ANODIC OXIDATION OF PHENOXYACETIC AND {2-[(PHENYLIMINO)METHYL]PHENOXY}ACETIC ACIDS

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Acizii fenoxiacetic şi {2-[(fenilimino)metil]fenoxi}acetic au fost supuşi oxidării anodice pe anozi de patină şi grafit, la diferite densităţi de curent, în metanol, etilenglicol, dietilenglicol şi dimetilformamidă. Produşii obţinuţi au fost analizaţi prin ^{1}H-NMR, GC-MS. Electrosintezele realizate urmează mecanismele clasice de oxidare anodică, formîndu-se polieteri, ca metoximetoxibenzenul sau 1,2-difenoxietanul, cu selectivităţi ridicate.

Phenoxyacetic and {2-[(phenylimino)methyl]phenoxy} acetic acid were subjected to anodic oxidation on platinum and graphite electrodes, at different current densities, in methanol, ethylene glycol, diethylene glycol and N,N-dimethylformamide. The obtained products were analyzed by ^{1}H-NMR, GC-MS. The performed electrosyntheses follow the classical mechanisms for anodic oxidation processes; polyethers, like methoxymethoxybenzene and 1,2-diphenylethane were formed with high selectivity.

Keywords: phenoxyacetic acid, {2-[(phenylimino)methyl]phenoxy} acetic acid, anodic oxidation, methanol, ethylene glycol, diethylene glycol, N,N-dimethylformamide.

1. Introduction

Anodic oxidation is a useful tool in organic synthesis discovered for over 150 years ago by Kolbe. According to the recognized mechanisms, anodic oxidation of carboxylic acids can be classified in: one-electron oxidation (Kolbe oxidation or Kolbe dimerization) and two-electron oxidation (non-Kolbe oxidation) [1]. Anodic oxidation is involved in industrial processes for synthesizing a lot of organic substances with good yield and selectivity. For example, a Kolbe dimer, the dimethyl sebacate is obtained for commercial purposes by anodic oxidation of monomethyl adipate with 92% selectivity [2].

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It has been shown that by choosing the right parameters for the factors which influences the process, anodic oxidation can be directed towards obtaining a certain product [6]. These factors are the structure of the raw material (electronic and steric effects) and conditions related to the nature of the electrode, current density, solvent, pH, additives, temperature, and pressure [1].

A great number of anodic oxidations of carboxylic acids in specific conditions for one- and two-electron oxidations are described in the literature [1-5]. Our research group studied the anodic oxidations of 3-phenylpropionic [6], benzoic, phthalic [7], N-acetyl-ε-amino-capronic [8], citric, benzylic [9], malic [10] and glutaric [11] acids and established mechanisms for their oxidations [12]. This paper focuses on the anodic oxidations of phenoxyacetic acid (**1**) and {2-[(phenylimino)methyl]phenoxy}acetic acid (**3**) in order to find an easier way to obtain polyethers, like methoxymethoxybenzene (**5**) which is difficult to be obtained by usual chemical synthesis [13, 14]. Consequently, we studied an electrochemical pathway to synthesize this compound.

2. Experimental part

Reagents

Phenol, chloroacetic acid, sodium hydroxide, methanol (M), ethylene glycol (EG), diethylene glycol (DEG), N,N-dimethylformamide (DMF), salicylaldehyde and aniline were from Merck and used as received. A sodium methoxide solution in methanol (0.32 M) was obtained by dissolving sodium in methanol and fractional distillation as previously described [6].

Phenoxyacetic acid (**1**) was synthesized from a method adapted from [15] for obtaining *o*-formylphenoxyacetic acid (**2)**. A solution of 8 g NaOH (0.2 moles) in 20 mL distilled water was added to a mixture of 9.4 g (0.1 moles) phenol and 9.45 g (0.1 moles) chloroacetic acid in 80 mL water. The resulting solution was heated under reflux (4h); acidified to pH=3 with concentrated hydrochloric acid and filtered. The precipitated product was recrystallized from water resulting a white solid; m.p. = 99 ^{0}C; yield=78%. ^{1}H-NMR (δ, ppm, TMS): 4.67 (2H, s, methylene protons); 6.93 (2H, d, ortho protons); 7.01 (1H, t, para proton); 7.3 (2H, t, meta protons).

o-Formylphenoxyacetic acid (**2**) was prepared according to [15]. A mixture of 10.6 mL (0,1 moles) salicylaldehyde, 9.45 g (0.1moles) chloroacetic acid and a solution of 8 g (0.2 moles) NaOH in 100 mL water was heated under reflux (4h) ; the resulting mixture was acidified to pH=3 with concentrated hydrochloric acid; the solution was steam-distilled to remove unreacted salicylaldehyde; then was cooled to 20 ^{0}C; the precipitated product was recrystallized from water. A solid was obtained (m.p.= 131 ^{0}C; 77 %).

