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SYNTHESIS AND STRUCTURE OF 5-ALKYL(ARYL)PYRROL-2-ONES

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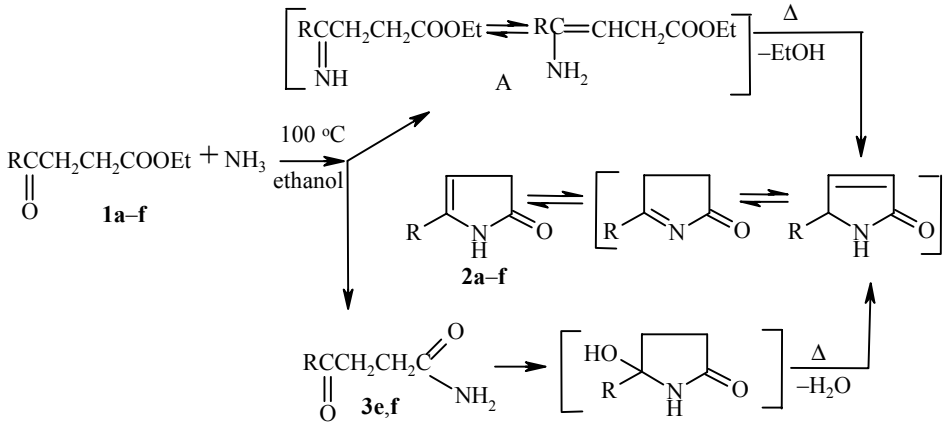
The amination of 4-oxoalkanoic acids and their esters by the action of ammonia and ammonium acetate leads to the formation of N-unsubstituted 5-alkyl(aryl)pyrrol-2-ones, which exist in solution in the form of a mixture of isomers in a ratio depending on the nature of the substituent at position 5 of the heterocycle.

Keywords: amides of 4-oxoalkanoic acids, N-unsubstituted 5-alkyl(aryl)pyrrol-2-ones, 4-oxoalkanoic acids, amination, tautomerism.

The heterocyclization of 4-oxoalkanoic acids and their derivatives by the action of aromatic amines, leading to the production of N-aryl-substituted pyrrol-2-ones, was discussed in our earlier paper [1]. However, questions concerning the synthesis and structure of N-unsubstituted pyrrol-2-ones were not examined. There are papers in which the production of N-unsubstituted pyrrol-2-ones by the oxidation of pyrroles with hydrogen peroxide [2] and also the production of 5-phenyl-3H-pyrrol-2-one by the reaction of β-benzoylpropionic acid with ammonia [3] are described.

In the present work we present the results of the production of 5-alkyl(aryl)-3H-pyrrol-2-ones from 4-oxoalkanoic acids and their esters and also β-benzoylpropionic acid by reaction with ammonia and ammonium acetate as aminating agents.

Ethyl 4-oxoalkanoates **1a-f** react with ammonia in a ratio of 1:3 in ethanol at 100°C in an autoclave with the formation of N-unsubstituted 5-alkyl-3H-pyrrol-2-ones **2a-f**.



1, **2**, **3** **a** R = C_3H_7, **b** R = C_5H_{11}, **c** R = *i*-C_5H_{11}, **d** R = C_6H_{13}, **e** R = C_7H_{15}, **f** R = C_8H_{17}

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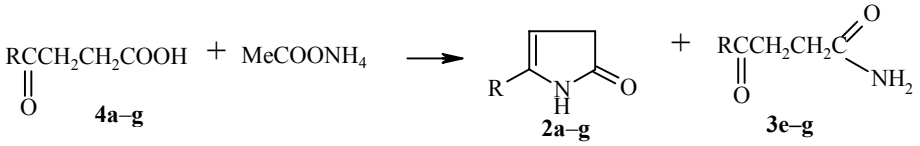
The ammonia can attack at the carbon atom of the oxo group with the formation of the intermediate A or at the carbon of the ethoxycarbonyl group with the formation of 4-oxoalkanamides. Ammonolysis of the esters **1e**,**f** leads to amides **3e**,**f**, which were isolated by evaporation of the reaction mixtures. In the amides the open-chain and cyclic forms are fairly stable, and a tautomeric equilibrium is not established.

The noncyclic structure of amides **3e**,**f** is confirmed by the IR spectra. In the region of 1580-1540 cm^{-1} there are the absorption bands of the amide carbonyl, the carbonyl group absorbs at 1690-1660, and the two narrow bands in the region of 3200 and 3325 cm^{-1} are characteristic of the primary amino group. Further cyclodehydration of amides **3e**,**f** to pyrrol-2-ones **2e**,**f** takes place during vacuum distillation.

