ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 7, pp. 1053–1059. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © R.I. Khusnutdinov, A.R. Baiguzina, R.R. Mukminov, I.V. Akhmetov, I.M. Gubaidullin, S.I. Spivak, U.M. Dzhemilev, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 7, pp. 1054–1060.

New Synthesis of Pyrrole-2-carboxylic and Pyrrole-2,5-dicarboxylic Acid Esters in the Presence of Iron-Containing Catalysts

R. I. Khusnutdinov, A. R. Baiguzina, R. R. Mukminov, I. V. Akhmetov, I. M. Gubaidullin, S. I. Spivak, and U. M. Dzhemilev

Institute of Petroleum Chemistry and Catalysis, Russian Academy of Sciences, pr. Oktyabrya 141, Ufa, 450075 Bashkortostan, Russia
e-mail: ink@anrb.ru

Received July 13, 2009

Abstract—Alkyl 1*H*-pyrrole-2-carboxylates and dialkyl 1*H*-pyrrole-2,5-dicarboxylates were synthesized in quantitative yield by reactions of 1*H*-pyrrole, 2-acetyl-1*H*-pyrrole, and 1-methyl-1*H*-pyrrole with carbon tetrachloride and aliphatic alcohols in the presence of iron-containing catalysts. A probable reaction mechanism was proposed, and the rate constants and energies of activation of particular steps were determined on the basis of experimental data.

DOI: 10.1134/S1070428010070158

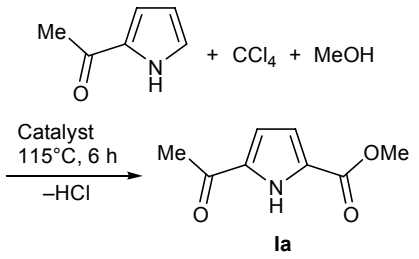
Pyrrolecarboxylic acids attract strong interest as starting compounds for the synthesis of porphyrins and biologically active substances [1, 2]. For instance, pyrrole-2-carboxylic acid derivatives exhibit antiviral activity, in particular against classical bird influenza viruses [3], whereas 5-arylpyrrole-2-carboxylic acid sodium salts were found to possess anticonvulsant activity [4].

A specific feature of pyrrolecarboxylic acids is that the carboxy group therein, regardless of its position, can readily be replaced by other functional groups. Replacement of carboxy group by the action of electrophilic reagents occurs more readily than replacement of hydrogen [5, 6]. For example, nitration of pyrrolecarboxylic acids with nitric acid in acetic anhydride gives mixtures of nitropyrrolecarboxylic acids and 2-nitropyrrole. The carboxy group in pyrrole-2-carboxylic acid is replaced most smoothly by halogen atoms.

Published data on the synthesis of pyrrolecarboxylic acids, in particular of an important representative of this series of compounds, 5-acetyl-1*H*-pyrrole-2-carboxylic acid, are very few in number. Difficulties in the synthesis of this acid are related to the effect of a strong electron-withdrawing substituent (COOH, $COOCH_3$, $COCH_3$) in position *2* of the pyrrole ring, which changes the regioselectivity intrinsic to pyrrole in electrophilic substitution reactions; as a result, a new substituent enters position *4* rather than free position *5* [6, 7]. Only in the reaction with *tert*-butyl hypochlorite, the desired 5-chloro-1*H*-pyrrole-2-carboxylic acid was obtained; this reaction is a very rare example of radical replacement in the pyrrole ring [8].

The goal of the present work was to develop a general procedure for the introduction of a carboxy group into compounds of the pyrrole series via reaction with the system CCl_4–MeOH–catalyst. We showed previously [9] that such reaction is successful with thiophene and its derivatives [9]. As model substrate we used 2-acetyl-1*H*-pyrrole. We found that the reaction of 2-acetyl-1*H*-pyrrole with carbon tetrachloride and methanol in the presence of a catalyst is regioselective and that the only product is methyl 5-acetyl-1*H*-pyrrole-2-carboxylic acid (**Ia**). As catalysts we used Ni, Cu, Mn, Pd, V, and Fe compounds and complexes which are known to activate C–Cl bond in CCl_4 molecule [9, 10]. The highest catalytic activity was observed for the following iron compounds: $Fe(OAc)_2$, $Fe(C_5H_5)_2$, $FeBr_2$, and $Fe(acac)_3$. The optimal conditions were temperature 115°C and reaction time 6 h; in this case the conversion of initial 2-acetyl-1*H*-pyrrole was complete, and the yield of ester **Ia** reached 98% (Scheme 1).

