Synthesis and Reduction of Some Mannich bases for Substituted Indol–2,3 -dione

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(Received: 30 / 12 / 2012 ---- Accepted: 22 / 7 / 2013)

Abstract

The present work involved two steps: First step include some Mannich bases of substituted Isatin has been synthesized by reacting Isatin with paraformaldehyde and secondary amine .

(4-Aminophenazone, Pyrazinamide,2,4-Diamino-6- phenyl-1,3,5- triazine, 2,6- Diamino- 6- methyl-1,3,5-triazine,2,4- Diamino- 6- hydroxy pyrimidin) to obtain Mannich bases (A-E) . The second step include reduction of all Mannich bases which prepared in first step by using Aluminum pure powder to obtain compounds (F-J). Some of the compounds were characterized by means of their UV, FT-IR, ^{1}H-NMR spectroscopic data .

Key words: Mannich Reaction, Reduction; Indol–2,3 –dione Dreivataves .

Introduction

Mannich reaction is one of the most important C-C bond forming reactions in organic synthesis for the preparation of secondary and tertiary amine derivatives [1], the Mannich reaction, an imino analogue of the aldol condensation, has been extensively studied by organic chemistry and has been the subject of numerous reviews[2] .

In the classical condensation, a single carbon atom is attached to an active methylene or methane group, using formaldehyde and an aimne, to generate β-amino carbonyl compounds (Mannich bases) .

These amines are further used for the synthesis of many intermediates, biologically active and natural products such as alkaloids and polyketids .

The products of Mannich reaction are mainly β-aminocarbonyl compounds and its derivatives that are used for the synthesis of amino alcohols, peptides, lactams and as precursors to optically active amino acids [3] .

In this study, some Mannich bases of substituted Isatin has been recently found to exhibit endogamous activity in mammals [4] . In recent years Schiffs' and Mannich bases of Isatin are reported to exhibit broad spectrum chemotherapeutic properties such as antibacterial, antifungal [5], anticonvulsant, antitubercular and anticancer effects [6,7]

2. Experimental

2.1 Chemicals

Melting points wsa determined by Gallen Kamp melting point apparatus and are uncorrected . ^{1}H-NMR spectra were recorded on Bruker specrospin ultra shield magnets 300 MHz instrument using tetramethyl slane (TMS) as an internal standared and DMSO – d_6 as a solvent in Ahl- Albate University in Jordan .