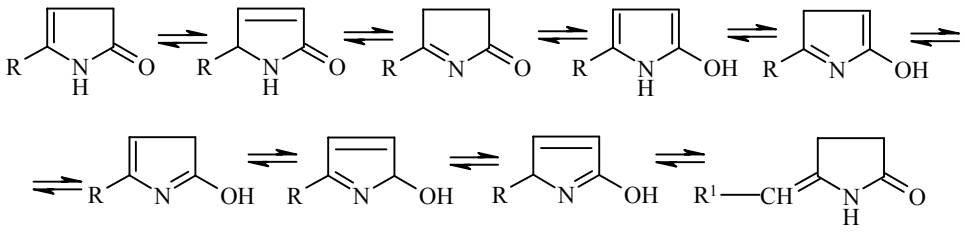
The reaction of 4-oxoalkanoic acids **4a-g** with ammonium acetate was realized by boiling in xylene or acetic anhydride. The required N-unsubstituted pyrrol-2-ones **2a-g** were obtained in acetic anhydride with yields of up to 70%.



2, **3**, **4 a** R = Pr, **b** R = C_5H_{11}, **c** R = *i*-C_5H_{11}, **d** R = C_6H_{13}, **e** R = C_7H_{15}, **f** R = C_8H_{17}, **g** R = Ph

By using xylene it is possible to obtain compounds **2e-g** with yields of up to 65% with the simultaneous release of amides **3e-g** (20%). In this case the reaction probably takes place through the formation of the amides of 4-alkanoic acids, the cyclization of which gives better yields in acetic anhydride.

The N-unsubstituted pyrrol-2-ones **2a-f** exhibit clearly defined tautomeric characteristics. Migration of a proton in the cyclic system makes it possible for various tautomeric forms to exist:



Study of the ^{1}H NMR and IR spectra showed that the transformation of one of the forms in the series of N-unsubstituted pyrrol-2-ones depends on the nature of the substituent at position 5 of the heterocycle (Table 1). In the ^{1}H NMR spectrum of compound **2g** there are signals for the methylene protons at $C_{(3)}$ in the region of 2.95 ppm, the vinyl proton at $C_{(4)}$ in the region of 5.32 ppm, and the proton at the nitrogen in the downfield region at 8.00 ppm. Apart from the above-mentioned signals belonging to the structure of the 3H form, there are signals for the protons belonging to the structure of the 3H, 4H form, and the signals of the methylene protons at $C_{(3)}$ and $C_{(4)}$ of the heterocycle are in the regions of 2.45 and 2.24 ppm.

Thus, 5-phenylpyrrol-2-one **2g** exists in solution in deuterochloroform as a mixture of the tautomeric forms 5-phenyl-1H,3H-pyrrol-2-one and 5-phenyl-3H,4H-pyrrole-2-one in proportions of 85 and 15% respectively.

Different conclusions can be reached during study of the ^{1}H NMR spectra of compounds **2c-f**, which have an alkyl substituent at position 5 of the heterocycle. In the spectra of these compounds there are signals at 2.92-2.95 ppm for the methylene protons at position 3; the vinylic proton gives a signal in the region of 5.19-5.21 ppm; in the upfield region there signals at 0.82-2.10 ppm for the protons of the alkyl substituent, and there is also a signal in the downfield region at 7.45-7.75 ppm for the proton at the nitrogen atom; the structure

TABLE 1. The ^{1}H NMR Spectra of 5-R-Pyrrol-2-ones **2e-g**

Compound	Chemical shifts, δ, ppm, *J* (Hz)
2c	2.92 (2H, dd, CH_2); 5.19 (1H, dd, =CH); 0.82-1.94 (m, H_R); 7.45 (1H, br. s, NH); 6.10 (1H, dd, =CH); 6.80 (1H, dd, J_{43} = 5.56, =CH)
2d	2.92 (2H, dd, =CH_2); 5.20 (1H, dd, =CH); 0.84-1.90 (m, H_R); 7.50 (1H, br. s, NH); 6.12 (1H, dd, =CH_2); 6.80 (1H, dd, J_{43} = 5.62)
2e	2.94 (2H, dd, CH_2); 5.21 (1H, dd, =CH); 0.82-2.05 (m, H_R); 7.65 (1H, br. s, NH); 6.10 (1H, dd, =CH); 6.82 (1H, dd, J_{43} = 5.60)
2f	2.93 (2H, dd, CH_2); 5.21 (1H, dd, =CH); 0.92-2.10 (m, H_R); 7.75 (1H, br. s, NH); 6.14 (1H, dd, =CH); 6.85 (1H, dd, J_{43} = 5.62
2g	2.95 (2H, dd, CH_2); 5.32 (1H, dd, =CH); 7.25-7.60 (5H, m, H_{Ar}); 8.00 (1H, s, NH); 2.45 (2H, dd, CH_2); 2.24 (2H, dd, CH_2)

