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A novel method for synthesis of some new heterocyclic compounds derived from (*E*)-2-benzylidenecyclohexanone with expected biological activity

Amira Atef Ghoneim

Chemistry Department, Faculty of Science, Zagazig University, Zagazig, (EGYPT)

E-mail: aa_amiraatef@yahoo.com

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ABSTRACT

We synthesized several heterocyclic compounds from (*E*)-2-benzylidenecyclohexanone 1. That was reacted with pyridine-2-amino 2, and also reacted with 4- ethylthiosemicarbazide followed by cyclization with 2-bromo-1-*p*-tolyehanone. On the other hands, a series of phenyl quinoline derivatives were prepared by the reaction with cyanoacetamide followed by ethylchloroacetate. The fused- ring pyrazole were obtained via the reaction of compound 1 with hydrazine hydrate in ethanol and hydrazine hydrate in acetic acid. The structure of the newly synthesized compounds has been established on the basis of their analytical and spectral data. The biological activity of the prepared compounds was also described.

KEYWORDS

Quinoline;
Hydrazine hydrate;
3-oxo-*N*-phenylbutanamide;
Cyanothioacetamide;
Antimicrobial activity.

INTRODUCTION

Many naturally occurring as well as synthetic compounds containing the pyridine scaffold exhibit interesting pharmacological properties[1, 2, 3]. α, β-Unsaturated ketones are versatile and convenient intermediates for synthesis of a wide variety of heterocyclic compounds. The α,β-enone moiety of the molecule is a favorable unit for dipolar cycloaddition with numerous reagents providing heterocyclic compounds of different ring sizes with one or several heteroatoms[4, 5]. Exocyclic α, β-unsaturated ketones are convenient starting materials for the synthesis of heterocyclic compounds of polycyclic skeletons. Quinoline derivatives possess diverse pharmacological activities, including antimicrobial[6], antimalarial[7], antiviral[8], and antitumor[9].

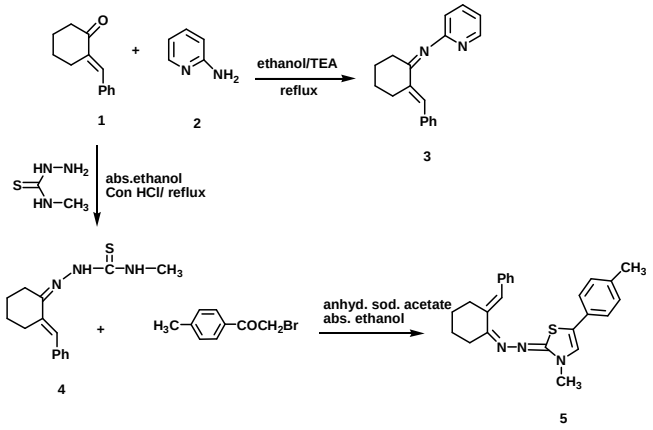
The 5, 6-dihydro-4H-pyrrolo [3, 2, 1-ij] quinoline ring constitutes the central core of different series of compounds exerting platelet activating factor production inhibition[10] or acting as 5-hydroxytryptamine (5-HT2c) receptor agonists and exerting antiepileptic or anti-obesity activities[11].

RESULTS AND DISCUSSION

(E)-2-benzylidenecyclohexanone 1[12] was prepared by treating of cyclohexanone with benzaldehyde in the presence of ethanol and sodium hydroxide solution. *(E)*-2-benzylidenecyclohexanone was reacted with pyridine-2-amine 2 in the presence of ethanol and triethylamine afforded ((6*Z*)-*N*-(*E*)-2-benzylidenecylohexylcidene) pyridine-2-amine 3 (Scheme 1). The IR spectrum of the latter compound showed the absorption band at 1634 cm^{-1} due to C=N and not found absorption band at 3225 and its mass spectrum showed a peak corresponding to its molecular ion at m/z = 262 [M+]. Sub-

sequent, treatment of compound 1 with 4-methylthiosemicarbazide[13] in refluxing absolute ethanol and concentrated hydrochloric acid yielded the corresponding thiosemicarbazide derivative 4 (Scheme 3). The compound 4 was established on the appearance of an NH absorption band at the 3235 cm^{-1} and absorption band at 1632 cm^{-1} for C=N. ^{1}HNMR spectrum revealed the presence of a signal due to NH proton in the 7.05 ppm and the mass spectra showed molecular ion at m/z = 273.14[M+].

