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Bairy Padma
University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Sammaiah Gadea
University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Corresponding Author:
Bairy Padma
University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Synthesis, characterization and evaluation of antioxidant activity of N-([1, 3, 4- Oxadiazino [6, 5-b] substituted indol-2-yl methyl) aniline

Bairy Padma and Sammaiah Gadea

Abstract
In the present study, a novel series of N-([1, 3, 4- Oxadiazino [6, 5-b] substituted indol-2-yl methyl) aniline have been synthesized in good yields and characterized by IR, NMR and mass spectral analyses. Compounds were evaluated for their antioxidant activity by standard DPPH assay method. Among the series the compounds VIIc, VIIo and VIIm, are potent antioxidant and remaining compounds showed significant antioxidant activity. Ascorbic acid was taken as standard drug.

Keywords: Synthesis, characterization, antioxidant activity, N-([1, 3, 4- Oxadiazino [6, 5-b]

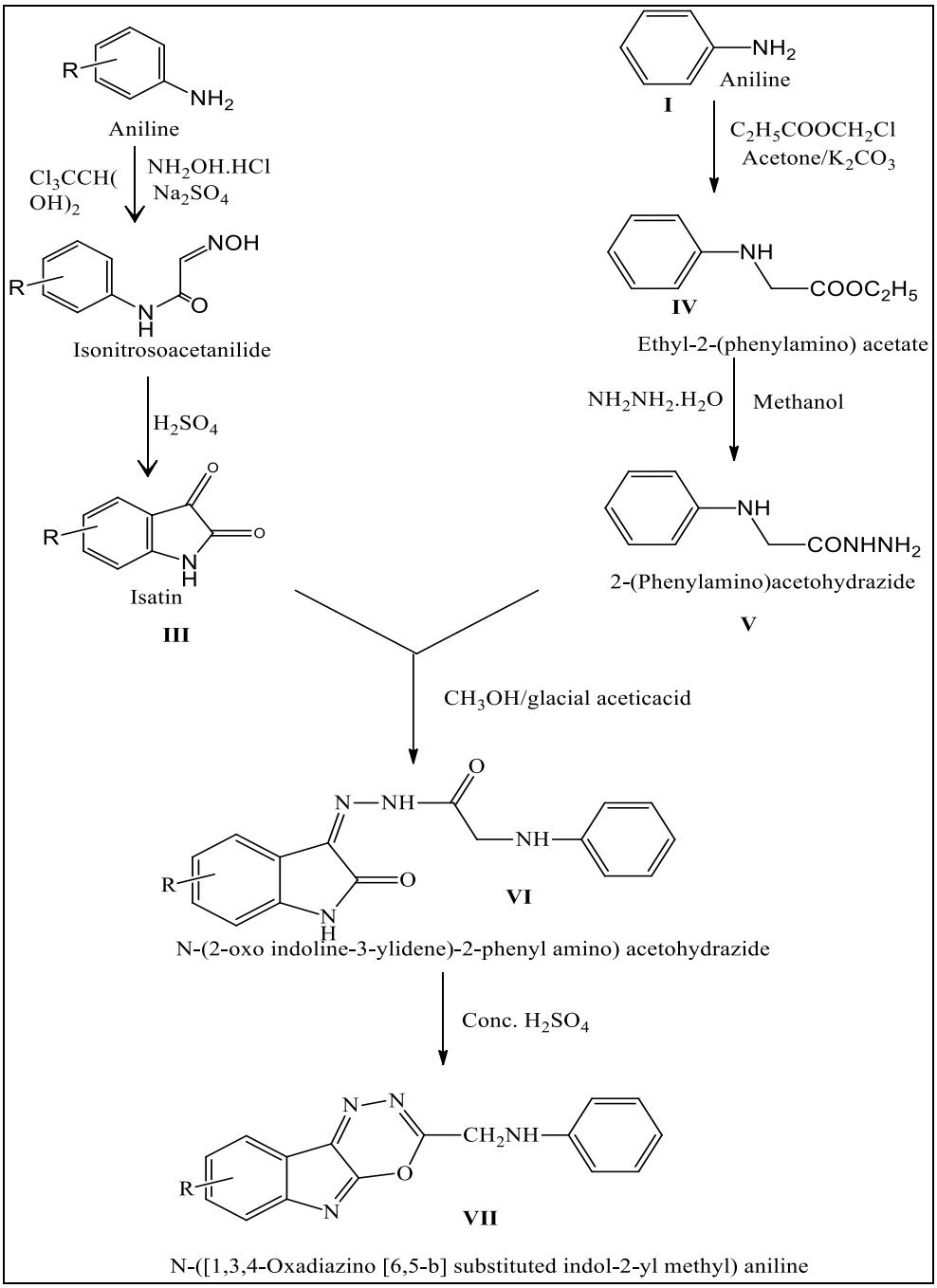
Introduction
Isatin [1] and its derivatives have led to extensive use of these compounds as key intermediates in organic synthesis. Isatin is a core constituent of many alkaloids and drugs as well as dyes, pesticides and analytical reagents. Several of their derivatives are also reported to exhibit a variety of biological and pharmacological activities, such as antimicrobial [2], antiviral [3], antimycobacterial [4], anti-inflammatory [5] and anticonvulsant [6] activities. Hence, this field has-ever-growing importance resulting in the development of new isatins. Keeping in view of an array of applications it has been considered worthwhile to synthesize some new biologically potent isatins with an aim to screen for antioxidant activity. The synthesized compounds has been purified and characterized with the help of their analytical and spectral (IR, ^{1}HNMR & Mass) data.

