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Synthesis and Characterization of Various Alkyl, Aryl and Hetero Aryl Substituted Hydrazines and Study of their Biological Activity

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ABSTRACT

Due to the presence of N-N linkage hydrazines are well-known for their diverse biological activity.N-N linkage has been used as a key structural motif in various bioactive agents. A series of aryl, alkyl and hetero aryl substituted hydrazine derivatives has been synthesized, for this diazotization of alkyl, aryl amines has been done, followed by reduction with stannous chloride or sodium sulfite. All synthesized compounds were characterized by elemental analysis, IR, 1H-NMR, Mass spectra and their biological activity has been studied.

Keywords: Hydrazine derivatives, N-N linkage,Biological activity, Diazotization.

INTRODUCTION

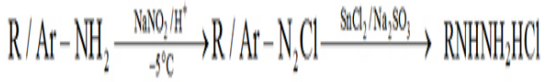
Among the nitrogen-nitrogen bond containing chemical the hydrazines are well-known for their diverse biological activity and as therapeutic agents in medicines. Many hydrazine derivatives are known to exhibit significant biological activity and several compounds with hydrazine moiety were shown to be effective for treatment of tuberculosis, Parkinson's disease and hypertension[1].Hydrazines shows neuroprotective, antitumor antidepressant and antimicrobial properties[2,3,4,5].

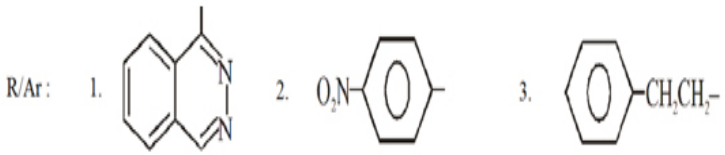
The hydrazine moiety has been used for modification of peptides[6].Azapeptides hydrazine based peptidomimetics, were found to be potent against hepapititas, AIDS & SARS[7,8,9].Hydrazines derivatives occur naturally in tobacco and mushrooms,p-tolylhydrazine(bioactive molecule) isolated as a degradation product from the mushroom Agaricus bisporus, was found to be highly active compared to 5-flourouracil in vitro anticancer studies [10].

Diacylhydrazines have been identified as one of the most important types of insect regulators[11-13]. Several commercial compounds, such as tebufenozide, methoxyfenozide, chromafenozide,and halofenozide, are all classified as diacylhydrazines, and all of these insecticides

affect the ecdysonereceptor complex, leading to precocious lethal molting, especially in caterpillars [14,15]. Diacylhydrazines have attracted significant attention because of their high insecticidal selectivity,simple structure, and low toxicity to vertebrates [13].

Aryl hydrazides and hydrazine compounds shows anticancer activity against 5 cancer cell lines namely A-549, SK-N-SH, HEP-2, PC-3 and MCF-7. Gallic acid hydrazide found to be most active,having high scores, indicating highest binding propensity towards the thymidylate synthase[16].





Scheme 1: Synthesis of Hydrazine Derivatives

MATERIALS AND METHODS

All the reactions were carried out with A.R. grade chemicals. The C.P. grade chemicals, whenever used, were purified by standard methods. All m.p. were determined on a Yanaco micro-melting point apparatus and were uncorrected. Elemental analysis was get done at CDRI Luckhnow. IR spectra were taken on a Perkin Elmer System 2000 FT-IR Spectrophotometer, in KBr pellets. EI-mass spectra were recorded on a VG Biotech Quattro 5022 spectrometer. 1H-NMR spectra were recorded on a Bruker AMX-500 in $CDCl_3$ and chemical shifts are given in ppm with TMS as internal standard .Silica gel was used for CC and silica gel 60 F-254 for TLC preparation. TLC optical rotations were measured using a Jasco DIP -370 Polarimeter in $CHCl_3$.

Table 1: physical characteristics and analytical data of the compounds investigated

Compound	Colour	Molecular mass g/Imole	Elemental Analysis				Melting Point °C	Molecular formula
			C%	H%	N%	O%		
1	Yellow Powder	160	60	5	35		172.50	$C_8H_8N_4$
2	Orange-red needle shaped crystal	153	47.05	4.5	27.4	20.9	156	$C_6H_7N_3O_2$
3	Clear Liquid	136	70.5	8.8	20.5		22, B.P.74	$C_8H_{12}N_2$

Table 2: IR spectral data of the compounds investigated in cm^{-1}

Compound	V_{N-H}	V_{N-N}	V_{C-H}	V_{C-C}	V_{C-N}	$V_{C=N}$
1	3304, 3411	1373	3000, 2976	1540, 1465	1289	1596, 1668
2	3322,3202	1377	3087	1532, 1501	1341, 1315	1600, 1559
3	3405	1395	3020, 2850	1610, 1118	1310	

Table 3: NMR and Mass spectral data of the compounds investigated

Compound	Mass Spectra m/z	NMR Spectra(ppm)
1	160	δ 9.25(d,J=1.8Hz,1H,),δ 8.05(m,J=7.4,1.7Hz,1H,aromatic),δ 7.91(m,2H),δ 7.88(m,2H,aromatic),δ 8.32(m,1H,aromatic),δ 4.73(2H,d,J=3.1Hz,NH_2) δ 4.58(1H,m,NH)
2	153	δ 8.14(m,J=8.4,1.4Hz,1H,aromatic),δ 7.7(m,J=8.4,1.6Hz,1H,aromatic) δ 7. 13(m,J=7.7,1.6Hz,1H,aromatic),δ 6.84(m,J=8.4,1.6Hz,1H,aromatic), δ 5.0 9(t,J=3.0Hz,0H,NH),δ 2.93(d,J=2.9Hz,1H,NH_2)
3	136	δ 2.07(d,J=3.5Hz,2H,NH_2),δ 2.84(tt,J=3.5,2.7Hz,1H,NH),δ 3.07(td,J=5.5, 2.6Hz,2H,CH_2),δ 2.74(tt,J=5.4,1.0Hz,2H,CH_2-C=C),δ 7.24(m,3H,aromatic),δ 7.29(m,2H,aromatic)

Synthesis of compounds

Alkyl,aryl and hetero aryl substituted hydrazine derivatives were synthesized.[17-19]

ANALYSIS

BIOLOGICAL ACTIVITY

All the synthesized compounds have been tested for their biological activity.

Compound 1 shows antihypertensive activity. It can be used to treat high blood pressure, which helps in preventing strokes, heart attacks and kidney problem. For thisNon-invasive (Tail cuff method) has been used.

Compound 2 shows anticancer activity against SK-N-SH (CNS) cancer cells.Thisactivity of the compounds have been test by MTT essay.

Compound 3 shows antidepressant activity . It is a non-selective momoamine oxidase (MAO) inhibitor commonly used to treat depression and panic disorder.It is checked by the behavioral despair test (porsolt –forced swimming test).

RESULTS and DISCUSSIONS

Compounds were synthesized from their respective amines. Synthesized compounds shows antihypertensive , antidepressant and anticarcinogenic activity.Compound 2 shows anticancer activity against SK-N-SH cancer cell line with IC_{50}= 29µg/ml.

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