SYNTHESIS OF BIOLOGICALLY ACTIVE 1-(ARYLIDENE-AMINO-ETHYL)-2-METHYL/PHENYL-4-(BENZYLIDENE)-IMIDAZOLIN-5-ONES

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ABSTRACT

1-(Arylidene-amino-ethyl)-2-methyl/phenyl-4-(benzylidene)-Imidazolin-5-ones [R = CH_3, C_6H_5; R_1 = C_6H_5, $C_6H_5CH = CH$, 3-CH_3O(4-CH_3O)-C_6H_3, 4-$CH_3O.C_6H_4$, 3-CH_3O-(4-HO)-C_6H_3, 4-$(CH_3)_2$.N-C_6H_4] were synthesised in 58-70% yield by the condensation of 2-methyl/phenyl-4-(benzylidene)-oxazolin-5-one and ethylenediamine in pyridine, followed by reaction with appropriate aldehyde in ethanol containing a few drops of glacial acetic acid. The compounds were screened for their CNS activity. The compounds were non-toxic. Their ALD_{50} ranged from 681 to 1000 mg/kg, intraperitoneally.

INTRODUCTION

THE benzylidene imidazolinone chemistry with its diverse biological properties like central nervous system depressant[1], anticonvulsant[2], and monoamine oxidase inhibitor[3] has received importance in recent years. The benzylidene imidazolinones has also been reported to possess the analgesic and muscle relaxant properties[4]. The structural modification with pharmacologically active grouping has shown excellent results in pharmacology. To extend the scope and validity of these observations, a few benzylidene imidazolinone derivatives have been synthesised to get compounds having pronounced central nervous system activity as well as potency.

EXPERIMENTAL

2-Methyl/phenyl-4-(benzylidene)-oxazolin-5-ones:

The procedure of Vogel[5] and Niederl *et. al*[6]., was used to synthesise the required oxazolin-5-ones.

1-(Amino-ethyl)-2-methyl/phenyl-4-(benzylidene)-imidazolin-5-ones:

A mixture of 2-methyl/phenyl-4-(benzylidene)-oxazolin-5-one (0.01 mole) and ethylenediamine (0.01 mole) in pyridine (30 ml) was heated under reflux for 8 hr and the solvent was distilled off under reduced pressure. The crude product was diluted with acidified water and allowed to stand for 4 hr at room temperature. The precipitate was filtered, washed with water and recrystallised from ethanol.

The comparison of I.R. spectra, with that of 2-methyl/phenyl-4-(benzylidene)-oxazolin-5-one indicated the absence of characteristic absorption band at 1755 cm position assigned for >C=O in γ-azlactone. The presence of sharp absorption peaks at 1690–1680 cm^{-1} (carbonyl stretching in -C(=O)-N-) and two sharp bands at 3450 10 cm^{-1} (N—H stretching vibration in NH_2) supported the structure of the compound.

1-(Arylidene-amino-ethyl)-2-methyl/phenyl-4-(benzylidene)-imidazolin-5-ones:

A mixture of 1-(amino-ethyl)-2-methyl/phenyl-4-(benzylidene)-imidazolin-5-one (0.01 mole), appropriate aldehyde (0.01 mole) and ethanol (50 ml) containing a few drops of glacial acetic acid was refluxed on a waterbath for 4 hr. The ethanol was distilled off and the crude product was washed with water, filtered and then washed with petroleum ether (b.p. 60–80° C) by trituration. The solid obtained was washed with ether. It was recrystallised from ethanol. The compounds thus synthesise are presented in table 1.

I.R. Spectra (KBr):

The presence of absorption bands at 1630 ± 10 cm^{-1}(for, ring C = N), 1690 ± 10 cm^{-1}(for ring N-C(=O)-group), 1600 ± 10 cm^{-1}(for C = C stretching), 3000 ± 10 cm^{-1}(-CH_2-stretching) supported the validity of compounds.

N.M.R. Spectra ($CDCL_3$):

The compound No. 10 showed spectrum, at δ 7.10 (1H of -OH group), δ 2.05 (3H of CH_3 group), δ 2.25 (4H of -CH_2-group), δ 7.55 (1H of CH =, arylidene), δ 6.85 (9H of aryl substitution), δ 7.65 (1H of -N = CH). It is compatible with the assigned structure.

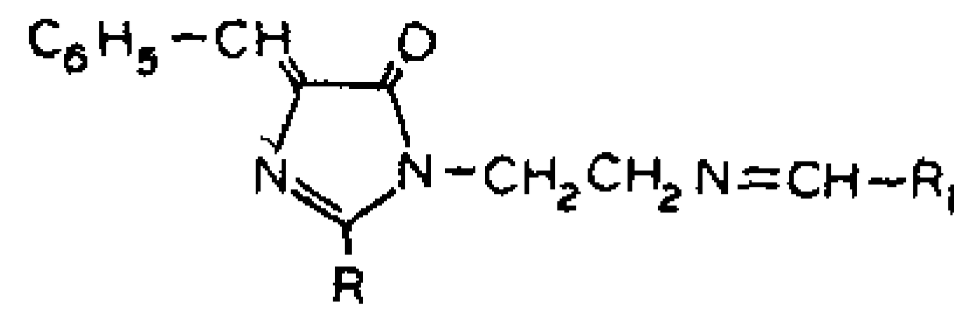
BIOASSAY

Approximate lethal dose (ALD_{50}) determination:

The method of Weil[7] was followed for this study.

