Electrosynthesis of 4-iodopyrazole and its derivatives

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Electrosynthesis of 4-iodo-substituted pyrazoles has been accomplished by iodination of the corresponding precursors on a Pt-anode in aqueous solutions of KI under conditions of the diaphragm galvanostatic electrolysis. Efficiency of the process depends on the donor-acceptor properties of substituents and their positions in the pyrazole ring. Thus, iodination of pyrazole, 3,5-dimethylpyrazole, 3-nitropyrazole, 1-methylpyrazole, 1,3-dimethylpyrazole, pyrazole-3(5)-carboxylic acid or methyl esters furnished 4-iodo derivatives in 57, 86, 2, 5, 35, 30, and 40% yields, respectively.

Key words: electrosynthesis, pyrazoles, iodination.

It is known that 4-iodopyrazoles are important intermediate products in the synthesis of biologically active compounds possessing antiviral, antitumor, and antibacterial activity,[1—4] they are used for obtaining purine and nucleoside derivatives[5] and as reagents in organic synthesis (cross-coupling reactions with terminal acetylenes,[6] reactions with organotin aryl derivatives,[7] or alkylboronic acids[8]). This is the reason for the interest to search new efficient methods for the synthesis of 4-iodo derivatives of pyrazole. In the present work, we for the first time study their preparation by electrochemical method.

To solve the problem, we proceeded from the data on electrosynthesis of 4-chloro- and 4-bromo-substituted pyrazoles,[9—11] as well as from the results reported on chemical iodination of pyrazole[12] and its derivatives.[13,14]

Iodination of pyrazoles was studied under conditions of galvanostatic diaphragm electrolysis of aqueous solutions of KI or methanol solutions of NaI.

Results and Discussion

There are literature data on electroiodination (EI) of terminal acetylenes[15] under conditions of the diaphragm electrolysis of solutions of NaI in MeOH, which leads to the corresponding 1-iodoacetylenes in high (70—90%) yields. On the authors' opinion,[15] the process proceeds through the intermediate formation of highly reactive cation I^+, present apparently in the solution as a complex with involvement of MeOH. Therefore, we started attemption of EI of pyrazoles exactly under these conditions using unsubstituted pyrazole. Due to the consumption of NaI during the EI reaction, supporting electrolyte $NaClO_4$ ($C = 0.3$ mol L^{-1}) was used to maintain electroconductivity of the anolyte.

The yield of the target product under these conditions (see Table 1, entry *1*) turned out to be not high enough (39%), and in this case the reaction mixture contained, together with 4-iodopyrazole, considerable amount of iodine (the current efficiency was 29%). Variations in the electrolysis conditions (current density, the ratio pyrazole/NaI in the reaction mixture) did not led to the increase in the yield of 4-iodopyrazole (see Table 1, entries *1—3*), amount of iodine virtually did not decrease either. Apparently, the rate of EI of pyrazole in methanol solutions has proved low. Intensification of the process by the removal of HI formed in the course of the reaction due to the addition of a base (NaOAc) failed. The yield of 4-iodopyrazole was even lower by 6% (see Table 1, entries *6* and *9*). This fact, as well as a decrease in the amount of iodine in the reaction mixture (the current efficiency decreased by 17%), indicate a noticeable contribution of a side process, *viz.*, the reaction of I_2 with MeOH with oxidation or iodination of the latter.

Further, we studied EI of pyrazoles in aqueous solutions, where the side processes indicated previously are not possible. However, iodine generated on the anode was poorly soluble in water and mainly precipitated. This was the reason that we started to carry out the EI in the two-phase system (aqueous KI—$CHCl_3$), using $NaNO_3$ as a supporting electrolyte. The yield of 4-iodopyrazole under indicated conditions (see Table 1, entry *5*) was low (28%), and the final reaction solution contained a large amount of iodine (the current efficiency was 47%). The formal process of EI of pyrazole, proceeding through the intermediate formation of *N*-iodo derivative,[16] is given in Scheme 1.