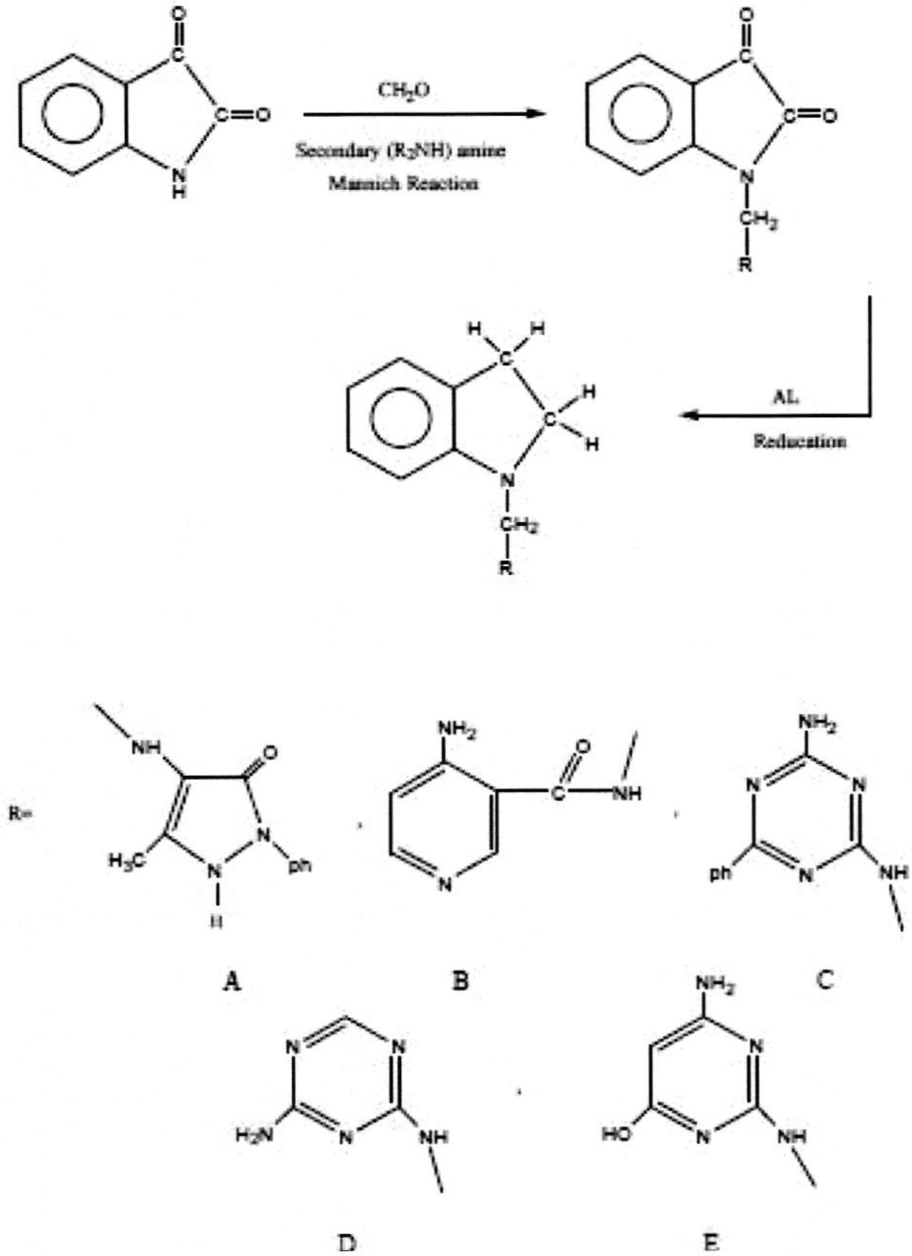
FT-IR spectra were recorded on shimadzu FT –IR 8400 Fourier Transform infrared spectrophotometer using KBr disk .

2.2 Synthesis of Mannich base[8]

Amixture of (0.9 gm, 0.01 mole) of paraformaldehyde solution and (0.015 mole) of different secondary amines in abs. ethanol (10 ml) was refluxed for about (1 hour) then to this solution added hot solution from (0.6 gm, 0.004 mole) of Isatin in 10 ml abs. ethanol. The reaction mixture was stirred for 5 hours. Then cooling the reaction mixture when poured on crushed ice . The precipitated Mannich base was filtered and recrystalized from ethanol. The physical properties for the synthesized compounds are given in Table (1).

2.3 - Reduction of Mannich bases[9,10]

Dissolved (0.5 gm, 1.08 mmol) from Mannich bases (A-E) in (10 ml) (of 10% sodium hydroxide and the reaction mixture was refluxed for until most of the mixture has been clear, then adding power of pure aluminum slowly for 1 hours till hydrogen gas evolution has been stopped after that the mixture was filtered in order to remove the unreacted aluminum. Then the reaction mixture was acidified with (10%) HCL to precipitate the acid . The resulting product was filtered and recrystallzed from chloroform. Table (1) lists the physical properties of the synthesized compounds .



Scheme (1)

Results and discussion

The present work involved two steps

First step: includes the preparation of five Mannich bases of Isatin (A-E) by condensation of Isatin with different substituted secondary amines and Paraformaldehyde .

