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Synthesis of new 6-substituted-3-(4-substitutedphenyl) Diazenyl)-2, 4-dimethyl quinoline derivatives

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Abstract
A synthesis of new (E)-6-substituted-3-((4-substitutedphenyl) diazenyl)-2,4-dimethyl quinolines has been achieved by the Combs reaction. The synthesis of the derivatives is based on diazonium coupling reaction. The intermediate compound (E)-3-((4-substitutedphenyl)diazenylpentane-2,4-dione derivatives (I-VI) was obtained from diazonium coupling reaction between primary aromatic amines with acetyl acetone, then condensation to a (Z)-3-((E)-(4-substituted phenyl)diazenyl)-4-((4-substituted phenyl)imino)pentan-2-one derivatives (VII – XIV) followed by elimination of a water molecule and cyclisation of the result by the heating and elimination of water in presence Sulphuric acid to afford final compounds (E)-6-substituted-3-((4-substitutedphenyl)diazenyl)-2,4-dimethylquinoline derivatives (XV – XXII) The identities and purity of synthesized compounds were elucidated through the thin layer chromatography (TLC), melting point and spectroscopy data such as (IR, UV, ^{1}HNMR, and mass spectroscopy).

Keywords: quinoline; synthesis; combs reaction; diazonium coupling reaction; acetyl acetone; *p*. substituted aromatic amines

Introduction
Quinoline moiety is of great importance to chemists as well as biologists as it is found in a large variety of naturally occurring compounds and also chemically useful molecules having diverse biological activities. Amongst the various activities of their derivatives, antimicrobial activity is noteworthy. (Eswaran *et al.*, 2010) [5]. Quinoline synthesis and its derivatives has been prevalent in biomedical studies and attracted both synthetic and biological chemist because of its diverse chemical and pharmacological properties and synthetic methods as well as the relative low-cost production of these compounds. Apart from classical method for the synthesis of quinoline ring available like Skraup, Doebner-Miller, Friedländer, Pfitzinger, Conrad-Limpach, Camps, Nimentowski, Pictet, Gould-Jacobs's, Miscellaneous, Povarov and Combes syntheses (Kumar *et al.*, 2009) [7].
The quinoline nucleus is an important class of heterocyclic compounds found in many synthetic and natural products with wide range pharmacological activities such as antiviral (Nayak *et al.* 2016) [8], anticancer (Denny *et al*., 2006) [3], antibacterial (El Faydy *et al*., 2016) [4], antifungal (Wang *et al*., 2010) [11], anti-inflammatory (Zarghi and Ghodsi 2010) [12], antileishmanial (Boa *et al*., 2005) [1], anti-tuberculosis (De Souza *et al*., 2009) [2], and anti-HIV (Mouscadet and Desmaële 2010) [9], which can be illustrated by the large number of drugs in the market containing this heterocyclic class. Quinoline and its derivatives are well known for their antimalarial drugs, such as chloroquine, quinine and mefloquine are main stays of chemotherapy against malaria (Zibaseresht *et al*., 2013) [13]. Quinolines have been attracted considerable interest because a large number of natural products and drugs contain this heterocyclic moiety. Further, these compounds are used to building blocks of various other compounds (Hajalsiddig and Saeed 2019) [6]. The present study, was focused on synthesize of disubstituted quinoline derivatives by the developing Combs reaction to form final compounds in multi-step reaction. The synthesized compounds were characterized by IR, UV, ^{1}HNMR and mass spectroscopy.

Experimental Section
General equipment
All chemical reagents are obtained from commercial suppliers and used without further purification. Melting points of all synthesized compounds were determined on an electro thermal melting point ST 150SA.UK. Ultraviolet Spectroscopy (UV) data was carried out at (UV.3101PC. Shimadzu-Japan. TLC for progress of all synthesized compounds was carried out on Aluminum per-coated plates with different mobile phases and visualizing the spots in Iodine crystalized. IR spectra were carried out as KBr discs on model FTIR-84005 Spectrometer (Shimadzu, Japan). ^{1}HNMR spectra were scanned on Vario Germany instrument model ultrashield-300MH using DMSO as solvent. The mass spectral recorded on (GC-MS) Shimadzu Qp-1000 EX. Japan.

Synthesis

General method for synthesis (*E*)-3-((4-substitutedphenyl)diazenylpentane-2,4-dione derivatives (I-VI)

p-substituted aniline (0.01mole) was dissolved in a mixture of concentrated HCl (8 ml) and water (6 mL) and cooled to 0-5ºC on ice bath. A cold aqueous solution of sodium nitrite (0.02mole) was added. The cold diazonium salt solution was filtered into a cooled solution of acetyl acetone in presence of sodium nitrite (0.01mole) and sodium acetate (0.05mole) in aqueous ethanol (20 mL) and stirred for 2 hours and resulting solid was filtered, dried and purified by recrystallization from ethanol to afford compounds (I – VI) intermediate (1) see scheme (1).

