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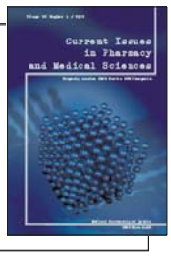

Synthesis of new derivatives ofm 1-[1-(2-pyridyl) -imidazolidine-2-ylidene]-3-aryl(arylakyl)ureas

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ABSTRACT

The synthesis and physicochemical properties of new 1-[1-(2-pirydyl)imidazolidine-2-ylidene]-3-aryl(arylalkyl)ureas [I-VIII]. The title compounds were obtained by condensation of 1-(2-pirydyl)-2-aminoimidazoline-2 with aryl isocyanate or arylalkyl isocyanate in dichloromethane under the atmosphere of dry nitrogen. The reaction was conducted in the room temperature for 24 h. Considering the structure of obtained compounds it can be expected that these compounds can reveal pharmacological activity.

Keywords: 1-(2-pirydyl)-2-aminoimidazoline-2, phenyl isocyanate, 3-chlorphenyl isocyanate, benzyl isocyanate, phenethyl isocyanate

INTRODUCTION

The synthetic carbonyl derivatives of 1-aryl-2-imino-imidazolidine containing urea moiety form are various and important group of medicines. In the search for new derivatives with potential pharmacological activity new 1-(1-arylimidazolidine-2-ylidene)-3-substituted ureas [6] were obtained. Some derivatives of N-aryl urea show anti-inflamatory, antibacterial, antifungal activity [7], have antidepressant activity [5] and are smoothened antagonist [4].

In the recent years at the Department of Synthesis and Technology of Drugs, a number of simple and fused derivatives of imidazoline was synthesized. In many cases [3] they exhibited analgesic activity, especially when the additional carbonyl group was present. To find out the part of their structure that can be a possible analgesic 'pharmacophor', a series of chain carbonyl derivatives of 1-aryl-2-iminoimidazoline were synthesized [2].

Pain is still considered a very complex process involving multiple neurotransmitters and neuro modulators. Some types of pain can be treated now with efficiency, but the side effects associated with using of these drugs makes the search for new approaches inevitable. The search for new for new biological targets [8] or new drugs that are more selective is the most important approach.

Commonly, for the pharmacophore models of opioid-receptor activity some groups are important. The amino-carbonyl derivatives of 1-aryl-2-imidazolidine-2 have significant antinociceptive activity connected with activation of the MOP (μ opioid protein) receptor [3].

RESULTS AND DISCUSSION

New 1-[1-(2-pirydyl)imidazolidine-2-ylidene]-3-aryl (arylakyl)urea derivatives were received as a result of condensation of 1-(2-pirydyl)-2-aminoimidazoline-2 with respective aryl(alkyl) isocyanate in dichloromethane under the atmosphere of dry nitrogen. The reaction was conducted in the room temperature for 24 h. The reaction leading to the formation of [I-VIII] is outlined in the Fig. 1.

New compounds were characterized by elemental analysis as well as by the ^{1}H NMR, MS spectra.

Taking into account the possibility of existing of two isomeric form 1-[1-(2-pirydyl)imidazolidie-2-ylidene)-3-aryl (arylakyl)ureas (in scheme A) or 1-(2-pirydyl)-2-amino -3-aryl(arylakyl)aminocarbonyloimidazoilidines (in Fig. 1B) in the obtained products exist 1-[1-(2-pirydyl)imidazolidine-2-ylidene]-3-aryl(arylakyl)ureas (Fig. 1) [I-VIII]. The spectral data of obtained compounds are presented in Table 1.

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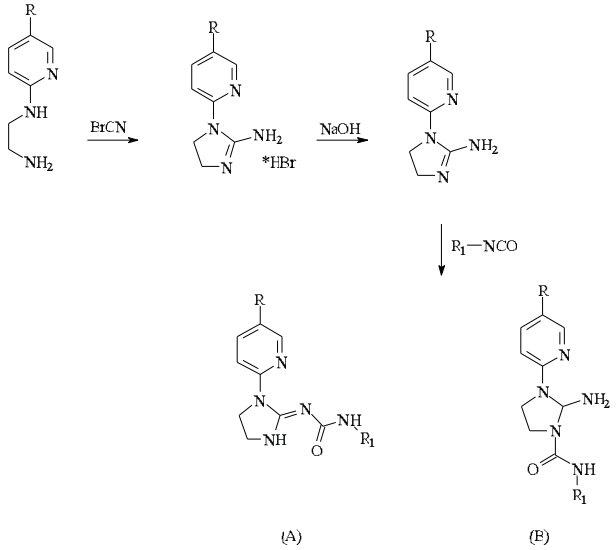

Fig. 1. Synthesis of new of 1-[1-(2-pirydyl)imidazolidine-2--ylidene]-3-aryl(arylakyl)urea derivatives

from propan-2-ol. Purity was checked by TLC on Merc Co. TLC was performed on commercial Merc SiO_2 Plates with chloroform-methanol (10:2) solvent system, visualization with UV.