Scheme 1.



Catalyst	Yield of **Ia**, %
$Fe(C_5H_5)_2$	98
$Fe(acac)_3$	95
$Fe(OAc)_2$	90
$FeBr_2$	87

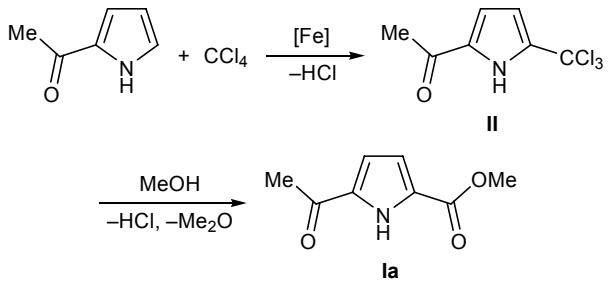
The classical procedure for the preparation of compound **Ia** by acylation of methyl 1*H*-pyrrole-2-carboxylate with acetic anhydride is not selective: as a result, a mixture of ester **Ia** and isomeric methyl 4-acetyl-1*H*-pyrrole-2-carboxylate is formed. Furthermore, the latter is obtained as the major product (yield 73%) in the presence of $AlCl_3$ as catalyst, while the yield of **Ia** does not exceed 8% [11]. The reaction in the presence of $HClO_4$ gives an equimolar mixture of ester **Ia** and methyl 4-acetyl-1*H*-pyrrole-2-carboxylate [12]. Ethyl 5-acetyl-1*H*-pyrrole-2-carboxylate was synthesized in 37% yield by reaction of ethyl 1*H*-pyrrole-2-carboxylate with acetyl chloride in the presence of $ZnCl_2$ [13].

The structure of compound **Ia** was determined by ^1H and ^{13}C NMR spectroscopy, including two-dimensional correlation techniques (HSQC, HMBC). Signals from directly coupled protons and carbon atoms in the acetyl and methoxycarbonyl groups, as well as from the endocyclic CH groups (δ_C 116.04, δ 6.84 ppm; δ_C 115.58, δ 6.89 ppm), were unambiguously assigned on the basis of ^1H–^{13}C heteronuclear correlation experiments (HSQC). The substitution pattern in the pyrrole ring was reliably determined by analysis of the HMBC heteronuclear correlation spectra. The most informative was the signal from protons in the acetyl group at δ 2.48 ppm which displayed geminal coupling with the carbonyl carbon atom (C^8) and vicinal coupling with the C^5 atom in the pyrrole ring. The C^5 nucleus (δ_C 134.20 ppm) showed in turn a cross peak with 4-H (δ 6.84 ppm). A considerably weaker correlation between 4-H and C^2 (δ_C 126.93 ppm) corresponds to long-range vicinal heteronuclear interaction, which confirms the position of the CO_2CH_3 and $COCH_3$ groups at C^2 and C^5 of the pyrrole ring.

Special experiments showed that the examined reaction can be performed successfully with other tetrahalomethanes such as CBr_4 and $BrCCl_3$ and that chloroform, bromoform, and methylene chloride failed to react. The reactions with CBr_4 and $BrCCl_3$ require lower temperature (105°C) and are complete in 3 h.

The following reaction mechanism seems to be the most probable. Taking into account aromaticity of 2-acetyl-1*H*-pyrrole and the presence of a Lewis acid ($FeBr_2$), the formation of compound **Ia** via alkylation with carbon tetrachloride, followed by methanolysis of trichloromethyl derivative **II**, is possible (Scheme 2). Although our attempts to detect intermediate compound **II** in the reaction mixture were unsuccessful, its participation provides the best rationalization for the formation of methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (**Ia**). The proposed mechanism is detailed in Scheme 3.

Scheme 2.

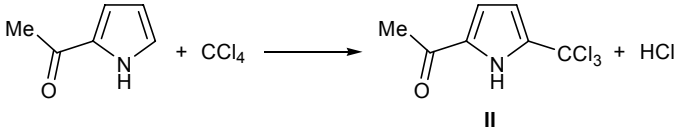


We also derived a kinetic model for the formation of methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (**Ia**). The kinetic model includes mathematical description as nonlinear differential equations for concentrations of compounds involved in the process. The laboratory reactor was simulated by the ideal mixing model [14], for which the material balance equations are given by the system

$$\frac{\partial x_i}{\partial t} = \frac{F_i - x_i F_N}{N}; \quad F_i = \sum_{j=1}^{m} \nu_{ij} w_j \qquad (1)$$

