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NOTE

Synthesis of New Piperazino Oxadiazoles as Antiparkinsonian Agents

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Some novel piperazino oxadiazoles have been synthesised and their biological activity have been evaluated. These compounds exhibited moderate to good antiparkinsonian activity.

Key Words: Piperazine, Oxadiazole, Antiparkinsonian activity.

Piperazine and its derivatives have been found to be associated with a wide range of biological properties such as antiinflammatory, antibacterial, antifungal, anticonvulsant activities[1-3]. Oxadiazoles are also known for antiparkinsonian, antitremor, antirigidity and antihypokinetic activities[4]. This study prompted us to synthesise some new piperazino oxadiazoles and to evaluate their biological activity. Compound **III** on reaction with $FeCl_3$ in acetic acid underwent oxidative intra molecular cyclization to yield 1,4-di-(5-aryl-1,3,4-oxadiazole-2-yl-methyl)piperazine.

Piperazine (**I**) was converted into 1,4-di-piperazine acetic acid hydrazide (**II**) on reaction with chloroacetic acid and hydrazine hydrate, respectively by the known procedures[5].

1,4-Piperazine acetic acid arylidene hydrazide (III): An equimoler (0.01 mol) mixture of **II** and an appropriate aryl aldehyde in ethanol containing acetic acid (0.5 mL) was refluxed for 4 h. The excess of solvent was distilled off and residue kept in the cold. The solid separated was filtered, washed and recrystallized to give **III**. m.p. 138 ºC, yield 78 % IR (KBr, ν_{max}, cm^{-1}): 1640 (C=N), 3300 (NH), 1680 (C=O) and 2910 (CH_2).

1,4-(1,3,4-Oxadiazol-2-yl-methyl)piperazine (IV): To a solution of **III** (0.01 mol) in warm glacial acetic acid (10 mL) was added ferric chloride (2 g) in water while shaking. The mixture was stirred for 2 h and diluted with water kept at room temperature for 2 days. The solid thus separated was filtered and washed with water, dried and recrystallized from aqueous ethanol to give **IV** (**Scheme-I**). IR (KBr, ν_{max}, cm^{-1}): 1640 (C=N), 1310 (C-N), 1610 (N=N).

Biological activity: It was determined in albino mice and rats of either sex. The number of animals in each group was 6. All the synthesised compounds were tested by the known method of evaluation of antiparkinsonian activity[4]. The results are given in Table-1.

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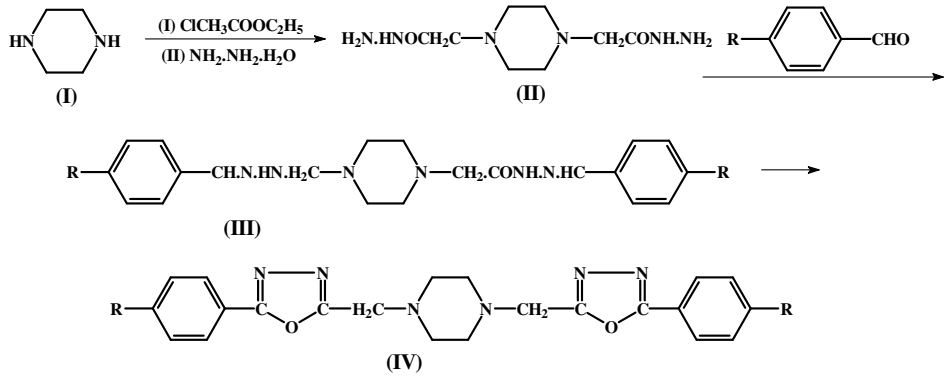

Scheme-I

TABLE-1
CHEMICAL CHARACTERIZATION OF THE COMPOUNDS

Comp. no.	R	m.p. (ºC)	Yield (%)	m.f.	Nitrogen (%) Found	Nitrogen (%) Calcd.	Oxotremorine induced in mice (0.5 mg/kg)
$\mathbf{IV_a}$	-H	168	77	$C_{22}H_{22}N_6O_2$	20.9	20.7	2.5 ± 0.23
$\mathbf{IV_b}$	-CH_3O	188	69	$C_{24}H_{26}N_6O_4$	19.5	19.4	2.7 ± 0.00
$\mathbf{IV_c}$	-Cl	196	72	$C_{22}H_{20}N_6O_2Cl_2$	20.1	20.1	2.3 ± 0.22
$\mathbf{IV_d}$	2-OH	133	78	$C_{22}H_{22}N_6O_4$	20.0	20.1	2.2 ± 0.22
$\mathbf{IV_e}$	-NO_2	194	81	$C_{22}H_{20}N_8O_6$	21.6	21.9	2.0 ± 0.21
$\mathbf{IV_f}$	-Br	142	73	$C_{22}H_{20}N_6O_2Br_2$	15.3	15.5	2.2 ± 0.19
$\mathbf{IV_g}$	-NH_3	183	72	$C_{22}H_{26}N_6O_2$	23.7	23.5	2.0 ± 0.22

The various substituted piperazino oxadiazoles have been synthesized in good yield, melting points were taken in open capillary tubes and are uncorrected. Synthesized compounds were checked for their purity on silica gel G. The structure of all the synthesized compounds have been established on the basis of spectral data and elemental analysis. IR spectra in KBr were recorded on Perkin-Elmer 157 spectrophotometer. It has been observed that the compound $\mathbf{IV_c}$, $\mathbf{IV_e}$, $\mathbf{IV_g}$ showed better antiparkinsonian activity while other compounds showed moderate activity.

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