Synthesis, Characterization and the Biological Activity of Some new a (Thiadiazolidine and Thiatetrazanonanes Hetrocbiyclic Derivatives from Azine

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Abstract

mixture of p-chlorobenzaldehyde with P-hydroxybenzaldehyde, Then was reacted with hydrazine sulphate in the presence of ammonia solution to synthesis Azin derivative (N) , by addition reaction of acetylchloride to azomethene groups and disodiumsulphide tp prepare new derivative of (1,3,4-thiadiazolidine), and bicycle rings (1,3,5,6,8-thiatetrazanonanes). (TLC) technique was used to follow the reaction and after purification of the prepared derivative the melting degrees were measured, the infrared (FTIR-spectra, 1H-NMR-Spectra, 13C-NMR-spectra). Some of these compounds were tested against bacterial activity via E-coli and staphylococcus.

Keywords: Hetrobicylic, Azine, thiadiazolidine, thiatetrazanonanes, Bacaterial activity.

1. Introduction

Azine has two meanings in chemistry: in heterocyclic chemistry, azines are aromatic six-membered rings containing one (pyridine) to six N atoms (hexazine). In alicyclic chemistry, azines are compounds resulting from the reaction of two molecules of identical carbonyl compounds symmetrical azines, or more commonly from the reaction of two different carbonyl compounds unsymmetrical azines with hydrazine. The compounds are called aldazines or ketazines depending on whether the carbonyl compound is an aldehyde or a ketone, respectively [1]. Azines that are N–N-linked diimines are 2, 3-diaza analogs of 1,3-butadiene. They are a class of compounds with interesting chemical properties and undergo a wide variety of chemical processes [2].

Azine compounds containing azomethine group (–CH=N–) are known as Schiff bases. [3] Hydrazones and azines are special class of compounds in the Schiff bases family. [4] Hydrazones are used as intermediate in synthesis, as functional groups in metal carbonyls, as herbicides, insecticides and plant growth regulators [5]. They also act as drug and possible a ligands for metal complexes, organocatalyzed and also are used for the synthesis of heterocyclic compounds [6]. Azines have also been extensively used in bond formation reaction polymerization, and in the design of liquid crystal [7].

Thiadiazolidine heterocycles containing nitrogen and sulfur are very interesting compounds in organic synthesis as well as in medicinal chemistry due to their significant biological and pharmacological properties [8, 9]. The sulfonylureas and cyclosulfamoyl urea's are an important class of compounds, the sulfonylureas derivatives are the first oral hypoglycemic agents which are known of their use for the treatment of type II diabetes [10]. In addition, these molecules exhibited other therapeutic uses such as ACAT inhibitors [11], herbicidal, antifungal [12], antimicrobial [13], and anticancer activities [14].

Thiatetrazanonanes, Synthesis of Fused Heterocycles Based on 1-Amino-1H-tetrazole-5-thiol and α,β-Unsaturated Aldehydes 8-Phenyltetrazolo [5,1-b][1,3,4] thiadiazepine was obtained as a result of intermolecular cyclization of 1-amino-1H-tetrazole-5-thiol and 3-phenyl-2-propynal. The reaction of α-bromocinnamaldehyde with 1-amino-1H-tetrazole-5-thiol led to the formation of -tetrazolo[5,1-b][1,3,4]thiadiazine , Erupian petant in biheterocycle contain tetrazoi-thaiol derivatives

In recent years tetrazole scaffolds have been attracted interest in the field of synthetic and medicinal chemistry research.). The newly synthesized of thio-1H-tetrazole derivatives are characterized by spectral characterization and screened for their antifungal activity. Among these, some of the newly synthesized compounds show potent antifungal activity [7].

The first synthesis of new Hetero icyclic Pentazanonane and Thiatetrazanonane from cyclizide azin derivatines

2. Experimental

Synthesis of bezaldazine (N)

4-(4chlorobenzylidene) hydrazineylidene) methyl) phenol

Amixture of p-chlorobenzaldehyde (7gm, 0.2mol) and p-hydroxy benzaldehyde (6.1gm, 0.2mol) with hydrazine sulphate (6.5gm, 0.2mol) in ammonia solution (20ml) in 100ml distilled water with stirring for (2hrs) then allowed to cool to room temperature and the solid product was filtered and recrystalyzed from ethanol as yellow-needle crystals

Synthesis (N1), N, N`-di acetyl-N, Ń-di-α-chlorobenzyl hydrazine

A suspension of acetylchloride (3.5ml, 4gm, and 0.05mol) in 50ml of dry benzene was added dropwise to asolution of benzaldazine (5.16gm, 0.02 mol) in 50ml of dry benzene with cooling and continuous stirring for (5hrs).

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the reaction process was followed up with TLC, purified by filtration and crystallized with absolute ethanol and aceton.

Synthesis (NZ) (1,1-(2-(4-chlorophenyl)-5-(4-hydroxy phenyl) 2-5-diphenyl-3,4-di acetyl-1,3,4-thiadiazolidine [15]

A mixture of compound (N1) (0.38gm, 0.001mol) and Sodium sulphide (0.6gm,0.0076 mol) in ethanol 50ml was stirred at room temperature for (8hrs). The reaction process was followed up with TLC. Then reaction mixture was poured into 100ml of ice-cooled distilled water and separated crystals purified by filtration and recrystallized from absolute ethanol.

Synthesis (NZ1) (4-(5-(4-chlorophenyl) -1, 3, 4-thiadiazolidine-2-yl) phenol-2, 5-diphenyl – 1, 3, 4-thiadiazolidine

A mixture of compound NZ (0.376gm, 0.001mol) in 10ml of 30% HCl was shaken at room temperature for (8hrs). Then the resulting mixture was made alkaline with sodium bicarbonate. The reaction process was followed up with TLC. Then purified by filtration and recrystallized from absolute ethanol.