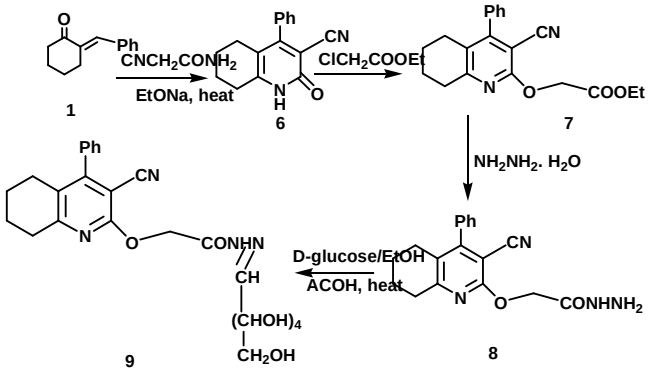
(13*Z*)-1-((*E*)-2-benzylidenecyclohexylidene)-2-(3-methyl-5-*p*-tolylthiazol-2(3H)-ylidene) hydrazine 5 was prepared by refluxing compound 4 with 2-bromo-1-*p*-tolylethanone in the presence of anhydrous sodium acetate in absolute ethanol. The compound 5 was characterized by the IR, ^{1}HNMR, MS spectral and CHN analysis.



Scheme 1 : Synthetic pathway for the preparation of compounds 3-5.

In another side, treatment of (*E*)-2-benzylidenecyclohexanone 1 with 2-cyanoacetamide in the presence of sodium ethoxide and ethanol yielded 1, 2, 5, 6, 7, 8-hexahydro-3-hydroxy-1-phenylisoquinoline-4-carbonitrile 6. Compound 7 was synthesized in a good yield by electrophillic substitution on 2-oxo-4-phenylquinoline-3-carbonitrile derivative 6 using ethyl chloroacetate under the reflux condition. Compound 7 was reacted with hydrazine hydrate in ethanol to give the corresponding hydrazide 8, which was reacted with D-glucose in acetic acid to afford nucleoside derivative 9. The structures of the products were established on the basis of spectroscopic (IR,^{1}H NMR, and MS) data of the pure compounds.

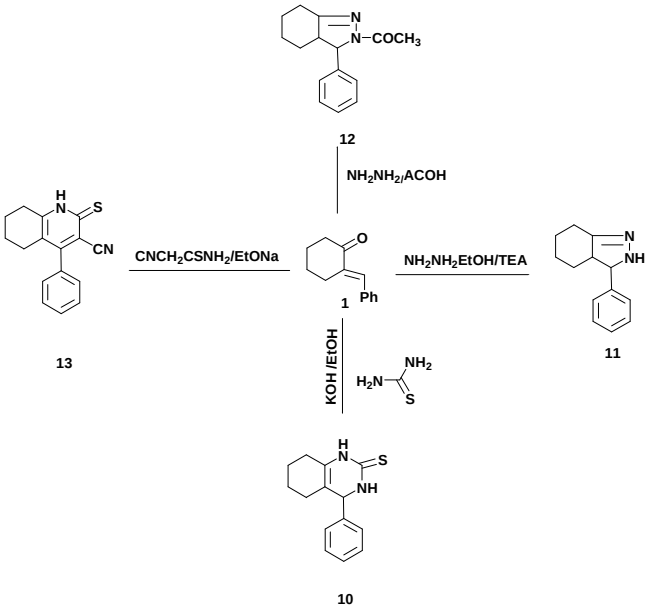
Treatment of compound 1 with thiourea in ethanolic



Scheme 2 : Synthetic pathway for the preparation of compounds 6-8.

potassium hydroxide solution afforded 3, 4, 5, 6, 7, 8-hexahydro-4-phenylquinazoline-2(1H)-thione 10. The IR spectrum of compound 10 showed absorption bands from 3394 to 3411 cm^{-1} for NH and from 1157 to 1184 cm^{-1} for C=S groups. The ^{1}H NMR spectrum of compound 10 showed singlet at 4.67 ppm due to methine. The two NH protons of the pyrimidine ring were seen as two broad singlets at 8.24 to 8.29 ppm. The aromatic protons resonated as a complex multiplet in the region from 7.23 to 8.17 ppm.