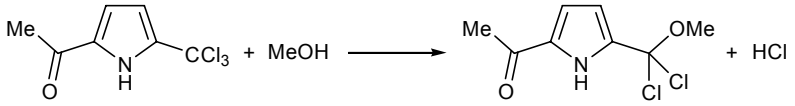
with the following entry conditions: at $t = 0$: $x_i = x_i^o$, $N = 1$; here, $N = c/c_0$ is the relative change in the number of moles in the reaction mixture; c and c_0 are the molar density and its initial value; x_i are the concentrations of the components (mole fractions); $i = 1$ (2-acetyl-1*H*-pyrrole), $i = 2$ (CCl_4), $i = 3$ (2-acetyl-5-trichloromethyl-1*H*-pyrrole), $i = 4$ (HCl), $i = 5$ (MeOH), $i = 6$ [2-acetyl-5-dichloro(methoxy)methyl-1*H*-pyrrole], $i = 7$ [2-acetyl-5-chloro(dimethoxy)methyl-1*H*-pyrrole], $i = 8$ (2-acetyl-5-trimethoxymethyl-

Scheme 3.

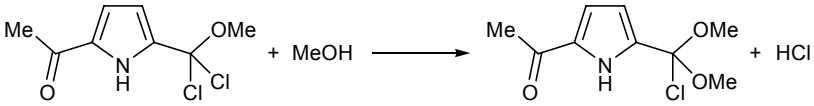


II

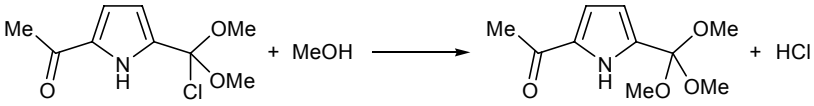
E_1 = 96.7 kJ/mol; k_1 = 0.044 (105°C), 0.052 (110°C), 0.1 h^{-1} (115°C).



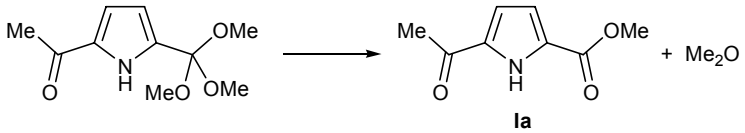
E_2 = 7.96 kJ/mol; k_2 = 0.015 (105°C), 0.016 (110°C), 0.017 h^{-1} (115°C).



E_3 = 7.58 kJ/mol; k_3 = 0.013 (105°C), 0.014 (110°C), 0.015 h^{-1} (115°C).



E_4 = 7.75 kJ/mol; k_4 = 0.0013 (105°C), 0.0014 (110°C), 0.0015 h^{-1} (115°C).



Ia

E_5 = 7.67 kJ/mol; k_5 = 1.756 (105°C), 1.812 (110°C), 1.87 h^{-1} (115°C).

1*H*-pyrrole), i = 9 [methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (**Ia**)], i = 10 (dimethyl ether).

The right parts of system (1) look as follows:

$$F_1 = -w_1;\ F_2 = -w_1;\ F_3 = w_1 - w_2;\ F_4 = w_1 + w_2 + w_3 + w_4;$$
$$F_5 = w_2 - w_3 - w_4\ ;\ F_6 = w_2 - w_3;\ F_7 = w_3 - w_4;\ F_8 = w_4 - w_5;$$
$$F_9 = w_5;\ F_{10} = w_5;\ F_{11} = F_N = w_5.$$

The developed model appropriately describes the experimental findings: deviations between the calculated and experimental variations in the reactant concentrations do not exceed 7%. In this work we used an informational analytical system of inverse problems of chemical kinetics [15]. With the aid of mathematical model (1) we solved the reverse kinetic problem and determined the kinetic parameters (rate constants and energies of activation of particular steps). There is no universal method for the solution of inverse problem [16]. In any way, it is solved by searching over a series of primal problems according to a specified program to minimize the deviation between the calculated and experimental data. The kinetic constants were estimated by random search followed by parabolic descend at a selected direction with an accuracy of 10^{-3} [17]. As a result, we found several sets of constants which equally conformed to the experimental data. To remove ambiguity in the determination of the rate constants, experimental data obtained at different temperatures were treated. Correction of the rate constants at different temperatures with the aid of the Arrhenius equation allowed us to define a single set of constants describing the entire experimental temperature range. The constants k_i (h^{-1}) are some reduced quantities with a dimension of reciprocal time, which are related to the true constants K_i (l mol^{-1} h^{-1}) by the equations $k_i = K_i c_0$ (i = 1–4), $k_5 = K_5$. In keeping with the proposed kinetic model, the rate-determining step is alkylation of 2-acetyl-1*H*-pyrrole with carbon tetrachloride.

