Synthesis of *N*-methacryloyl- and *N*-allyl-substituted derivatives of ethyl 5-oxo-2-pyrrolidinecarboxylate

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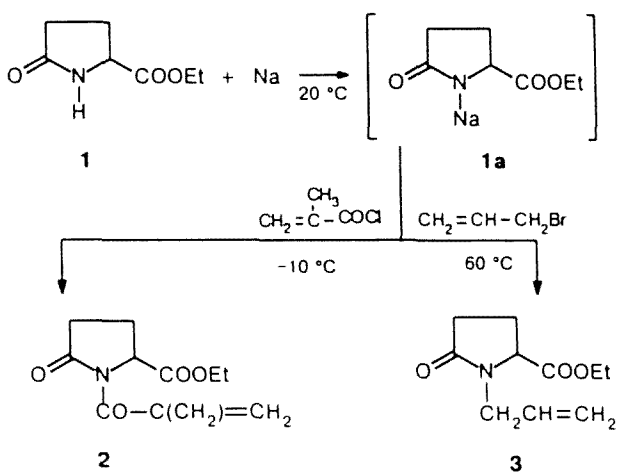
A method for the preparation of previously unknown *N*-methacryloyl- and *N*-allyl-derivatives of ethyl 5-oxo-2-pyrrolidinecarboxylate has been developed.

Key words: 5-oxo-2-pyrrolidinecarboxylic acid, unsaturated derivatives.

5-Oxo-2-pyrrolidinecarboxylic (pyroglutamine) acid (OPCA) and its derivatives are used in medicine and the food industry, as well as for preparation of physiologically active compounds. Some of its derivatives are applied for medical treatment of alcoholism and mental disorders.[1]

Preparation of *N*-arylmethyl derivatives of OPCA esters by the action of corresponding arylmethyl halides in the presence of strong bases,[2] as well as preparation of their carbobenzoxy- and *tert*-butoxy-substituted derivatives using 1,8-diazabicyclo[5.4.0]undecene-7 (DBU),[3] are described in the literature. *N*-Alkyl- and *N*-acyl-substituted 5-oxo-2-pyrrolidinecarboxylates are usually obtained in good yields from corresponding *N*-substituted derivatives of glutamic acid by pyrrole ring closure in the presence of dehydrating agents under rather drastic conditions.[4]

We propose methods for preparative synthesis of unsaturated derivatives of ethyl 5-oxo-2-pyrrolidinecarboxylate (**1**) bearing methacryloyl or allyl groups at position 1 of the pyrrole ring. Interaction of Na-derivative (**1a**), preliminarily obtained by the reaction of ester **1** with a suspension of sodium in *p*-xylene, which remains in solution (which is very important for successful interaction), with methacryloyl chloride (**2**) or allyl bromide (**3**) is carried out under mild conditions. The reaction proceeds in a high yield and affords the corresponding derivatives of ethyl 5-oxo-2-pyrrolidinecarboxylate bearing unsaturated substituents at the N atom only. In this case we managed to avoid the procession of side reactions and formation of polymers. A similar method was not used for preparation of other *N*-substituted OPCA derivatives.



After the solvent was removed and the residue was distilled *in vacuo*, we obtained the monomers as individual compounds, according to elementary analysis and ^{1}H NMR spectral data.

Experimental

^{1}H NMR spectra were obtained on a Bruker HX-90 instrument with a working frequency of 200 MHz using $SiMe_4$ as the external standard. IR spectra were recorded on a UR-20 instrument in thin films in KBr. The starting ester **1**, m.p. 54—55 °C (from ligroin), was obtained by the known procedure.[5]