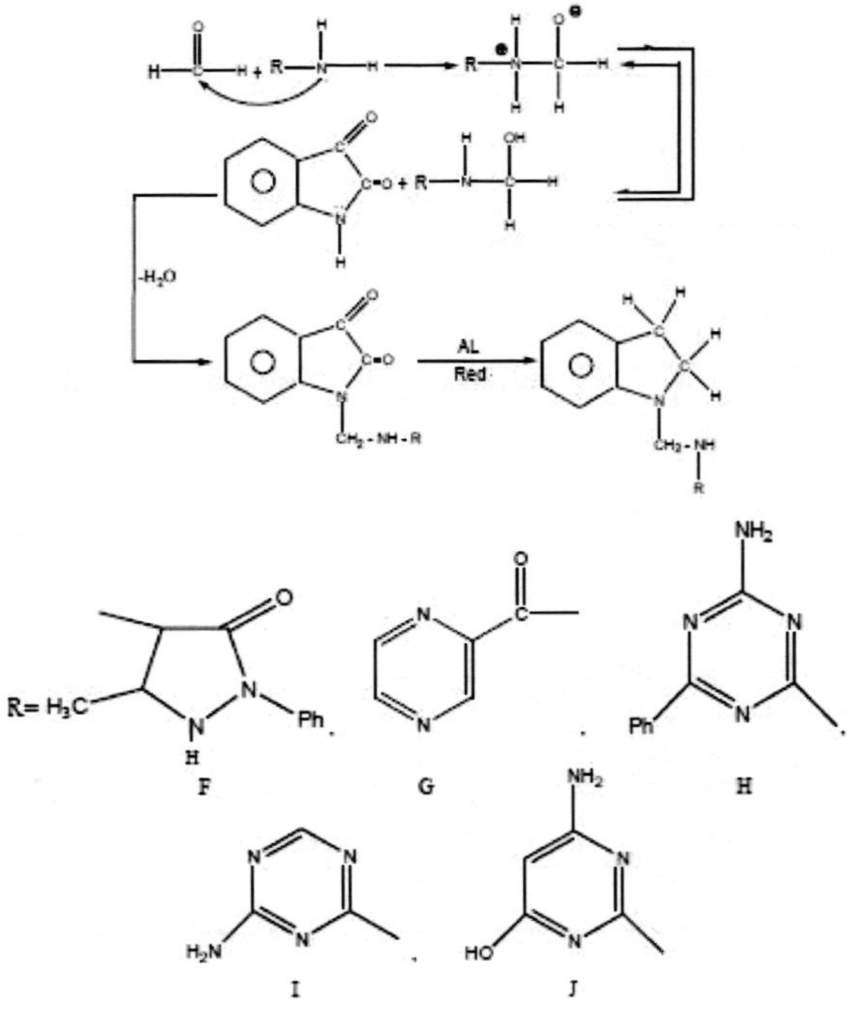
The synthesis of these compounds, was carried out as shown in scheme (1) . Mannich bases were isolated and characterized by melting point and spectroscopic data, all compounds prepared were found to be stable at room temperature, and the physical properties for Mannich bases (A-E) including melting point range of (90-160) C° and % yield were range of (76-85) which has been explained in Table (1). And these compounds were identified by UV. FT-IR and ^{1}H-NMR data .which shown in Table (2) . FT-IR spectrum of Mannish bases (A-E) showed clear absorption bands at (1724-1735) cm^{-1}, (3332-3425) cm^{-1}, (1411-1485) cm^{-1} , (3062- 3197) cm^{-1},(2889-2974) cm^{-1} and (1527-1624) cm^{-1} due to υ(C=O), r (N-H), υ(C-N), υ(C-H) aromatic, υ(C-H) alphatic and υ(C=C) aromatic[11-12], respectively which are displayed in Table (2), fig (5-7) UV. Spectrum of compound (A) showed an absorption λmax at (312) nm and (449) nm which attributed to (π→π) and (n→π*) the absorption is listed in Table (2) .

UV spectrum of copound (D) showed an absorption λmax at (302) nm and (349) nm which attributed to (π→π*) and (n→π*), The absorption is listed in table (2) .

UV. spctrum of compound (E) showen an absorption λmax at (304) nm and (416) nm which attributed to (π→π*) and (n-π*), the absorption is listed in table (2).H-NMR spectrum of compound (A). fig (9) showed characteristic signals at 7.286 - 8.087 ppm which assigned to the aromatic protons and siglet signal at (9.646)ppm duo to N-H grup[13] .

Second step: this step is including reduction all mannich bases (A-E) which prepred in first step by using aluminum pure powder to obtain compounds (F-J). The synthesis off these compounds was carried outlin in scheme (1), many a new compounds wrew isolated and characterzed by melting point and spectroscopic data .

