 Hz, H-2 and H-6), 7.76 (2H, d, J = 9.03 Hz, H-3′ and H-5′). ^{13}C NMR (400 MHz, d-Me_2SO) δ 14.3 (s, CH_3), 58.4 (s, α-CH), 59.6 (s, CH_2), 112.1 (s, C-2′, C-6′), 115.3 (d, J = 21.64 Hz, C-3, C-5), 117.3 (s, C-4′), 129.5 (d, J = 8.07 Hz, C-2, C-6), 130.6 (s, C-3′, C-5′), 134.2 (s, C-1), 151.0 (s, C-1′), 161.7 (d, J = 243.92 Hz, C-4), 165.7 (s, COOEt), 172.2 (s, COOH). ^{19}F NMR (200 MHz, d-Me_2SO) δ −114.0 (s). Anal. Calcd for $C_{17}H_{16}NO_4F$: C, 64.35; H, 5.05; N, 4.42. Found: C, 64.44; H, 5.10; N, 4.54. MS TOF LDI, 2.9×10^{14} eV, m/z (rel. int.): 273 $[M-COO]^+$ (30), 244 $[M-COOEt]^+$ (45), 243 $[M-COOEt-H]^+$ (100); 317 $[M]^-$ (35), 273 $[M-COO]^-$ (100).

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References

[1] V.P. Kukhar', V.A. Soloshonok (Eds.), Fluorine-containing Amino Acids, John Wiley and Sons Ltd., Chichester, England, 1995, p. 422.
[2] B.E. Smart, J. Fluorine Chem. 109 (2001) 3–11.
[3] V. Molteni, J. Penzotti, D.M. Wilson, A.P. Termin, L. Mao, C.M. Crane, F. Hassman, T. Wang, H. Wong, K.J. Miller, S. Grossman, P.D.J. Grootenhuis, J. Med. Chem. 47 (2004) 2426–2429.
[4] Y.S. Park, P. Beak, J. Org. Chem. 62 (1997) 1574–1575.
[5] F.M.D. Ismail, J. Fluorine Chem. 118 (2002) 27–33.
[6] S. Bajaj, S.S. Sambi, A.K. Madan, Acta Chim. Slov. 52 (2005) 292–296.
[7] Ch. Csongar, I. Muller, H. Slezak, H.-J. Klebsch, G. Tomaschewski, J. Prakt. Chem. 330 (1988) 1006–1014.
[8] J. Chaussard, J.-C. Folest, J.-Y. Nedelec, J. Perichon, S. Sibille, M. Troupel, Synthesis (1990) 369–381.
[9] G. Silvestri, S. Gambino, G. Filardo, Acta Chem. Scand. 45 (1991) 987–992.
[10] A.P. Tomilov, Russ. J. Electrochem. 36 (1994) 167–172 (Russ. Ver.).
[11] V.G. Koshechko, V.D. Pokhodenko, Teor. Exp. Khim. 33 (1997) 268–283.
[12] C.M. Sanchez-Sanchez, V. Montiel, D.A. Tryk, A. Aldaz, A. Fujishima, Pure Appl. Chem. 73 (2001) 1917–1927.
[13] U. Hess, R. Thiele, J. Prakt. Chem. 324 (1982) 385–399.
[14] G. Silvestri, S. Gambino, G. Filardo, Gazz. Chim. Ital. 118 (1988) 643–648.
[15] C. Saboureau, M. Troupel, S. Sibille, J. Perichon, J. Chem. Soc., Chem. Commun. 16 (1989) 1138–1139.
[16] M. Kyotani, C. Yamaguchi, A. Goto, K. Sasaki, H. Matsui, Y. Koga, S. Fujiwara, Carbon 40 (2002) 1583–1590.
[17] M. Rudolf, J. Electroanal. Chem. 529 (2002) 97–108.
[18] M. Rudolf, J. Electroanal. Chem. 543 (2003) 23–39.
[19] M. Rudolf, J. Electroanal. Chem. 571 (2004) 289–307.
[20] O. Scialdone, A. Galia, A.A. Isse, A. Gennaro, M.A. Sabatino, R. Leone, G. Filardo, J. Electroanal. Chem. 609 (2007) 8–16.
[21] V.D. Pokhodenko, A.A. Beloded, V.G. Koshechko, Redox-reactions of Free Radicals, Naukova Dumka, Kiev, 1977, p. 277.
[22] C.P. Andrieux, I. Gallardo, J.-M. Saveant, J. Am. Chem. Soc 111 (1989) 1620–1626.
[23] V.E. Titov, A.M. Mishura, V.G. Koshechko, Teor. Exp. Khim. 42 (2006) 217–221.
[24] S. Rondinini, A. Vertova, Electrochim. Acta 49 (2004) 4035–4046.
[25] D.R. Burfield, R.H. Smithers, J. Org. Chem. 43 (1978) 3966–3968.
[26] V.L. Minkin, V.A. Bren, Org. Reactiv. (USSR) 4 (1967) 112–123 (Russ. Ver.).
[27] M.F. Mayer, M.M. Hossain, J. Org. Chem. 63 (1998) 6839–6844.
[28] P. Bravo, S. Capelli, M. Crucianelli, M. Guidetti, A.L. Markovsky, S.V. Meille, V.A. Soloshonok, A.E. Sorochinsky, F. Viani, M. Zandaet, Tetrahedron 55 (1999) 3025–3040.
[29] J. Toullec, S. Bennour, J. Org. Chem. 59 (1994) 2831–2839.
[30] S.K. Dayal, S. Ehrenson, R.W. Taft, J. Am. Chem. Soc. 94 (1972) 9113–9122.