



Received on 09 September, 2015; received in revised form, 09 November, 2015; accepted, 05 January, 2016; published 01 March, 2016

SYNTHESIS OF QUINOLINE DERIVATIVES BY REACTION OF DIMETHYL(2R,3S,4R)-2-PHENYL-4-(PHENYLAMINO)-1,3,4-TRIHYDROQUINOLINE-2,3-DICARBOXYLATE WITH SOME AMINES

Isra' I. Salih Ad-Daraji ¹ and Abdulmajeed S.H. Al Samarrai ^{*2}

Department of Chemistry ¹, College of Education, University of Samarra, Salahalddin 13/1333, Iraq.

Department of Applied Chemistry 2, College of Applied Science, University of Samarra, Salahalddin 13/1333, Iraq.

Key words:

Quinolines, Diesters,
Dimethyl Acetylenedicarboxylate,
Amines, Ring Closure Reactions.

Correspondence to Author:

Dr. Abdulmajeed S. H. Al Samarrai

Department of Applied Chemistry,
College of Education, University of
Samarra, Saladdin 13/1333, Iraq.


Email: abdulmajeedsalihhamad@yahoo.com

ABSTRACT: In this work, quinoline derivatives were synthesized from reaction of aniline, benzaldehyde and dimethylacetylene dicarboxylate (DMAD) in sequent steps to provide quinoline derivative dimethyl (2R, 3S, 4R)-2-phenyl-4-(phenylamino)-1, 3, 4-trihydroquinoline-2,3-dicarboxylate (12). Compound (12), was reacted with some amines such as hydrazine hydrate, urea, thiourea, ethylenediamine, diaminopropane, dinitrophenylhydrazine and o-phenylenediamine to give (3aS,9R,9aS)-2-amino-3a-phenyl-9-(phenylamino)-4,9,9a-trihydro-pyrrolo[3,4-b]quinoline-1,3-dione (13), (3aR) - 1,3 - dioxo - 3a-phenyl-9-(phenylamino)-4,9,9a-trihydro-pyrrolo[3,4-b]quinoline-2-carboxamide (14), (3aS)-1,3-dioxo-3a-phenyl-9-(phenylamino)-4,9,9a-trihydro-pyrrolo[3,4-b] quinoline - 2-carbothioamide (15), 6a-phenyl-12-(phenylamino)-2,3,4,5,7,12,12a-heptahydro-[1,4]diazocino[6,7-b]quinoline-1,6-dione (16), (7aS)-7a-phenyl-13-(phenylamino)-2,3,4,5,6,8,13,13a-octahydro-[1,5]diazonino[7,8-b]quinoline-1,7-dione (17), 2-((2,4-dinitrophenyl)amino)-9-(phenylamino)- 4, 9, 9 a - trihydro-pyrrolo [3,4-b] quinoline-1,3-dione (18), and 2-(2-aminophenyl)-6a-phenyl-12-(phenylamino)-2, 4,5,7,12,12a-hexahydro-diazocino[3,4-b]quinoline-1,6- dione (19) respectively. Reaction of (12) sodium metal gave methyl 3-oxo-2-phenyl-5-(phenylamino)-1,2, 4,5-tetrahydro- benzo[b]azepine-4-carboxylate(20). These reactions were carried out with different solvents like acetonitrile, ethanol, and chloroform providing good yields of the new heterocyclic compounds (13-20) of quinoline derivatives. The identification of the compounds(13-20) were based on spectroscopic analysis such as IR, UV, ¹H-NMR, ¹³C-NMR, and the microanalysis of the elements (CHN) data.

INTRODUCTION: In recent years, the chemistry of nitrogen heterocyclic compounds especially quinolines has attracted attention due to their reactivity and biological activities like antibacterial ¹, antiasthmatic ², antihypertensive ³, anti-inflammatory agents ⁴, and antiobesity. ⁵ Quinolines also have antipyretic, antiperiodic ⁶ properties and are used as antimalarials and for preparing other antimalarial drugs. ⁷

Quinoline derivatives are prevalent in a variety of pharmacologically active synthetic and natural compounds. ⁸ A prominent example is quinine (1) which is found naturally in plants as alkaloids ⁹. The chloroquine (2) ¹⁰ is the most famous drug containing this active ingredient resulted in control and treatment of malaria for decades ⁷.