Chemistry
The new N-([1, 3, 4 – Oxadiazino [6,5-b] substituted indol-2-yl methyl) aniline have been synthesized by following Scheme-I and Characterized by IR,NMR and Mass data. Physical data of new compounds are presented in Table-1.

General Procedure for the synthesis of N-([1, 3, 4- Oxadiazino [6, 5-b] substituted indol-2-yl methyl) aniline

a. Synthesis of Ethyl-(2-phenyl amino) Acetate (IV)
Aniline (I, 0.01 mol) and ethyl chloro acetate (II, 0.01 mol) were taken into a round bottomed flask (250 ml). The reaction mixture was refluxed in dry acetone in presence of anhydrous potassium carbonate for 7 hours on water bath. Progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed to a possible extent by distillation under reduced pressure and cooled. The resultant product was triturated with ice cold water, filtered, washed with cold water and dried. It was purified by recrystallization from petroleum ether to get a brown crystalline solid m.p. 55 ^{o}C.

b. Synthesis of 2-(phenyl amino) acetohydrazide (V)
A mixture of ethyl-(2-phenyl amino) acetate (IV, 0.01mol) and hydrazine hydrate (0.02 mol) were taken into a RB flask and dissolved in minimum quantity of alcohol. The reaction mixture was refluxed on water bath for 4 hours. Progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed to a possible extent by distillation under reduced pressure and cooled. The resultant product was triturated with ice cold water, filtered, washed with cold water and dried. The compound was recrystallized form methanol to get a colourless crystalline solid yield 95%, mp. 125-127 ^{o}C.



Scheme-I

c. Synthesis of N-(2-oxo indoline-3-ylidene)-2-phenyl amino) acetohydrazide (VI)

2-(Phenyl amino) acetohydrazide **(**V, 0.001 mol) and an appropriate isatin (III 0.001 mol) was heated under reflux in alcohol for 2 hours. The solvent was concentrated and the product thus separated was filtered and purified by recrystallization from suitable solvent.

d. Synthesis of N-([1,3,4-Oxadiazino [6,5-b] substituted indol-2-yl methyl) aniline (VII)

A pure compound of N-(2-oxo indoline-3-ylidene)-2-phenyl amino) acetohydrazide (VI, 0.01mol) was refluxed for 4 hrs at 0-5 ^{0}C in the presence of concentrated sulphuric acid. Progress of the reaction was monitored by TLC. The resulting products was filtered and washed with distilled water. The new compound was purified by recrystallization from aqueous ethanol.