When effects of various factors on the efficiency of EI was studied, it was found that an increase in the amount

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Table 1. Effect of experimental conditions on the yield of 4-iodopyrazole (IP) upon anode iodination of pyrazole[a] (P)

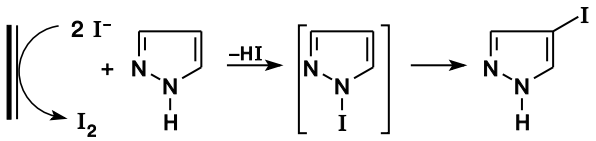
Entry	Medium[b]	Amount of metal iodide (M^+I^-)/mol	P : M^+I^-	T/°C	i_a/mA cm^{-2}	Product yields[c] (%)	
						IP on substance	iodine on the current
1	*A*	0.01	1 : 1	30	7.5	39	28
2	*A*	0.01	1 : 1	30	15.0	38	32
3	*A*	0.03	1 : 3	30	7.5	35	24
4	*A*	0.01	1 : 1	30	7.5	33	11
5	*B*	0.01	1 : 1	30	7.5	28	47
6	*B*	0.02	1 : 2	30	7.5	29	48
7	*B*	0.01	1 : 1	30	15.0	30	47
8	*B*	0.01	1 : 1	30	22.5	25	45
9	*B*	0.01	1 : 1	50	7.5	36	27
10	*B*	0.01	1 : 1	30	7.5	57	13
11	*B*	0.01	1 : 1	30	15.0	60	21
12	*B*	0.01	1 : 1	50	7.5	66	29
13	*B*	0.02	1 : 2	30	7.5	52	26
14	*B*	0.02	1 : 1	30	7.5	46	26

[a] Pt-anode, Cu-cathode, supporting electrolyte (C = 0.3 mol L^{-1}), $Q = Q_{calc} = 2\ F \cdot$ (mol P)$^{-1}$. In entries *1—13* amount of pyrazole was 0.01 mol, in entry *14*, 0.02 mol.

[b] *A*: MeOH as the solvent, NaI as the source of iodine, $NaClO_4$ as the supporting electrolyte, in entry *4* NaOAc (0.015 mol) was added as a base; *B*: the two-phase system H_2O—$CHCl_3$ (7 : 3), KI as the source of iodine, $NaNO_3$ as the supporting electrolyte, in entries *10—14* $NaHCO_3$ (0.015 mol) was added as a base.

[c] The yield of IP was calculated from the data on analysis of isolated mixture of the electrolysis products by ^{1}H NMR. The yield of iodine was determined by titration of a sample of the reaction mixture with 0.1 *N* aq. $Na_2S_2O_3$.

Scheme 1

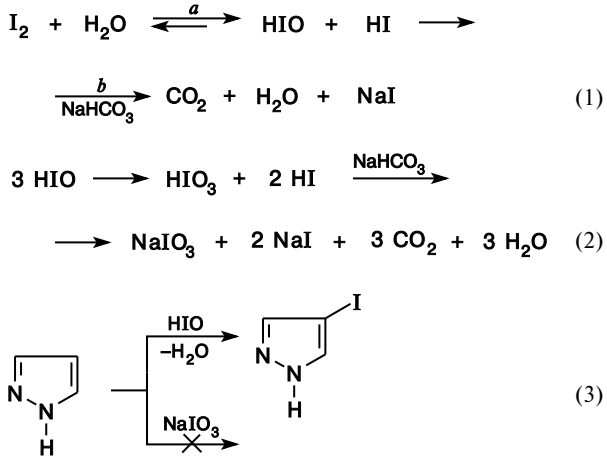


of KI from 0.01 to 0.02 moles (see Table 1, entries *5* and *6*) leads only to an insignificant (by ~2%) increase in the yield of the target product. The dependence of the yield of 4-iodopyrazole from the change of the current density passes the maximum (see Table 1, entries *5*, *7*, and *8*), reaching 30% at j = 15 mA cm^{-2}. An increase in the temperature of electrolysis from 30 to 50 °C caused a somewhat (to 36%) increase in the yield of 4-iodopyrazole and a considerable decrease in the content of iodine in the reaction mixture (the current efficiency of iodine decreased from 47 to 27%, see Table 1, entries *5* and *9*).

