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ORIGINAL ARTICLE

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NOVEL HYDRAZONES, SCHIFF'S BASE

Hamid Hussein Eissa
Assistant Professor in Physical organic Chemistry -Chemistry Department, Education and Applied College Sciences, University of Hajah, Yemen

ABSTRACT: A series of Schiff base derivatives have been synthesized by condensed of isophthalaldehyde and biphenyl-4,4'-dicarbaldehyde with various hydrazones in ethanol in the presence of acetic acide as catalyst to yield the Schiff base derivatives (I-V), The structure of synthesized compounds has been established on the basis of their spectral (FT-IR, Mass, ^{1}H, ^{13}C-NMR, elemental analysis)data. The purity of the compounds was confirmed by TLC. All these compounds were evaluated for their In vitro activity against several microbes (*Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Klebsiella pneumonia*).
KEYWORDS: Schiff Base, Hydrazone, Antibacterial Activity, *Staphylococcus Aureus, Escherichia Coli, Bacillus Subtilis, Klebsiella Pneumonia*.

INTRODUCTION

Schiff base, hydrazone derivatives are important heterocyclic molecules, it possess various type of biological activities such as anti-inflammatory analgesic (Patila *et al.,* 2007; Nataliya *et al.,* 2010; Özdemir *et al.,* 2012; Sonar and Crooks, 2009; Hosseini *et al.,* 2009) antimicrobial (Rollas and Güniz, 2007; Rauf *et al.,* 2008) anti-fungal (Sarikavakli and IREZ, 2005; Sondhi *et al.,* 2009) antitumor (Zulkepli *et al.,* 2009; Zhang *et al.,* 2004) and antimalarial (Terzioglu and Gursoy, 2003; Ashraf *et al.,* 2011). Schiff base hydrazones compounds have been extensively used as versatile ligands in coordination chemistry and Schiff base hydrazone complexes are also very attractive as model compounds for the elucidation of several biochemical processes. Transition metal complexes V=O with Schiff base chelating ligand has been reported In analytical chemistry hydrazones find applications as multidentate ligands for transition metals in colorimetric or fluorimetric determinations (Prakash *et al.,* 2009; Govindasami *et al.,* 2001; Sharma *et al.,* 2012). Hydrazones are being used extensively in detection and quantitative determination of several metals, for the preparation of compounds having diverse structures, analytical chemistry for the identification and isolation of carbonyl compounds (Govindasami *et al.,* 2001; Kucukguzel *et al.,* 2003; Mamolo *et al.,* 2003; Dimmock *et al.,* 2010; Kumar *et al.,* 2012). Hydrazones are used as plasticizers,and stabilizers for polymers polymerization initiators, antioxidants and etc. they act as intermediates in preparative chemistry. They also find applications as indicators and spot test reagents (Rollas and Kucukguzel, 2007). In search of potent molecules exhibiting anti-inflammatory and analgesic activities a number of novel Schiff bases hydrazone have been synthesized.

MATERIAL AND METHODS

Melting points were determined in open glass capillaries on agallenkamp apparatus and are uncorrected. TLC was performed to assess the reactions and the purity of the products. IR spectra were recorded in KBr (pellet forms) on aNicolet-Avatar-330 FT-IR spectrophometer and noteworthy absorption values (cm^{-1}) alone are listed. ^{1}H and ^{13}C NMR Spectra were recorded at 400 MH_Z Bruker AMX using $CDCl_3$ as solvent.

2.1. General procedure for the synthesis of hydrazones

2.1.1. Synthesis of 1-((E)-((Z)-(4aH-fluoren-9(9aH)-ylidene)hydrazono)methyl)-3-((Z)-((E)-(4aH-fluoren-9(9aH)-ylidene)hydrazono) methyl) benzene (I)

(3.88gr, 0.02mol) of fluoren-9-Hydrazone dissolved in boiling ethanol then(1.34g,0.01mol isophthalaldehyde) was added,2-3drops of con. HCl was added and the reaction mixture was refluxed for 4 hours on a water bath. The progress of reaction was monitored by TLC. After the complation of reaction, the reaction mixture was brought to room temperature. The

Corresponding Author: Hamid Hussein Eissa, Assistant Professor in Physical organic Chemistry-Chemistry Department, Applied College Sciences, University of Hajah, Yemen. **E-mail:** Hamedesia2003@yahoo.com

