Synthesis and Characterization of Some Compounds Derived from 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene) malonaldehyde

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Abstract
In this research, a series of new indole derivatives (C_1-C_4) were successfully synthesized by the condensation reaction of 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene) malonaldehyde with different amine compounds such as (2,4-dinitro phenyl hydrazine, thiosemicarbazide, P-Phenylendiamine). The compounds (C_5- C_6) were prepared through the reaction of compound (C_3) with anhydrous anhydride (malice anhydride, phthalic anhydride), while as compound (C_7) was synthesized by the condensation of compound(C_3) with 2-aminophenol. The purity of the compounds was confirmed by thin layer chromatography (TLC) and the structure of the synthesized compounds were deduced by using some spectroscopic techniques (FT-IR) and nuclear resonance spectroscopy Magnetic (^{1}H-NMR
Keywords: Schiff bases, malonoaldehyde, indole derivatives

1. Introduction

Heterocyclic compounds containe more than one of nitrogen atoms have excellent biological activities which have attracted many research attention In the years. These compounds, like the other members of the benzodiazepine series, have been widely applied as therapeutic agents due to their anti-cancer, cardiotonic and anti-inflammatory properties [1] At organic chemistry, heterocyclic compounds have constituted one of the largest areas for research [2]. They have performed a significant role in the evolution of pesticides, medicines and pharmaceutical applications [3-4]. Heterocycles have antiviral, antibiotic, antidepressant, antihypertensive, and anticancer activities. In the Comprehensive Medicinal Chemistry (CMC) database, more than 67% of the compounds listed contain heterocyclic rings. A large number of combinations of carbon, hydrogen, and heteroatoms can be designed, thereby providing compounds with the most diverse physical, chemical, and biological properties [5-6]. Heterocycles containing the indole ring system include some novel pharmacologically active compounds Schiff-bases are considered a very important class of organic compounds, having wide applications in many biological aspects, proteins, visual pigments, enzymic aldolization and decarboxylation reactions. Moreover, [7]. their complexes have been used as drugs and to possess a wide variety of biological activities against bacteria,[8]. antibacterial, antifungal, anticancer, antitumor.[9]. antidepressants, antiphlogogistic, nematocide, anti-carcinogenic and catalytic activity[10] Schiff base ligands have significant importance, especially in the development of Schiff base complexes, because Schiff base ligands are potentially capable of forming stable complexes with metal ions[11]. Inhibition efficiencies to the presence of unoccupied p*-orbitals in the Schiff base molecules [12] The Schiff bases are characterized by an imine group –N=CH-, which helps to clarify the mechanism of transamination and racemization reaction in biological system it exhibits antibacterial and antifungal effect in their biological properties . Metal-imine complexes have been widely investigated due to antitumor and herbicidal use. They can work as models for biologically important species [13].

2. 2.Experimental part

2.1. Materials

All chemicals and solvents used in this work were obtained from Sigma - Aldrich, Alpha and Merck companies {1,1,2-Trimethyl benz[e]indole, phosphoryl trichlorid ($POCl_3$), dimethylformamide (DMF), 2,4-dinitro phenyl hydrazine, thiosemicarbazide, P-phenylendiamine , Malice anhydride, phthalic anhydride, 2-aminophenol, absolute ethanol, glacial acetic acid , potassium carbonate}, chemicals are used as received. The compound 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2-ylidene) malonaldehyde was synthesized by the method previously described in reference [14]

2. 2. Methods of Identification

The purity of the synthesized compounds was checked by TLC sheet and the chemical structures were characterized by FT-IR, ^{1}H-NMR. The melting points of compounds were determined on GallenKamp (MFB-600) melting point apparatus and are uncorrected. FT-IR spectra of compounds were recorded PERKIN ELMER SPEACTUM-65 within the range [4000-400] using KBr disc. The ^{1}H-NMR spectra was recorded by Bruker 400 MHz spectrophotometer with TMS as internal standard and deuterated DMSO was used as a solvent.

2. 3. Synthetic methods

2.3.1. Synthesis of 2-[(1-(2,4-dinitrophenyl)-1H-pyrazol-4(yl)]1,1-dimethyl-1H- benzo[e]indole (C_1)

A mixture solution (0.2g, 0.75mmol) of 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2-ylidene) malonaldehyde with (0.1g , 0.75mmol) of 2,4-dinitro phenyl hydrazine dissolved in 30 mL ethanol , then refluxing at 78 °C for 24h in water bath. The solvent evaporated under the reduced pressure, and the brown residue was filtered off , washed with hexane and dried in the oven . The purity of this compound determined by using TLC (3:1) hexane: ethyl acetate with pre-coated silica gel , which gave one spot on the polar area. The physical properties of