Figures 1 and 2 compare the experimental (dark circles, squares, and triangles) and calculated data (continuous lines) on variation of the component concentrations x_1 and x_9 during the process. Excellent

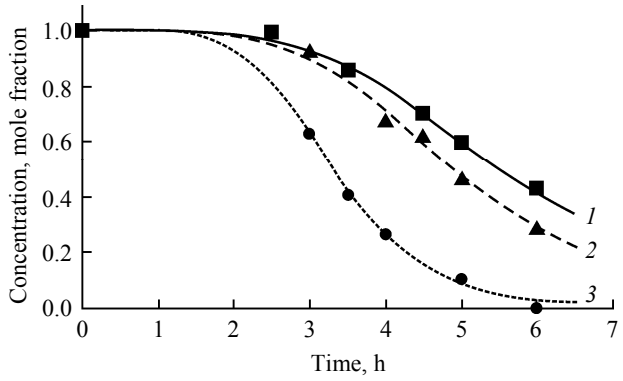


Fig. 1. Calculated and experimental data for the consumption of 2-acetyl-1*H*-pyrrole at (*1*) 105, (*2*) 110, and (*3*) 115°C.

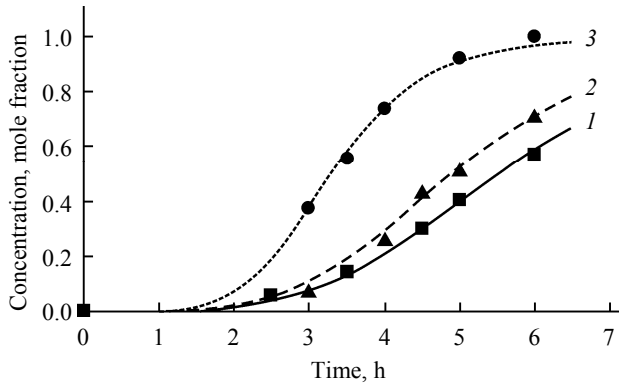


Fig. 2. Calculated and experimental data for the formation of methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (**Ia**) at (*1*) 105, (*2*) 110, and (*3*) 115°C.

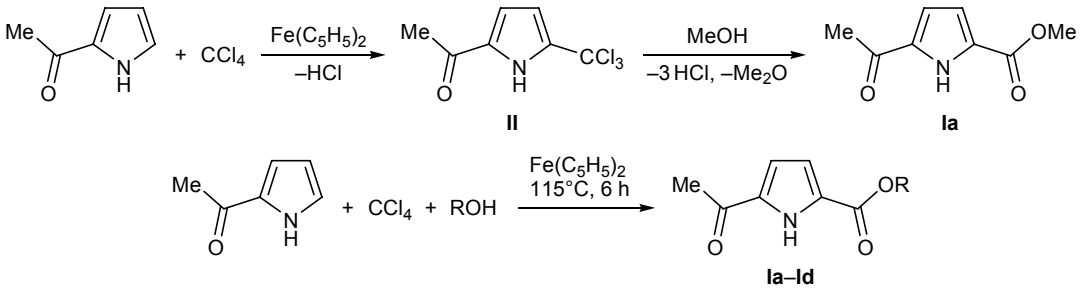
agreement is observed between the calculated and experimental data at any temperature: 105, 110, and 115°C. The energies of activation of the elementary steps decrease in the following order: $E_1 = 96.7 > E_2 = 7.96 > E_4 = 7.75 > E_5 = 7.67 > E_3 = 7.58$ kJ/mol. The energy of activation of the first elementary step exceeds those of the other steps by more than order of magnitude. Presumably, this is the reason why no intermediate products [in particular, 2-acetyl-5-trichloromethyl-1*H*-pyrrole (**II**)] were detected in the reaction mixture at any moment of time. On the other hand, the formation of 2-acetyl-5-trichloromethyl-1*H*-pyrrole (**II**) as intermediate is indirectly supported by the fact that replacement of methanol by ethyl, propyl, and isopropyl alcohols resulted in the formation of ethyl, propyl, and isopropyl 5-acetyl-1*H*-pyrrole-2-carboxylates **Ib**–**Id**, respectively, in fairly good yields (Scheme 4). In addition, hydrogen chloride and dimethyl ether were detected in the reaction mixture.