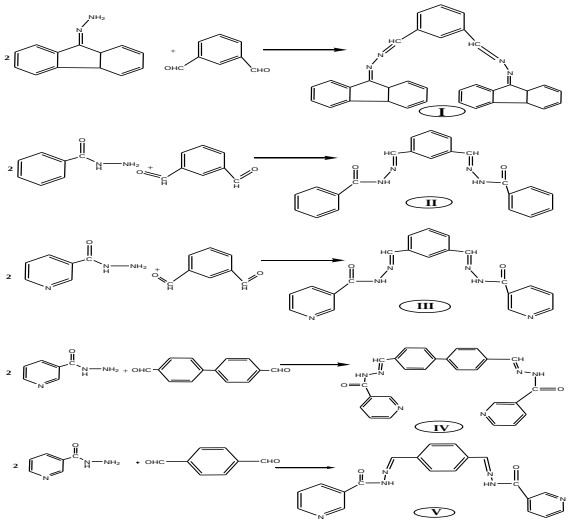
reaction mixture was filtered off and recrystallized from ethanol.

2.1.2. Synthesis of (1,3-phenylenebis (methanylylidene))di(benzohydrazide) (II)
(2.72 gr, 0.02 mol)of benzohydrazide dissolved in boiling ethanol then (1.34g,0.01mol) isophthalaldehyde was added,2-3drops of con. HCl was added and the reaction mixture was refluxed for 3 hours on a water bath. The progress of reaction was monitored by TLC. After the complation of reaction, the reaction mixture was brought to room temperature. The reaction mixture was filtered off and recrystallized from tolune.

2.1.3. Synthesis of (1,3-phenylenebis(methan-1-yl-1-ylidene))dinicotinohydrazide (III)
(2.74gr, 0.02 mol) of nicotinohydrazide dissolved in boiling ethanol then (1.34g,0.01mol) isophthalaldehyde was added, 2-3 drops of con. HCl was added and the reaction mixture was refluxed for 3 hours on a water bath. The progress of reaction was monitored by TLC. After the complation of reaction, the reaction mixture was brought to room temperature. The reaction mixture was filtered off and recrystallized from tolune.

2.1.4. Synthesis of (biphenyl-4,4'-diylbis(methan-1-yl-1-ylidene))dinicotinohydrazide(IV)
(2.74gr, 0.02 mol) of nicotinohydrazide dissolved in boiling ethanol then (4.2 gr, 0.01mol) biphenyl-4,4'-dicarbaldehyde was added,2-3drops of con. HCl was added and the reaction mixture was refluxed for 3 hours on a water bath. The progress of reaction was monitored by TLC. After the complation of reaction, the reaction mixture was brought to room temperature. The reaction mixture was filtered off and recrystallized from mixture of (ethanol:DMF,9:1).

2.1.5. Synthesis of (1,4-phenylenebis(methan-1-yl-1-ylidene))dinicotinohydrazide(V)
(2.74gr, 0.02 mol) of nicotinohydrazide dissolved in boiling ethanol then (1.34g,0.01mol) terephthalaldehyde,2-3drops of con. HCl was added and the reaction mixture was refluxed for 3 hours on a water bath. The progress of reaction was monitored by TLC. After the complation of reaction, the reaction mixture was brought to room temperature. The reaction mixture was filtered off and recrystallized of tolune.



Scheme 1: synthesis of compounds.

2.2. Biological Activity
The synthesized Schiff bases were screened for antibacterial and antifungal activity.

2.3. Antibacterial Testing
The bacterial cultures for *B. subtilis, S. aureus*, *Klebsiella pneumonia* and *E. coli* were obtained from Department of Microbiology University of Hajja, Yemen. The bacterial cultures were incubated at 30 ±0.1°C for 24 hours by inoculation into nutrient agar. Schiff bases were stored dry at room temperature and dissolved 20mg/ml in dimethylsulfoxide (DMSO). Antibacterial activities of each compound were evaluated by the agar disc-diffusion method. Mueller Hinton Agar Media (15 cm^3) kept at 45°C was poured in the Petri dishes and allowed to solidify. Poured Petri plates (9 cm) were incubated with 50µL of normal saline solution of above culture media (105-106 bacteria per ml). Discs injected with prepared Schiff bases (50µL) were applied on the solid agar medium by pressing tightly. The Petri plates were placed at 37°C for 24 hours. At the end of period the inhibition zones formed on media were measured with a zone reader in millimeters (Espinel-Ingroff, 2007).