Synthesis (NZ2) (1,1`-(1,8-bis(4-chlorophenyl) -4,5-bis(4-hydroxy phenyl) 6H-[1,3,4] thiadiazolo [3,4-α] [1,2,4,5] tetrazine -2,3(1H, 4H,)diyl)bis ethan-1-one

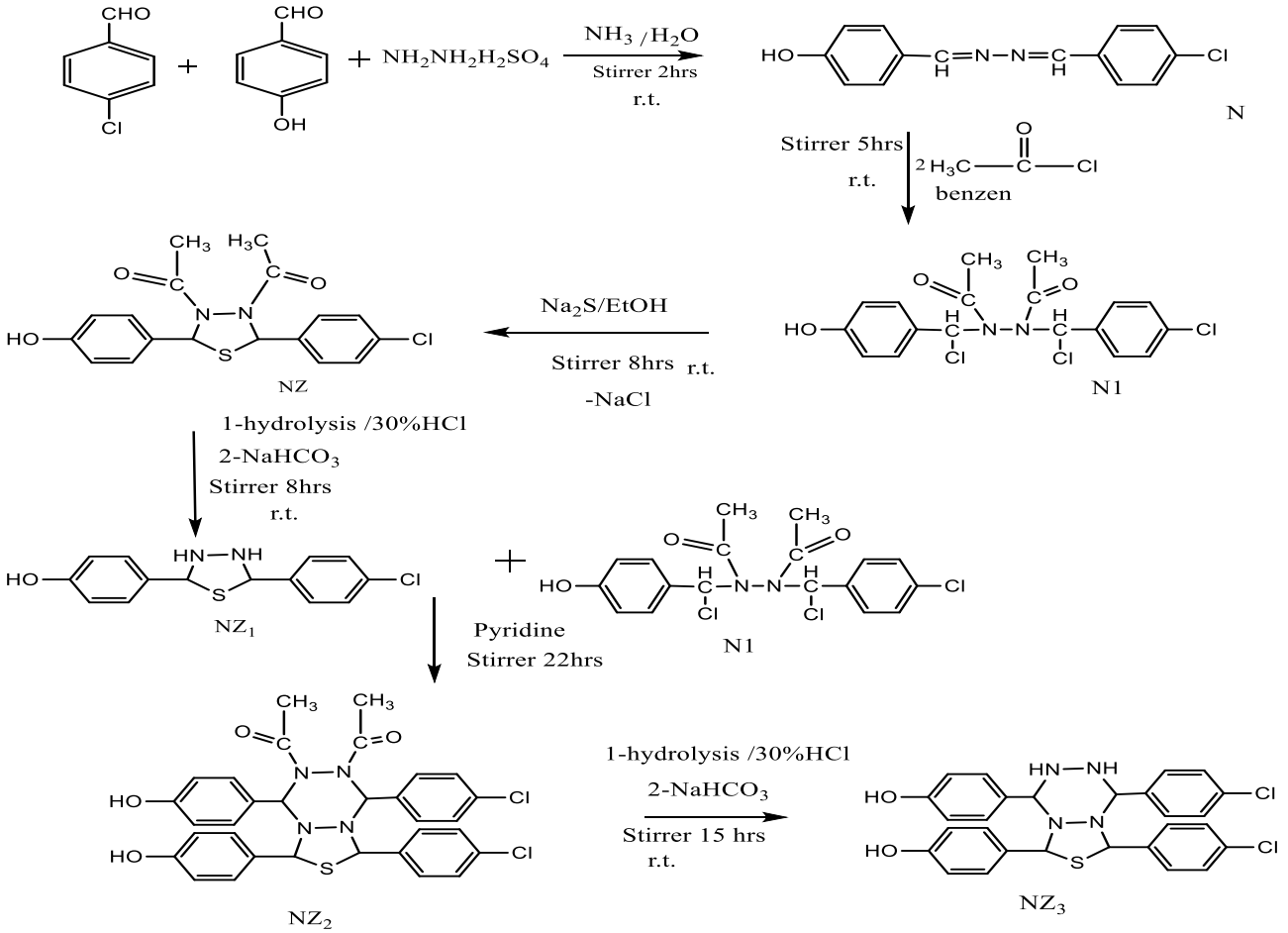
A mixture of N1 (0.38gm, 0.001 mol) and NZ1 (0.292gm, 0.001mol) in (30ml) pyridine was stirred at room temperature for 22hrs the reaction process was followed up with TLC. The reaction mixture was poured into 100ml of Ice-cooled distilled water-Purified by filtration and recrystallized from absolute ethanol.

Synthesis NZ3 (4,4'-(4,6-bis(4-chlorophenyl) tetrahydro-6H,8H-[1,3,4] thiadiazolo [3,4,α] [1,2,4,5] tetrazine-1,8-diyl) di phenol [16]

A mixture of compound NZ2 (0.635gm, 0.001 mol) in 30ml of 30% HCl was shaken at room temperature for 15 hrs. The resulting mixture was made alkline with sodium bicarbonate and the final product was fill and recrystallized from absolute.

Table 1: physical properties and other characteristics for the synthesized compounds

No	M.F	M.Wt	MP°C	Color	Rf	Yield%
N	C14H11N2O1Cl1	258	220	Yellow	0.66	90
N1	C18H17N2O3Cl2	380	227	Light – yellow	0.88	90
Nz	C18H17N2O3S1Cl1	376	219	Deep-Yellow	0.8	82
NZ1	C14H13N2O1S1Cl1	292	222	Pale Broun	0.75	75
NZ2	C32H28N4O4S1Cl2	635	230	Yellow	0.66	77
NZ3	C28H24N4O2S1Cl2	551	220	White	0.85	63



Scheme.1: Synthesis of compound (N-Nz3)

3. Results and Discussion

Identification (N), the FT-IR spectrum (Cm-1) figure (1) shows of at (OHphenolic 3446), (CHArom = 3047 – 3101), (CHAlph = 2941 – 2997), (C=N azin = 1664), (N – N = 1087), (C – Cl = 705)

HNMR the proton magnetic resonance spectrum of compound (N) showed the following signals. (OHsignals = 11.55 ppm), (CH=NAzin = 8.02 – 8.29 ppm), (Haromatic = multiplet signals at 7.45 – 7.94 ppm), DMSO = 2.52)

13C.NMR. the carbon magnetic resonance spectrum of compound (N) showed the following a signal at (156) refers to the carbon of (C-OH) another signal of appeared at (131) refers to carbon of the (CH=NAzin), the appearance of several signals refers to the carbon atoms in the aromatic rings at (117 – 125).