According to the experimental data, the optimal reactant ratio iron-containing catalyst–2-acetyl-1*H*-pyrrole–CCl_4–ROH is 1 : 100 : 750 : 6500. We made an attempt to involve unsubstituted pyrrole and *N*-methylpyrrole in analogous reaction with CCl_4 and CH_3OH under the optimal conditions. Freshly distilled pyrrole reacted quite readily to produce dimethyl 1*H*-pyrrole-2,5-dicarboxylate (**IIIa**) in quantitative yield (Scheme 5). The reaction with pyrrole may be catalyzed by the following iron compounds: $Fe(acac)_3$, $Fe(OAc)_2$, and $FeBr_2$. Ferrocene showed no catalytic activity.

Analogous reaction with *N*-methylpyrrole gave rise to a mixture of methyl 1-methyl-1*H*-pyrrole-2-carboxylate (**IVa**) and dimethyl 1-methyl-1*H*-pyrrole-2,5-dicarboxylate (**IVb**). In this case, the effect of the catalyst nature was especially strong. The reaction in the presence of $FeBr_2$ afforded dimethyl 1-methyl-1*H*-pyrrole-2,5-dicarboxylate (**IVb**) with high selectivity, whereas methyl 1-methyl-1*H*-pyrrole-2-carboxylate (**IVa**) was formed as the major product in the reaction catalyzed by ferrocene (Scheme 6). When the reaction was carried out at lower temperature (~85–105°C), a more complex mixture was obtained due to formation of condensation products at the free 5-position of the pyrrole ring [18].

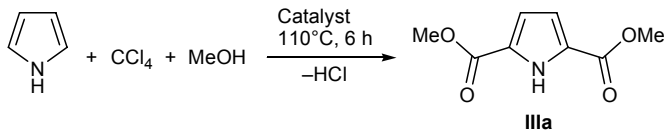
To conclude, we have developed a general procedure for the introduction of a carboxy group into the

Scheme 4.



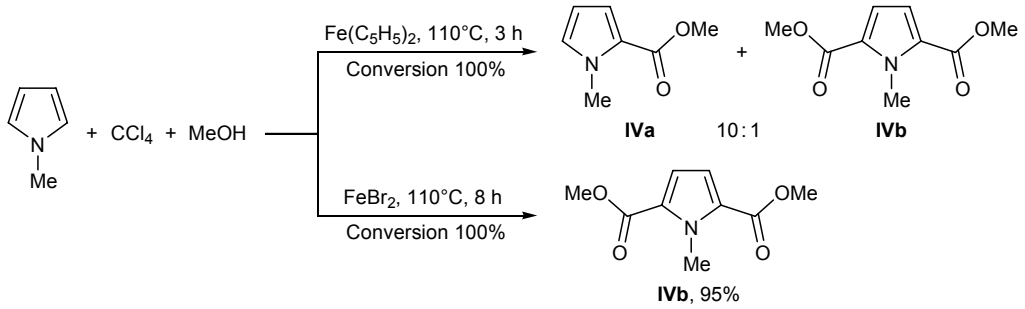
R = Me (**a**, yield 98%), Et (**b**, 97%), Pr (**c**, 81%), *i*-Pr (**d**, 62%).

Scheme 5.



Catalyst = $Fe(acac)_3$ (yield of **IIIa** 99%), $Fe(OAc)_2$ (97%), $FeBr_2$ (95%).

Scheme 6.



pyrrole ring using unsubstituted pyrrole, 2-acetyl-1*H*-pyrrole, and 1-methyl-1*H*-pyrrole as examples. Probable reaction mechanism was studied with the aid of mathematical simulation.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance-400 (400.13 and 100.62 MHz, respectively) and Jeol FX-90Q (90 and 22.5 MHz, respectively) spectrometers using $CDCl_3$ as solvent; the chemical shifts are given relative to tetramethylsilane. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT-112S GC–MS system. Chromatographic analysis was performed on a Shimadzu GC-9A instrument (2-m × 3-mm column packed with 5% of SE-30 on Chromaton N-AW-HMDS; oven temperature programming from 50 to 270°C at a rate of 8 deg/min; carrier gas helium, flow rate 47 ml/min).

Commercially available 2-acetyl-1*H*-pyrrole, pyrrole, *N*-methylpyrrole, methanol, ethanol, propan-1-ol, propan-2-ol, and carbon tetrachloride were distilled prior to use. Tris(acetylacetonato)iron(III), iron(II) acetate, ferrocene, and iron(II) bromide (from Acros) were recrystallized and dried in a vacuum desiccator prior to use. The reactions were carried out under continuous stirring in a glass 10-ml ampule which was placed into a 17-ml stainless steel high-pressure reactor maintained at a required temperature.