Spectral characterization data of the compound (VIIf)

IR (KBr, Cm^{-1}) ν

3453 (-NH of Aniline), 3004 (C-H, aromatic) 2912 (C-H of aliphatic), and 1594 (C=C, aromatic), 1409.80(C-N stretch).

^{1}H NMR (CDCl$_3$, 300 MHz, ppm) δ

4.99 (1H, -NH)**,** 3.94 (2H, CH_2) 6.95-7.10 (3H, Aromatic), 7.70-7.92 (5H, Aromatic).

Mass spectrum

Recorded its heaviest ion at m/z 294, which is in agreement with the mass (mol.wt.) of its assigned structure.

Thus based on the spectral data the compound has been characterized as N-([1, 3, 4- Oxadiazino [6, 5-b] 5-fluoro-indol-2-yl methyl) aniline (VIIf; R= F).

Antioxidant activity

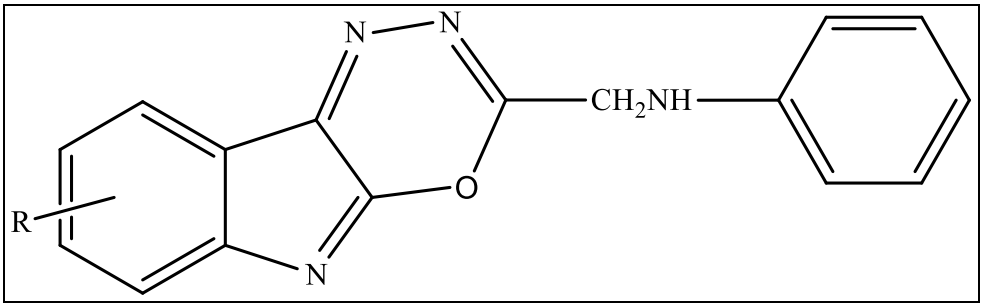
DPPH radical scavenging method

Blois [7] showed that α, α-diphenyl-β-picryl hydrazyl radical (DPPH) can be used for determining antioxidant activity. DPPH in ethanol shows a strong absorption band at 517 nm and the solution appears to be deep violet in color. As the DPPH radical is scavenged by the donated hydrogen from the antioxidant, the absorbance is diminished according to the stoichiometry. Briefly, 0.5 mL of DPPH solution (0.2 mM) was mixed with 0.1 mL of various concentrations of test compounds and 1.5 mL ethanol was added. The mixture was kept at room temperature for 30 min, and then the absorbance (OD) was read at 517 nm against blank. The % reduction of free radical concentration (OD) with different concentration of test compounds was calculated and compared with standard, ascorbic acid. The results were expressed as IC_{50} values (the concentration of test required to scavenge 50% free radicals).

Results and Discussion

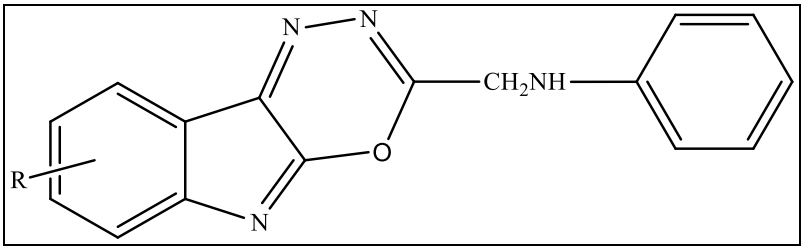
The antioxidant activity of all the synthesized compounds performed using DPPH method and the results given in Table 2. The values are expressed in IC_{50} that is, ability of the test compound required to decrease the concentration of test free radical by 50%. Among all the test compounds, compounds VIIc, VIIo, VIIm, exhibited more potent antioxidant activity against DPPH. Remaining compounds showed mild to modetare antioxidant activity. It is proposed that DPPH may be scavenged by an antioxidant through donation of hydrogen ($H^{\cdot}$) to form a stable DPPH-H molecule which does not absorb at 517 nm. Thus the results show that synthesized compounds possess antioxidant activity. It was observed that the test compounds with electron withdrawing groups (halogens) on the aromatic ring favors anti-oxidant activity.