Identification (N1), the FTIR spectrum (cm-1) figure (2) showed of at (OHPhenolic = 3377), (CH Arom = 3047), (CH Alph = 2941 – 2997), (C=O Keton = 1759), (N-N= 1192) (C-Cl = 705)

H.NMR spectrum showed the following signals (OH signal at 11.5ppm), (Haromatic=multiplet signals at 7.05–7.94ppm), (CH-Cl singlet signal at 4.54ppm) (H aliphatic = singlet signals at 1.81) DMSO=2.51.

13C.NMR spectrum showed the following signals at (182) refers to the carbon of (C=O), another signal of appeared at (155) refers to carbon (C-OH), the appearance of several signal refers to carbon atoms in the aromatic rings at (112 – 130), the appearance of a signal at (77.4) refer to the (—CH—Cl) and signal at (64.1) refer to the (C-Cl) a signal appeared at (23.4) due to the carbon (CH3)

Identification (NZ), the FTIR Spectrum (Cm-1) figure (3) showed off at (OHphenolic = 3423),(CHArom = 3150),(CHAlph = 2910), (C=OKeton = 1666), (N-N = 1004), (C-S = 1138)

H.NMR spectrum showed the following signals. (OH singlet signal at 11.5 ppm), (Haromatic =multiplet signals at 7.12 – 7.31 ppm), (HS—CH(N)—Ph) singlet signal at 5.32 ppm) (Haliphatic = singlet signal at 1.92 ppm), DMSO=2.5)

13C.NMR spectrum showed the following signals.

A signal at (175) refers to the carbon of (C=O), A signal appeared at (155) related to the (C-OH). and signal at (130) belonged to the (C-Cl), the appearance of several signal refer to the carbon atoms in the aromatic rings at (112-127), another signal of appeared at (85) refers to carbon (HS—CH(N)—Ph) the appearance of signal at (24) due to the carbon (CH3) Al compounds measured in 13C-NMR spectroscopy appeared at (39-40) due to the solvent used for measurement dmos-d6.

Identification (NZ1), the FTIR Spectrum (Cm-1) figure (4) showed of at (OHphenolic=3417),(CHAromatic=3001),(C-S=1209), (HN-NH=1168),(C-Cl= 768).

Identification (NZ2), the FTIR Spectrum (Cm-1) figure (5) showed of at (OHphenolic = 3450),(CHAromatic = 3005),(CHAlpha = 2910), (C=OKeton = 1757), (C-S = 1213) , (N-N = 1166), (C-Cl = 778).

Identification (NZ3), the FTIR Spectrum (Cm-1) figure (6) showed of at (OHphenolic = 3406),(CHAromatic = 3005), (C-S = 1203) , (NH-NH = 1170), (C-Cl = 769).