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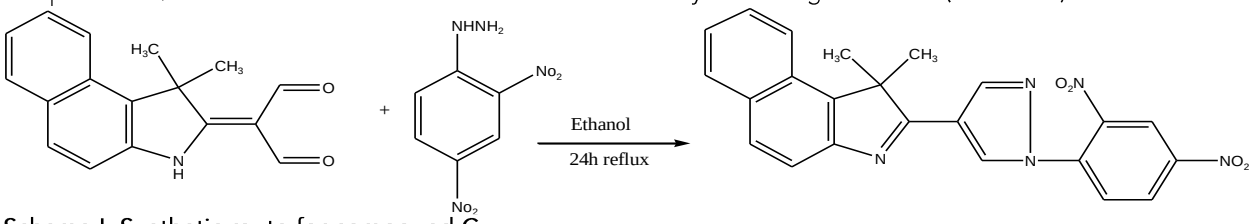
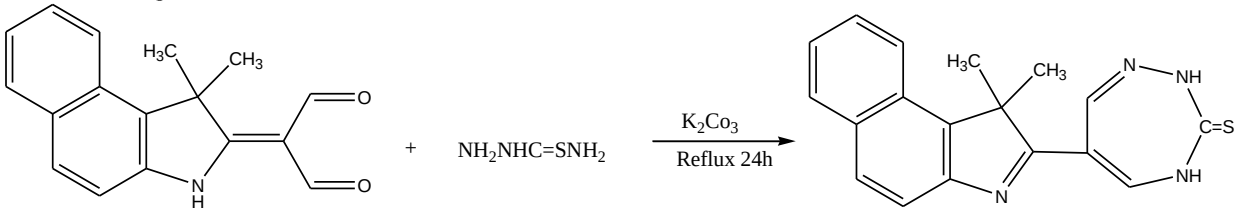
compounds C_1 are listed in table 1 and the scheme of synthesis is given below (scheme I)



Scheme I: Synthetic route for compound C_1

2.3. 2. Synthesis of 6-(1,1-dimethyl-1H-benzo[e]indol-2-yl)-2,4-dihydro-[1,2,4-triazepine-3-thione (C2)

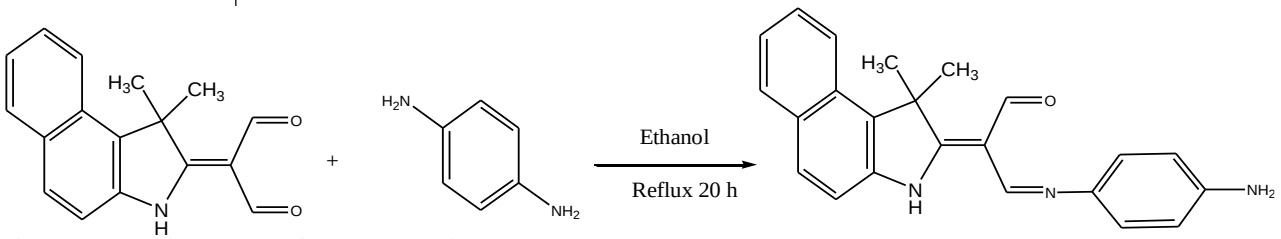
Equimolar quantities (0.5g, 1.8mmol) of 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2- ylidene)malonaldehyde and (0.1g , 1.8mmol) of thiosemicarbazide were dissolved in 20 mL ethanol, (0.5g, 3.6mmol) of potassium carbonate dissolved in (50ml) distilled water was added to the mixture , then refluxing for 24h in water bath, the mixture cooled to room temperature, then acidified the mixture with glacial acetic acid. The solution was filtered, and the yellow crystals formed, dried, and recrystallized from ethanol. The physical properties of compounds C_2 are listed in table 1 and the scheme of synthesis is given below (scheme II)



Scheme II: Synthetic route for compound C_2

2.3. 3. Synthesis of 3-((4-aminophenyl) imino)-2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)propanal (C3)

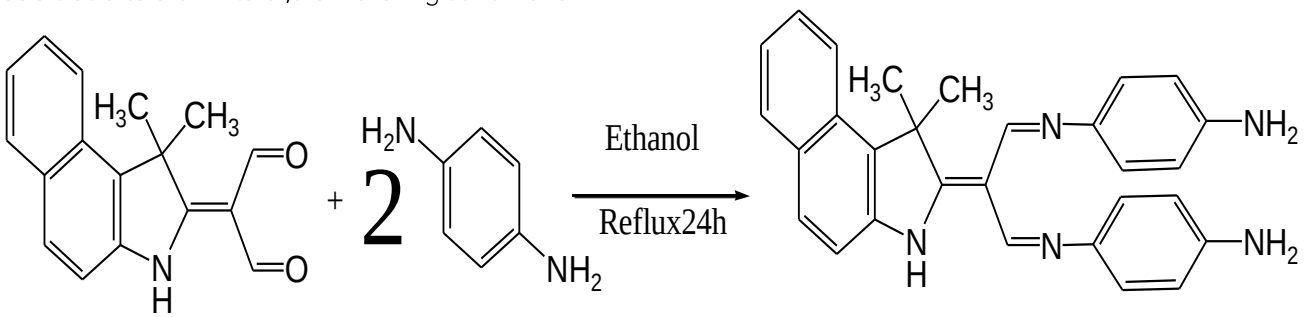
A mixture solution of (0.2 g, 0.75mmol) of 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2- ylidene) malonaldehyde with (0.07g, 0.75mmol) of P-Phenylendiamine dissolved in 20 mL ethanol with the addition (5-6) drops of glacial acidic acid to the mixture, then refluxing at 78 ° C for 20h in water bath. The completion of the reaction was checked by using T.L.C, mobile phase (hexane: ethyl acetate 3:1). After cooling to room temperature, the solid precipitate was filtered, washed with hexane and dried in the oven. The physical properties of compounds C_3 are listed in table 1 and the scheme of synthesis is given below (scheme III)