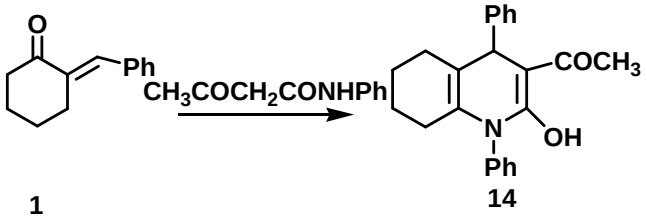
3, 3a, 4, 5, 6, 7-hexahydro-3-phenyl-2H-indazole 11 was prepared by the condensation of compound 1 with hydrazine hydrate in the presence of ethanol. The IR spectrum of compound 11 showed absorption bands at 3230 cm^{-1} for NH and band at 1645 cm^{-1} for C=N. ^{1}H NMR spectrum of compound 11 showed multiple



Scheme 3 : Synthetic pathway for the preparation of compounds 10-13.

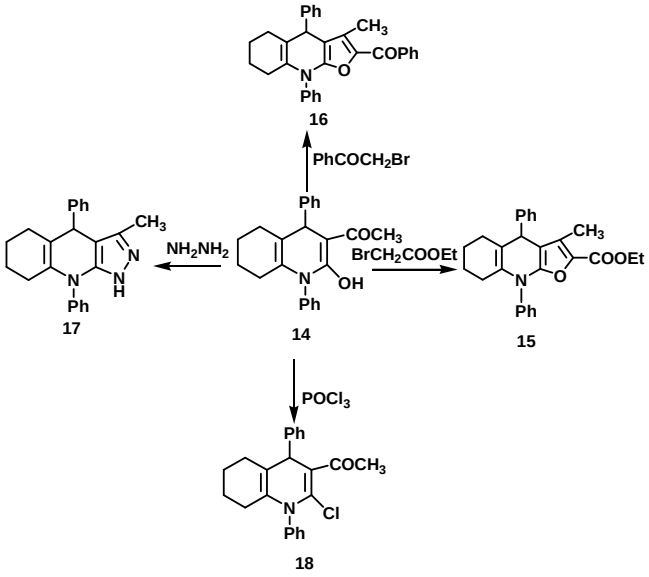
signals at δ 7.04-7.15 ppm due to aromatic protons and at δ 8.23 for NH groups. And also compound 1 reaction with hydrazine hydrate in the presence of acetic acid afforded 1-(3, 3a, 4, 5, 6, 7-hexahydro-3-phenylindazol-2-yl) ethanone 12. Treatment of compound 1 with 2-cyanothioacetamide in ethanol containing catalytic amount of sodium ethoxide yielded thioxoquinoline derivative 13.

The condensation of the compound 1 with 3-oxo-*N*-phenylbutanamide in the presence of sodium ethoxide afforded the desired 1-(1, 4, 5, 6, 7, 8-hexahydro-2-hydroxy-1, 4-diphenylquinolin-3-yl) ethanone 14 in high yield (Scheme 4). The structure of compound 14 was characterized by IR, ^{1}HNMR and MS spectral data. Where The IR spectrum of compound 14 showed absorption bands at 3438 cm^{-1} for OH and at 1695 cm^{-1} for C=O groups. The ^{1}H NMR spectrum of compound 14 showed singlet at 13.43 ppm due to hydroxyl group.



Scheme 4 : Synthesized pathway for the preparation of compound 14.

Ethyl - 4, 5, 6,7, 8, 9- hexahydro-3-methyl-4, 9-diphenylfuro [2,3-b] quinoline-2-carboxylate 15 and 4, 5, 6,7, 8, 9- hexahydro-3- methyl- 4, 9-diphenylfuro[2, 3-b] quinoline-2-yl- (phenyl) mehanone 16 were synthesized by the reaction of compound 14 with ethylbromoacetate and bromophenylethanone respectively in the presence of sodium ethoxide. (Scheme 5). The structures of the products were established on the basis of spectroscopic (IR, ^{1}HNMR, and MS) data of the pure compounds. Compound 14 was reacted with hydrazine hydrate in the presence of ethanol afforded the cyclization compound 4, 5, 6, 7, 8, 9-Hehahydro-3-methyl-4, 9-diphenyl-1H-pyrazolo [3, 4-b] quinoline 17. 1-(2-Chloro-1, 4, 5, 6, 7, 8-hexahydro-1, 4-diphenylquinolin-3-yl) ethanone 18 was prepared by the reaction of compound 14 with phosphoryltrichloride in refluxing. (Scheme 5). The structures of the products were established on the basis of spectroscopic (IR, ^{1}HNMR, and MS) data of the pure compounds.