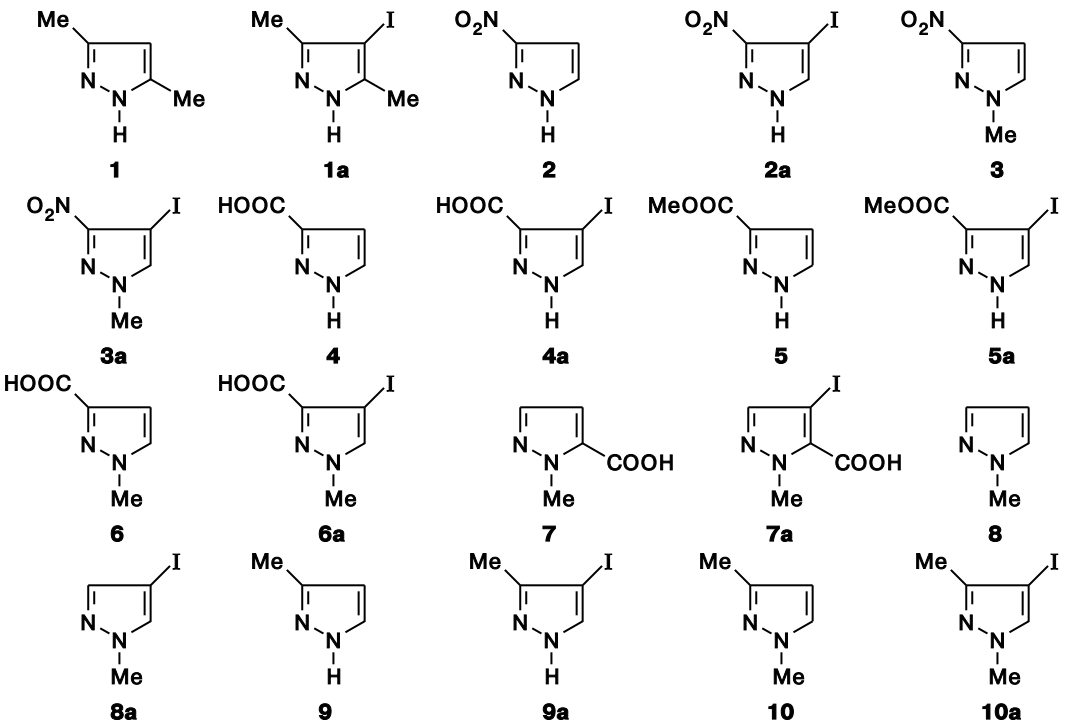
When the temperature has been increased, the rate of iodination was apparently increased, however, since the boiling point of the aseotrope $CHCl_3/H_2O$ is[17] 56 °C, further increase in the temperature under these conditions is impossible.

To optimize the EI process, we carried out the electrolysis in the presence of a base ($NaHCO_3$) combining with HI (Scheme 2). Under these conditions, the yield of 4-iodopyrazole rises more than two-fold (see Table 1, entries *5* and *10*). An increase in the amount of KI from 0.01 to 0.02 moles (see Table 1, entries *10* and *13*) results in the decrease (by ~5%) in the yield of the target product. An increase in the current density (from 7.5 to 15 mA cm^{-2}, see Table 1, entries *10* and *11*) is accompanied by only small (by ~2%) increase in the yield of the target product.

Scheme 2



An increase in the temperature of electrolysis from 30 to 50 °C, though led to the increase in the yield of 4-iodopyrazole (by ~8%, see Table 1, entries *10* and *12*), however, the content of the "active" iodine (electro-



generated free iodine and products of its reaction with water, *i.e.*, HIO and $NaIO_3$) considerably increased (see Scheme 2) (an increase in the current efficiency by ~16%) in the reaction mixture.

According to Scheme 2 (see reaction (1)), an equilibrium *a* exists in the solution of electrolyte, which in the presence of $NaHCO_3$ is significantly shifted to the right due to the rapid ionic reaction in step *b*. In this case, an efficient removal of HI takes place, whereas HIO (a weak acid) is formed and accumulated in the solution. At elevated temperatures, HIO has a tendency to disproportionation[18] (see Scheme 2, Eq. (2)), leading to the strong acids HIO_3 and HI, which in the presence of $NaHCO_3$ form $NaIO_3$ and NaI, respectively. Unlike HIO capable to iodinate pyrazole, $NaIO_3$ does not react with it under these conditions (alkaline solution) (see Scheme 2, reaction (3)). This is the reason that elevated temperature, though assists in the increase in the yield of 4-iodopyrazole, but efficiency of the use of KI in the electrosynthesis is decreased, and some iodine generated by anode oxidation of KI is not used in the synthesis of the target product.