Scheme III: Synthetic route for compound(C_3)

2.3. 4. Synthesis of N1, N1'-(2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene) propane-1,3-diylidene) bis(benzene-1,4-diamine) (C4)

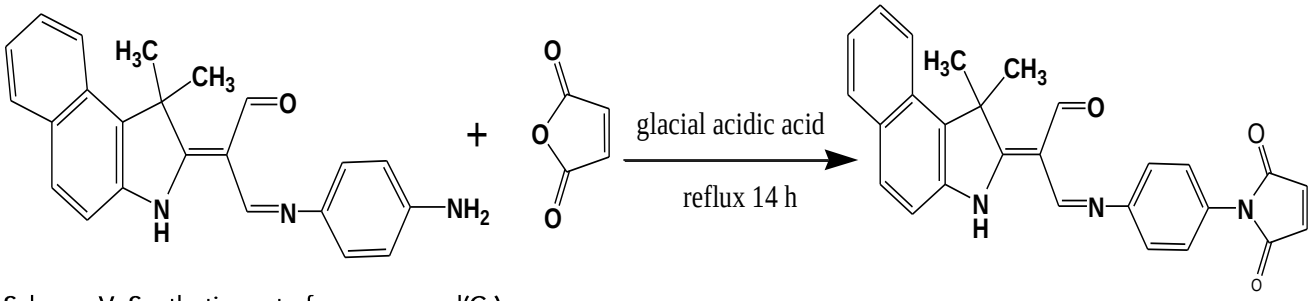
A mixture solution of (0.2g,0.75mmol) of 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2- ylidene) malonaldehyde with (0.1g, 1.5mmol) of P-Phenylendiamine dissolved in 20 mL ethanol with the addition (5-6) drops of glacial acidic acid to the mixture ,then refluxing at 78 ° C for 24h in water bath. The solvent evaporated under the reduced pressure, and the brown residue was filtered off, washed with water and dried in the oven. The purity of this compound determined by using TLC (3:1) hexane: ethyl acetate with pre-coated silica gel, which gave one spot on the polar area. The physical properties of compounds C_4 are listed in table 1 and the scheme of synthesis is given below (scheme **IV**)



Scheme IV: Synthetic route for compound(C_4)

2.3. 5. Synthesis of 2-(1,1-Dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-3-[4-(2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-phenylimino]-propionaldehyde (C_5)

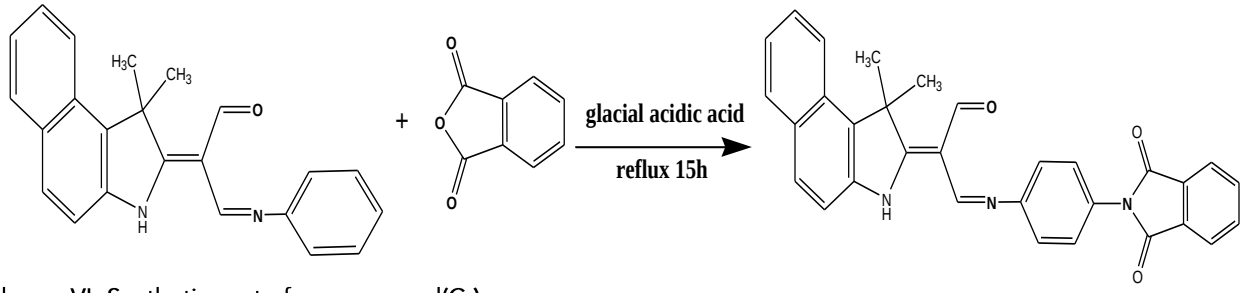
A mixture of Schiff bases compound (C_3) (0.2g , 0.56mmol) was dissolved in 20 mL of glacial acetic acid, then added (0.07g , 0.56mmol) of malice anhydride to the mixture , and refluxing for 14h in water bath, then refrigerate, collected the precipitate, washed with water and re-crystallized from methanol . The physical properties of compounds C_5 are listed in table 1 and the scheme of synthesis is given below (scheme **V**)



Scheme V: Synthetic route for compound(C_5)

2.3. 6. Synthesis of 2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)-3-((4-(1,3-dioxoisoindolin-2-yl) phenyl) imino)propanal(C6)