Scheme 5 : Synthetic pathway for the preparation of compounds 15-18.

Antimicrobial activity

The synthesized were tested for their antibacterial activity *in vitro* in comparison with gatifloxacin as a reference drug using the standard agar disc diffusion method[14] against six bacterial species: *Bacillus cereus* (AUMC B70), *Staphylococcus aureus* (AUMC B71) as representatives of the Gram-positive strains, while the Gram-negative strains were represented by *Escherichia coli* (AUMC B69), *Pseudomonas aeruginosa* (AUMC B72), and *Serratia marcescens* (AUMC B67). Cell suspension of bacterial strains was prepared from 48 h old cultures on nutrient agar (NA) in sterile water. One milliliter of suspension was added to a Petri dish of 9 cm diameter and then 15 mL of NA was poured into the plate. The plate was shaken gently to homogenize the inocula. Sterile 5-mm filter paper disc (Whatman, UK) was saturated with 10 mL of the solution of test compound and gatifloxacin as a reference drug (53 mmol mL–1 in DMSO). In addition, another disc was impregnated with the solvent (DMSO) and served as a negative control. The discs were then dried for 1 h and placed in the center of each plate. The seeded plates were incubated at 35 ± 2 °C for 24–48 h. The radii of inhibition zones (in

mm) of triplicate sets were measured and the results are given in TABLE 1.

The examination of data (TABLE 1) reveals that most of compounds showed excellent antibacterial activity when compared with gatifloxacin. From the results, it is obvious that compound 6, 17 showed the highest degree of inhibition against *Staphylococcus aureus*, *Serratia marcescens*, *Escherichia coli* EC and *Bacillus subtilis* BS. Moreover, compounds 9, 11 and 15 have weak inhibition against *Escherichia coli* and *Cereus Bacillus*. While 10 had a considerable degree of inhibition against *Bacillus Cereus and Pseudomonas aeruginosa*, compounds 9 and 10 had only weak inhibition against *Escherichia coli* EC.

TABLE 1 : Results of antibacterial activity of the tested compounds

Compound	Microorganisms				
	Antibacterial activity (in mm/conc. 1mg/ml^{-1})				
	Staphylococcus aureus	Serratia marcescens	Pseudomonas aeruginosa	Escherichia coli	Bacillus Cereus
6	8	9	7	7	8
9	6	7	6	2	5
10	4	7	4	4	6
11	8	3	8	3	3
12	7	5	6	8	7
15	6	3	4	4	3
17	7	4	7	8	8
Gatifloxacin	8	10	10	9	15

MATERIALS AND METHODS

General

Melting points were determined with an Electro Thermal Mel-Temp II apparatus and are all uncorrected. IR spectra were obtained in the solid state as potassium disc using a Perkin-Elmer model 1430 Spectrometer. 1H NMR were recorded on aVarian/Gemini 200/MHZ spectrometer in DMSO-d6 as a solvent and TMS as an internal standard (chemical shift in δ, ppm). Mass spectra were measured on an instrument "VG-7035" spectra were recorded at 70 or 15 electron volt. Elemental analysis was performed at the Micro analytical centre, Cairo University, Giza, Egypt.

(6Z)-N-((E)-2-benzylidenecyclohexylidene) pyridin-2-amine (3)

A mixture of compound 1 (0.186g, 1 mmol) and the appropriate pyridine-2-amine 2 (0.094g, 1 mmol) in ethanol (50 ml) was refluxed for 4 h. The formed solid product was collected by filtration, washed with ethanol and dried. Recrystallization from ethanol afforded the corresponding imine derivative 3. Yield: 89%; m.p 227-229°C IR: (KBr) 3048, 1634, 1621, 1443 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 7.48-7.21 (m, 4H, C_5H_4), 7.23-7.13 (m, 5H, C_6H_5), 5.92 (s, 1H, CH) 1.96-1.81 (4s, 8H, $4CH_{2)}$. Anal. Calcd. for $C_{18}H_{18}N_2$ (262.35): C, 82.41; H, 6.92; N, 10.68; Found C, 82.71; H, 6.93; N, 10.60.