SYNTHESIS OF 1-[1-(2-PIRYDYL) IMIDAZOLIDINE-2-YLIDENE]-3-ARYL(AKYL) UREA DERIVATIVES [I-VIII]

General procedure: Aryl(arylalkyl) isocyanate was solved in 25 mL of dichloromethane under the atmosphere of dry nitrogen and added to the solution free base (0.02 mol) of 1-(2-pirydyl)-2-aminoimidazoline-2 solved in 100 mL of dichloromethne. The mixture was shaken for 24 h in room temperature. The solvent was removed by distillation and the rubber-like residue was treated with warm propan-2-ol. The solid product was filtrated off and recrystallized from propan-2-ol.

Table 1. The physical data of new compounds

No	R	R_1	Formula Molecular Weight	M.p.°C Yield %	Analysis Calculated/Found			
					C	H	N	Cl
I	H	C_6H_5	$C_{15}H_{15}N_5O$ 281.32	147-148 40	64.04 64.20	5.37 5.44	24.89 24.95	—
II	H	3-ClC_6H_5	$C_{15}H_{14}ClN_5O$ 315.77	165-167 73	57.05 57.11	4.79 4.88	22.18 22.25	11.23 11.30
III	H	$C_6H_5CH_2$	$C_{16}H_{17}N_5O$ 295.35	173-175 44	65.07 65.22	5.80 5.91	23.70 23.65	—
IV	H	$C_6H_5CH_2CH_2$	$C_{17}H_{19}N_5O$ 309.38	165-167 54	66.00 65.89	6.19 6.32	22.64 22.78	
V	NO_2	C_6H_5	$C_{15}H_{14}N_6O_3$ 326.33	179-180 46	55.21 55.30	4.32 4.44	25.75 25.67	—
VI	NO_2	3-ClC_6H_5	$C_{15}H_{13}ClN_6O_3$ 360.77	215-216 50	49.93 49.88	3.63 3.70	23.30 23.44	9.82 9.88
VII	NO_2	$C_6H_5CH_2$	$C_{16}H_{16}N_6O_3$ 340.35	163-165 51	56.46 56.55	4.74 4.86	24.69 24.72	—
VIII	NO_2	$C_6H_5CH_2CH_2$	$C_{17}H_{15}N_6O_3$ 354.38	154-155 37	57.62 57.72	5.12 5.20	23.72 23.81	—

^{1}H NMR (DMSO-d_6) ; (ppm) for :
Comp. I : 10.11 (s, 1H, N3); 7.44 (s, 1H, N8); 6.95-7.44 (m, 9H, $CH_{aromat.}$); 3.21-3.45 (dd, 2H,C4); 3.08-3.10 (dd, 2H, C5)
Comp. II : 9.18 (s, 1H, N3); 7.55 (s, 1H, N8); 7.05-7.55 (m, 8H, $CH_{aromat.}$); 3.25-3.45 (dd, 2H,C4); 3.08-3.21 (dd, 2H, C5)
Comp. III : 9.30 (s, 1H, N3); 8.30 (s, 1H, N8); 6.93-7.86 (m, 9H, $CH_{aromat.}$); 4.34-4.44 (dd, 2H, C4); 3.98-4.01 (dd, 2H, C5); 2.48-2.51 (m, 2H, C_{benzyl})
Comp. IV : 10.01 (s, 1H, N3); 9.21 (s, 1H, N8); 6.91-8.31 (m, 9H, $CH_{aromat.}$);3.42-3.47 (dd, 2H,C4); 3.32-3.41 (dd, 2H, C5); 2.76-2.80 (m, 2H, $C_{phenylethyl}$); 2.49-2.51 (m, 2H, $C_{phenylethyl}$)
Comp. V : 8.58 (s, 1H, N3); 7.85 (s, 1H, N8); 7.05-7.55 (m, 8H, $CH_{aromat.}$); 3.78-3.85 (dd, 2H,C4); 3.48-3.51 (dd, 2H, C5)
Comp. VI : 8.38 (s, 1H, N3); 7.76 (s, 1H, N8); 6.68-7.25 (m, 8H, $CH_{aromat.}$); 3.48-3.75 (dd, 2H,C4); 3.18-3.35 (dd, 2H, C5)
Comp. VII : 8.53 (s, 1H, N3); 7,86 (s, 1H, N8); 6.88-7.36 (m, 8H, $CH_{aromat.}$); 3.45-3.78 (dd, 2H, C4); 3.44-4.01 (dd, 2H, C5); 2.18-2.28 (m, 2H, $C_{benzyl.}$)
Comp. VIII : 10.11 (s, 1H, N3); 9.45 (s, 1H, N8); 7.11-8.22 (m, 8H, $CH_{aromat.}$);3.22-3.37 (dd, 2H,C4); 3.02-3.11 (dd, 2H, C5); 2.76-2.80 (m, 2H, $C_{phenylethyl}$); 2.29-2.41 (m, 2H, $C_{phenylethyl}$)

EXPERIMENTAL

Chemistry

Melting points were determined on a Böetius apparatus and are given uncorrected. The ^{1}H NMR spectra were recorded on Brucker 300 MHz spectrometers in d_6-DMSO. The mass spectra were recorded using mass spectrometers parameters of EI source: Electron energy 70 eV. Elemental analyses were performed on a Perkin-Elmer analyzer and were in the range of ±0.4% for each elemental analyses (C, H, Cl, N,). All the compounds were recrystallized

The physical data of new compounds are shown in Table 1.

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