{2-[(Phenylimino)methyl]phenoxy}acetic acid (**3**) was obtained according to the general procedure for Schiff bases [16]. A mixture of 2.7 g (0.015 moles) of **2** and 1.5 g (0.016 moles) of aniline dissolved in ethanol was stirred (30 min) and then filtered on a Buchner funnel. The precipitate was washed with ethanol and dried. Yield=78%. ^{1}H-NMR (δ, ppm, TMS) data are shown in Fig.1.

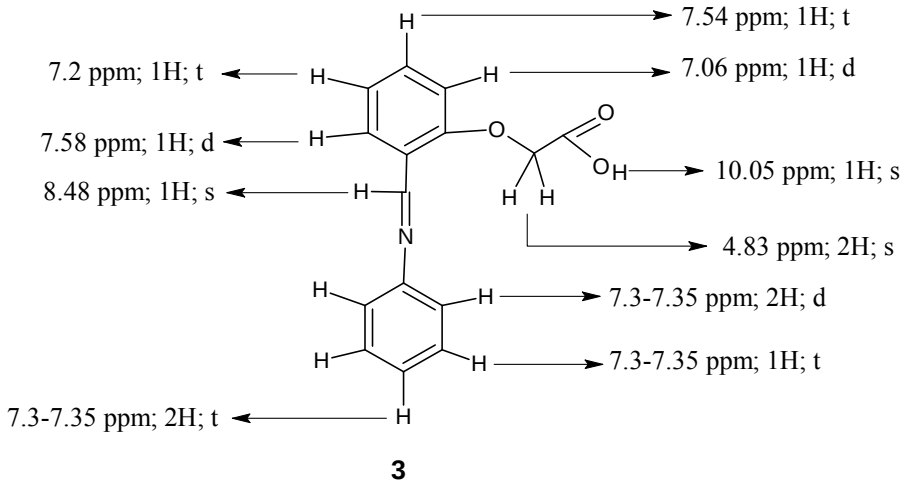

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Fig.1. Assignment of ^{1}H-RMN signals for {2-[(phenylimino)methyl]phenoxy} acetic acid

Anodic oxidations have been performed in electrolyte solutions obtained by dissolution of organic acids in ~10 mL solvent and partial neutralisation (10 %) with CH_3ONa solution (0.32 M) in CH_3OH.

Procedure

Anodic oxidations were performed in an undivided cell on graphite (2 cm^2) and platinum electrode sheets (5 cm^2) under galvanostatic conditions. The amount of electricity used was bigger than the theoretical quantity. In electrolyses whre methanol was used as a solvent the obtained mixture was evaporated and water was added. When EG and DEG were used as solvents a solution of 20 % NaOH was added. The organic compounds were then extracted with ethyl ether; the ether layer was dried ($MgSO_4$) and evaporated. When DMF was used as solvent the products were isolated by adding water and filtration.

The concentrates were analyzed by ^{1}H-NMR (300 MHz Varian spectrometer; $CDCl_3$, DMSO-d^6), and GC-MS (Varian 3400 Saturn 2 System gas chromatograph-mass spectrometer on a 25 m capillary glass column DBS; T_{inj} = 250 ^{0}C; 80 - 250 ^{0}C with 10 ^{0}C/min).

3. Results and discussions

The anodic oxidation of **1** and **3** has been performed in conditions favoring either one- or two-electron oxidation, respectively on platinum at high current densities (cd), and on graphite at low current densities, in four solvents (Table 1).