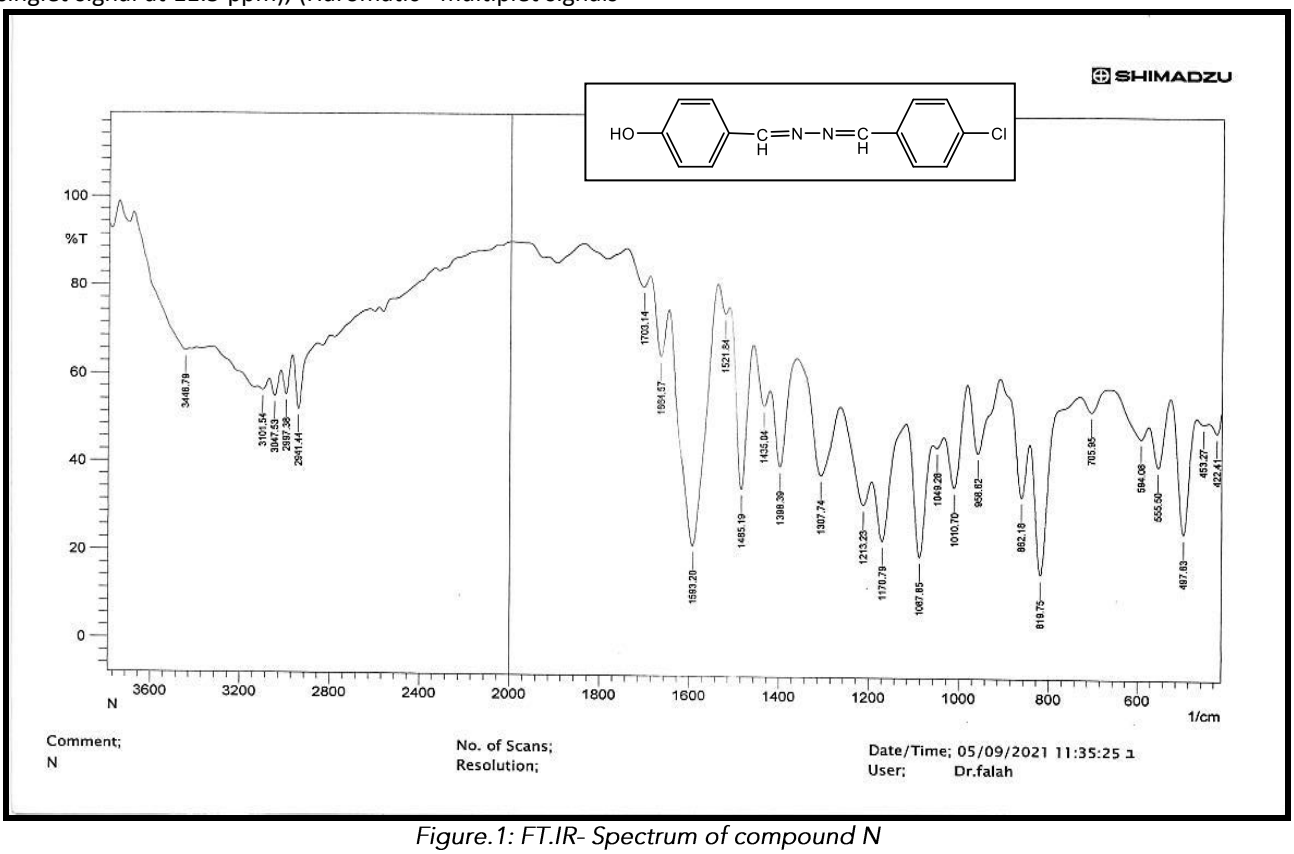


Figure.1: FT.IR- Spectrum of compound N

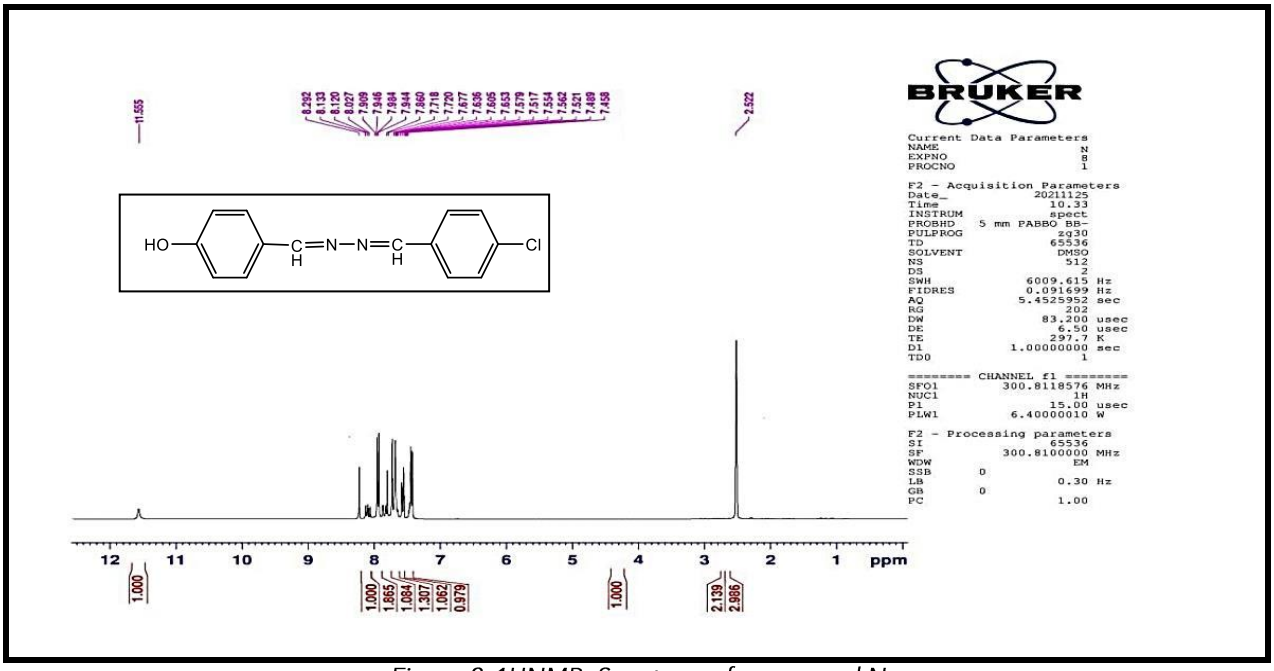


Figure.2: 1HNMR- Spectrum of compound N

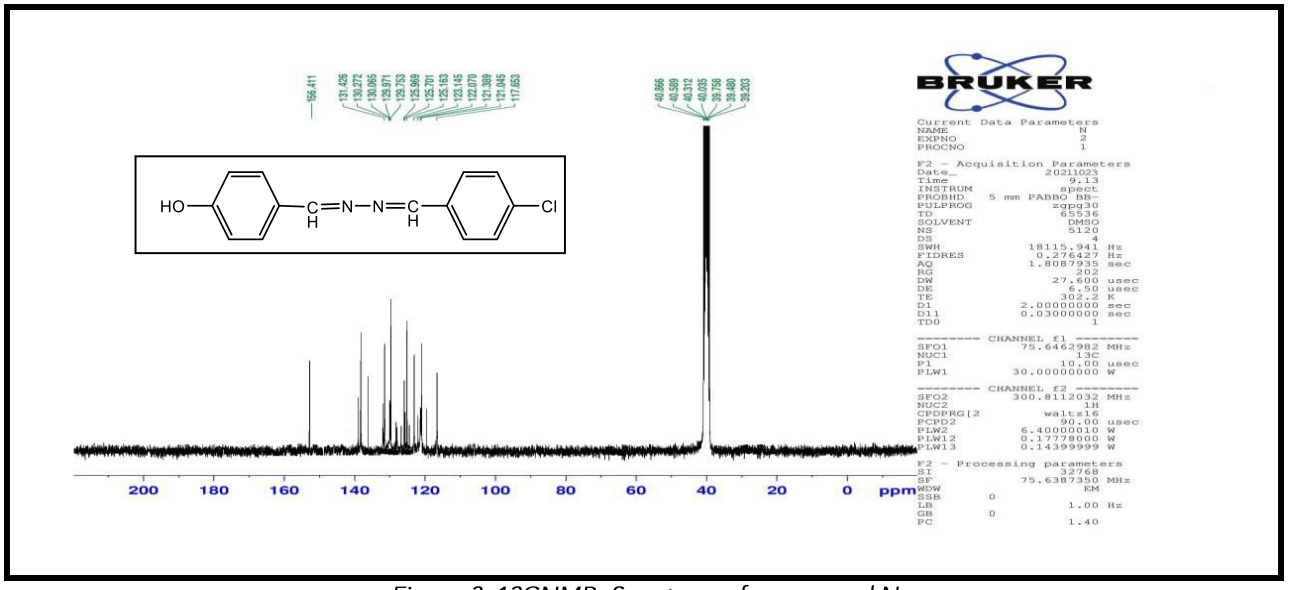


Figure.3: 13CNMR- Spectrum of compound N

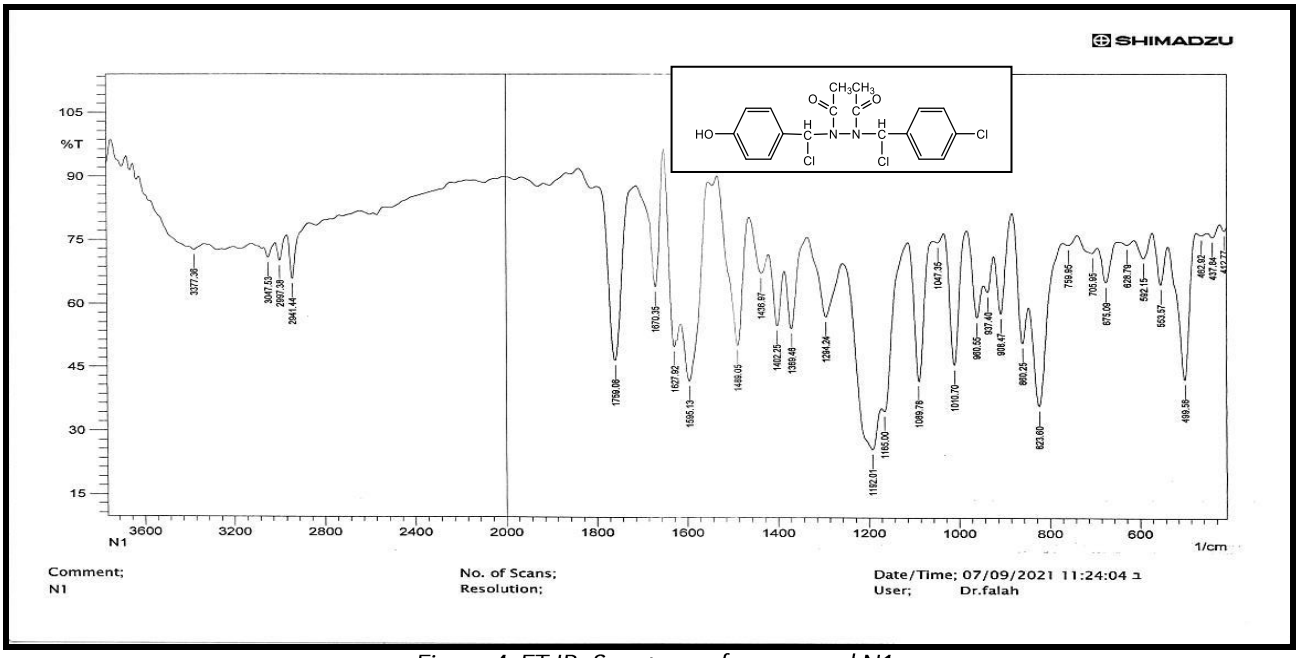


Figure.4: FT.IR- Spectrum of compound N1

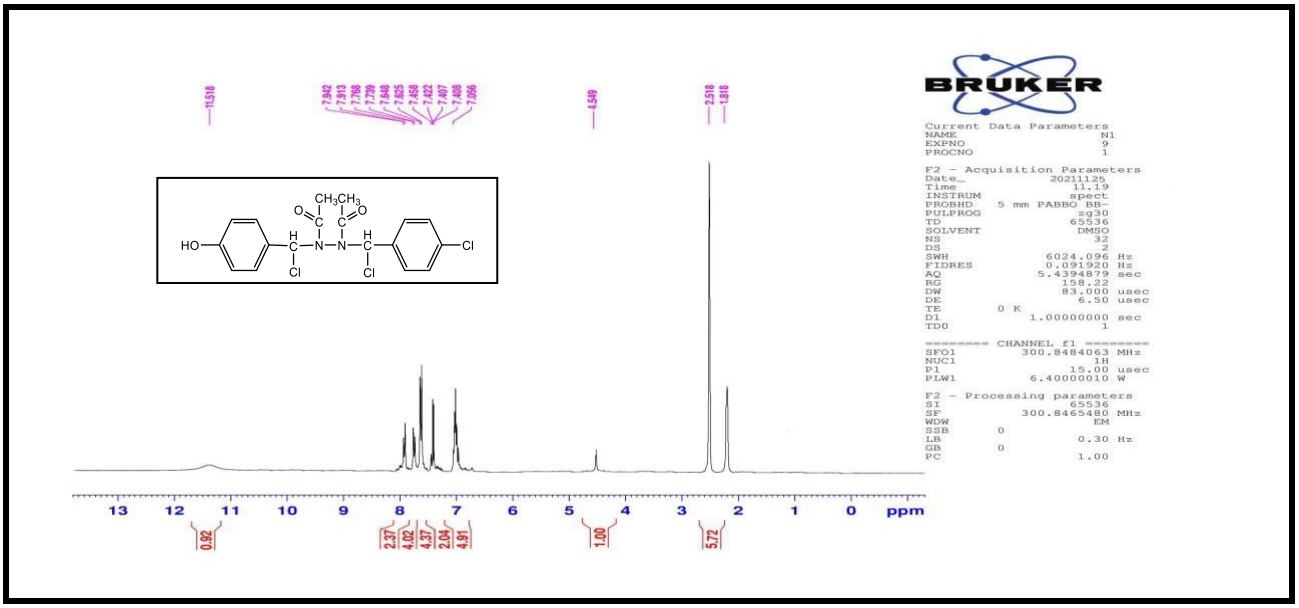