Summarizing this part of the study, it should be noted that EI of pyrazole under optimum conditions (electrolysis in the heterophase system aqueous KI—$CHCl_3$ (7 : 3), Pt-anode, amounts of pyrazole and KI of 0.01 mol, j_a = 7.5—15 mA cm^{-2}, T = 30 °C) allows us to obtain 4-iodopyrazole in 57—60% yield calculated on the starting pyrazole.

The works[9–11] on electrochemical chlorination and bromination of pyrazoles reported that efficiency of halogenation strongly depends on the nature of substituent in the pyrazole ring. This prompted us to study EI of pyrazoles with electron-donating and electron-withdrawing substituents.

Table 2. Effect of experimental conditions on the yield of 4-iodo-substituted pyrazoles upon anode iodination of pyrazoles in the heterophase system aq. KI—$CHCl_3$[a]

Entry	Pyrazole	Iodination product	Product yields[b] (%)	
			of iodination on substance	of "active" iodine on the current
1	**1**	**1a**	86	14
2	**2**	**2a**	2	95
3	**3**	**3a**	0	98
4	**4**	**4a**	30	51
5	**5**	**5a**	40	55
6	**6**	**6a**	0	91
7	**7**	**7a**	0	96
8	**8**	**8a**	5	90
9	**9**	**9a**	71	27
10	**10**	**10a**	35	64

[a] Pt-anode, Cu-cathode, amount of pyrazoles and KI was 0.01 mole, $NaNO_3$ (0.3 *M*) was a supporting electrolyte, amount of $NaHCO_3$ was 0.015 mole, $Q = Q_{calc} = 2\,F$ (mole of the starting pyrazole)$^{-1}$, j_a = 7.5 mA cm^{-2}.

[b] The yield of IP was calculated from the ^{1}H NMR data of isolated mixture of the electrolysis products, the yield of "active" iodine (a mixture of I_2 and HIO) was determined by iodometric analysis.

Comparison of the results obtained on the EI of pyrazole and 3,5-dimethylpyrazole **1** (*cf.* Table 1, entry *10* and Table 2, entry *1*) showed that the presence of two methyl groups at carbon atoms in the pyrazole ring leads to a considerable increase in the yield of 4-iodo derivative **1a** (from 57 to 86%, calculated on the amount of pyrazole used).

3-Nitropyrazole (**2**) was the following object for our study. No data on its chemical iodination have been found in the literature, therefore, initially we studied this process.

It turned out that chemical iodination of compound **2** takes place only under drastic conditions (AcOH as a solvent with additives of H_2O and CCl_4; a mixture of I_2, KIO_3, and H_2SO_4 as a iodination agent; the reaction temperature of 80—85 °C; the reaction time 21 h). As a result, 4-iodo-3-nitropyrazole (**2a**) was obtained in 86% yield (calculated on the amount of pyrazole **2** used).

Further, we found that the presence of an NO_2 group in the pyrazole ring sharply decreases efficiency of EI. For instance, upon EI of pyrazole **2** under the same conditions as in the EI of pyrazole (see above), the yield of its iodo derivative **2a** was only 2% calculated on the starting pyrazole **2** (see Table 2, entry *2*). EI of pyrazoles with other less electron-withdrawing groups (COOH, COOMe) showed that under the optimum conditions electrolysis of pyrazol-3(5)-carboxylic acid (**4**) leads to 4-iodopyrazol-3(5)-carboxylic acid (**4a**) in relatively low (~30% calculated on the amount of the acid used) yield (see Table 2, entry *4*). In this case, the yield of "active" iodine (I_2, HIO) has proved high enough (~50% on the current). We suggest that this effect is due to the relatively low rate of chemical reaction of the electrogenerated iodine with acid **4**. On replacement of the COOH group with less electron-withdrawing COOMe group going from pyrazole **4** to methyl pyrazol-3(5)-carboxylate (**5**), it was found that upon the EI of the latter, the yield of iodination product (methyl 4-iodopyrazol-3(5)-carboxylate (**5a**)) increased more than 1.3-fold (see Table 2, entries *4* and *5*).

Earlier,[10,11] during study of electrohalogenation (chlorination, bromiination) processes, it was found that replacement of H atom on the nitrogen atom of the pyrazole ring with the electron-donating Me group facilitates the process indicated. Therefore, it could have been expected that upon EI of 1-methyl-3-nitropyrazole (**3**) the yield of the target product would be higher than upon EI of pyrazole **2**. However, we obtained an unexpected result: under the same experimental conditions, which were used in the EI of unsubstituted pyrazole (see above), pyrazole **3** was not subjected to EI (see Table 2, entry *3*). Note that on the replacement of H atom on the nitrogen atom in 3(5)-pyrazolecarboxylic acid with the Me group (going from acid **4** to 1-methylpyrazol-3-carboxylic (**6**) and 1-methylpyrazol-5-carboxylic (**7**) acids), the EI of such pyrazoles does not occur (see Table 2, entries *6* and *7*).