Because the chloroquine prevent the development of malaria parasites in the blood so it is used by doctors to both prevent and treat malaria. ¹¹ Simple quinoles (3-6) are isolated from the bark of *Galipea longiflora* trees of the Rutaceae family ¹²⁻¹⁴ used effectively against the parasites *Leishmania* sp., which are the agents of Leishmaniasis, a protozoan disease of the tropical areas in South Africa,

QUICK RESPONSE CODE	DOI: 10.13040/IJPSR.0975-8232.7(3).961-67
	Article can be accessed online on: www.ijpsr.com
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7(3).961-67	

particularly in the amazonian forest.¹⁵ Previous publications have clearly demonstrated many reactions in various synthetic applications which give rise to quinoline nucleus.¹⁶⁻¹⁹ The most versatile method available for the synthesis of quinoline derivatives is the reaction of 2-aminoacetophenon and ethyl acetoacetate in the presence of chloramine-T and acetonitrile as a solvent to afford (7).^{20, 21}

There is a facile and efficient iron-catalyzed intramolecular allylic amination of 2-aminophenyl-1-en-3-ols which proceeds smoothly to afford 1,2-dihydroquinoline and quinoline derivatives such as (8) and under further mild reaction conditions gives

good yields of (9).²² Also, 1,4-dihydroquinolines such as (11) has been reported through sequential N-acylamide (10) methylenation-enamide ring-closing metathesis.²³

As a part of our continued interest in the development of new synthetic methods for further highly substituted fused rings to quinoline nucleus, we have developed a new synthetic route mainly to the synthesise of pyrroloquinolines derivatives through unprecedented approach from dimethyl (2R,3S,4R)-2-phenyl - 4 - (phenylamino)-1,3,4-trihydroquinoline-2,3-dicarboxylate (12) and amines.

(1)

(2)

MATERIALS AND METHOD:

Infrared (IR) spectra were recorded on Shimadzu FT-IR 8400S instrument, and were calibrated using a polystyrene film. Solid compounds were recorded in potassium bromide disks (KBr). Ultraviolet (UV) spectra were recorded on Shimadzu UV-1800 spectrophotometer, $^1\text{H-NMR}$ spectra were recorded on 400 MHz AV III-HD-800 Bio Spin spectrometer while $^{13}\text{C-NMR}$ were recorded on 300 MHz Bruker spectrometer instrument using dimethyl sulfoxide (DMSO-d_6) as a solvent solution, using tetramethylsilane (TMS) as an internal standard. Chemical shifts were quoted in parts per million (ppm) downfield from TMS. Elemental analysis was performed on the CHN elemental (Eur Vector EA 3000A) Germany, see **Table 1**. Analytical thin layer chromatography (T.L.C.) was carried out on already made 5x5 cm plates coated with silica gel 0.25 cm N-HR/UV₂₅₄, while column chromatography was carried out using silica gel (60-230 mesh) as a stationary phase and different solvent systems as mobile phases.

Reaction of aniline, dimethyl acetylene dicarboxylate (DMAD), and benzaldehyde in the presence of p-toluene sulfonic acid as a catalyst:

Dimethyl acetylenedicarboxylate (1.136g, 8mmol) was added to a solution of aniline (1.48g, 15.91 mmol) in ethanol (5ml) and the mixture stirred overnight at room temperature. Benzaldehyde (0.848g, 8 mmol) and p-toluene sulfonic acid (0.344g, 2 mmol) were added to the solution with further stirring for 48h. Solid product separated out, was collected, washed with cold ethanol, and recrystallized from ethanol to give pale green crystals for dimethyl(2R,3S,4R)-2-phenyl-4-(phenylamino)-1,3,4-trihydroquinoline-2,3-dicarboxylate (12), m.p., 177-179°C, (yield : 1.66g, 48%). λ_{max} (EtOH) : 207, 253, and 292 nm. ν_{max} (KBr) : 3260, 3210 (N-H); 3050 ($-\text{C}_6\text{H}_5$); 2930 (CH-aliph.); 1700, 1680 (2C=O); 1230 (C-O), and 1060 cm^{-1} (C-N).