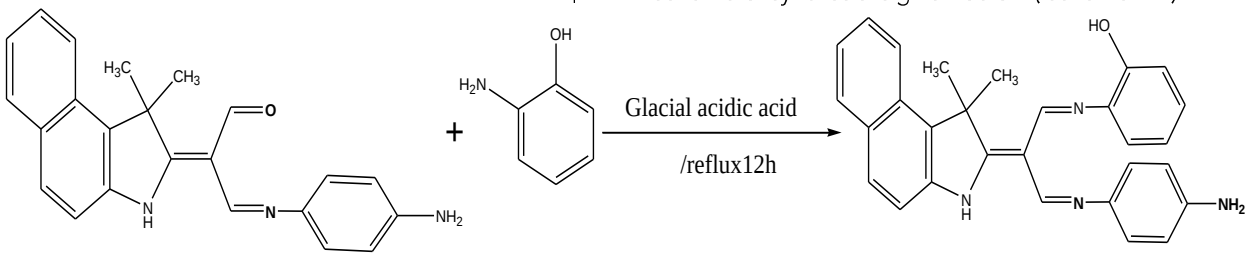
A mixture of Schiff bases compound (C_3) (0.25g, 0.7mmol) was dissolved in 20 mL of glacial acetic acid, then added (0.1g, 0.7mmol) of phthalic anhydride to the mixture and refluxing for 15h in water bath, then refrigerate, collected the precipitate, washed with water and re-crystallized from methanol . The physical properties of compounds C_6 are listed in table 1 and the scheme of synthesis is given below (scheme **VI**)



Scheme VI: Synthetic route for compound(C_6)

2.3. 7. Synthesis of 2-[3-(4-Amino-phenylimino)-2-(1,1-dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-propylideneamino]-phenol (C7)

(0.2g , 0.56mmol) of 3-((4-aminophenyl)imino)-2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)propanal(C_3) was dissolved in 20 mL absolute ethanol with added(5-6) drops of glacial acetic acid, (0.06g, 0.56mmol) of 2-aminophenol was added to the mixture , then refluxing at 78 ° C for 12h in water bath. After cooling to room temperature, the solid precipitate was filtered, washed with water and re-crystallized from methanol. The physical properties of compounds C_7 are listed in table 1 and the scheme of synthesis is given below (scheme **VII**)



Scheme VI: Synthetic route for compound(C_7)

3.Results and Discussion

The new synthesized compounds were subjected to TLC; spectral studies like ^{1}HNMR, and FTIR, and their results are discussed below. The physical properties such as the percentage yield, melting point and color of the compounds (C_1- C_7) are represented in Table 1

Table 1. Physical properties of the synthesized compounds (C_1-C_7)

Comp. No.	Molecular formula	Molecular weight	Percentage Yield	Melting Point °C	Color
C_1	$C_{23}H_{19}N_5O_4$	429.43	68%	230-232	Brown
C_2	$C_{18}H18N_4S$	322.43	65%	212-216	Yellow
C_3	$C_{23}H_{21}N_3O$	355.43	88%	278-280	Brown
C_4	$C_{29}H_{27}N_5$	445.57	96%	288-290	Brown
C_5	$C_{27}H_{21}N_3O_3$	435.47	89%	173-175	Brown
C_6	$C_{31}H_{23}N_3O_3$	485.53	85%	190-195	Brown
C_7	$C_{29}H_{26}N_4O$	446.54	88%	186-190	Brown

3. 1. FT-IR and ^{1}H-NMR Study

The compound (C_1) was prepared in this work by the reaction of 2-(1,1-Dimethyl1,3-dihydro-benzo [e] indol-2-ylidene)- malonaldehyde with 2,4-dinitro phenyl hydrazine. The structure of prepared compound has been characterized by both FT-IR and ^{1}H-NMR spectra. The FT-IR of compound (C_1) demonstrate the following stretching bands: The bands at 3094 cm^{-1} to the (C-H aromatic), 2976-2865cm^{-1} to (C-H aliphatic), 1646 cm^{-1} for stretching vibration of C=N , while 1613-1578 cm^{-1} for stretching vibration of (C= C). The bands of stretching vibration of NO_2 group at (1541-1339 cm^{-1}). While as the ^{1}H-NMR spectrum of compound (C_1) was extracted the following data: 10.09(s,1H,HC=CH-Pyrazole) 8.92(s,1H,CH=N Pyrazole), 8.58 -7.62 (m,9H,Ar-H) and 1.99(s,6H,2xCH_3).

The 2-(1,1-Dimethyl1,3-dihydro-benzo [e] indol-2-ylidene)-malonaldehyde was reacted with thiosemicarbazide to give compound (C_2). The structure of the synthesized compound has been characterized by both FT-IR and ^{1}H-NMR spectra. The FT-IR of compound (C_2) demonstrate the