We carried out additional experiments on the influence of the Me substituent in the pyrazole ring on the efficiency of EI. Pyrazoles containing Me groups on both the nitrogen atom (1-methylpyrazole (**8**), 1,3-dimethylpyrazole (**10**)) and carbon atom of the pyrazol ring (3(5)-methylpyrazole (**9**)) were chosen as the starting compounds. It turned out that exchange of the H atom on the nitrogen atom in unsubstituted pyrazole for the Me group leads to a sharp (more than ten-fold) decrease in the yield of the iodinated product (4-iodo-1-methylpyrazole (**8a**)) (*cf.* Table 1, entry *10* and Table 2, entry *8*). The content of electrogenerated "active" iodine in the reaction mixture also sharply increased. And vice versa, replacement of the H atom with the Me group on the carbon atom in unsubstituted pyrazole led to the expected result: an increase in the yield of the target product (4-iodo-3(5)-methylpyrazole **9a**) (*cf.* Table 1, entry *10* and Table 2, entry *9*). This indicates a strong decrease in the rate of iodination going from unsubstituted pyrazole to 1-methylpyrazole.

An exchange of the H atom for the Me group on the carbon atom in 1-methylpyrazole (pyrazole **10**) leads to a certain decrease in the "wrong" influence of the Me substituent on the nitrogen atom and, consequently, to the increase in the yield of 4-iodo derivative from 5 to 35% (see Table 2, entries *8* and *10*).

The data on nontypical (as compared to chlorination and bromiination) effect of the Me group in the reaction of EI mentioned above are of special interest. To explain such facts, we have thoroughly analyzed available literature information on chemical iodination of pyrazoles.

In the work,[19] it was found that the rate of iodination of unsubstituted pyrazole is inversely proportional to the concentration of H_3O^+. This was an evidence that not pyrazole itself undergoes iodination, but its anion. Pyrazole anion is much more reactive (the ratio of the iodination rate constants of the ionized and unionized forms of pyrazole[20] is equal to $3 \cdot 10^9$).

Since 1-methylpyrazole cannot give anion, only its unionized form undergoes iodination. This leads to a strong decrease in the reaction rate. By analysis of the data[19,20] on kinetics of iodination, we found that going from pyrazole to 1-methylpyrazole the reaction rate decreases ~300-fold. Note that replacement of the H atom with the Me group on the carbon atom in the pyrazole ring increases the rate of iodination (going from pyrazole to 3(5)-methylpyrazole, the iodination rate increases[20] 150-fold).

In connection with the aforementioned facts, it becomes clear why the yields of 4-iodopyrazoles decrease on the exchange of the H atom for the Me group at the nitrogen atom and the yield of the target product increases going from 1-methylpyrazole to 1,3-dimethylpyrazole.

In conclusion, the presence of electron-donating substituents at the carbon atom of the pyrazole ring facilitates

EI, whereas the presence of electron-withdrawing substituents makes the process more difficult. In addition, position of substituents in the ring play a significant role. The presence of alkyl substituents at the nitrogen atom of the pyrazole ring retards the EI process.

Experimental

Experiments were carried out in the galvanostatic regime, using a source of direct current B-5-8 and a glass cell with a diaphragm made of porous glass with Pt-anode ($S = 30$ cm^2) and Cu-cathode thermostated by a U-1 thermostat. A coulometer constructed in the SCB of IOCh of the RAS was included into the electric chain. A magnetic stirrer was used to stir solutions during electrolysis.

Pyrazole, 3,5-dimethylpyrazole (**1**), and 3(5)-methylpyrazole (**9**) (Acros) were used as purchased. 1,3-Dimethylpyrazole (**10**)[21], 3-nitropyrazole (**2**)[22], 1-methyl-3-nitropyrazole (**3**)[14], pyrazol-3(5)-carboxylic (**4**), 1-methylpyrazol-3-carboxylic (**6**), and 1-methylpyrazol-5-carboxylic acids (**7**)[23], as well as methyl pyrazol-3(5)-carboxylate (**5**),[24] were synthesized according to the procedures described earlier.