Alkyl 5-acetyl-1*H*-pyrrole-2-carboxylates Ia–Id (*general procedure*). An ampule was charged under argon with 0.001 g (0.0045 mmol) of $Fe(C_5H_5)_2$, 0.05 g (0.45 mmol) of 2-acetyl-1*H*-pyrrole, 0.34 ml (3.5 mmol) of carbon tetrachloride, and 29 mmol of the corresponding alcohol (1.2 ml of methanol, 1.7 ml of ethanol, 2.2 ml of propan-1-ol, or 2.2 ml of propan-2-ol). The ampule was sealed and placed into a high-pressure reactor which was hermetically capped and heated for 6 h at 115°C under continuous stirring. When the reaction was complete, the reactor was cooled to 20°C, the ampule was opened, the reaction mixture was filtered through a layer of silica gel (2 g), the sorbent was washed with hexane–diethyl ether (1 : 1), the solvent was distilled off, and the residue was recrystallized from benzene–hexane.

Methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (Ia). Yield 98%, mp 112.5°C; published data: mp 109–110 [11], 110–111.5°C [12]. ^1H NMR spectrum, δ, ppm: 2.48 s (3H, CH_3CO), 3.90 s (3H, OCH_3), 6.80–6.95 m (2H, 3-H, 4-H), 9.89 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 25.85 ($CO\mathbf{C}H_3$), 52.04 (OCH_3), 115.58 (C^3), 116.04 (C^4), 134.18 (C^2), 155.50 (C^5), 161.50 ($\mathbf{C}OOCH_3$), 188.59 ($\mathbf{C}OCH_3$). Mass spectrum, m/z (I_{rel}, %): 167 (96) $[M]^+$, 43 (25), 53 (15), 64 (12), 92 (24), 118 (20), 120 (100), 136 (45), 152 (80), 153 (100).

Ethyl 5-acetyl-1*H*-pyrrole-2-carboxylate (Ib). Yield 98%, mp 59–60°C; published data: mp 54–57 [13], 60–60.5°C [19]. ^1H NMR spectrum, δ, ppm: 1.38 t (3H, $C\mathbf{H}_3CH_2$, J = 6.8 Hz), 2.48 s (3H, $COCH_3$), 4.36 q (2H, OCH_2, J = 7.2 Hz), 6.75–6.95 m (2H, 3-H, 4-H), 9.81 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.32 ($CH_2\mathbf{C}H_3$), 25.85 ($CO\mathbf{C}H_3$), 61.15 (OCH_2), 115.48 (C^3), 116.05 (C^4), 134.18 (C^2), 155.52 (C^5), 161.68 (COO), 188.65 ($\mathbf{C}OCH_3$).

Propyl 5-acetyl-1*H*-pyrrole-2-carboxylate (Ic). Yield 81%, mp 42–44°C. ^{1}H NMR spectrum, δ, ppm: 1.02 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 1.7–1.9 m (2H, CH$_3$C**H**$_2$), 2.42 s (3H, CH$_3$CO), 4.26 t (2H, OCH$_2$, ^3J = 6.8 Hz), 6.80–7.28 m (2H, 3-H, 4-H), 9.89 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 9.76 (**C**H$_3$CH$_2$), 21.48 (CH$_3$**C**H$_2$), 25.68 (CO**C**H$_3$), 66.55 (OCH$_2$), 115.44 (C^3), 116.07 (C^4), 127.34 (C^2), 146.19 (C^5), 160.46 (COO), 188.61 (**C**OCH$_3$).

Isopropyl 5-acetyl-1*H*-pyrrole-2-carboxylate (Id). Yield 62%, mp 67°C. ^{1}H NMR spectrum, δ, ppm: 1.36 d [6H, (C**H**$_3$)$_2$CH, ^3J = 6 Hz], 2.42 s (3H, CH$_3$CO), 4.95–5.5 m (1H, OCH), 6.80–7.72 m (2H, 3-H, 4-H), 9.83 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 21.92 [(**C**H$_3$)$_2$CH], 25.84 (CO**C**H$_3$), 68.86 (OCH), 115.39 (C^3), 116.09 (C^4), 124.56 (C^2), 134.53 (C^5), 159.92 (COO), 188.65 (**C**OCH$_3$).