RESULTS AND DISCUSSION

3.1. Synthesized
Five new Schiff bases have been synthesized from the condensation of hydrazone with dialdhyde (isophthalaldehyde, biphenyl-4,4'-dicarbaldehyde, terephthalaldehyde) (Scheme 1). The analytical and physical data are listed in Table (1,2,3).

3.2. IR Spectroscopy
The IR Spectral data are shown in table 2 are assigned to the prepared Schiff bases The five

bands at 1635.23, 1600.92, 1643.35, 1600.92, 1642.0 cm^{-1} are attributed to imine group (-C=N) for (I-IV) (Figures 1-5), respectively The bands in the spectra at 1546.9, 1573.91, 1548.91, 1593.20,1579.8, and 1611.5cm^{-1} is due to (C=C) of aromatic rings. The IR spectra of (I,II,III) show characteristic absorption bands at 1442.75-1489.05, 1442.75-1519.91, and 1481.33-1554.63cm-1 due to v(-N=N-) stretching vibrations, respectively. The bands at, 3060.5,3055.24,3051.39,3062.96 and ,3054.5 cm^{-1} are attributed to (C-H aromatic) for (I-IV) respectively (Salih and Hamid, 2008).

3.3. NMR Spectroscopy

The data of ^{1}H-NMR Spectra of prepared compounds are shown in table 3. The ^{1}H-NMR spectra of (I-V) in Figures shows a singlet signal at11.94,12.13,12.09 and 12.17 ppm assigned to the proton(-CO-NH) of Compounds (II-V), respectively. The singlet signals 8.46,8.49,9.095,9.093, and9.094 ppm due to (CH=N) of compounds (I-V). The multiple signals7.28,7.53,7.57,8.97, and 8.197-6.575 ppm are due to the aromatic pro-tons for (I-V) respectively.

3.4. Antibacterial activity

The results of the antibacterial screening of the Schiff bases at a concentration of 20mg/ml against all bacteria have been found. The inhibition zones were measured in mm and results are shown in Table 4. The results of antimicrobial screening indicate that Schiff bases show significant activity against *Staphylococcus aureus, Escherichia coli, and Bacillus subtilis*. More than *Klebsiella pneumonia* Antibacterial activity of these compounds show ascending order. When we increase concentration, area of inhibited growth also increased.

Table 1: Physical properties for new Schiff compounds

Compound	M.P (^{0}C)	yield	R.F.	*Formula*	M.Wt	Color
I	241	% 82	0.75	$C_{34}H_{22}N_4$	486	Yellow
II	300.2 < **Δ**	85%	0.53	C22H18N4O2	370	White
III	290	% 90	0.78	$C_{33}H_{32}N_2O_2$	370	White
IV	258	% 80	0.79	$C_{33}H_{32}N_2O_2$	370	White
V	300.2 < **Δ**	% 78	0.67	$C_{33}H_{32}N_2O_2$	372	White

Table 2: FT-IR spectral data of compounds (I-V)

Comp. No.	v (C=N)	v(C=C)	v (C=O)	v (C-H(aliph))	v (C-H) arom	v (N-H)
I	1635.23	1546.9-1496.78	---------	---------	3060.5	---------
II	1600.92	1548.91-1508.33	1654.92	---------	3055.24	3259.70
III	1643.35	1558.48-1593.20	1678.07	---------	3051.39	3194.12-3417.15
IV	1600.92	1579.8-1420.4	1651.07	2858.5-2933.5	3062.96	3248.13
V	1642.0	1594.4-1611.5	1679.6	---------	3054.5	3189.5-3437.3