Compounds obtained upon EI of pyrazoles were identified by ^{1}H NMR spectroscopy using comparison with the spectra of standard samples described in the literature (4-iodopyrazole,[25] 4-iodo-3,5-dimethylpyrazole (**1a**),[26] 4-iodo-1-methyl-3-nitropyrazole (**3a**),[14] methyl 4-iodopyrazol-3(5)-carboxylate (**5a**),[27] 4-iodo-3(5)-methylpyrazole (**9a**),[25] 4-iodo-1-methylpyrazole (**8a**), and 4-iodo-1,3-dimethylpyrazole (**10a**)[28]), 4-iodopyrazol-3(5)-carboxylic acid (**4a**) obtained according to the known procedure,[22] and 4-iodo-3-nitropyrazole (**2a**) alternatively synthesized by us (see below).

^{1}H NMR spectra were recorded on a Bruker AC-300 spectrometer, using DMSO-d_6 as a solvent.

Electrochemical iodination of pyrazole in aqueous KI (using entry *10* as an example, see Table 1). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole (0.68 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. A solution of $NaNO_3$ (0.3 *M*, 150 mL) was placed into the cathode compartment. Electrolysis was carried out using current of 225 mA at 30 °C. After passing 2 *F* of electricity per 1 mol of the starting compound ($Q = 1930$ C), the electrolysis was stopped, the reaction mixture was stirred for 1.5 h. The aqueous and organic fractions were separated using a separatory funnel. An aliquot of the solution was taken from each fraction, and the content of "active" iodine (I_2 and HIO) was determined by titration with $Na_2S_2O_3$.[29] Using the analysis results, the total (both fractions) yield of the "active" iodine was determined (13%). Then the aqueous and organic fractions were mixed, acidified with concentrated HCl (2 mL), followed by addition of Na_2SO_3 with stirring (to combine with iodine) until the solution became colorless. Then, the reaction mixture was neutralized by addition of Na_2CO_3 (to pH 7—8), the aqueous and organic fractions were separated using a separatory funnel. Then, solid NaCl was added to the aqueous solution (for the salting off the products from the aq. solution), and the products were additionally extracted with $CHCl_3$ (2×30 mL). The organic solutions were combined and dried with $CaCl_2$. The solvent was evaporated to obtain 4-iodopyrazole (1.11 g, 57%) identified by the m.p. 108 °C (*cf.* Ref. 12: m.p. 108.5 °C) and characteristics of the ^{1}H NMR spectrum.

Electrochemical iodination of pyrazole in methanol solution of NaI (using entry *2* as an example, see Table 1). A methanol solution (100 mL) containing NaI (1.5 g, 0.01 mol), $NaClO_4$ (3.67 g, 0.03 mol), and pyrazole (0.68 g, 0.01 mol) was placed into the anode compartment of a cell, a solution of $NaClO_4$ in methanol (0.3 *M*, 150 mL) was placed into the cathode compartment. Electrolysis was carried out with current of 445 mA, the rest of conditions were analogous to those given above. The content of iodine in the reaction mixture was determined (see above), and these data were used to find its current efficiency (32%). Then, MeOH was evaporated from the reaction mixture under reduced pressure, followed by addition of water (20 mL), conc. HCl (1 mL), and Na_2SO_3 (to combine with iodine, see above) to the residue formed. The mixture obtained was neutralized with Na_2CO_3 (to pH 7—8), and organic products were extracted with $CHCl_3$ (3×30 mL). After drying (see above) the organic extract and evaporation of the solvent, 4-iodopyrazole was obtained (0.74 g, 38%), which was identified by the m.p. 108 °C and characteristics of the ^{1}H NMR spectrum.

Electrochemical iodination of 3,5-dimethylpyrazole (1) (using entry *1* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole **1** (0.96 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine, and isolation of the products were carried out as described above. The yield of "active" iodine on the current was 14%. The yield of 4-iodo-3,5-dimethylpyrazole (**1a**) was 1.91 g (86%), it was identified by the m.p. 137 °C (*cf.* Ref. 13: m.p. 137—138 °C) and characteristics of the ^{1}H NMR spectrum.