Figure.5: 1HNMR- Spectrum of compound N1

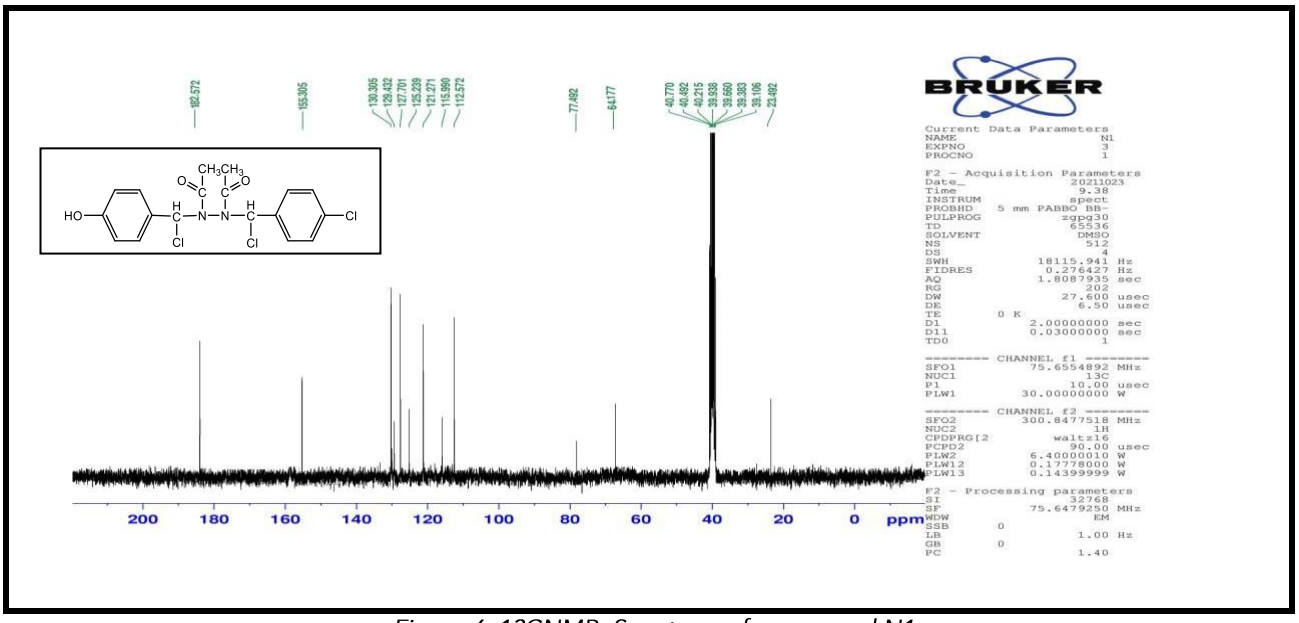


Figure.6: 13CNMR- Spectrum of compound N1

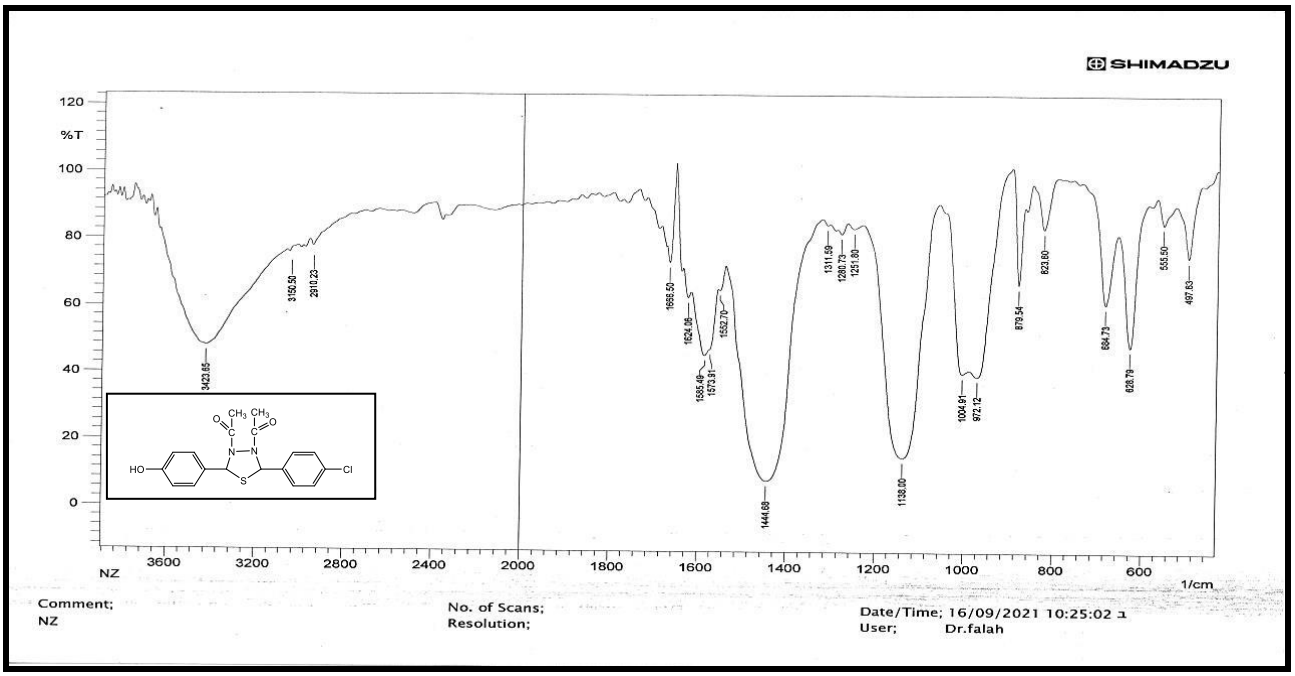


Figure.7: FT.IR- Spectrum of compound Nz

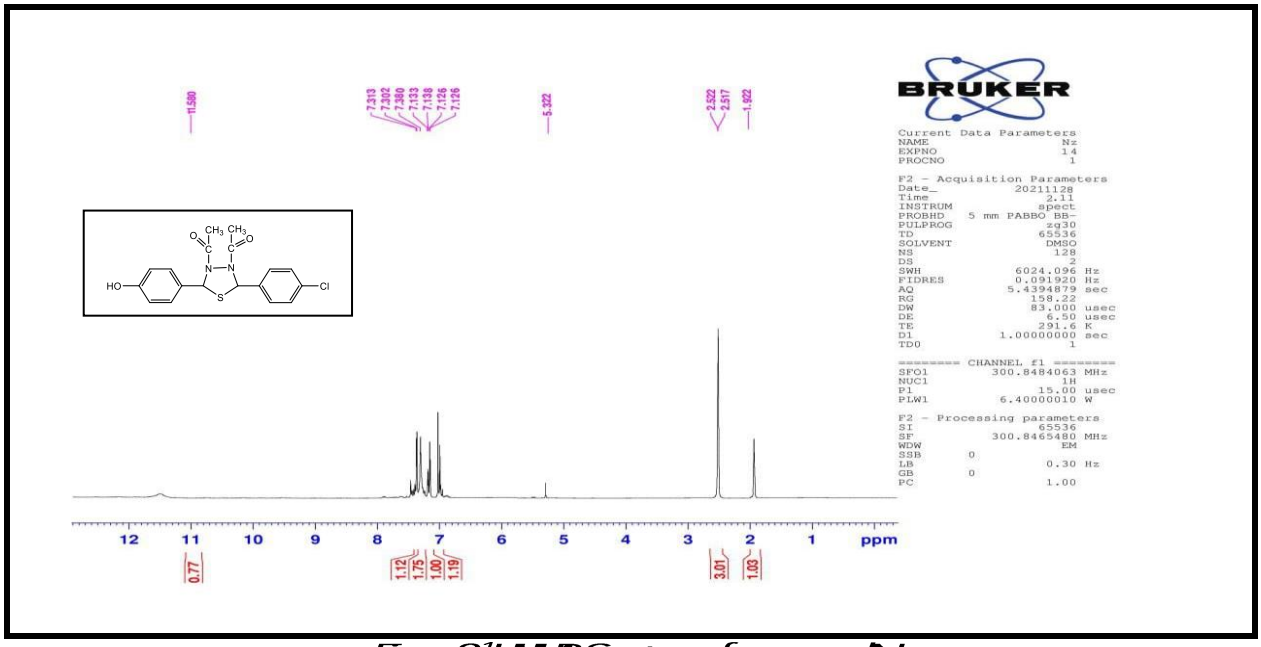


Figure.8: ^{1}H-NMR-Spectrum of compound Nz

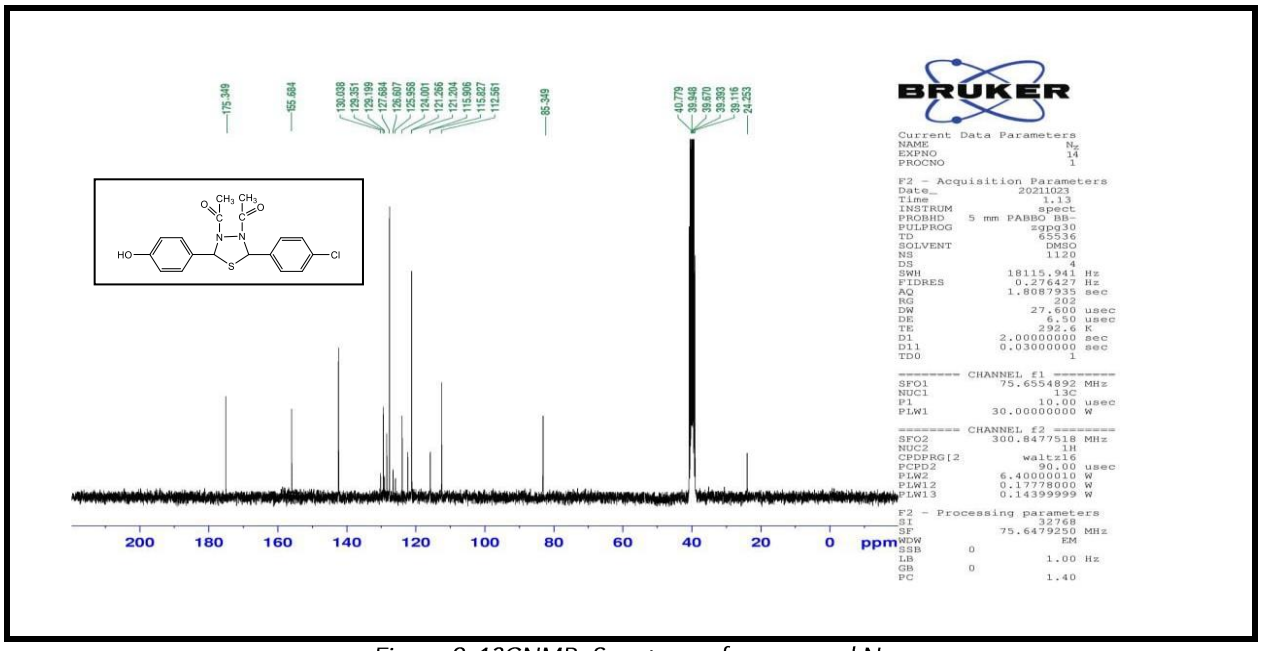


Figure.9: 13CNMR- Spectrum of compound Nz