Table 3: ^{1}H-NMR spectral data for the prepared compounds

Chemical shifts	**Compound No**
^{1}H-NMR(CDCl3-400MHz) δ = 8.461-8.498 (s,2H,CH=N) , 7.284 - 8.123 (m,20 H, Ar), 1.611-1.613(Solvents organic).	**I**
1H-NMR(CDCl3-400MHz) δ =11.9418 (s,2H, CO-NH-), 8.498 (s,2H,CH=N) , 7.532 - 7.992 (m,14H, Ar), 2.509 -3.346 (DMSO,H2O).	**II**
1H-NMR(CDCl3-400MHz) δ =12.1329 (s,2H, CO-NH-), 9.095 (s,2H,CH=N) , 7.578 - 8.975 (m,12H, Ar), 2.510 -3.372 (DMSO,H2O).	**III**
^{1}H-NMR(CDCl3-400MHz) δ =12.0957(s,2H, CO-NH-), 9.093 (s,2H,CH=N) , 7.591 - 8.979 (m,16H, Ar), 2.508 -2.677(DMSO,H2O).	**IV**
1H-NMR(CDCl3-400MHz) δ =12.1707 (s,2H, CO-NH-), 9.094 (s,2H,CH=N) , 7.527 - 8.971 (m,12H, Ar), 2.509 -3.370 (DMSO,H2O).	**V**

Table 4: Antimicrobial activity for prepared compounds

Compound no.	Zone of inhibition of sample (mm)			
	E.coli	*B.subtilis*	*S.auerus*	*K.pneumonia*
I	34	21	30	18
II	42	31.5	49	20
III	39.5	20	36	18
IV	22	16	30	19
V	35	22	32	16
Std.drug (Amoxycillin)	18	12	14	15

*Concentration of sample =20mg/ml of Damso

Concentration of standard drug (Amoxycillin) =10µg 1 disc , =No activity

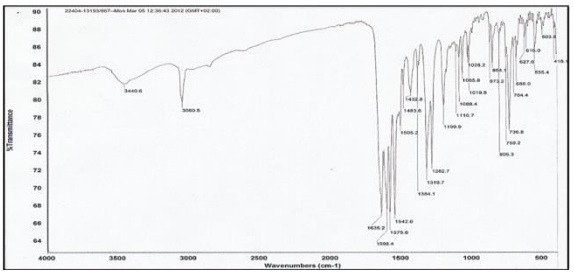


Figure 1: IR spectra of compound (I)

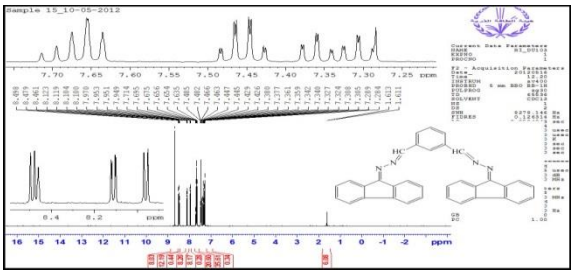


Figure 6: 1-HNMR spectra of compound (I)

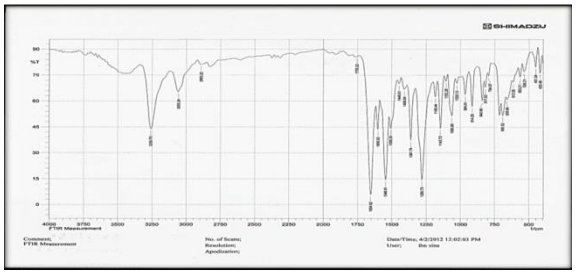


Figure 2: IR spectra of compound (II)

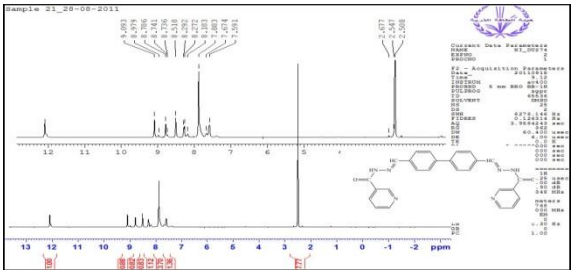


Figure 7: 1-HNMR spectra of compound (II)

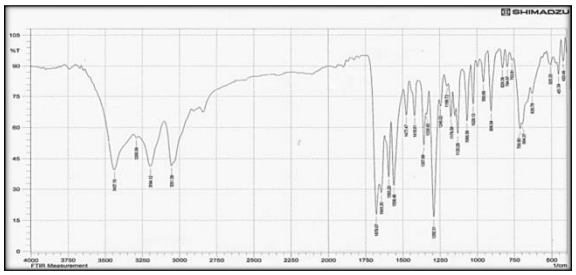


Figure 3: IR spectra of compound (III)