Chemical iodination of 3-nitropyrazole (2). Iodine (6.12 g, 0.024 mol), KIO_3 (2.56 g, 0.012 mol), H_2O (9 mL), conc. H_2SO_4 (2.2 mL), and CCl_4 (4.8 mL) were added to a solution of pyrazole **2** (6.78 g, 0.06 mol) in AcOH (40 mL). The reaction mixture was heated to 80—85 °C and stirred at this temperature for 21 h. After the reaction mixture was cooled, CCl_4 was evaporated under reduced pressure. Then, the mixture was poured on ice, discolored (from unreacted I_2) by addition of Na_2SO_3, and the mineral acid was neutralized with Na_2CO_3. A precipitate formed was filtered off, washed with water, and dried at 100 °C to obtain 4-iodo-3-nitropyrazole (**2a**) (12.32 g, 86%), m.p. 227—228 °C. ^{1}H NMR, δ: 8.05 (s, 1 H, H(5)). Found (%): C, 15.16; H, 0.86; I, 53.07; N, 17.45. $C_3H_2IN_3O_2$. Calculated (%): C, 15.06; H, 0.84, I, 53.14; N, 17.57.

Electrochemical iodination of 3-nitropyrazole (2) (using entry *2* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), compound **2** (1.13 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis and analysis of the reaction mixture for the "active" iodine were carried out as described above. The yield of "active" iodine on the current was 95%. The reaction mixture after electrolysis was acidified with conc. HCl (2 mL), treated with Na_2SO_3 (see above), then neutralized with Na_2CO_3 (to pH 7—8), and the aqueous and organic fractions were separated. Products were isolated from the organic fraction as described above to obtain yellowish powder (0.32 g), which (^{1}H NMR spectroscopic data) was a mixture of **2a—2**. The molar ratio of these compounds in the reaction mixture (1 : 11.25) was

determined using the integral intensities of the signals for compounds **2a** with δ 8.05 (s, 1 H, H(5)) and **2** with δ 7.80 (s, 1 H, H(5)). The solvent from aqueous fraction was evaporated under reduced pressure. The residue obtained was treated with Me_2CO (4×25 mL), then the solvent was evaporated, the residue was washed with water (1×7.5 mL) and dried at 100 °C to obtain yellow powder (0.36 g), which was (^{1}H NMR spectroscopic data) the starting pyrazole **2**. The yield of product **2a** was 2%.

Electrochemical iodination of 1-methyl-3-nitropyrazole (3) (using entry *3* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole **3** (1.27 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine, and isolation of products were carried out as described in the preceding experiment. The yield of "active" iodine on the current was 98%. The products of electrolysis contained (^{1}H NMR spectroscopic data) only the starting pyrazole **3** (no formation of 4-iodo-1-methyl-3-nitropyrazole (**3a**) was detected).

Electrochemical iodination of pyrazol-3(5)-carboxylic acid (4) (using entry *4* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), acid **4** (1.12 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis and analysis of the reaction mixture for the "active" iodine was carried out as described above. The yield of "active" iodine on the current was 51%. The reaction mixture was separated for aqueous and organic fractions. The aqueous* fraction was acidified with conc. HCl (2 mL) and treated with Na_2SO_3 (see above).

A precipitate formed was filtered off, washed with water (2×5 mL), and dried at 100 °C to obtain 4-iodopyrazol-3(5)-carboxylic acid (**4a**) (0.53 g, 22%), which was identified by the m.p. 240 °C (*cf.* Ref. 22: m.p. 240—241 °C) and characteristics of the ^{1}H NMR spectrum. Water was evaporated under reduced pressure from the mother liquor formed after isolation of the major product. The residue obtained was treated with Me_2CO (2×25 mL) and EtOH (2×25 mL), the solvents were evaporated, the residue was washed with water (2×4 mL) and dried at 100 °C to obtain a powder (0.2 g), which was (^{1}H NMR spectroscopic data) a mixture of compounds **4a**—**4**. The molar ratio of these compounds in the reaction mixture (27.5 : 1) was determined from the integral intensities of the signals for compounds **4a** with δ 7.88 (s, 1 H, H(3(5))) and **4** with δ 6.70 (s, 1 H, H(4)). The total yield of product **4a** was 30%.