following stretching bands: The bands at 3384 cm^{-1} assigned for the stretching vibration of (N-H) ,3163 cm^{-1} to the (C-H aromatic), 2970-2870 cm^{-1} to (C-H aliphatic), 1604 cm^{-1} for stretching vibration of (C=N) , while 1519-1458 cm^{-1} for (C= C) stretching vibration. The spectrum ^{1}H-NMR of compound (C_2) was extracted the following data: 13.43 (s,1H, NH-N), 10.19 (s,14,NH-C=), 6.68 (s,2H,2CH of triazpine), 8.17- 7.45 (m,6H,Ar-H), 1.94(s,6H,2xCH_3). The malonaldehyde compound of indole was reacted with P-phenylendiamine to give compound (C_3).The structure of synthesized compounds has been characterized by FT-IR and ^{1}H-NMR spectra. The FT-IR of compound (C_3) demonstrate the following stretching bands: The bands at 3400-3333 cm^{-1} assigned for the stretching vibration of (NH_2), 3210 cm^{-1} to the(N-H), 3060 cm^{-1} to the(C-H aromatic), 2967-2927 cm^{-1} to (C-H aliphatic), 1709 cm^{-1} to (C= O), 1620 cm^{-1} to (C=N), and the bands at 1606-1556 cm^{-1} to (C= C). The spectrum of ^{1}H-NMR to compound (C_3) appears the following data: 14.20(s,1H, NH), 9.60(s,1H,CHO), 8.40(s,1H,CH=N), 7.97-7.27(m,10H,Ar-H), 6.65(s,2H,NH_2), 1.85(s,6H,2xCH_3). The malonaldehyde compound of indole was reacted with P-phenylendiamine (2 Equivalent) to give compound (C_4). The FT-IR of compound (C_4) shows the following stretching bands: The bands at 3520-3443 cm^{-1} assigned for the stretching vibration of (NH_2), 3300 cm^{-1} due to the(N-H), 2968 cm^{-1} to (C-H aliphatic), 1637 cm^{-1} to (C=N) , 1605-1555 to (C= C) and 1494 cm^{-1}(CH_3 bending) . The spectrum of ^{1}H-NMR to compound (C_4) appears the following data: 13.91(s,1H,NH),8.89(s,2H,2xCH=N), 8.14-6.5 (m,14H,Ar-H), 5.2(s,4H,2XNH_2), 1.98(s,6H,2xCH_3).

The compounds (C_5-C_6) were synthesized by the reaction of compound (C_3) with anhydrous anhydride (malice anhydride , phthalic anhydride) .The structure of thus prepared compounds has been characterized by both FT-IR and ^{1}H-NMR spectra. The FT-IR of compound (C_5) demonstrate the following stretching bands: The bands at 3425 cm^{-1} assigned for the stretching vibration of (N-H), 3041 cm^{-1} to the(C-H aromatic), 2927-2860 cm^{-1} to (C-H aliphatic), 1723 cm^{-1} to (C= O), 1622 cm^{-1} to (C=N) , 1517-1450 cm^{-1} to (C= C) and 1379 cm^{-1}(CH_3 bending) . The spectrum of ^{1}H-NMR to compound (C_5) appears the following data: 14.22(s,1H, NH), 9.67(s,1H, CHO), 8.30(s,1H, CH=N),8.14-7.52 (m,10H,Ar-H), 6.73(d,2H,CH=CH),and 1.94(s,6H,2xCH_3). The spectrum of ^{1}H-NMR to compound (C_6) appears to show the following data: 14.22(s,1H, NH), 9.59(s,1H, CHO), 8.622(s,1H,N=CH), 7.33-8.18(m,14H,Ar-H) and 1.93(s,6H,2xCH_3).

Compound (C_3) was reacted with 2-aminophenol to give compound (C_7).The structure of thus prepared compounds has been characterized by both FT-IR and ^{1}H-NMR spectra. The FT-IR of compound (C_7) demonstrate the following stretching bands: The band at 3418 cm^{-1} to the (O-H) phenol, the band of (N-H) over lapping with (OH) , 3062 cm^{-1} to the(C-H aromatic), 1672 cm^{-1} to (C=N) , 1570-1470 cm^{-1} to (C= C) and 1407 cm^{-1} (CH_3 bending)[15] . The spectrum of ^{1}H-NMR to compound (C_7) appears the following data: 14.22(s,1H,NH), 9.56(s,1H,OH), 8.88(s,2H,2CH=N), 8.01- 6.81 (m,14H,Ar-H), 6.46(s,2H,NH_2), 1.84(s,6H,2xCH_3).

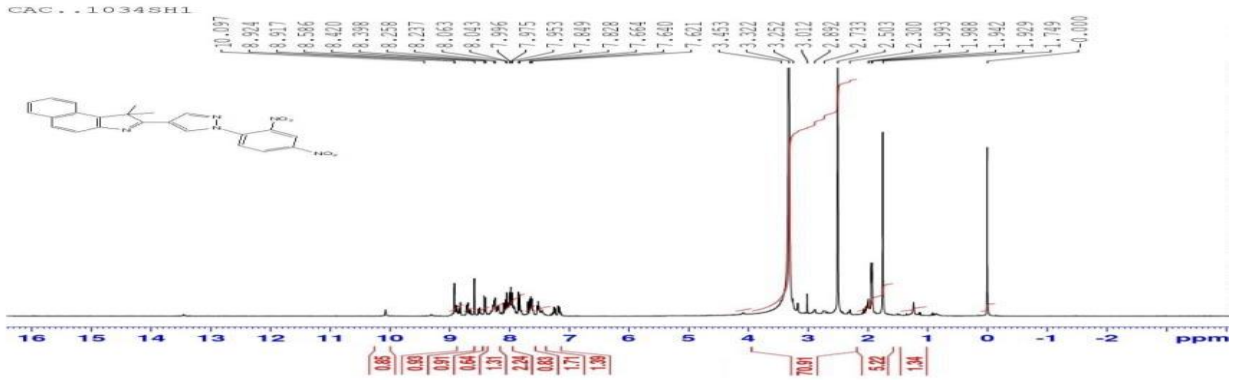


Figure 2. The ^{1}H-NMR spectra of the compound (C_1).