The physical proparites for these compounds (F- J) including melting point rang of (145-193) C° and % yield were range of (40-70) which explaine in Table (1), and these compounds were identified by UV, FT-IR and ^{1}H-NMR spectroscopy which explaine in Table (2) .FT-IR spectrum for compounds (F-J) showed clear absorption bands at (3320-3448) cm^{-1}, (1450-1480) cm^{-1} (3070-3160) cm^{-1}, (2875-2980) cm^{-1}, and (1590-1635) cm^{-1}, due to υ(N-H), υ(C-N) , υ(C-H) aromatic , υ(C-H) aliphatic and υ(C=C) aromatic respectively which expline in table (2), fig (8). In FT-IR for compounds (F-J) disappearance of υ(C=O) imide strtching frequency is good evidence for success of this step of reaction . UV. spectrum of compound (F), showed an absorption λ max at (301) nm which attributed (π→π*) . The absorption is listed in table (2) . While ^{1}H-NMR spectrum of compound (F) fig (10) showed characteristics signals at (4.250) ppm (5.496) ppm and (6.772) ppm duo to (CH_2) wich reducted from carbonyl group appeared there signals is dood evidence for success of this step of raction and multiplet signals at 7.425 to (7.729) ppm which were qssigned to the aromatic protons while signlet signal at 9.003ppm duo to N-H group.[14] .



Scheme (2)