$^1\text{H-NMR}$ (DMSO-d_6) : δ 2.1 (3H, s, $(\text{CH}_3\text{O})_3$); 2.3 (1H, d, CHNH); 3.0 (3H, s, $(\text{CH}_3\text{O})_3$); 5.4 (1H, d, CH), and 7.1-7.6 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO-d_6): δ 27.1 (C_3); 30.1 (C_2); 33.2 (C_4); 125-145 (C-aromatic); 145.3 (C_{9a} -ipso); 148.4 (C_{4a} -ipso); 175.1 ($\text{C}_3=\text{O}$); 179.5 ppm ($\text{C}_3=\text{O}$).

General procedure for the synthesis of the compounds (13-19):

An equivalent amount of (12) was added to solutions containing the amines, hydrazine hydrate, urea, thiourea, ethylene diamine, 1,3-propane diamine, 2,4-dinitrophenylhydrazine, and phenylene diamine with stirring at various temperature (see **Table 2** further reaction conditions). Solid products separated out were filtered off and recrystallized to give compounds (13-19) respectively.

(3aS,9R,9aS) - 2 - amino- 3 a - phenyl - 9 - (phenylamino)-4,9,9a - trihydro - pyrrolo [3, 4-b]quinoline-1,3-dione (13).

(Yield: 0.14g, 68%), λ_{max} (EtOH) : 202, 222, 254, and 284 nm. ν_{max} (KBr) : 3213 (N-H); 3051 (C_6H_5); 2956 (CH-aliph.); 1610, 1620 (2C=O); 1230 (C-O), and 1050 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO-d_6) : δ 2.4 (1H, d, CHNH); 2.6 (1H, s, NH); 4.1 (2H, s, NH_2); 5.5 (1H, d, CHCO), and 7.3-7.7 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO-d_6) : δ 28.0 (C_{9a}); 32.5 (C_{3a}); 34.1 (C_9); 127-146 (C-aromatic); 147.0 (C_{4b} -ipso); 149.1 (C_{8b} -ipso); 178.9 ($\text{C}_1=\text{O}$); 180 ppm ($\text{C}_3=\text{O}$).

(3aR)-1,3-dioxo-3a-phenyl - 9 - (phenylamino)-4,9,9a-trihydro - pyrrolo [3,4-b] quinoline-2-carboxamide (14).

(Yield: 0.057g, 20%), λ_{max} (EtOH) : 203, 253, and 291 nm. ν_{max} (KBr) : 3261, 3209 (N-H); 3050 ($-\text{C}_6\text{H}_5$); 2950, 2922 (CH-aliph.); 1710, 1683 (2C=O); 1240 (C-O), and 1065 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO-d_6) : δ 2.6 (1H, d, CHNH); 2.65 (1H, s, NH); 4.4 (2H, s, NH_2); 5.6 (1H, d, CHCO), and 7.0-7.6 ppm (ph-protons). $^{13}\text{C-NMR}$ (DMSO-d_6) : δ 27.5 (C_{9a}); 31.1 (C_{3a}); 34.0 (C_9); 130-147 (C-aromat); 145.0 (C_{4b} -ipso); 149.5 (C_{8b} -ipso); 177.3 ($\text{C}_1=\text{O}$); 180.0 ($\text{C}_3=\text{O}$); 183.1 ppm (C=O-NH₂).

(3aS)-1,3-dioxo-3a-phenyl - 9 - (phenylamino)-4,9,9a-trihydro - pyrrolo [3,4-b] quinoline - 2-carbothioamide (15).

(Yield: 0.108g, 40%), λ_{max} (EtOH) : 210, 253, and 295 nm. ν_{max} (KBr) : 3257, 3207 (N-H); 3006 ($-\text{C}_6\text{H}_5$); 2956 (CH-aliph.); 1703, 1680 (C=O); 1232 (C-O); 1201 (C=S), and 1075 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO-d_6) : δ 2.67 (1H, d, CHNH); 2.7 (1H, d, NHCH); 3.1 (1H, s, NH); 4.9 (2H, s, NH_2); 5.68 (1H, d, CHCO), and 7.2-7.8 ppm (Ph-

protons). $^{13}\text{C-NMR}$ (DMSO- d_6) : δ 28.5 (C_{9a}) ; 31.5 (C_{3a}) ; 32.9 (C_9) ; 130-149 (C-aromatic) ; 146.0 (C_{4b} -ipso) ; 149.5 (C_{8b} -ipso) ; 178.4 ($\text{C}_1=\text{O}$) ; 179.0 ppm ($\text{C}_3=\text{O}$).