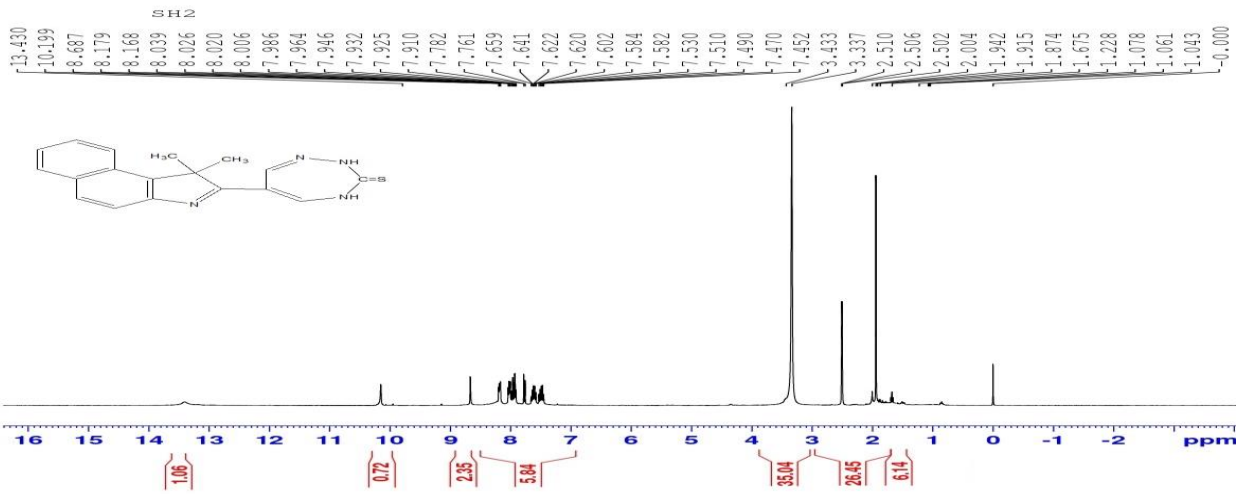


Figure 2. The ^{1}H-NMR spectra of the compound (C_2).

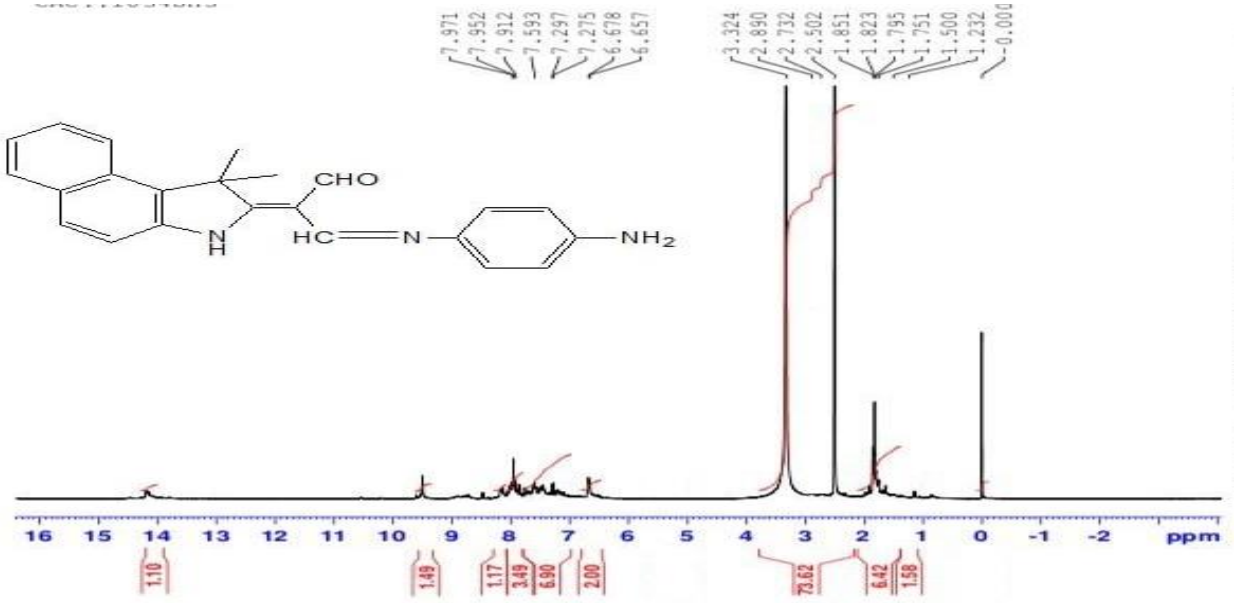


Figure 3. The ^{1}H-NMR spectra of the compound (C_3).