Table 1

Electrochemical parameters in the performed electrolyses of phenoxyacetic (1) and {2-[(phenylimino)methyl]phenoxy}acetic (3) acids

Entry	Acid/ concentration (M)	Anode	Solvent	Curent density $A*cm^{-2}$	$(Q_p/Q_t)^*$	Results	
						GC-MS	^{1}H-NMR
1.	**1**/ 0.65	Platinum	Methanol (M)	0.1	3	~50% **4**	**4** is the main product (97,5%) **5** is the by-product
2.	**1** /0.65	Graphite	Methanol (M)	0.015	3	~80% **5**	**5** is the main product (70%) **4** is the by-product
3.	**1** /0.34	Graphite	Ethylene glycol (EG)	0.015	2	-	**6** is formed
4.	**1** /0.23	Graphite	Diethylene glycol (DEG)	0.002	2	-	**7** is formed
5.	**3** /0.15	Graphite	N,N-dimethylformamide (DMF)	0.025	3	-	**8** is the main product

Q_t = theoretical amount of electricity for one-electron oxidation; Q_t = practical amount of electricity.

Anodic oxidations has been done on platinum anode at high cd (Entry 1, Table 1) in order to obtain Kolbe products and on graphite anode at low cd (Entries 2-5, Table 1) for non-Kolbe products. Different solvents were used M, EG, DEG and DMF.

The ^{1}H-NMR and GC-MS spectra of the mixture resulted from anodic oxidation in conditions favoring Kolbe oxidation (Entry 1, Table 1) contain signals mainly for 1,2-diphenoxyethane (**4**):

^{1}H-NMR (δ, ppm, TMS): 4.33 (4H, s, methylene protons); 6.93 (4H, d, ortho protons); 7.06 (2H, t, para protons); 7.26 (4H, t, meta protons);

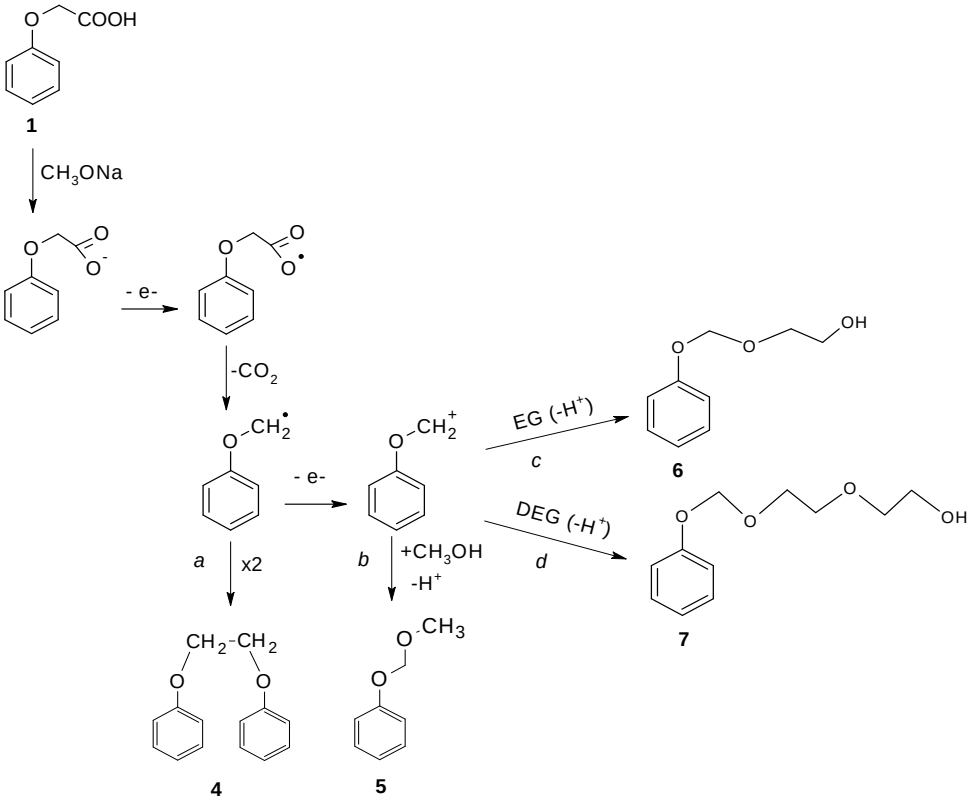
GC-MS (70eV, m/z): 213 (48%), (M-1); 121 (48%), (Ph-O-CH_2-CH_2**.**$^+$); 93 (45%), (Ph-OH**.**$^+$); 77 (100%), (Ph**.**$^+$).