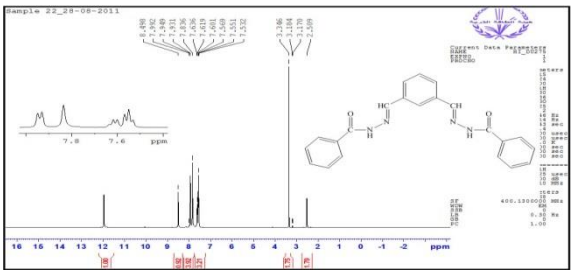


Figure 8: 1-HNMR spectra of compound (III)

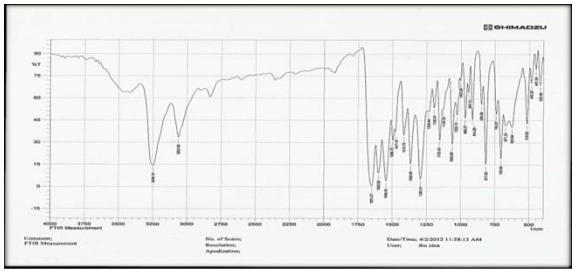


Figure 4: IR spectra of compound (IV)

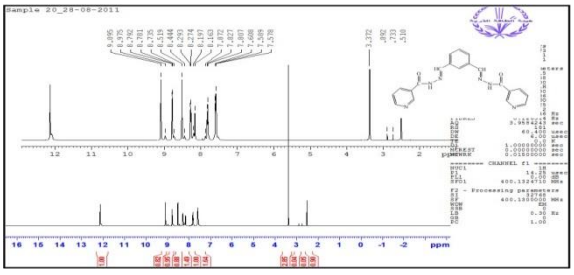


Figure 9: 1-HNMR spectra of compound (IV)

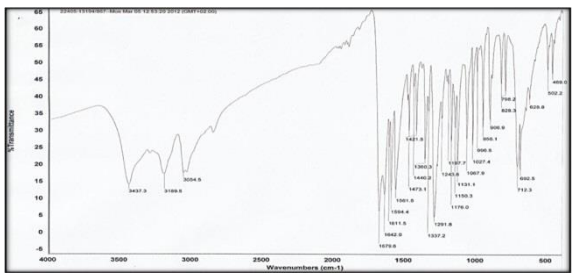


Figure 5: IR spectra of compound (V)

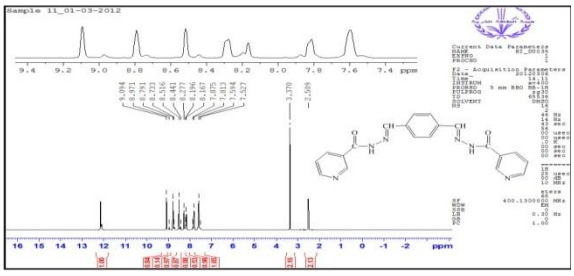


Figure 10: 1-HNMR spectra of compound (V)

REFERENCES

Ashraf MA, Mahmood K, Wajid A. Synthesis, Characterization and Biological Activity of Schiff Bases. 2011 International Conference on Chemistry and Chemical Process IPCBEE 2011;10:25.

Dimmock JR, Vasishtha SC, Stables JP. Anti-convulsant Properties of Various Acetylhydrazones, Oxa- moylhydrazones and Semicarbazones Derived from Aro-matic and Unsaturated Carbonyl Compounds. European Journal of Medicinal Chemistry 2010;35(2):241- 248.

Espinel-Ingroff A. Standardized Disk Diffusion Method for Yeasts. Clinical Microbiology Newsletter 2007;29(13):97-100.

Govindasami T, Pandey A, Palanivelu N, Pandey A. Synthesis, Characterization and Antibacterial Activity of Biologically Important Vanillin Related Hydrazone Derivatives. International Journal of Organic Chemistry 2011;1:71-77.