TABLE 1

1-(Arylidene-amino-ethyl)-2-methyl/phenyl-4-(benzylidene)-imidazolin-5-ones



Sl. No.	R	R_1	Molecular formula	Melting Point °C	Nitrogen analysis %		ALD 50 (mg/kg)	Gross central nervous system activity: Special tests at 1/5th of the ALD 50			
					Calcd.	Found	i.p.	SMA	React.	Resp.	Writhing
1.	C_6H_5	C_6H_5	$C_{25}H_{21}N_3O$	159–60	11.08	11.00	>1000	↑	↑	↑	(–)
2.	C_6H_5	$4-CH_3O.C_6H_4$	$C_{26}H_{23}N_3O_2$	179–80	10.27	10.13	1000	↑	↑	↑	(+)
3.	C_6H_5	$C_6H_5CH\ \ CH$	$C_{27}H_{23}N_3O$	170	10.37	10.00	1000	↑	↑	↑	(–)
4.	C_6H_5	$4-HO(3-CH_3O)-C_6H_3$	$C_{26}H_{23}N_3O_3$	116	9.88	9.53	>1000	↑	↑	(–)	(–)
5.	CH_3	$4-CH_3O.C_6H_4$	$C_{21}H_{21}N_3O_2$	169	12.10	11.95	>1000	↓	↓	↓	(–)
6.	CH_3	C_6H_5	$C_{20}H_{19}N_3O$	108–9	13.25	13.05	1000	↓	↓	↓	(–)
7.	CH_3	$4-CH_3O(3-CH_3O)-C_6H_3$	$C_{22}H_{23}N_3O_3$	155	11.14	11.10	681	↑	↑	↑	(–)
8.	CH_3	$4-HO(3-CH_3O)-C_6H_3$	$C_{21}H_{21}N_3O_3$	112	11.57	11.41	>1000	↑	↑	↑	(–)
9.	CH_3	$4-(CH_3)_2N-C_6H_4$	$C_{22}H_{24}N_4O$	105	15.56	15.61	1000	↓	↓	↓	(–)
10.	CH_3	$4-HO.C^6H_4$	$C_{20}H_{19}N_3O_2$	134–35	12.61	12.17	681	↑	↑	↑	(+)

The compounds were recrystallised from ethanol. The yield percentage ranged from 58–70%.
↑ = increase, ↓ = Decrease; (+) = Presence; (—) = uneffected; > = Greater than.
SMA = spontaneous motor activity; Resp. = Respiration rate; React. = Reactivity to external influences.

Graded doses of the compounds were administered intraperitoneally in groups of four mice each. The dose of compound killing two animals out of four was taken as its ALD_{50}.

Gross behavioural effects:

The graded doses of the compounds were administered intraperitoneally in groups of five mice each. After the administration of a particular compound, the animals were observed for the resulting behavioural effects. If any like spontaneous motor activity (SMA), ataxia, loss of righting, pinna and corneal reflexes, straub tail and convulsions etc., in order to establish whether a particular compound had a stimulant effect, depressant effect or no effect on central nervous system.

Result And Discussion

The compounds recorded in table 1 were screened for the activity of their central nervous system. All the compounds were non-toxic. Their ALD_{50} ranged from 681 to > 1000 mg/kg, i.p. The compound Nos. 1, 2, 3, 4, 7, 8 and 10 increased the SMA and reactivity to external influences indicating the stimulant nature of these compounds. Compound Nos. 5, 6 and 9 were CNS-depressant. Compound Nos. 2 and 10 showed the presence of writhing (twisting of belly).

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NITROGEN FIXATION BY BLUE-GREEN ALGAE ASSOCIATED WITH DEEPWATER RICE

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ABSTRACT

A study of ^{15}N dilution and $^{15}N_2$ gas incorporation by deepwater rice demonstrated that blue green algae epiphytic on the aquatic tissues of deepwater rice could fix molecular nitrogen and a part of the fixed nitrogen was transferred to the aerial portions that were not exposed to $^{15}N_2$ gas.

Introduction

Farmers growing deepwater or floating rice could neither derive the benefit from short-stature, high yielding rice varieties, nor apply chemical fertilizer. In comparison to irrigated rice or shalow-water rainfed rice, the improvement of rice varieties and cultural method has ben neglected. Yields as low as 1 ton per ha are fairly common; yields higher than 3 tons per ha are seldom obtained[1].

Because the ratio of straw weight to grain weight is four or more due to long stems and growth period, deepwater rice can accumulate considerable biomass despite low grain yield. Farmers have been growing deepwater rice without nitrogen fertilizer, but still considerable biomass production has been obtained. Little is known about the sources of nitrogen to support such biomass without nitrogen fertilizer.

From the nodes under water, clusters of roots grow. Often the roots in the soil are rotted. Aquatic roots are suspected to have the ability to absorb nitrogen from the floodwater, but the extent of this ability is not known; neither is the contribution of biological nitrogen fixation to its nitrogen nutrition.

Studies of epiphytic N_2-fixation in rice and weeds a shallow-water rice field by Roger *et al*[2] and Kulasoo-