The ^{1}H-NMR and GC-MS spectra of the mixture resulted from anodic oxidation in conditions favoring the non-Kolbe oxidation (Entry 2, Table 1) contain signals mainly for methoxymethoxybenzene (**5**):

^{1}H-NMR (δ, ppm, TMS): 3.48 (3H, s, methyl protons); 5.17 (2H, s, methylene protons); 7.02 (2H, d, ortho protons); 7.05 (1H, t, para proton); 7.26 (2H, t, meta protons);

GC-MS (70eV, m/z): 137 (19%), (M-1); 108 (13,2%), (Ph-O-CH_2**.**$^+$); 94 (6,6%), (Ph-OH**.**$^+$); 77 (26,5%), (Ph**.**$^+$)

The results from Entry 1 and 2 could be explained using the mechanism depicted in Scheme 1 in which the one- and two-electron oxidation pathways *a* and *b* respectively are followed leading to either **4** or **5** products.



Scheme 1

The results in Table 1 show a high selectivity in obtaining the eters **4** or **5** (Entries 1 and 2). They have been calculated from ^{1}H-NMR spectra (using the

ratio between the methylene protons in **4** and **5**). This behavior is due to conjugation of in the intermediate carbocation with the neighbor oxygen atom which provides stability for the resulting species.

The mixtures obtained from anodic oxidation of phenoxyacetic acid in conditions favoring the non-Kolbe oxidation in EG and DEG (Entries 3 and 4, Table 1) were characterized by ^{1}H-RMN. The results show the formation of 2-(phenoxymethoxy)ethanol and 2-[2-(phenoxymethoxy)ethoxy] ethanol respectively. Their signals assignments are presented in Fig. 2.

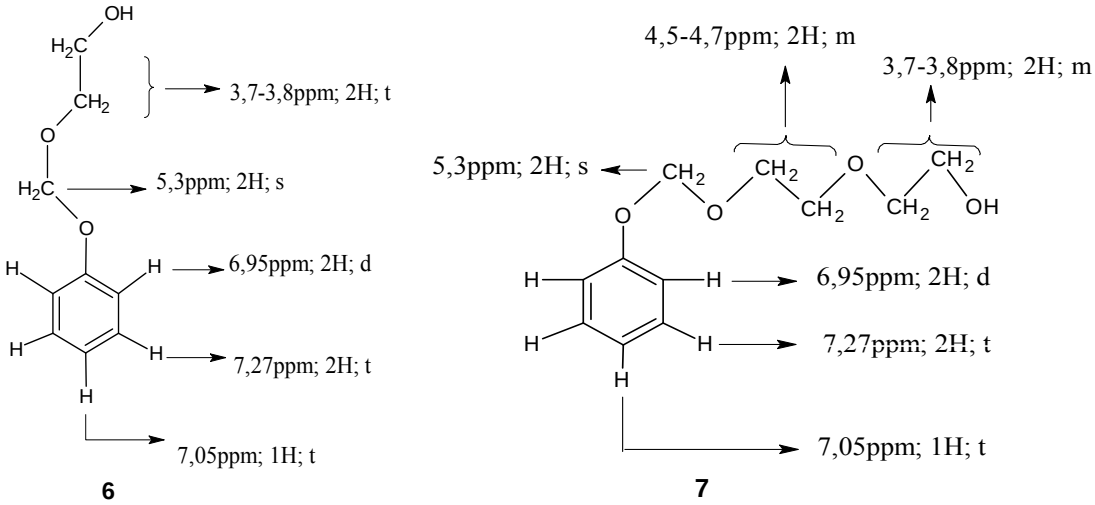


Fig.2. Assignments of ^{1}H-RMN signals for 2-(phenoxymethoxy)ethanol **6** and 2-[2-(phenoxymethoxy)ethoxy] ethanol **7**

These results for Entries 3 and 4 could be rationalized using the mechanism described in Scheme 1, pathways *c* and *d*. The solvent plays an essential role in obtaining a certain structure for the final product of anodic oxidation. On graphite anode the main product is always the ether (Entries 2-4, Table 1), which gives to this method a preparative value. The examples given in Table 1 show that this method can be extended to the preparation of different ethers by changing the alcohol.

The mixture obtained from anodic oxidation on graphite anode in DMF (Entry 5, Table 1) of {2-[(phenylimino)methyl]phenoxy}acetic acid (**3**) was characterized by ^{1}H-RMN spectroscopy (in DMSO-d^6). The results show the formation of 6*H*-dibenzo[*b*,*f*][1,5]oxazocine (**8**), Fig. 3.