Ethyl *N*-methacryloyl-5-oxo-2-pyrrolidinecarboxylate (2). Compound **1** (7.9 g, 0.05 mol) was dissolved in dry xylene (20 mL) in a flask supplied with a magnetic stirrer. A suspension of Na (1.3 g) in xylene (15 mL) was added to the solution in the course of 1 h with vigorous stirring (liberation of hydrogen is observed in the course of the reaction). The reaction mixture was cooled to −10 °C, and freshly distilled methacryloyl chloride (6.3 g, 0.06 mol) was added dropwise to the flask. The mixture was filtered, the filtrate was evaporated, and, after the solvent was removed, the residue was distilled *in vacuo* to give 9.5 g (84 %) of ether **2**, b.p. 145—146 °C (2 Torr), n^{20}_D 1.4790. Found (%): C, 58.33; H, 7.15; N, 6.23. $C_{11}H_{15}NO_4$. Calculated (%): C, 58.67; H, 6.67; N, 6.22. IR, ν/cm^{-1}: 1640 (C=O), 1692 (CONH), 1753 (COOR). ^{1}H NMR, $CDCl_3$, δ: 1.00 (t, 3 H, CH_3); 3.92 (q, 2 H, CH_2O); 4.40 (m, 1 H, CH); 5.12 (s, 2 H, $=CH_2$).

Ethyl *N*-allyl-5-oxo-2-pyrrolidinecarboxylate (3). Compound **1** (7.9 g, 0.05 mol) was dissolved in dry xylene (30 mL)

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in a flask supplied with a magnetic stirrer and a reflux condenser. A suspension of Na (1.3 g) in xylene (5 mL) was added to the solution with vigorous stirring for 0.5 h, and then allyl bromide (7.3 g, 0.06 mol) was added dropwise. The reaction was accompanied by heating. The reaction mixture was stirred for 1 h at 60 °C, left for 12 h, and after that filtered. The residue on the filter was washed with xylene. After the solvent was removed, the residue was distilled *in vacuo* to give 9.2 g (93 %) of ether **3**, b.p. 126—127 °C (1 Torr), $n^{20}D$ 1.4730. Found (%): C, 60.40; H, 7.66; N, 7.10. $C_{10}H_{15}NO_3$. Calculated (%): C, 60.89; H, 7.66; N, 7.10. IR, ν/cm^{-1}: 1640 (C=O), 1690 (CONH), 1755 (COOR). ^1H NMR, $CDCl_3$, δ: 1.05 (t, 3 H, CH_3); 3.30 (m, 1 H, CH); 3.95 (m, 2 H, CH_2O); 4.96 (m, 2 H, $=CH_2$); 5.5 (m, 1 H, =CH).

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Over-pressure TLC variant on a plate with an enclosed sorbent layer

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An over-pressure TLC variant with an enclosed sorbent layer and forced flow of the mobile phase was suggested. A simple new type device for its realization was developed.

Key words: over-pressure TLC, plate with closed sorbent layer, device for over-pressure TLC.

Thin-layer chromatography is widely used in science and industry for determination of the composition of various objects.[1—6] However, the most popular TLC variant has several restrictions: (1) rather long duration of analysis; (2) low reproducibility of the chromatographic parameters of the process; and (3) nonoptimum efficiency of the process, which is explained by a sharp change in the flow rate of the mobile phase during experiments.

Hungarian researchers (see, *e.g.*, Refs. 5—9) suggested a TLC variant with forced flow of the mobile phase, in which the plate placed in a special device becomes a planar column during chromatographic separation due to application (under high pressure) of a polymeric material on its sorption layer, and the mobile phase under the action of pressure is supplied to the beginning of this planar column. Despite fine results, the method described did not find wide application, because the device is rather expensive and complicated. In this work, a new simplified TLC variant with forced flow of the mobile phase is proposed. The method is based on the use of TLC plates with the standard plate adsorption layer enclosed in a transparent polymeric film.[10,11]

The device,[12] which allows one to realize TLC with forced flow of the mobile phase using the new type plates, is presented in Fig. 1. Its work is based on creation of a pressure drop on the layer, because an eluent is supplied at an elevated pressure equal to an excessive gas pressure in the chamber, and the air space of the layer is connected with the atmosphere and exists at normal pressure. The value of the pressure drop (≤ 4 atm) depends on the pressure of the gas supplied from the pressure source and is determined by the design of the chamber (ability to "hold" pressure).

The demountable hermetic chamber is made of organic glass and consists of the body (*1*) and transparent lid (*2*), which are sealed with screw clamps (*3*) by the gasket (*4*) that has the form of a rectangular frame. The chamber contains the plate (*5*) with an enclosed sorbent

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