6a-phenyl-12-(phenylamino)-2, 3, 4, 5, 7, 12, 12a-heptahydro-[1,4]diazocino[6,7-b]quinoline - 1, 6-dione (16).

(Yield: 0.357g, 70%), λ_{max} (EtOH) : 209 , 255 , and 305 nm. ν_{max} (KBr) : 3450 (N-H) ; 3028 (- C_6H_5) ; 2954 (CH-aliph.) ; 1700 , 1685 (2C=O) ; 1228 (C-O) , and 1076 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO- d_6) : δ 2.5 (1H , d , CHNH) ; 2.6 (1H , d , NHCH) ; 3.0 (1H , s , NH) ; 4.1 (1H , t , 2NHCH $_2$) ; 5.4 (1H , d , CHCO) ,and 7.0-7.9 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO- d_6) : δ 27.0 (C_{12a}) ; 31.5 (C_{12}) ; 32.1 (C_{6a}) ; 62 ($\text{C}_{3,4}$) ; 128-140 (C-aromatic) ; 145.3 (C_{7b} -ipso) ; 148.4 (C_{11b} -ipso) ; 179.0 ($\text{C}_1=\text{O}$) ; 181.0 ppm ($\text{C}_6=\text{O}$)

1,3- Diaminopropane(7aS) -7a – phenyl -13-(phenylamino)-2,3,4,5,6,8,13,13a-octahydro-[1,5] diazonino[7,8-b]quinoline-1,7-dione (17).

(Yield: 0.46g, 79%), λ_{max} (EtOH) : 206 , 262 , and 313 nm. ν_{max} (KBr) : 3327 (N-H) ; 3060 , 3029 (C_6H_5) ; 2949 (CH-aliph.) ; 1689 (C=O) ; 1228 (C-O) , and 1031 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO- d_6) : δ 2.51 (1H , d , CHNH) ; 2.61 (1H , d , NHCH) ; 2.9 (1H , s , NH) ; 4.0 (1H , t , 2NHCH $_2$) ; 5.1 (1H , d , CHCO) ,and 7.0-7.8 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO- d_6) : δ 21.5 (C_4) ; 26.5 (C_{13a}) ; 30.8 (C_{13}) ; 33.0 (C_{7a}) ; 62.7 ($\text{C}_{3,5}$) ; 126.5-141 (C-aromatic) ; 146.0 (C_{8b} -ipso) ; 149.3 (C_{12b} -ipso) ; 178.7 ($\text{C}_1=\text{O}$) ; 181.5 ppm ($\text{C}_7=\text{O}$).

2-((2,4-dinitrophenyl)amino) - 9 -(phenylamino)-4,9,9a-trihydro-pyrrolo[3,4-b]quinoline - 1, 3-dione (18).

(Yield: 0.58g, 60%), λ_{max} (EtOH) : 205 , 245 , and 363 nm. ν_{max} (KBr) : 3350 (N-H) ; 3050 (C_6H_5) ; 2910 , 2925 (CH-aliph.) ; 1695 (C=O) ; 1225 (C-O) , and 1080 cm^{-1} (C-N).

$^1\text{H-NMR}$ (DMSO- d_6) : δ 2.6 (1H , d , CHNH) ; 2.75 (1H , d , NHCH) ; 3.2 (1H , s , NH) ; 4.7 (1H , s , NHNCO) ; 5.4 (1H , d , CHCO) ,and 7.3-8.1 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO- d_6): δ 28.1 (C_{9a}) ; 31.5 (C_9) ; 34.1 (C_{3a}) ; 127.1-142 (C-aromatic) ; 147.3 (C_{4b} -ipso) ; 150.4 (C_{8b} -ipso) ; 179.5 ($\text{C}_1=\text{O}$) ; 182.3 ppm ($\text{C}_3=\text{O}$).

g- O-phenylendiamine2-(2-aminophenyl) - 6a - phenyl-12-(phenylamino)-2, 4, 5, 7, 12, 12a-hexahydro-diazocino[3,4-b]quinoline- 1, 6- dione (19).