Table (1) physical properties of Mannich bases and Their Reduction Products

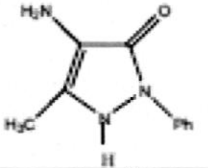
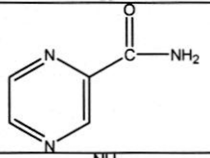
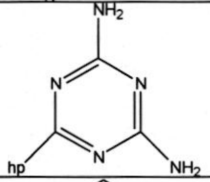
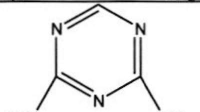
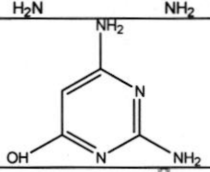
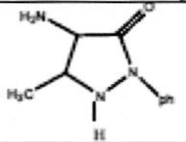
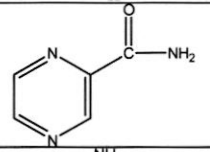
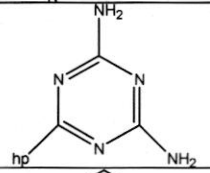
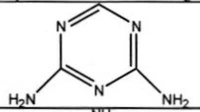
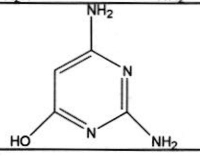
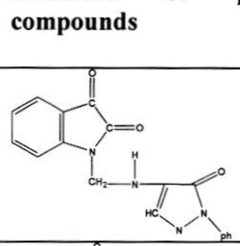
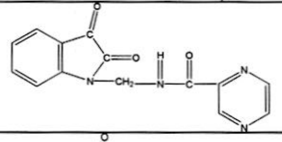
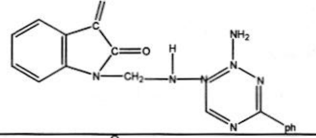
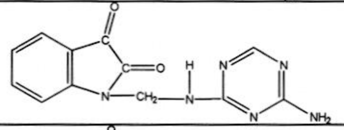
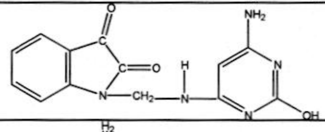
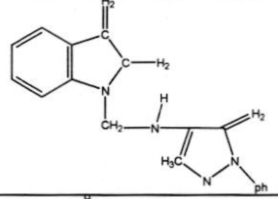
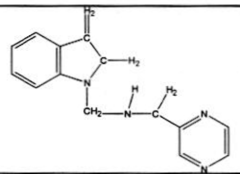
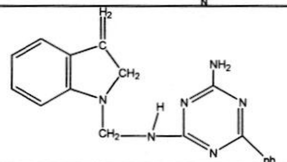
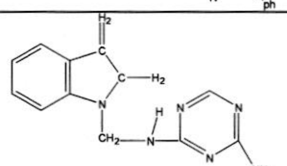
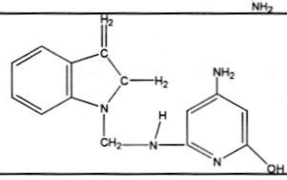
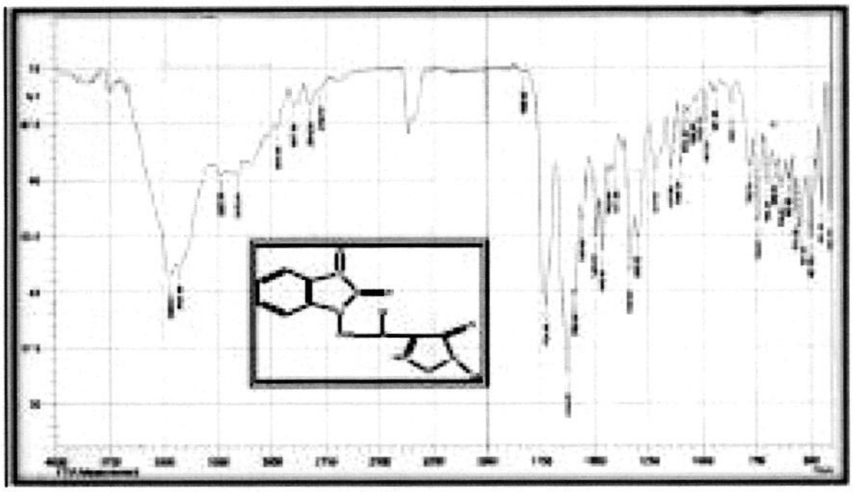
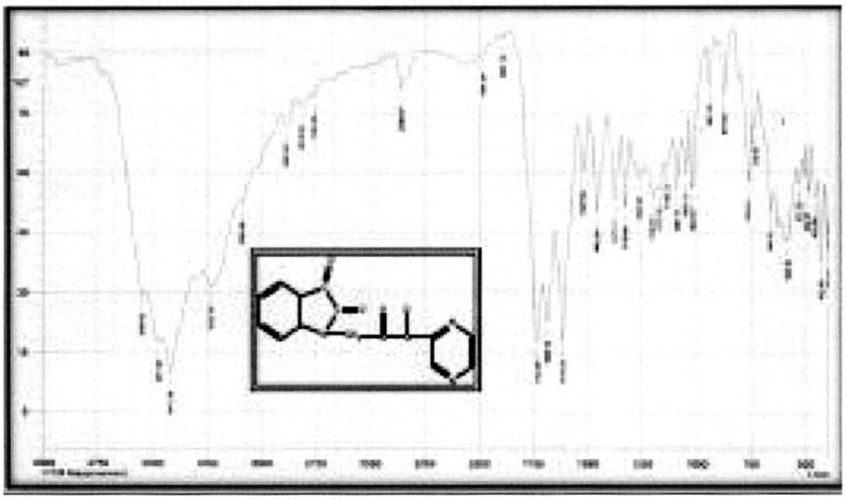
Comp. No	R	Colour	%Yeild	m.pc°	Solvent of crystallsation
A		red	81	132 – 134	Ethanol + THF
B		brown	76	134 – 136	1,4 – Dioxan
C		dark orange	77	90 – 92	Ethanol + THF
D		red	85	114 – 115	Ethanol + THF
E		brown	83	160 – 164	Ethanol + THF
F		white	65	145 – 148	chloroform
G		Pale brown	70	190 – 193	benzene
H		dark green	55	188 – 191	chloroform
I		brownish red	40	171 – 173	chloroform
J		yellow	60	163 - 165	DMF

Table (2) FT – IR and UV. Spectral data of Mannich bases and Their Reduction Products