(1Z)-1-((E)-2-benzylidenecyclohexylidene)-4-methylthiosemicarbazide (4)

A mixture of compound 1 (3.74 g, 2 mmol) and 4-methylthiosemicarbazide (2.11g, 2 mmol) in absolute ethanol (100 mL) was refluxed for 2 h. The separated white solid was filtered off and recrystallized from ethanol and dimethylformamide to give the compound 4. Yield: 87%; m.p 204-206°C; IR: (KBr) 3235-3140, 3025, 1640, 1576, 1443 cm^{-1}; ^{1}HNMR (DMSO-d6) δ 7.38-7.21 (m, 5H, C_6H_5), 7.05 (s, 1H, NH), 6.32 (s, 1H, CH), 3.45 (s, 3H, NH), 2.53 (s, 3H, CH_3), 1.94-1.83 (4s, 8H, $4CH_{2)}$. Anal. Calcd. for $C_{15}H_{19}N_3S$ (273.14): C, 65.90; H, 7.00; N, 15.37; S, 11.73; Found C, 65.71; H, 6.92; N, 15.62; S, 11.43.

(13Z)-1-((E)-2-benzylidenecyclohexylidene)-2-(3-methyl-5-p-tolylthiazol-2(3H)-ylidene) hydrazine (5)

A solution of thiosemicarbazone derivative 4 (0.273 gm, 0.001 mol), anhydrous sodium acetate (0.08 gm, 0.001 mol) and 2-bromo-1-*p*-tolylethanone (0.46 g) in absolute ethanol (30 mL) was heated under reflux for 10-21h, concentrated and left overnight. The product was filtered, dried and crystallized from absolute ethanol to give the compound 5. Yield: 67%; m.p. 253-256°C. IR: (KBr) 3025, 1635, 1621, 1576, 1443 cm^{-1}; ^{1}HNMR (DMSO-d6) δ 7.18-7.21 (m, 9H, C_6H_4, C_6H_5), 7.32 (s, 1H, CH), 6.42 (s, H, CH of thiazoline), 3.45 (s, 3H, NCH_3), 2.73 (s, 3H, CH_3), 1.96-1.81 (4s, 8H, $4CH_{2)}$. Anal. Calcd. for $C_{24}H_{25}N_3S$ (387.54):

C, 74.38; H, 6.50; N, 10.84; S, 8.27; found C, 74.31; H, 6.22; N, 10.92; S, 8.13.

1, 2, 5, 6, 7, 8-Hexahydro-2-oxo-4-phenylquinoline-carbonitrile (6)

A mixture of compound 1 (0.3 g, 1.27 mmole), sodiumethoxide (0.02 g) and cyanoacetamide (0.1 g) in ethanol was heated under reflux for 6 hrs, then allowed to cool, poured into water, the solid product formed was filtrated off and recrystallized from ethanol to afford a pale yellow crystals. Yield: 87%; m.p 310 ^{o}C IR (KBr): 3450-3200, 3020, 2215, 1675, 1664, 1631 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 9.63 (s, IH, NH), 7.12-7.21 (m, 5H, H-aromatic), 1.95 (2t, 4H, 2CH$_2$), 1.65 (2t, 4H, 2CH$_2$) Anal. Calcd. for C $_{16}$H$_{14}$ N$_2$O (250.3): C, 76.78; H, 5.64; N, 11.19; Found C, 76.56; H, 5.82; N, 11.02.