Dimethyl 1*H*-pyrrole-2,5-dicarboxylate (IIIa). An ampule was charged under argon with 0.0016 g (0.0045 mmol) of Fe(acac)$_3$, 0.03 g (0.45 mmol) of pyrrole, 0.54 g (3.5 mmol) of CCl$_4$, and 0.94 g (29 mmol) of MeOH. The reaction was carried out, and the reaction mixture was treated, as described above for compounds **Ia**–**Id**. Yield 99%, mp 129–130°C; published data [20]: mp 132°C. ^{1}H NMR spectrum, δ, ppm: 3.93 s (6H, OCH$_3$), 6.89 s (2H, 3-H, 4-H), 9.64 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 34.12 (NCH$_3$), 51.96 (OCH$_3$), 115.56 (C^3, C^4), 119.69 (C^2, C^5), 162.00 (COO).

Methyl 1-methyl-1*H*-pyrrole-2-carboxylate (IVa) and dimethyl 1-methyl-1*H*-pyrrole-2,5-dicarboxylate (IVb). An ampule was charged under argon with 0.001 g (0.0045 mmol) of Fe(acac)$_2$ (in the synthesis of **IVa**) or 0.001 g (0.0045 mmol) of FeBr$_2$ (in the synthesis of **IVb**), 0.036 g (0.45 mmol) of *N*-methylpyrrole, 0.54 g (3.5 mmol) CCl$_4$, and 0.94 g (29 mmol) of MeOH. The ampule was sealed and placed into a high-pressure reactor, and the reactor was hermetically closed and heated at 110°C for 3 (**IVa**) or 8 h (**IVb**) under continuous stirring. When the reaction was complete, the reactor was cooled to 20°C, the ampule was opened, the reaction mixture was filtered through a layer of silica gel (2 g), the sorbent was washed with hexane–diethyl ether (1 : 1), and the solvent was distilled off. Compound **IVa** was distilled under reduced pressure, while compound **IVb** was recrystallized from benzene–hexane (1 : 1).

Methyl 1-methyl-1*H*-pyrrole-2-carboxylate (IVa). Yield 90%, bp 62–63°C (1 mm); published data: bp 46–47°C (0.6 mm) [21], 95–98°C (28 mm) [22]. ^{1}H NMR spectrum, δ, ppm: 3.80 s (3H, NCH$_3$), 3.91 s (3H, OCH$_3$), 6.10–7.10 m (2H, 3-H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 36.26 (NCH$_3$), 50.46 (OCH$_3$), 107.58 (C^4), 117.56 (C^3), 129.31 (C^2), 127.54 (C^5), 161.26 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 139 (60) [*M*]$^+$, 45 (15), 53 (28), 80 (25), 94 (15), 108 (100), 124 (4).

Dimethyl 1-methyl-1*H*-pyrrole-2,5-dicarboxylate (IVb). Yield 95%, mp 78–80°C; published data [22]: mp 80–80.5°C. ^{1}H NMR spectrum, δ, ppm: 4.16 s (3H, NCH$_3$), 3.75 s (6H, OCH$_3$), 6.8 s (2H, 3-H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 34.12 (NCH$_3$), 51.18 (OCH$_3$), 116.07 (C^3, C^4), 127.63 (C^2, C^5), 161.07 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 197 (72) [*M*]$^+$, 45 (18), 69 (10), 79 (10), 97 (8), 108 (10), 120 (14), 138 (8), 152 (15), 166 (100), 182 (5).

Kinetic study on the formation of methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (Ia). A series of experiments on the synthesis of compound (**Ia**) from 2-acetyl-1*H*-pyrrole were performed according to the above described procedure with variation of the reaction time (2.5, 3, 3.5, 4, 4.5, 5, 6 h) and temperature (105, 110, 115°C). The conversion of initial 2-acetyl-1*H*-pyrrole and the yield of methyl 5-acetyl-1*H*-pyrrole-2-carboxylate (**Ia**) were determined by GLC using decane as internal standard.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 09-03-00472) and by the Ministry of Education and Science of the Russian Federation (project no. NSh 2349.2008.3).