(*E*)-3-((4-Chlorophenl) diazenyl)pentane-2,4-dione (I)

Color: yellow, Yield: 94%, m.p: 133-135 ºC, M.W.: 238.67, Rf.: 0.79, IR (KBr, cm-1): 3431 (N-H), 3095 (Ar-C-H), 1668 (C=O), 1623 (C=N), 1519 (C=C), 1305 (N=N), 1417 (-C-CH_3), 1188 (Ar-C-N), 769 (C-Cl).

(*E*)-4-((2,4-dioxopentan-3-yl)diazenyl)benzene sulfonamide (II)

Color: yellow, Yield: 45 %, m.p.: 117-119 ºC, M.W.: 283.30, Rf.: 0.59, IR (KBr, cm-1): 3257 (N-H), 3022 (Ar-C-H), 1679 (C=O), 1633 (C=N), 1504 (C=C), 1321 (N=N), 1417 (-C-CH_3), 1147 (Ar-C-N).

(*E*)-3-((4-bromophenyl)diazenyl)pentane-2,4-dione (III)

Color: yellow, Yield: 90 %, m.p.: 99-103 ºC, M.W.: 283.13, Rf.: 0.75, IR (KBr, cm-1): 3533 (N-H), 3085 (Ar C-H), 1668 (C=O), 1625 (C=N), 1504 (C=C), 1315 (N=N), 1182 (Ar-C-N), 1421 (-C-CH_3), 624 (Br).

(*E*)-3-(phenyldiazenyl) pentane-2,4-dione (IV)

Color: deep yellow, Yield: 53 %, m.p.: 85-87 ºC, M.W.: 204.23, Rf.: 0.62, IR (KBr, cm-1): 3533 (N-H), 3093 (Ar C-H), 1674 (C=O), 1623 (C=N), 1519 (C=C), 1417 (-C-CH_3), 1188 (Ar-C-N), 1309 (N=N).

(*E*)-3-((4-acetylphenyl)diazenyl)pentane-2,4-dione (V)

Color: brown, Yield: 78 %, m.p.: 144-146 ºC, M.W.: 246.27, Rf.: 0.66, IR (KBr, cm-1): 3446 (N-H), 3051 (Ar C-H), 1674 (C=O), 1600 (C=N), 1506 (C=C), 1303 (N=N), 1419 (-C-CH_3), 1195 (Ar-C-N).

(*E*)-4-(2-(2, 4-dioxopentan-3-yl)diazenyl)benzoic acid (VI)

Color: brown, Yield: 88 %, m.p.: 272-274 ºC, M.W.: 248.24, Rf.: 0.72, IR (KBr, cm-1): 2977 (N-H), 2663 (Ar C-H), 1679 (C=O), 1614 (C=N), 1510 (C=C), 1301 (-N=N-), 1423 (-C-CH_3), 1166 (Ar-C-N), 3776 (O-H).

General method for Synthesis (*Z*)-3-((*E*)-(4-substituted phenyl) diazenyl)-4-((4-substituted phenyl) imino) pentan-2-one derivatives (VII – XIV)

Add to a mixture of 5.32g (0.05 mole) of aniline *p*. substituent and 5.1g (0.05mole) of (*E*)-3-((4-substitutedphenyl)diazenylpentane-2, 4-dione (I - VI) contained in a 100 ml round bottomed flask 10g of granular anhydrous calcium sulphate. Attach an air condenser fitted with calcium chloride guard-tube to the flask and heat the mixture on a steam bath for 1 hour, with occasional shaking. Cool, add 40 ml of ether to the reaction mixture and filter. Wash the calcium sulphate in the filter funnel with 40 ml ether and evaporate the combined ether filtrates. Drying and recrystallization the solid obtained from hexane to afford compounds (VII – XIV) intermediate 2 see scheme 2.

(*Z*)-3-((*E*) -(4-chlorophenyl)diazenyl)-4-((4-chlorophenyl)imino)pentan-2-one (VII)

Color: yellow, Yield: 68 %, m.p.: 139-142 ºC, M.W.: 348.23, Rf.: 0.84, IR (KBr, cm-1): 3078 (Ar-C-H), 3001 (C-H), 1668 (C=O), 1625 (C=N), 1519 (C=C), 1305 (-N=N-), 1417 (-C-CH_3), 1188 (Ar-C-N), 1305 (-N=N-), 3436 (O-H), 769 (C-Cl).