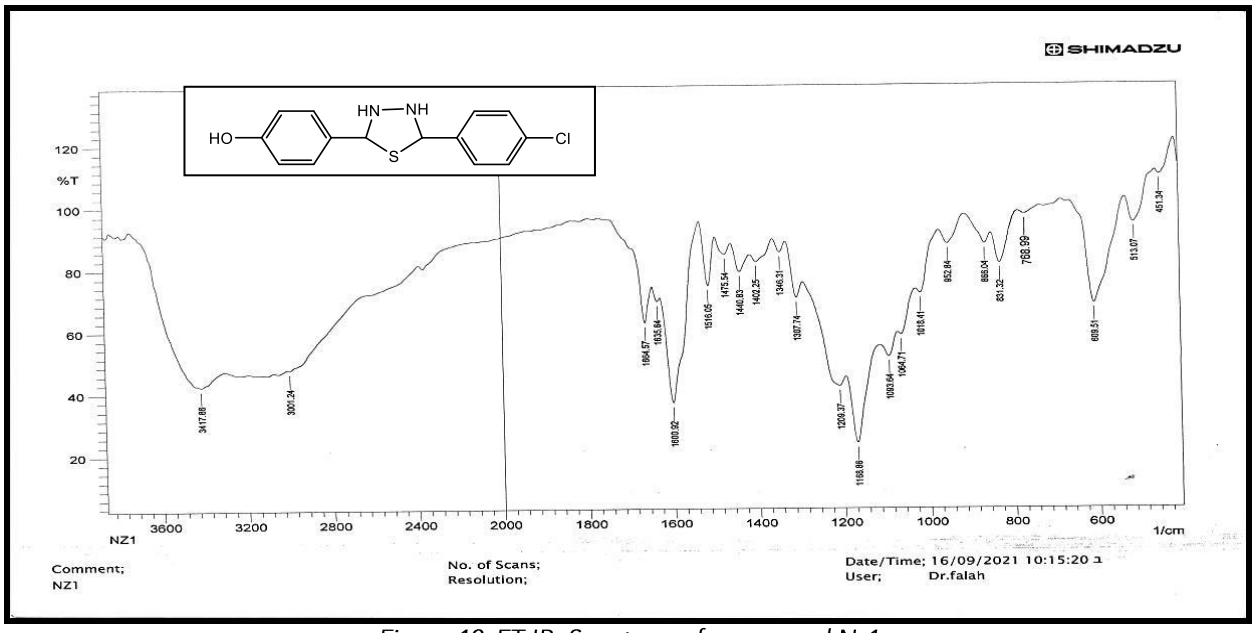


Figure.10: FT.IR- Spectrum of compound Nz1

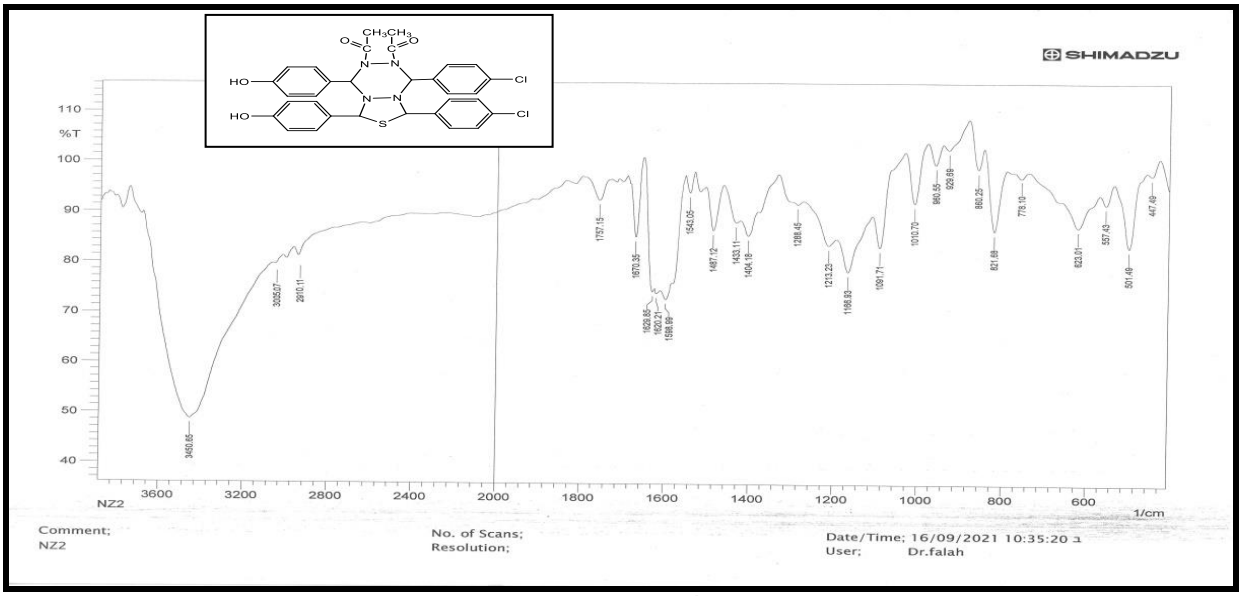


Figure.11: FT.IR- Spectrum of compound Nz2

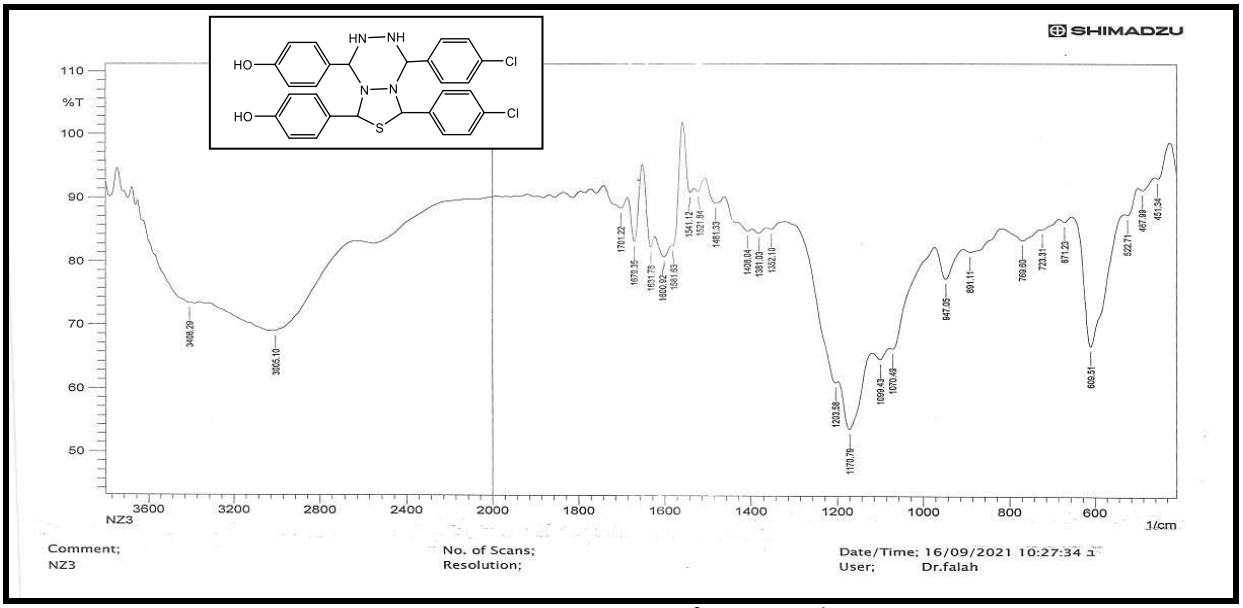


Figure.12: FT.IR- Spectrum of compound Nz3

Biological activity

In this research Biological activity is studied to some of compounds (3) by using wells diffusion method. And studing its effect on two type of bacteria which are G+ (Staphylococcus aurous) for and G- (Escherichia Coli). Product agar and petri dishes were sterilized by autoclaving for 20min at 121oC for both bacteria. DMSO was used as a solvent to prepare solutions of the different compounds were (1X10-2M, 1x10-4M, 1x10-6M). The inhibition region caused the various compound.

Table2. the biological effectiveness of the heterocyclic compound were the zone inhibiters, (-) no inhibition, (+) 5-14 mm, (++) 15-20 mm

Comp	Staph-aurous 1x10-2M	E.coli 1x10-2M	Staph-aurous 1x10-4M	E.coli 1x10-4M	Staph aurous 1x10-6M	E.coli 1x10-6M
N	+	++	-	++	+	-
NZ	+	+	+	+	-	-
NZ3	+	++	-	+	-	+

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