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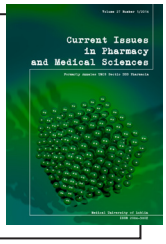

Synthesis of new derivatives of 9-(2-pyridyl)-3-aryl(arylalkyl)--2,4,5(9H)trioxo-7,8-dihydroimidazo[1,2-a][1,3,5]triazepine

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ABSTRACT

A series of new derivatives of 9-(2-pyridyl)-3-aryl(arylalkyl)-2,4,5(9H)trioxo-7,8-dihydroimidazo [1,2-a][1,3,5] triazepine was obtained by condensation of 1-[1-(2-pyridyl) imidazolidine-2-ylidene]-3-aryl(arylalkyl)ureas) with diethyl oxalic acid ester. Considering the structure of the obtained compounds, it can be expected that these compounds can reveal pharmacological activity.

INTRODUCTION

In the recent years at the Department of Synthesis and Technology of Drugs, a number of fused derivatives of triazepine has been synthesized [11,13].

The synthetic derivatives of triazepine form various and important group of medicines. In the search for new structures with potential pharmacological activity, a set of novel imidazo[1,2-a][1,3,5]triazepines has been obtained. Some known derivatives of imidazotriazepine show activity as muscle relaxants [1], the others have antifungal [8], anti-diabetic [3,9,10], antimicrobial [2,4,5], antiviral [7,14], anticancer [7] and analgesic [6] properties. This heterocyclic system has been obtained by us in a two-step reaction. It seemed worthwhile to synthesize new imidazo[1,2-a][1,3,5]triazepine derivatives to estimate their pharmacological activity.

MATERIALS AND METHODS

General procedure for the synthesis of 9-(2-pyridyl)-3-aryl(arylalkyl)-2,4,5(9H)-trioxo-7,8-dihydroimidazo [1,2-a][1,3,5] triazepines

Diethyl oxylate acid ester (0,01 mole) was added to 1-[1-(2-pyridyl)imidazolidine-2-ylidene]-3-aryl(arylalkyl) ureas) (0.01 mole) dissolved in 50 cm^3 of DMF. The mixture was heated under reflux for 10-12h. The solvent was evaporated under reduced pressure to ca. a half its volume. The precipitate was filtered off and finally recrystallized.

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RESULTS AND DISCUSSION

New 9-(2-pyridyl)-3-aryl(arylalkyl)-2,4,5(9H)-trioxo-7,8-dihydroimidazo[1,2-a][1,3,5]triazepines were received as a result of condensation of 1-[1-(2-pyridyl)imidazolidine-2-ylidene]-3-aryl(arylalkyl)ureas [6,12] with diethyl oxalic acid ester. The reaction was conducted in the boiling temperature of the solvent. The reaction sequence leading to the formation of small molecules (I-V) is outlined in Scheme 1.

Melting points were determined on a Boetius apparatus and given uncorrected. The ^{1}H NMR spectra were recorded on AVANCE 300 MHz spectrometers stiffy Brucer in DMSO-d_6 as an internal standard. Elemental analyses were performed on a Perkin-Elmer analyzer. All the compounds were recrystallized from propan-2-ol. Chemicals for synthesis were purchased from Merck Co or Fluka Lab. and used without purification. Purity of the compounds was checked by thin layer chromatography (TLC).TLC was performed on commercial Merck SiO_2 plates with chloroform-methanol (10:2) solvent system and visualization under UV light at 254 nm.

The physical data of new compounds are shown in Table 1, whereas their spectral data are provided underneath Table 1.

^{1}H NMR (DMSO-d_6); (ppm) for:
Comp.I: 6.65-6.90 (m.9H.CH_{arom});3.52-3.80 (m.4H.2CH_2),
Comp.III: 7.50-7.85 (m.8H.CH_{arom}); 3.33-3.60 (m.4H.2CH_2);
Comp.IV: 7.10-7.30 (m.7H.CH_{arom}); 3.68-3.90 (m.4H.2CH_2),
Comp.V: 7.11-7.16 (m.9H.CH_{arom}); 3.52-3.80 (m.4H.2CH_2) ;2.29-2.41 (m.4H.2CH_2)

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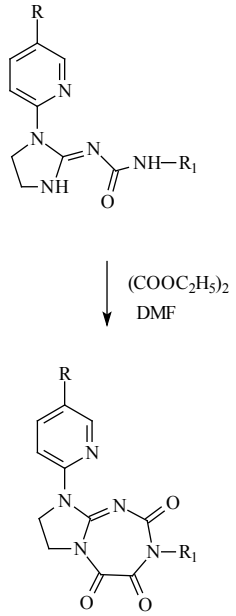

R = H, NO_2 R_1 = C_6H_5, 3-ClC_6H_4, $CH_2CH_2C_6H_5$

Scheme 1. Synthetic route to small molecules (I-V) under study

Table 1. The physical and spectral data of new compounds

Comp.	R R_1	Formula (mol.wght.)	M.p. (°C) Yield (%)	Analyses (calcd/found)			
				% C	% H	% Cl	% N
I	H C_6H_5	$C_{17}H_{13}N_5O_3$ 367.33	235-37 36	55.59 55.53	3.57 3.60		21.78 21.60
II	4-NO_2 C_6H_5	$C_{17}H_{12}N_6O_5$ 380.33	253-55 40	53.67 53.59	3.18 3.16		23.00 23.02
III	H 3-ClC_6H_4	$C_{17}H_{12}ClN_5O_3$ 369.78	234-36 42	55.22 55.24	3.27 3.27	9,59 9,67	21.63 21.66
IV	4-NO_2 3-ClC_6H_4	$C_{17}H_{11}ClN_6O_5$ 414.48	203-05 32	49.26 49.20	2.68 2.67	8.55 8.58	20.28 20.00
V	H $CH_2CH_2C_6H_5$	$C_{19}H_{17}N_5O$ 363.38	218-20 40	62.80 62.82	4.72 4.77		19.27 19.20

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