Ethyl-2-(3-cyano- 5, 6, 7, 8-tetrahydro-4-phenylquinolin-2-yloxy) acetate (7)

To a solution of 6 (4.6 g, 0.018 mmol) in absolute ethanol and sodium acetate anhydrous, followed by (1.6 gm, 0.018 mmol) of ethylchloroacetate the reaction mixture was refluxed under anhydrous condition, and filtered, the filtrate was poured into (100 ml) water of ice cold water. The separated ester was extracted with ether and dried over anhydrous magnesium sulphate. m.p. 198-201 ^{o}C; IR (KBr) : 3342, 2981, 2221, 1732, 1637, 1339 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 7.08-7.21 (m, 5H, aromatic-H), 4.49 (q, 2H, CH$_2$), 4.12(s, 2H, CH$_2$), 2.82 (t, 2H, CH$_{2)}$, 2.52 (t, 2H, CH$_{2)}$, 1.82 (m, 4H, 2CH$_{2)}$, 1.35 (t, 3H, CH$_3$). Anal. Calcd. for C $_{20}$H $_{20}$N $_2$O$_3$ (336.38): C, 71.41; H,5.99; N, 8.33; Found C, 71.76; H, 5.82; N, 8.02.

2-(3-Cyano-5, 6,7, 8-tetrahydro-4-phenylquinolin-2-yloxy) acetohydrazide (8)

A solution of 7 (3.8 g, 0.011 mmol) and hydrazine hydrate (0.022 mol) in 50 ml of ethanol was refluxed for 3 hr. The hydrazide which separated on cooling, was collected by filtration m.p. 280-283^{o}C IR (KBr): 3240-3210, 2960, 2231, 1680, 1645 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 9.35 (s, 1H, D2O exchangeable, NHNH$_2$).7.22-7.39 (m, 5H, aromatic-H), 4.34 (s, 2H, D2O exchangeable, NHNH$_2$), 4.24(s, 2H, CH$_2$), 2.92 (t, 2H, CH$_{2)}$, 2.53 (t, 2H, CH$_{2)}$, 1.65(2t, 4H, 2CH$_2$) Anal. Calcd. for $C_{18}H_{18}N_4O_2$ (322.36): C, 67.07; H, 5.36; N, 17.38; Found C, 67.76; H, 5.82; N, 17.02.

2-(3-Cyano -5, 6, 7, 8-tetrahydro-4-phenylquinolin-2-yloxy) acetohydrazono-D-glucose (9)

A solution of 8 (0.32 g, 2.03 mmole) dissolved in warm methanol (30 ml) and acetic acid (2 ml) was added to D-glucose (0.653 g, 1.67 mmole). The reaction mixture was stirred for 6 hrs and then allowed to cool to room temperature. Then the solvent was removed by evaporation in vacuo to dryness, the residue was dissolved in water and washed with aqueous sodium bicarbonate. The organic layer was dried in vacuo, and the residue was recrystallized from ethanol to give yellow crystal yield, 51%, m.p. 210-220^{o}C; ^{1}H-NMR (DMSO-d6) δ 10.23 (s, 1H, NH), 7.12-7.29 (m, 5H, aromatic-H), 6.79 (d, 1H, H-1‘), 5.24 (s, 2H, OH-1, OH-2), 5.03(s, 3H, OH-3, 4, 5), 3.89-3.55 (m, 6H, H-2,3,4,5,6,6‘), 4.53 (s, 2H, CH$_2$), 2.51 (d, 1H, CH), 1.85-2.95 (s, 8H, 4CH$_2$). Anal. Calcd. for $C_{24}H_{32}N_4O_7$ (488.53): C, 59.00; H, 6.60; N, 11.47; Found C, 58.96; H, 6.52; N, 11.32.

3, 4, 5, 6, 7, 8-Hexahydro-4-phenylquinazoline-2(1H)-thione (10)

A mixture of 1 (1.86 gm, 0.01 mol) and thiourea (0.76 gm, 0.01 mol) in ethanolic potassium hydroxide (0.56 gm, in 5 mL) was refluxed for 4–7 h. The volume of the reaction mixture was reduced to half of its original volume, diluted with ice-cold water, then acidified with dilute hydrochloric acid and kept overnight. The solid thus obtained was filtered, washed with water and recrystallized from ethanol. Yield: 81%; mp. 244-246 ^{o}C; IR (KBr) : 3394-3411, 1157, 1184, 1463, 1375 cm-1; 1H-NMR (DMSO-d6) δ 8.24-8.29 (brs, 2H, 2NH), 7.23-8.17 (m, 5H, aromatic-H), 7.50 (s, 1H, NH), 1.73 (2t, 4H, 2CH$_2$), 4.67 (s, 1H, CH), 1.95 (2t, 4H, 2CH$_2$). Anal. Calcd. for $C_{14}H_{16}N_2S$ (244.36): C, 68.81; H, 6.60; N, 11.46; S, 13.12; Found C, 68.96; H, 6.82; N, 11.32; S, 13.32.