Table 1: Physical data of N-([1, 3, 4- Oxadiazino [6,5-b] substituted indol-2-yl methyl) aniline



S. No	Compound	Substituent (R)	Mol. Formula	Mol. Wt.	m.p (ºC)	% Yield
1	VIIa	H	$C_{16}H_{12}N_4O$	276	192-194	62
2	VIIb	5-Cl	$C_{16}H_{11}N_4OCl$	310	224-226	70
3	VIIc	7-Cl	$C_{16}H_{11}N_4OCl$	310	224-226	70
4	VIId	5-CH_3	$C_{17}H_{14}N_4O$	290	235-237	54
5	VIIe	7-CH_3	$C_{17}H_{14}N_4O$	290	235-237	51
6	VIIf	5-F	$C_{16}H_{11}N_4OF$	294	276-278	84
7	VIIg	7-F	$C_{16}H_{11}N_4OF$	294	276-278	84
8	VIIh	5-Br	$C_{16}H_{11}N_4OBr$	354	310-312	82
9	VIIi	7-Br	$C_{16}H_{11}N_4OBr$	354	310-312	82
10	VIIj	5-NO_2	$C_{16}H_{11}N_5O_3$	321	269-271	74
11	VIIk	7-NO_2	$C_{16}H_{11}N_5O_3$	321	269-271	72
12	VIIl	5-OH	$C_{16}H_{12}N_4O_2$	292	256-258	69
13	VIIm	7-OH	$C_{16}H_{12}N_4O_2$	292	256-258	70
14	VIIn	5-COOH	$C_{17}H_{12}N_4O_3$	320	222-224	61
15	VIIo	5-$COOC_2H_5$	$C_{19}H_{16}N_4O_3$	348	216-218	59

Table 2: Antioxidant activity of N-([1,3,4- Oxadiazino[6,5-b] substituted indol-2-yl methyl) aniline



S.No	Compound	R	IC_{50} (µg/ml)
1	VIIa	H	72
2	VIIb	5-Cl	25
3	VIIc	7-Cl	22
4	VIId	5-CH_3	55
5	VIIe	7-CH_3	54
6	VIIf	5-F	103
7	VIIg	7-F	106

8	VIIh	5-Br	86
9	VIIi	7-Br	75
10	VIIj	5-NO_2	118
11	VIIk	7-NO_2	115
12	VIIl	5-OH	58
13	VIIm	7-OH	37
14	VIIn	5-COOH	46
15	VIIo	5-$COOC_2H_5$	33
16	Standard	Ascorbic Acid	5.95

Conclusions

A series of N-([1, 3, 4- Oxadiazino [6, 5-b] substituted indol-2-yl methyl) aniline has been synthesized as shown in Scheme 1. The synthesized compounds were subjected to antioxidant activity, amongst the compounds tested substituent with an electron withdrawing group on the aromatic ring showing significant activity than the other substituted compounds.

References

1. Erdmann, J. Prakt. Chem. 1841, 24, 1.
2. Pandeya SN, Sriram D. Synthesis and screening for antibacterial activity of Schiff's and Mannich bases of Isatin and its derivatives. Acta. Pharm. Turc. 1998; 40:33-38.
3. Verma RS, Nobles W. Lantiviral, antibacterial and antifungal activities of isatin-N-Mannich bases. J. Pharm. Sci. 1975; 69:881-882.
4. Gao F, Yang H, Lu T, Chen Z, Ma L, Xu Z, *et al.* Design, synthesis and anti-mycobacterial activity evaluation of benzofuran-isatin hybrids Eur J Med Chem. 2018; 159:277-281.
5. Sridhar SK, Sreenivasulu M. Synthesis, Analgesic and Anti-inflammatory activity of N-Mannich bases of (4'-Substituted)-2-Phenylindoles. Indian drugs. 2001; 38:531-34.
6. Varma M, Pandeya SN, Singh KN, Stables JP. Anticonvulsant activity of Schiff bases of isatin derivatives. Acta Pharm. 2004; 54:49-56.
7. Blois MS. Antioxidant determinations by the use of a stable free radical. Nature. 1958; 181(4617):1199-1200.