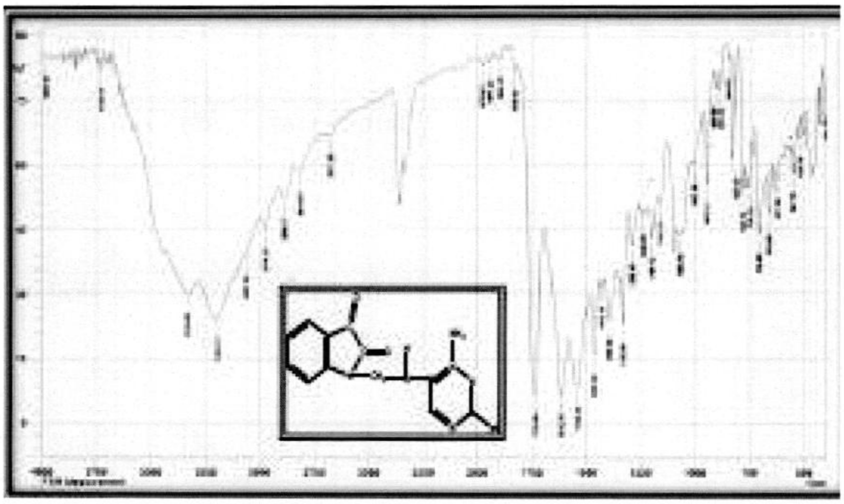
Comp. No.	Structure of prepared compounds	ν(c=o)cm⁻¹	ν(N–H) cm⁻¹	ν(C-N) cm⁻¹	ν(C-H) cm⁻¹ aromatic	ν(C-H) cm⁻¹ aliphtic	ν(c=c)	UV
A		1724	3425	1411	3155	2897 – 2970	1589 1624	312 – 449
B		1732	3417	1462	3089	2893	1527 1685	304
C		1732	3332	1462	3062	2889 – 2974	1539 1616	304 407
D		1735	3406	1469	3128	2897 – 2974	1558 1616	302 349
E		1710	3414	1462	3062	2889	1616	304 416
F		----	3448 -3236	1454	3140	2980	1635	301
G		----	3320	1450	3130	2960	1590	235 358
H		----	3410	1467	3070	2875	1600	240 351
I		----	3370	1480	3080	2890	1630	247 299
J		----	3416	1455	3160	2962	1624	269 317



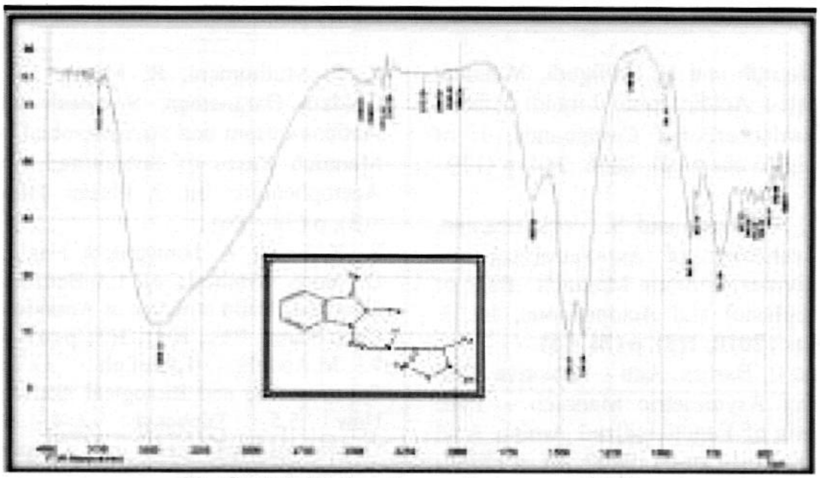
Fig(5): FT-IR Spectrum of compound (A)