Electrochemical iodination of methyl pyrazol-3(5)-carboxylate (5) (using entry *5* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), compound **5** (1.26 g, 0.01 mol) and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis and analysis of the reaction mixture for the "active" iodine was carried out as described above. The yield of "active" iodine on the current was 55%. After performing electrolysis, the reaction mixture was acidified with conc. HCl, treated with Na_2SO_3 (see above), then the aqueous and organic fractions were separated. The products were additionally extracted from the aqueous fraction with $CHCl_3$ (2×30 mL). The organic solutions were combined and dried with Na_2SO_4. The solvent was evaporated to obtain white powder (1.37 g), which was (^{1}H NMR spectroscopic data) a mixture of compound **5** and methyl 4-iodopyrazol-3(5)-carboxylate (**5a**). The molar ratio of these compounds (1.32 : 1) in the reaction mixture was determined from the integral intensities of the signals of compounds **5a** with δ 7.95 (s, 1 H, H(3(5))) and **5** with δ 6.75 (s, 1 H, H(4)). The aqueous fraction was concentrated under reduced pressure to 10 mL and the products were extracted with $CHCl_3$ (2×15 mL). The organic extracts were combined and dried with Na_2SO_4. The solvent was evaporated to obtain white powder (0.1 g), which was (^{1}H NMR spectroscopic data) a mixture of **5a**—**5**. The molar ratio of these compounds was 0.07 : 1. The total yield of product **5a** (40%) was determined from the ^{1}H NMR spectroscopic data of the products isolated.

Electrochemical iodination of 1-methylpyrazol-3-carboxylic acid (6) (using entry *6* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), acid **6** (1.26 g, 0.01 mol) and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine and isolation of products were carried out similarly to those described above for compound **4**. The yield of "active" iodine on the current was 91%. The products isolated contained (^{1}H NMR spectroscopic data) only the starting acid **6** (no formation of 4-iodo-1-methylpyrazol-3-carboxylic acid (**6a**) was observed).

Electrochemical iodination of 1-methylpyrazol-5-carboxylic acid (7) (using entry *7* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), acid **7** (1.26 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine and isolation of the products were carried out as described in the preceding example. The yield of "active" iodine on the current was 96%. The products isolated contained (^{1}H NMR spectroscopic data) only the starting acid **7**.

Electrochemical iodination of 1-methylpyrazole (8) (using entry *8* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole **8** (0.82 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine and isolation of products were carried out similarly to those described above for compound **1**. The yield of "active" iodine on the current was 90%. After isolation of the products, an oil was obtained (0.78 g), which (^{1}H NMR spectroscopic data) was a mixture of 4-iodo-1-methylpyrazole (**8a**), pyrazole **8**, and $CHCl_3$. The molar ratio of these compounds (1 : 12.67 : 4) was determined from the integral intensities of the signals for compounds **8a** with δ 7.72 (s, 1 H, H(5)), **8** with δ 6.20 (s, 1 H, H(4)), and $CHCl_3$ with δ 8.30 (s, 1 H). The yield of product **8a** was 5%.

Electrochemical iodination of 3(5)-methylpyrazole (9) (using entry *9* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole **9** (0.82 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine and isolation of products were carried out as described in

* Organic fraction contained no acids **4** and **4a**.

the preceding example. Compound **9a** was obtained (1.48 g, 71%), which was identified by the m.p. 110—111 °C (*cf.* Ref. 12: m.p. 110.5 °C) and characteristics of the ^{1}H NMR spectrum.

Electrochemical iodination of 1,3-dimethylpyrazole (10) (using entry *10* as an example, see Table 2). An aqueous solution (70 mL) containing $NaNO_3$ (1.79 g, 0.021 mol), KI (1.66 g, 0.01 mol), $NaHCO_3$ (1.26 g, 0.015 mol), pyrazole **10** (0.96 g, 0.01 mol), and $CHCl_3$ (30 mL) was placed into the anode compartment of a cell. Electrolysis, analysis of the reaction mixture for the "active" iodine and isolation of products were carried out as described in the preceding example. The yield of "active" iodine on the current was 64%. After isolation of the products, an oil was obtained (1.47 g), which (^{1}H NMR spectroscopic data) was a mixture of 4-iodo-1,3-dimethylpyrazole (**10a**), pyrazole **10**, and $CHCl_3$. The molar ratio of these compounds (2.08 : 3.02 : 1) was determined from the integral intensities of the signals for compounds **10a** with δ 7.75 (s, 1 H, H(5)), **10** with δ 6.95 (s, 1 H, H(4)), and $CHCl_3$ with δ 8.30 (s, 1 H). The yield of product **10a** was 35%.

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