(Yield: 0.38g, 57%), λ_{max} (EtOH) : 206 , 244 , 276 , 360, 370 , and 400 nm. ν_{max} (KBr) : 3275 (N-H) ; 3025 (- C_6H_5) ; 2990 (CH-aliph.) ; 1675 (C=O) ; 1240 (C-O) , and 1070 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO- d_6) : δ 2.83 (1H , d , CHNH) ; 2.9 (1H , d , NHCH) ; 3.3 (1H , s , NH) ; 4.6 (1H , s , 2NH) ,and 7.3-7.9 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO- d_6) : δ 27.4 (C_{12a}) ; 29.7 (C_{12}) ; 33.0 (C_{6a}) ; 126.3-141.1 (C-aromatic) ; 145.1 (C_{7b} -ipso) ; 149.0 (C_{11b} -ipso) ; 177.7 ($\text{C}_1=\text{O}$) ; 181.4 ppm ($\text{C}_6=\text{O}$).

Reaction of (12) with sodium metal:

Small pieces of sodium metal (0.081g, 3.6 mmol) was added to a suspension of (10) (0.5 g, 1,2 mmol) in dry diethyl ether (15 ml). Mixture was stirred at room temperature for 72 h accompanied by change of colour from pink to yellow during reaction time. Solid material was separated out, filtered off, washed with diethyl ether and recrystallized from acetonitrile to give methyl 3-oxo-2-phenyl-5-(phenylamino)-1,2,4,5-tetrahydro - benzo[b]azepine-4-carboxylate(20), m.p., 270-272 $^{\circ}\text{C}$, (yield: 0.35g , 60%). λ_{max} (EtOH) : 209 , 261 ,and 315 nm. ν_{max} (KBr) : 3350 (N-H) ; 3060 , 3030 (- C_6H_5) ; 2997 , 2947 (CH-aliph.) ; 1703 (C=O) ; 1238 (C-O) ,and 1076 cm^{-1} (C-N). $^1\text{H-NMR}$ (DMSO- d_6) : δ 2.2 (3H , s , CH_3OCO) ; 2.8 (1H , d , CHph) ; 2.83 (1H , s , NHCH) ; 2.85 (1H , d , CHNH) ; 3.25 (1H , s , NH) ,and 7.1-7.8 ppm (Ph-protons). $^{13}\text{C-NMR}$ (DMSO- d_6) : δ 30.1 (C_4) ; 31.5 (C_5) ; 34.8 (C_2) ; 127-144 (C-aromatic) ; 143.7 (C_{9a} -ipso) ; 147.9 (C_{5a} -ipso) ; 176.5 ($\text{CH}_3\text{C}=\text{O}$) ; 180.6 ppm ($\text{C}_3=\text{O}$).

RESULTS AND DISCUSSION: Besides the importance of quinoline and its derivatives as biologically active agents, they are also useful synthons and building block for many heterocyclic products and probably used as biologically agents also. Condensation of anilines and benzaldehyde and acetylenic ester has been extensively used for the preparation of nitrogen heterocyclic compounds, especially in the preparation of condensed heterocycles such as the compound (21), as it can be seen below:

TABLE 1: CHN ANALYSIS OF COMPOUNDS (12-20).