3, 3a, 4, 5, 6, 7-Hexahydro-3-phenyl-2H-indazole (11)

A mixture of compound 1 (0.01 molo) and hydrazine hydrate (99%; 0.02 mole) in ethanol (30 ml) in presence of triethylamine was heated under reflux for 5 h, and then allowed to cool. The solid product was collected by filtration and recrystallizod from ethanol to

give 11. Yield: 73%; m.p. 264-265 °C; IR (KBr) : 3204-3143, 1645, 1460, 1378 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 8.23 (brs, 1H, NH), 7.04-7.15 (m, 5H, Ar-H), 2.13 (m, 1H, CH), 3.74 (d, 1H, CH-NH), 1.42 -1.43 (m, 8H, $4CH_2$);Anal. Calcd. for $C_{13}H_{16}N_2$ (200.28): C, 77.96; H, 8.05; N, 13.99; Found C, 77.76; H, 8.12; N, 13.92.

3, 3a, 4, 5, 6, 7-Hexahydro-3-phenyl-2-acetyl-indazole (12)

A mixture of compound 1 (0.01 molo) and hydrazine hydrate (0.02) was refluxed in glacial acetic acid (20 ml) for 6 hrs. The reaction mixture was left to cool; the formed precipitate was filtered, dried washed with water and crystallized. Yield: 66%; m.p. 254-255 °C ^{1}H-NMR (DMSO-d6) 7.08-7.21 (m, 5H, Ar-H), 4.74 (d, 1H, CH), 2.63 (m, 1H, CH), 1.32 -1.43 (m, 8H,$4CH_2$), 2.03 (s, 3H, CH3); Anal. Calcad. for $C_{15}H_{18}N_2O$ (200.28): C, 74.35; H, 7.49; N, 11.56; found C, 74.66; H, 7.12; N, 11.92.

1, 2, 5, 6, 7, 8-Hexahydro - 4 - phenyl - 2 - thioxoquinoline -3-carbonitrile (13)

A mixture of compound 1 (1 mmol), sodium ethoxide (0.03 g) in ethanol (30 ml) and cyanothioacetamide (1 mmol) was added. The mixture was heated under reflux for 5 h; the reaction was cooled and poured onto ice/HCl. The solid was filtered off and dried. Recrystallization from ethanol (71%) afforded 13. m.p. 264-265 °C. ^{1}H-NMR (DMSO-d6) 7.14-7.31 (m, 5H, Ar-H), δ7.23 (s, 1H, NH), 1.92 (2t, 4H, $2CH_2$), 1.65 (2t, 4H, $2CH_2$); Anal. Calcd. for $C_{16}H_{14}N_2S$ (266.36): C, 72.15; H, 5.30; N, 10.52; S, 12.02; Found C, 72.36; H, 5.12; N, 10.92; S, 12.13.

1-(1, 4, 5, 6, 7, 8-Hexahydro-2-hydroxy-1, 4-diphenylquinolin-3-yl) ethanone (14)

A mixture of 1 (1mmol), sodium ethoxide (0.02 g) and 3-oxo-N-phenylbutanamide (1 mmol) in ethanol was heated under reflux for 6 hrs, then allowed to cool, poured into water containing on Con HCl, the solid product formed was filtrated off and recrystallized from ethanol to afford a pale yellow crystals. mp 210 °C; IR: (KBr) 3438 brs, 3025,1695,1631, 1576, 1440 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ13.43 (s, 1H, OH); 7.04-7.15 (m, 10H, Ar-H); 4.34 (s, 1H, CH), 2.33 (s, 3H, CH_3), 1.98 (2t, 4H, $2CH_2$), 1.72 (2t, 4H, $2CH_2$); Anal. Calcd. for $C_{23}H_{23}NO_2$ (345.43): C, 79.97; H, 6.71; N, 4.05; Found C, 79.80; H, 6.42; N, 3.97.