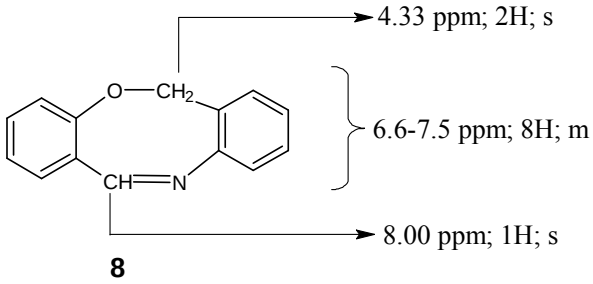
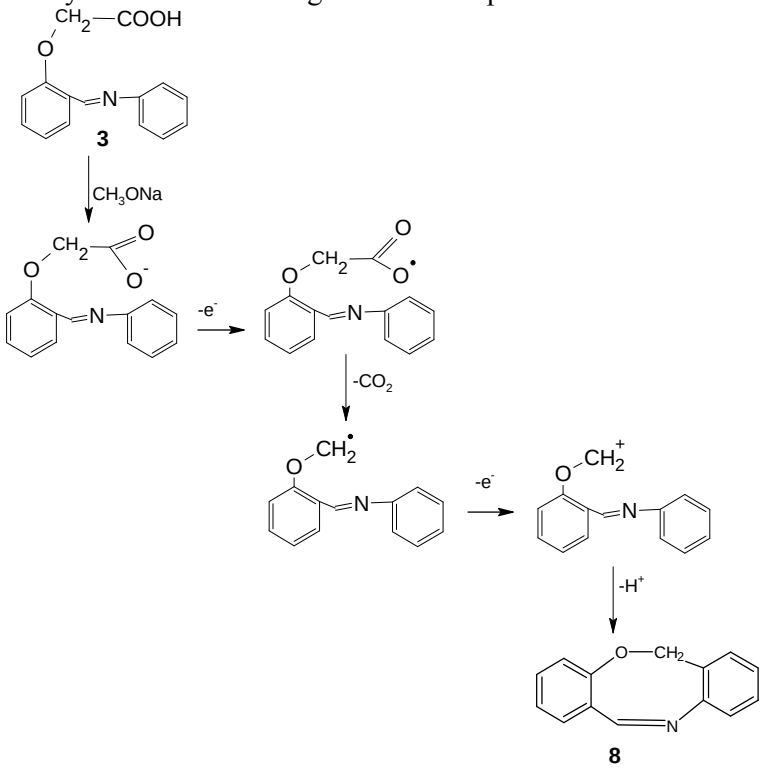


Fig.3. Assignment of ^{1}H-RMN signals for 6*H*-dibenzo[*b*,*f*][1,5]oxazocine

Based on these results we proposed the mechanism decribed in Scheme 2 in which the carbocation formation is as a consequence of two-electron anodic oxidation. The carbocation stabilization could occur by reaction with a nucleophile such as nitrogen atom, double bond, aromatic cycle (if the geometry allows) or solvent (DMF). In our case the 6*H*-dibenzo[*b*,*f*][1,5]oxazocine formation is a cycle closing by the nucleophilic attack of the formed carbocation to the aromatic cycle and not to nitrogen atom as expected.



Scheme 2

4. Conclusions

The phenoxyacetic acid was electrochemically oxidized in conditions favoring either one or two-electron oxidation. The anodic oxidation processes follow the classical mechanisms of anodic oxidation and therefore radicals and carbocations intermediates are formed.

In the case of the anodic oxidation of phenoxyacetic acid in methanol on platinum anode we obtained 1,2-diphenoxyethane (the Kolbe product) as main product with a high selectivity, while on graphite anode the anodic oxidation lead to the non-Kolbe product with a very high selectivity due to the stabilization of the intermediate carbocation by conjugation with the neighbor oxygen atom.

Two-electron anodic oxidation of **3** determined the aromatic cycle closure by the nucleophilic attack of the formed carbocation to the aromatic cycle and not to nitrogen atom as expected.

The solvent plays an essential role in obtaining a certain structure for the final product of anodic oxidation. On graphite anode the main product is always the ether which gives to this method a preparative value. The method can be extended to the preparation of different ethers by changing the alcohol.

R E F E R E N C E S

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