Comp. No.	Molecular Formula	Found				Calculated			
		C%	H%	N%	S%	C%	H%	N%	S%
12	C ₂₅ H ₂₄ N ₂ O ₄	72.11	5.76	6.73	72.15	5.71	6.77
13	C ₂₃ H ₂₀ N ₄ O ₂	73.01	5.29	14.81	72.89	5.32	14.79
14	C ₂₄ H ₂₀ N ₄ O ₃	69.90	4.85	13.59	69.83	4.91	13.45
15	C ₂₄ H ₂₀ N ₃ O ₂ S	69.56	4.83	10.14	7.72	69.66	4.92	10.17	7.75
16	C ₂₅ H ₂₄ N ₄ O ₂	72.81	5.82	13.59	72.74	5.88	13.62
17	C ₂₅ H ₂₅ N ₄ O ₂	72.63	6.05	13.55	72.69	6.01	13.57
18	C ₂₉ H ₂₂ N ₆ O ₆	66.15	4.18	15.96	66.22	4.25	16.10
19	C ₂₉ H ₂₄ N ₄ O ₂	75.65	5.21	12.17	75.73	5.19	12.20
20	C ₂₄ H ₂₂ N ₂ O ₃	74.61	5.69	7.25	74.66	5.61	7.31

TABLE 2: REACON CONDITION, PHYSICAL PROPERTIES, AND YIELD % OF SYNTHESIZING COMPOUNDS (13-20).

Products	Mmoles of (12)	Mmoles of Amine	Reaction Time (H)	Reaction Temp. °C	Solvent	Colour	Recrystall. Solvent	M.P. (°C)	Yield %
13	0.6	0.6	48	R.T.	Chloroform	Pink	Ethanol	190	68
14	0.6	0.6	240	R.T.	acetonitrile	white	ethanol	182-5	20
15	0.6	0.6	72	R.T.	Acetonitrile	white	acetonitrile	196-8	40
16	1.2	1.2	0.5 min.	40	Acetonitrile	white	ethanol	150	70
17	1.2	1.2	4 min.	40	Acetonitrile	white	ethanol	193	79
18	1.2	1.2	12	80	Acetonitrile	orange	acetonitrile	195-7	60
19	1.2	1.2	12	80	Acetonitrile	orange	ethanol	248	57
20	1.2	3.6*	72	R.T.	diethyl ether	yellow	acetonitrile	270-2	60

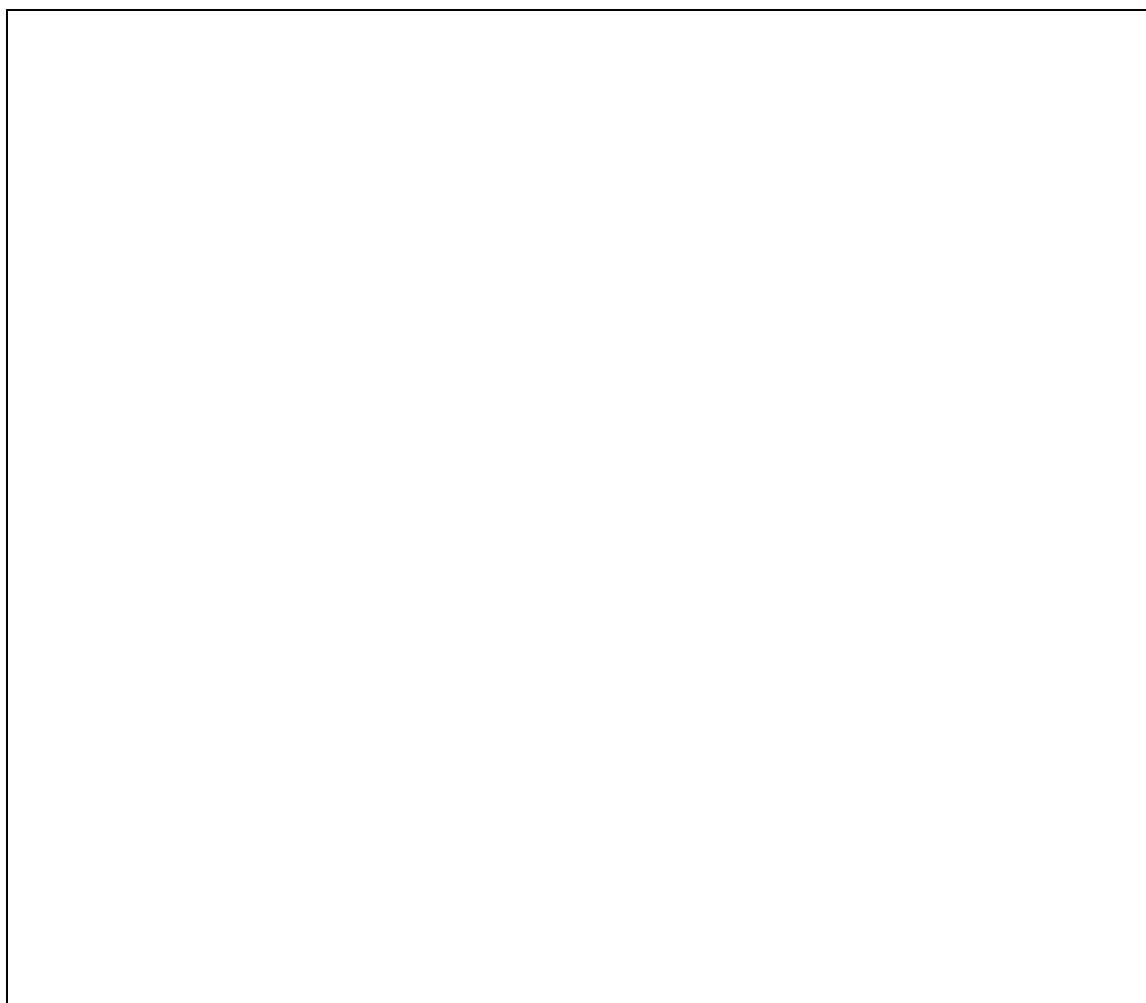
In view of significant interest in the synthesis of these heterocyclic, we herein report in a detailed account of the synthetic methods available for the synthesis of (12). In a typical experiment, aniline, dimethyl acetylenedicarboxylate (DMAD) and benzaldehyde were reacted in presence of p-toluene sulfonic acid in absolute ethanol with stirring to afford the corresponding product, dimethyl (2R,3S,4R)-2-phenyl-4-(phenylamino)-1,3,4-trihydroquinoline-2,3-dicarboxylate (12) in moderate yield. The reaction was completed within 72 hours, as it can be seen below:

The mechanism apparently do not differ from that of forming (21) and involves the nucleophilic attack of aniline on the dimethyle acetylenedicarboxylate with formation of compound (21), through the following mechanism:

Compound (12) was further converted into their cyclic imide derivatives by treatment with different amines. The reaction of (12) with hydrazine hydrate at room temperature afforded the heterocyclic compound (13). The compound (13) was characterized by IR which showed a fundamental stretching band (doublet) due to NH_2 at 3261 and 3209 cm^{-1} . Compounds (14) and (15) prepared from reaction of (12) with urea and thiourea at room temperature, also showed a fundamental stretching bands (doublet) due to NH_2 at 3250 , 3200 and 3255 and 3205 cm^{-1} respectively. In general, IR spectra of the rest of the compounds (16-20) showed N-H stretching at about 3450 to 3210 cm^{-1} . In addition to that, the compounds (13-20) also showed two carbonyl ($\text{C}=\text{O}$) stretching absorption band for imides compounds at around 1710 to 1610 cm^{-1} , methoxy ($\text{C}-\text{O}-\text{C}$) band absorption at around 1240 to 1225 and C-N absorption band at around 1080 to 1031 cm^{-1} .

$^1\text{H-NMR}$ spectra of the compounds (12-20) showed characterization signals at around δ 2.3 to 2.85 for CHNH, signals for NH at around δ 2.6 to 3.3, signals at around δ 5.1 to 5.65 for CHCO, aromatic protons signals were appeared at about δ 7.0 to 8.1 ppm.

Regarding $^{13}\text{C-NMR}$ spectra for the same compounds (12-20), signals at around δ 27.1 to 30.1 for CH group adjacent to carbonyl group, signals for CH adjacent to NH group at around δ 30.8 to 34.4, signals at around δ 30.1 to 34.8 for tertiary carbon adjacent to the other carbonyl group. Signals that due to aromatic carbon appeared at around δ 125 to 149, the ipso-carbon showed signals at around δ 143.7 to 150.4 and important signals were observed due to carbonyl group carbons at about δ 175.1 to 182.3 ppm. Microanalysis (CHN) of the compounds (12-20) confirms the molecular weight of the desired compounds.



SCHEME 1: REACTION OF COMPOUND (12) WITH SOME AMINES.