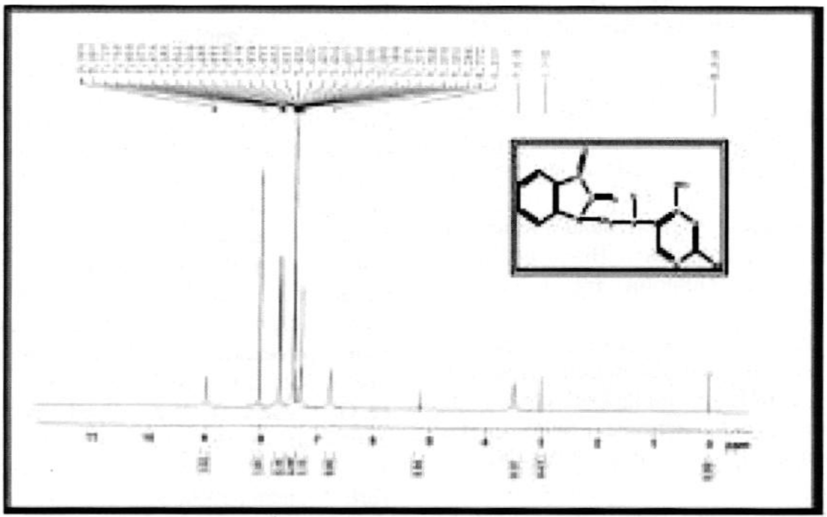
Fig(6): FT-IR Spectrum of compound (B)



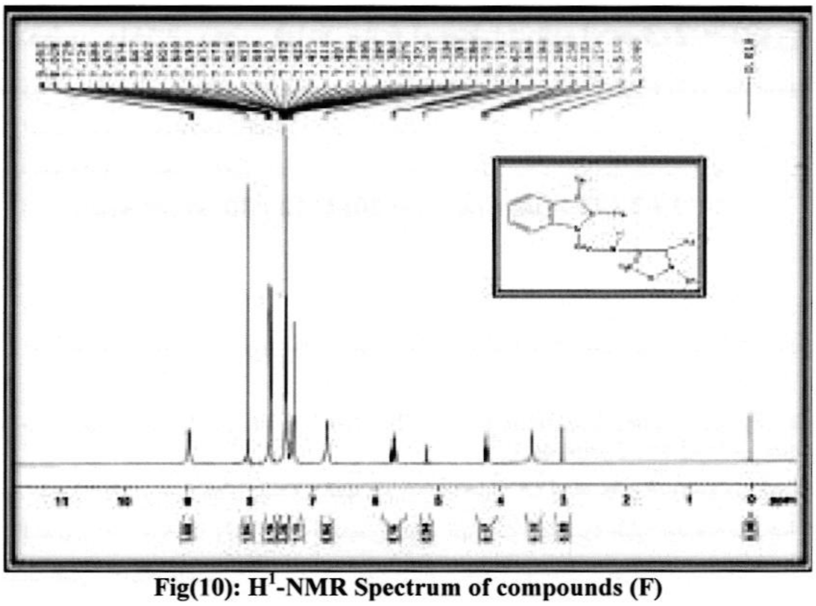
Fig(7): FT-IR Spectrum of compound (C)



Fig(8): FT-IR Spectrum of compound (F)



Fig(9): H^1-NMR Spectrum of compounds (A)



Fig(10): H^1-NMR Spectrum of compounds (F)

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تحضير واختزال بعض قواعد مانخ لمعوضات اندول – 3،2 – دايون

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(تاريخ الاستلام: 30 / 12 /2012 ---- تاريخ القبول: 22 / 7 / 2013)

الملخص

يتضمن البحث خطوتين ، الخطوة الأولى هي تحضير بعض قواعد مانخ بواسطة تفاعل كل من اندول–2،–3 دايون مع البارافورمالديهايد وبأستخدام امينات ثانوية
(4-Aminophenazone, Pyrazinamide, 2,4-Diamino- 6- Phenyl-1,3,5-Triazine, 2,6- Diamino- 6- Methyl 1,3,5-Traizine, 2,4-Diamino- 6- Hydroxy Pyrimidin) .
حيث نحصل على قواعد مانخ (A-E) . اما الخطوة الثانية ، ففيها تتم عملية اختزال كل قواعد مانخ المحضرة في الخطوة الأولى وذلك باستخدام مسحوق الألمنيوم النقي للحصول على مركبات (F-J) . تم تشخيص جميع المركبات المحضرة طيفياً بواسطة مطيافية UV و FT-IR وكذلك مطيافية الرنين النووي المغناطيسي ^{1}H- NMR.