Hosseini Monfareda H, Pouralimardana O, Janiakb C. Synthesis and Spectral Characterization of Hydrazone Schiff Bases Derived from 2,4-Dinitro phenylhydrazine. Crystal Structure of Salicylaldehyde-2,4-Dinitrophenylhydrazone. Molecules 2009;13:1920-1949.

Kucukguzel SG, Mazi A, Sahin F, Ozturk S, Stables J. Synthesis and Biological Activities of Diflunisal Hydrazide-Hydrazones. European Journal of Medicinal Chemistry 2003;38(11-12):1005-1013.

Kumar RK, Raghavendra A, Prasad G, Srilalitha V, Narayana Swami G, Ravindranath LK. Synthesis and Characterization of Iron Complexes of Resacetophenone Salicyloyl Hydrazone. ROMANIA Series of Chemistry and Environmental Engineering 2012;57(71):1.

Mamolo MG, Falagiani V, Zampieri D, Vio U, Banfi E, Scialino G. Synthesis and Antimycobacterial Activity of (3,4-Diaryl-3H-thiazol-2-ylidene)-hydrazide Derivatives. IL Farmaco 2003;58(9):631- 637.

Nataliya P, Belskaya A, Dehaen W, Bakuleva VA. Synthesis and properties of hydrazones bearing amide, thioamide and amidine functions. J ARKIVOC 2010;(i):275-332.

Özdemir A, Turan-Zitouni G, Kaplancikli ZA, Altintop MD. The synthesis of some new hydrazone derivatives containing the benzothiazole moiety. J Serb Chem Soc 2012;77(2):141–146.

Patila BR, Machakanura SS, Hunoora RS, Badigera DS, Gudasia KB, Blighb A. Synthesis and anti-cancer evaluation of cyclotriphosphazene hydrazone derivatives. J Der Pharma Chemica 2011;3(4):377-388.

Prakash A, Kumar CH, Sangamesh A, Shivananda N, Nagaraju C. Synthesis, spectral characterization, in–vitro microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazine. European Journal of Medicinal chemistry 2009;44:3552-3559.

Rauf A, Bandaya MR, Mattoo RH. Synthesis, Characterization and Antimicrobial Activity of Long-Chain Hydrazones. Acta Chim Slov 2008;55:448–452.

Rollas S, Küçükgüzel G. Biological Activities of Hydrazone Derivatives. Molecules 2007;12:1910-1939.

Salih I, Hamid T. The synthesis and spectral studies of macrocyclic Cu (II), Ni (II) complexes. J Chem 2008;6(2):227-284.

Sarikavakli N, Irez G. Synthesis and Complex Formation of Some Novel vic-Dioxime Derivatives of Hydrazones. Turk J Chem 2005;29:107–115.

Sharma CS, Gunjan J, Singh HP, Ankalgi AD, Ranawat MS, Diwaker AK. Synthesis, spectral and biological evaluation of some hydrazone Derivatives. IJARPB 2012;2(1):28-33.

Sonar VN, Crooks PA. Synthesis and antitubercular activity of a series of hydrazone and nitrovinyl analogs derived from heterocyclic aldehydes. J Enzyme Inhib Med Chem 2009;(1):117-24.

Sondhi SM, Dinodia M, Jain SH, Kumar A. Synthesis of biologically active novel bis Schiff bases, his hydrazone and bis guanidine derivative. Indian journal of chemistry 2009;48B:1128-1136.

Terzioglu N, Gursoy A. Synthesis and anticancer evaluation of some new hydrazone derivatives of (2,6-Dimethyl- N'-(2-hydroxyphenylmethylidene) imidazo[2,1-b][1,3,4] thiadiazole-5-carbohydrazide. Eur J Med Chem 2003;38:781-6.

Zhang H, Drewe J, Tseng B. Discovery and SAR of indole-2-carboxylic acid benzylidenehydrazides as a new series of potent apoptosis inducers using cell based HTS assay. Bioorg Med Chem 2004;12:3649-55.

Zulkepli NA, Kai Rou KV, Hidayati WN, Sulaiman W, Salhin A, Saad B, Seeni A. A Synthetic Hydrazone Derivative Acts as an Apoptotic Inducer with Chemopreventive Activity on a Tongue Cancer Cell Line. Asian Pacific Journal of Cancer Prevention 2011;12:259-263.