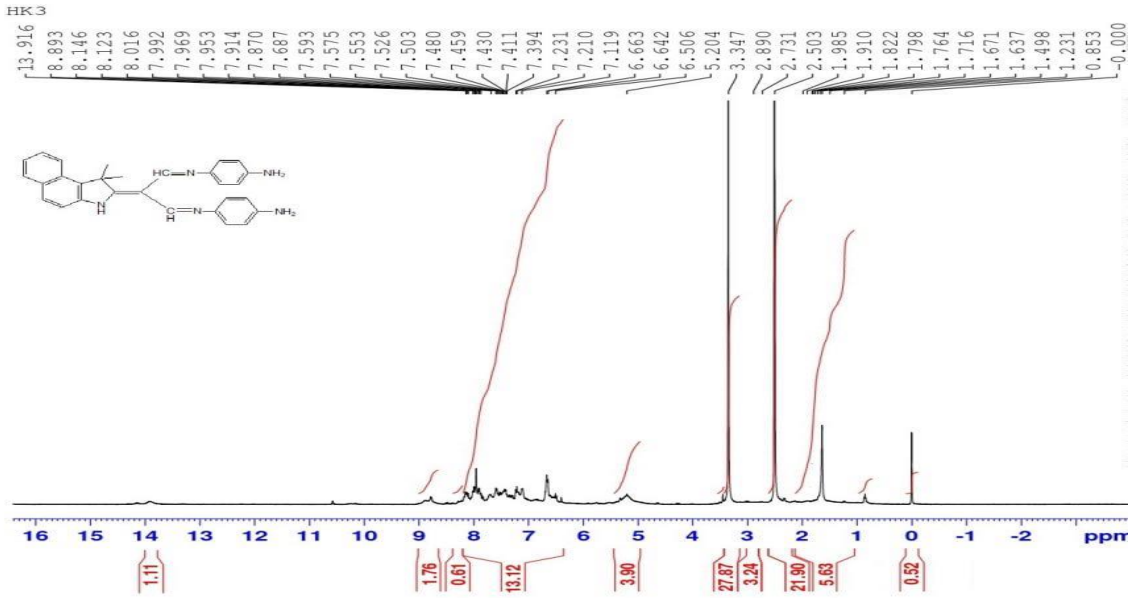


Figure 4. The ^{1}H-NMR spectra of the compound (C_4).

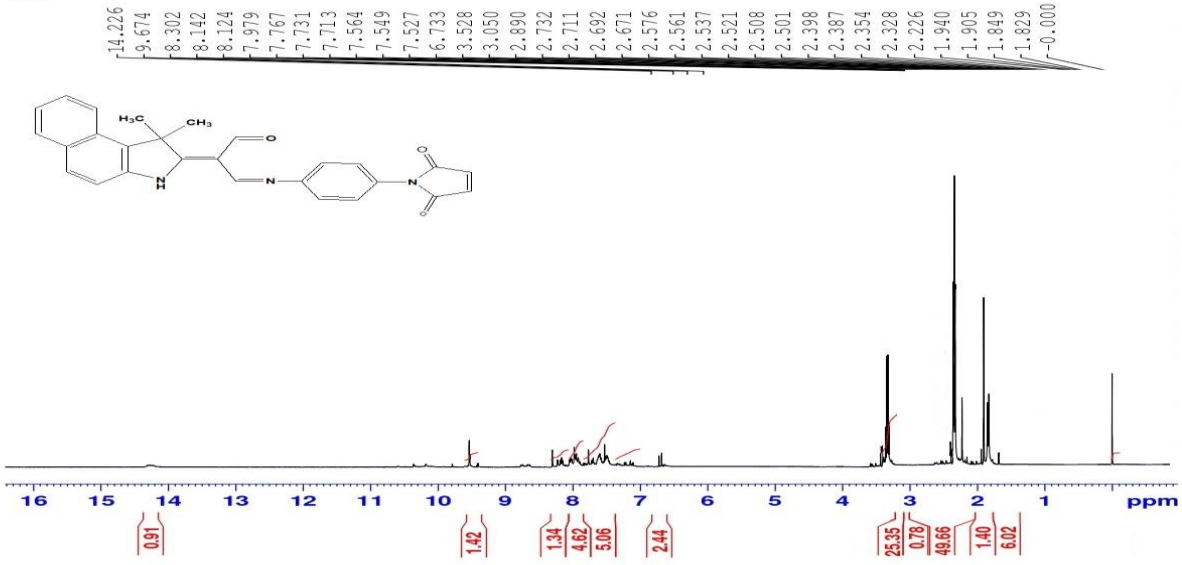


Figure 5. The ^{1}H-NMR spectra of the compound (C_5).