CONCLUSIONS: Quinoline and its derivatives are important heterocyclic systems which have great significance as a biologically active compounds as well as being useful synthon for synthesis of many heterocyclic compounds. This work describes the synthesis of new heterocyclic compounds from quinoline derivatives and amines.

ACKNOWLEDGMENT: We thank the department of chemistry, college of applied science, university of Samarra, Iraq for funding this project. Also, we thank Samarra drug industry (SDI) (Samarra) for providing some instrumental facilities.

REFERENCES:

1. M. E. Welsch, S. A. Snyder, B. R. Stockwell, Privileged scaffolds for library design & drug discovery. *Curr. Opin. Chem. Biol.*, 2010, 14: 347.
2. M.A.,Nasser, B.Zakerinassab, S.Kamayestani, Proficient Procedure for Preparation of Quinoline Derivatives Catalyzed by NbCl₅ in Glycerol as Green Solvent. *Journal of Applied Chemistry*, 2014, 2015: 1.
3. C. N. Warshakoon, J. Sheville, T. R. J. Bhatt, L. J. Mendez Andino, M. K. Meyers, N. Kim, A.J. Wos, C. Mitchell, L. Jeennifer, L. P. Paris, B. Benth, B. B. Pinney, O.Ofer Reizes, X. E. Hu, Design & synthesis of substituted quinolines as novel & selective MCHA as antiobesity agents. *Bioorg. Med. Chem. Lett.*, 2006, 16: 5207.
4. S. Mukherjee, M. Pal, Medicinal chemistry of quinolines as emerging anti-inflammatory agents: an overview. *Curr. Med. Chem.*, 2013, 20 (35): 4386.
5. Y. L. Chen, K. C. Fang, J. Y. Sheu, S. L. Hsu, C. C. Tzeng, Synthesis & antibacterialevaluation of certain quinolone derivatives. *J. Med. Chem.*, 2001, 44: 2374.
6. A. U. Malik, M. Adeel, I. Ullah, M. K. Baloch, M. Mustaqeem, M. Akram, Solubility of 3-{3,5-Bis(trifluoromethyl)phenyl}quinoline Using Micellar Solutions of Surfactants. *Journal of Solution Chemisry*, 2015, 44(6): 1191.
7. C. Mullié, N. Taudon, C. Degrouas, A. Jonet, A. Pascual, P. Agnamey, P. Sonnet, Enantiomerically pure amino-alcohol quinolines: in vitro anti-malarial activity in combination with Dihydroartemisinin, cytotoxicity and in vivo efficacy in a plasmodium berghei mouse model. *Malaria Journal*, 2014, 13: 407.
8. L. V. Reddy, S. B. Nallapati, S. S. Beevi, L. N. Mangamoori, K. Mukkanti, S, Pal, A "green" synthesis of N-(quinoline-3-ylmethylene)benzohydrazide derivatives and their cytotoxicity activities. *J. Braz. Chem. Soc.*, 2011, 22, 1742.
9. T. K. Milugo, L. K. Omosa, J. O. Ochanda, B. O. Owuor, F. A. Wamanyokoli, J. O. Oyugi, J. W. Ocheing, Antagonistic effect of alkaloids and saponins on bioactivity in the quinine tree (*Rauvolfia caffra* sond.): further evidence to support biotechnology in traditional medicinal plants. *BMC Complementary and Alternative Medicine*, 2013, 13, 285.
10. P. Kurup, Y. Zhang, Aβ-mediated NMDA receptor endocytosis in Alzheimer's diseas involves ubiquitination of the tyrosine phosphatase STEP 61. *Neurobiology of Disease*, 2010, 30: 5948.

How to cite this article:

Ad-Daraji IIS and Al Samarrai ASH: Synthesis of Quinoline Derivatives by Reaction of Dimethyl(2r,3s,4r)-2-Phenyl-4-(Phenylamino)-1,3,4-Trihydroquinoline-2,3-Dicarboxylate with Some Amines. *Int J Pharm Sci Res* 2016; 7(3): 961-67.doi: 10.13040/IJPSR.0975-8232.7(3).961-67.

All © 2013 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **ANDROID OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)