REFERENCES

1. Vogel, E., Richert, K., Benninghaus, T., Muller, M., and Cross, A.D., US Patent no. 5179120, 1993; *Chem. Abstr.*, 1993, vol. 119, no. 72432t.
2. Kleinspehn, G.G. and Corwin, A.H., *J. Am. Chem. Soc.*, 1960, vol. 82, p. 2750.
3. Korobchenko, L.V., Vladyko, G.V., Borenko, E.I., Sobenina, L.N., Mikhaleva, A.I., Sergeeva, M.P., and Trofimov, B.A., *Khim.-Farm. Zh.*, 1992, p. 57.
4. Sobenina, L.N., Mikhaleva, A.I., Bakhareva, E.V., Vasil'eva, N.N., Pushechkina, T.Ya., Kazimirovskaya, V.B., Sergeeva, S.E., Korostova, S.E., Nesterenko, R.N., Golovanova, N.I., and Polovnikova, R.I., *Khim.-Farm. Zh.*, 1992, p. 26.
5. Joh, Y., *Seikagaku*, 1961, vol. 33, p. 787; *Chem. Abstr.*, 1962, vol. 57, p. 11144.
6. Joule, J.A. and Mills, K., *Heterocyclic Chemistry*, Malden, MA: Blackwell Science, 2000, 4th ed. Translated under the title *Khimiya geterotsiklicheskikh soedinenii*, Moscow: Mir, 2004, p. 728.

7. Belanger, P., *Tetrahedron Lett*., 1979, vol. 20, p. 2505.
8. Joule, J.A. and Smith, G.F., *Heterocyclic Chemistry*, London: Van Nostrand Reinhold, 1972. Translated under the title *Osnovy khimii geterotsiklicheskikh soedinenii*, Moscow: Mir, 1975, p. 398.
9. Khusnutdinov, R.I., Shchadneva, N.A., Baiguzina, A.R., Mukminov, R.R., Mayakova, Yu.Yu., Smirnov, A.A., and Dzhemilev, U.M., *Neftekhimiya*, 2008, no. 6, p. 467.
10. Khusnutdinov, R.I., Shchadneva, N.A., Baiguzina, A.R., Lavrent'eva, Yu.Yu., Burangulova, R.Yu., Atnabaeva, A.M., and Dzhemilev, U.M., *Neftekhimiya*, 2004, p. 329.
11. Anderson, H.J. and Huang, C.W., *Can. J. Chem*., 1967, vol. 45, p. 897; *Ref. Zh., Khim*., 1967, no. 23Zh334.
12. Loader, C.E. and Anderson, H.J., *Tetrahedron*, 1969, vol. 25, no. 17, p. 3879.
13. Martyn, D.C., Vernall, A.J., Clark, B.M., and Abell, A.D., *Org. Biomol. Chem*., 2003, vol. 1, p. 2103.
14. Slin'ko, M.G., *Osnovy i printsipy matematicheskogo modelirovaniya kataliticheskikh protsessov* (Fundamentals and Principles of Mathematical Modeling of Catalytic Processes), Novosibirsk: Inst. Kataliza imeni G.K. Boreskova Sib. Otd. Ross. Akad. Nauk, 2004, p. 488.
15. Gubaidullin, I.M. and Spivak, S.I., *Sist. Uprav. Inform. Tekhnol*., 2008, no. 1.1, p. 150.
16. Yablonskii, G.S., Bykov, V.I., and Gorban', A.N., *Kineticheskie modeli kataliticheskikh reaktsii* (Kinetic Models of Catalytic Reactions), Novosibirsk: Nauka, Sib. Otd., 1983, p. 254.
17. Spivak, S.I., *Sovremennye problemy biokinetiki* (Current Problems in Biokinetics), Varfolomeev, S.D., Ed., Moscow: Mosk. Gos. Univ., 1987, p. 150.
18. *Heterocyclic Compounds*, Elderfield, R.C., Ed., New York: Wiley, 1951, vol. 1. Translated under the title *Geterotsiklicheskie soedineniya*, Moscow: Inostrannaya Literatura, 1953, vol. 1, p. 556.
19. Tani, M., Ariyasu, T., Nishiyama, C., Hagivara, H., Watanabe, T., Yokoyama, Y., and Murakami, Y., *Chem. Pharm. Bull*., 1996, vol. 44, p. 48.
20. *Dictionary of Organic Compounds*, Heilbron, J. and Bunbury, H.M., Eds., London: Eyre and Spottswoode, 1953, vol. 3. Translated under the title *Slovar' organicheskikh soedinenii*, Moscow: Inostrannaya Literatura, 1949, vol. 3, p. 977.
21. Williams, A. and Salvadori, G., *J. Chem. Soc., Perkin Trans. 2*, 1972, no. 7, p. 883.
22. Shirley, D.A., Gross, B.H., and Roussel, P.A., *J. Org. Chem*., 1955, vol. 20, p. 225.