TABLE 2. The Characteristics of the Synthesized Compounds

Com-pound	Empirical formula	Found, % / Calculated, %			bp, °C/mm Hg mp,°C	n_D^{20}	Yield, %
		C	H	N			
2a	$C_7H_{11}NO$	67.15 / 67.20	8.92 / 8.80	11.35 / 11.20	120-122/3 / —	1.5170	70
2b	$C_9H_{15}NO$	70.43 / 70.58	9.64 / 9.80	9.46 / 9.15	126-128/3 / —	1.5122	66
2c	$C_9H_{15}NO$	70.73 / 70.58	9.87 / 9.80	9.05 / 9.15	130-132/3 / —	1.5112	60
2d	$C_{10}H_{17}NO$	72.10 / 71.85	10.27 / 10.18	8.19 / 8.38	140-142/3 / —	1.4985	70
2e	$C_{11}H_{19}NO$	73.01 / 72.99	10.63 / 10.58	7.50 / 7.74	156-157/3 / 42	—	60
2f	$C_{12}H_{21}NO$	73.53 / 73.79	10.88 / 10.84	6.78 / 7.17	170-172/3 / 46	—	65
2g	$C_{10}H_9NO$	75.35 / 75.47	5.70 / 5.66	8.66 / 8.80	— / 119	—	60
3e	$C_{11}H_{21}NO_2$	66.83 / 66.39	10.57 / 10.64	6.85 / 7.04	— / 121	—	20
3f	$C_{12}H_{23}NO_2$	67.60 / 67.61	10.79 / 10.80	6.40 / 6.57	— / 126	—	18
3g	$C_{10}H_{11}NO_2$	67.56 / 67.79	6.35 / 6.21	7.78 / 7.90	— / 130	—	18

(the 3H form) of compounds **2c-f** is supported by the form and position of the signals. The spectra also contain signals confirming the existence of the 5H isomer of compounds **2c-f**: The signals of the vinylic protons at $C_{(3)}$ and $C_{(4)}$ are observed in the regions of 6.10-6.14 and 6.80-6.85 ppm respectively; the signal of the proton at position 5 is downfield in the region of the absorption of the protons of the alkyl substituent (Table 1). The signals of other isomers were not detected.

Thus, pyrrol-2-ones **2c-f** having a bulky alkyl substituent at position 5 of the heterocycle exist in solution in deuterochloroform as mixtures of the two tautomeric forms 5-alkyl-3H-pyrrol-2-ones and 5-alkyl-5H-pyrrolin-2-ones in proportions of 88-90 and 12-10% respectively.

The IR spectra of compounds **2a-g**, recorded in thin layers, contain absorption bands characteristic of the unconjugated 3H form of pyrrol-2-ones. In the region of 1690-1670 cm^{-1} there is an absorption band for the carbonyl group, and the absorption of the unconjugated C=C bond appears in the region of 1650-1660 cm^{-1}.

Thus, 4-oxoalkanoic acids and their esters are suitable synthons for the synthesis of N-unsubstituted pyrrol-2-ones, which exist in solutions in deuterochloroform as mixtures of tautomers. The ratio of the tautomers depends on the nature of the substituent at position 5 of the heterocycle.

EXPERIMENTAL

The IR spectra were recorded on an IKS-29 instrument, and the ^{1}H NMR spectra were recorded on a Varian FT-80A instrument (80 MHz) in deuterochloroform with TMS as internal standard. The yields and characteristics of the obtained compounds are given in Tables 1 and 2. The ethyl 4-oxoalkanoates (**1a-g**) were obtained by the method in [4]. The 4-oxoalkanoic acids were obtained by the method in [5]. β-Benzoylpropionic acid was obtained by the method in [6].

5-Alkyl-3H-pyrrol-2-ones (2a-f) Based on Ethyl 4-Oxoalkanoates. To the compound **1a-f** (0.02 mol) we added ethanol that had been previously saturated with ammonia. (A threefold excess of ammonia was used.) The reaction mixture was heated at 100°C in a rotating autoclave for 6 h, after which the excesses of ammonia and solvent were distilled. The residue was distilled under vacuum.

5-Alkyl-3H-pyrrol-2-ones (2a-g) Based on 4-Oxoalkanoic Acids. To the compound **4a-g** (0.02 mol) we added ammonium acetate (0.05 mol). After boiling for 3 h in acetic anhydride or *o*-xylene the solvent was distilled, and the residue was distilled under vacuum.

4-Oxoalkanamides (3e,f). To absolute ethanol (30 ml) that had been previously saturated with ammonia we added the compound **1e**,**f** (1 mmol) (ratio of reagents 3:1). The reaction mixture was heated for 6 h in an autoclave with a capacity of 50 cm^3 at 100°C, after which the excess of the ammonia was distilled. The residue was recrystallized from benzene. The further transformation of 4-alkanamides **3e**,**f** into pyrrol-2-ones **2e**,**f** occurred during fractional distillation under vacuum.

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