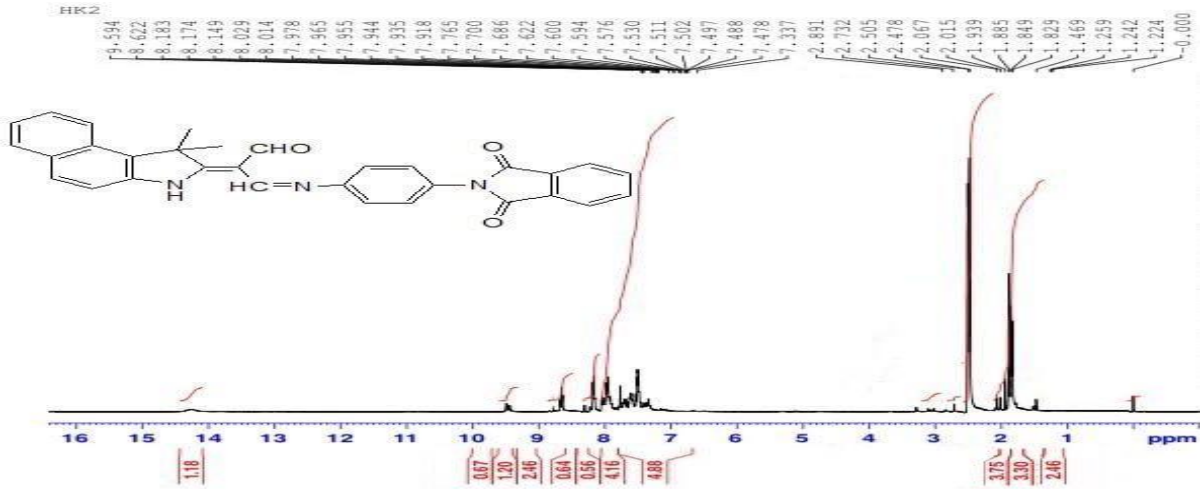


Figure 6. The ^{1}H-NMR spectra of the compound (C_6).

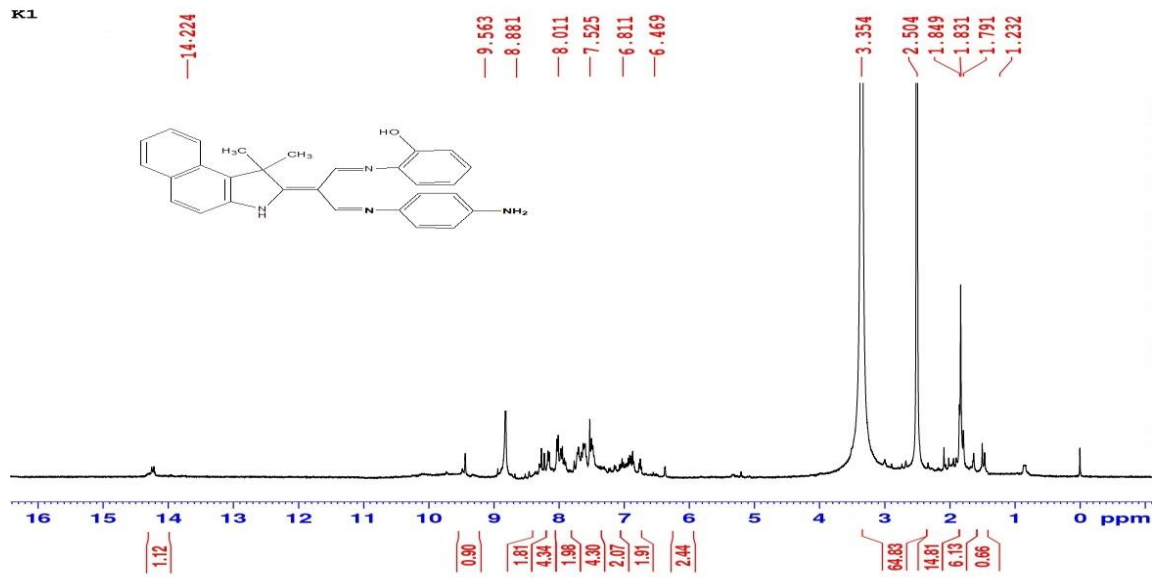


Figure 7. The ^{1}H-NMR spectra of the compound (C_7)

3. Conclusions

New derivatives of indole were synthesized (C_1-C_7) and identified by melting point, TLC, FT-IR, and ^{1}H-NMR spectroscopy technique. The synthesized compounds are 2-[(1-(2,4-dinitrophenyl)-1H-pyrazol-4(yl)]1,1-dimethyl-1H-benzo[e]indole **(C_1)** , 6-(1,1-dimethyl-1H-benzo[e]indol-2-yl)-2,4-dihydro-[1,2,4-triazepine-3-thione **(C_2)** , 3-((4-aminophenyl)imino)-2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)propanal **(C_3)**, N1,N1'-(2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)propane-1,3-diylidene)bis(benzene-1,4-diamine) **(C_4)**, 2-(1,1-Dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-3-[4-(2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-phenylimino]-propionaldehyde **(C_5)** , 2-(1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene)-3-((4-(1,3-dioxoisoindolin-2-yl)phenyl)imino)propanal**(C_6)**, 2-[3-(4-Amino-phenylimino)-2-(1,1-dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-propylideneamino]-phenol**(C_7)**.

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