Ethyl 4, 5, 6, 7, 8, 9-hexahydro-3-methyl-4, 9-diphenylfuro [2, 3-b] quinoline-2-carboxylate (15)

To a solution of 14 (1mmol) in absolute ethanol sodium ethoxide (30 ml) was added (10 mmol) sodium in 20 ml absolute ethanol), followed by (1mmol) of ethyl bromoacetate. The reaction mixture was refluxed under anhydrous condition for 3hr. and filtered; the filtrate was poured on to 100 ml of ice –water. The separated ester was extracted with ether and dried over anhydrous magnesium sulphate. Excess ether was removed by distillation the remaining crude was 45%; mp. 233-235 °C crystallized from ethanol; IR (KBr): 3120, 1692, 1631, 1460, 1440 cm^{-1}; ^{1}H-NMR(DMSO-d6) δ 7.01-7.14 (m, 10H, phenyl), 4.74 (s, 1H,CH), 4.26 (q, 2H, CH_2), 1.92 (s, 3H, CH_3), 1.34 (t, 3H, CH_3), 1.97 (2t, 4H, $2CH_2$), 1.67 (2t, 4H, $2CH_2$); Anal. Calcd. for $C_{27}H_{27}NO_3$ (413.51): C, 78.42; H, 6.58; N, 3.39; Found C, 78.51; H, 6.27; N, 3.05.

(4, 5, 6, 7, 8, 9- Hexahydro-3- methyl- 4, 9-dipheny lfuro [2, 3-b] quinoline-2-yl) (Phenyl) mehanone (16)

To a solution of 14 (1mmol) in absolute ethanol, sodium ethoxide (30 ml) was added (10 mmol) sodium in 20 ml absolute ethanol), followed by (1 mmol) of bromophenylethanone. The reaction mixture was refluxed under anhydrous condition for 6hr. and filtered; the filtrate was poured on to 100 ml of ice –water. The separated ester was extracted with ether and dried over anhydrous magnesium sulphate. Excess ether was removed by distillation the remaining crude was 65%; mp 245-247°C, crystallized from ethanol; IR (KBr): 3112, 1664, 1631, 1430 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 6.64-7.14 (m, 15H, phenyl), 4.50 (s, 1H, CH), 1.92 (s, 3H, CH_3), 1.98 (t, 4H, $2CH_2$), 1.68 (t, 4H, $2CH_2$) ; Anal. Calcd. for $C_{31}H_{27}NO_2$ (445.55): C, 83.57; H, 6.11; N, 3.14; Found C, 83.46; H, 5.98; N, 3.00.

1-(2-Chloro-1, 4, 5, 6, 7, 8-hexahydro-1, 4-diphenylquinolin-3-yl) ethanone (17)

A mixture of the compound 14 and phosphoryltrichloride (30 ml) was refluxed with stirring

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for 4hr. On cooling, the yellowish green precipitate with ether (50ml) and crystallized from large quantily of dioxane. m.p. 235 °C; IR (KBr): 3154, 1702, 1641, 1443 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ 7.00-7.24 (m, 10H, phenyl), 4.46 (s, 1H, CH), 2.12 (s, 3H, CH_3), 1.98 (t, 4H, $2CH_2$), 1.98 (t, 4H, $2CH_2$); Anal. Calcd. For C_{23} H_{22}ClNO (363.88): C, 75.92; H, 6.59; N, 3.85; Found C, 75.80; H, 6.38; N, 3.71.

4, 5, 6, 7, 8, 9-Hehahydro-3-methyl-4, 9-diphenyl-1H-pyrazolo [3, 4-b] quinoline (18)

A mixture of compound 14 (0.01 mol) and hydrazine hydrate (0.02 mol) in (30 ml) ethanol was refluxed for 4 h, and then left to cool. The solid product so formed was collected by filtration and recrystallized from ethanol m.p. 282-284 °C; IR (KBr) : 3304-3150, 1630, 1460, 1398 cm^{-1}; ^{1}H-NMR (DMSO-d6) δ12.23 (s, 1H, NH), 6.64-7.15 (m, 10H, Ar-H), 4.74 (s, 1H, CH), 2.53 (s, 3H, CH_3), 1.72 (2t, 4H,$2CH_2$), 1.98 (2t, 4H, $2CH_2$) ; Anal. Calcd. for $C_{23}H_{23}N_3$ (341.45): C, 80.90; H, 6.79; N, 12.31; Found C, 80.76; H, 6.82; N, 12.02.

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