(*Z*)-3-((*E*)-(4-chlorophenyl)diazenyl)-4-(*p*-tolylimino)pentan-2-one (VIII)

Color: yellow, Yield: 69 %, m.p.: 102-104 ºC, M.W.: 327.81, Rf.: 0.69, IR (KBr, cm-1): 3058 (Ar-C-H), 3224 (C-H), 1652 (C=O), 1589 (C=N), 1519 (C=C), 1433 (-C-CH_3), 1174 (Ar-C-N), 1280 (-N=N-), 3396 (O-H), 769 (C-Cl).

(((*Z*)-4-oxo-3-((*E*)-(4-sulfamoyophenyl)diazenyl)pentan-2-ylidene)amino)benzene sulfonamide (IX).

Color: pall yellow, Yield: 95 %, m.p.: 154 -156 ºC, M.W.: 437.49, Rf.: 0.81, IR (KBr, cm-1): (3321-3251) (NH_2), 1679 (C=O), 1591 (C=N), 1502 (C=C), 1147 (C-N), 1309 (-N=N-), 3477 (O-H), 1433 (-C-CH_3).

(*Z*)-3-((*E*)-(4-bromophenyl) diazenyl)-4-((4-bromophenyl)imino)pentane-2-one (X)

Color: brown, Yield: 73 %, m.p.: 78-80 ºC, M.W.: 437.14, Rf.: 0.79, IR (KBr, cm-1): 3087 (Ar C-H), 1668 (C=O), 1625 (C=N), 1506 (C=C), 1315 (-N=N-), 1186 (Ar-C-N), 1417 (C-CH_3).

(*Z*)-3-((*E*)-phenyldiazenyl)-4-(*p*-tolylimino)pentane-2-one (XI)

Color: yellow, Yield: 82 %, M.P.: 91-93 ºC, M.W.: 293. 37, Rf.: 0.83, IR (KBr, cm-1): 3095 (Ar C-H), 1674 (C=O), 1623 (C=N), 1519 (C=C), 1415 (-C-CH_3), 1188 (Ar-C-N), 3006 (C-H), 1309 (N=N).

(*Z*)-4-((4-acetylphenyl)imino)-3-((*E*)-phenyldiazenyl)pentan-2-one (XII)
Color: green yellow, Yield: 35 %, m.p.: 101-103 ^{o}C, M.W.: 238.67, Rf.: 0.66, IR (KBr, cm-1): 3394 (O-H), 1647 (C=N), 1589 (C=C), 1433 (-C-CH_3), 1170 (Ar-C-N), 1272 (-N=N-).

(*Z*)-3-((*E*)-(4-acetylphenyl)diazenyl)-4-((4-acetylphenyl)imino)pentane-2-one (XIII)
Color: yellow, Yield: 79 %, m.p.: 138-140 ^{o}C, M.W.: 363.42, Rf.: 0.78, IR (KBr, cm-1): 2995 (C-H), 3089 (Ar C-H), 1674 (C=O), 1596 (C=N), 1504 (C=C), 1303 (-N=N-), 1153 (Ar-C-N), 3452 (O-H).

((*E*)-((*Z*)-2-oxo-4-((4-sulfamoylphenyl)imino)pentan-3-yl)diazenyl)benzoic acid (XIV).
Color: yellow, Yield: 91 %, m.p.: 227-229 ^{o}C, M.W.: 384.41, Rf.: 0.80, IR (KBr, cm-1): 2977 (Ar C-H), 1677 (C=O), 1596 (C=N), 1508 (C=C), 1159 (Ar-C-N), 1423 (-C-CH_3), 1303(-N=N-), 3477 (O-H), 3317-3242 (NH_2).

General method for synthesis (*E*)-6-substituted-3-((4-substitutedphenyl)diazenyl)-2,4-dimethylquinoline derivatives (XV – XXII)
Add 6g (0.032mole) of above (*Z*)-3-((*E*)-(4-substitutedphenyl)diazenyl)-4-((4-substituted phenyl)imino)pentan-2-one (VII - XIV) in portions, to 25 ml of concentration sulphuric acid (*d*1.84) contained in a 250 ml conical flask. Swirl the mixture occasionally to ensure through mixing. The first portion of the enamine dissolve rather slowly but solution occurs more rapidly with later portions as the temperature of the mixture increase to 60 – 70 ^{0}C. When addition is complete, heat the mixture on water-bath at 100^{o} for 5 hr, then cool the brown solution at room temperature and cautiously pour into ice-water (200 ml) in 1-liter baker. Basify the resulting solution by adding solid sodium carbonate, and filter off then cool the mixture in an ice-water bath until the precipitated product from 60 % aqueous ethanol to afford compounds (XV - XXII) see scheme 3.

(*E*)-6-chloro-3-((4-chlorophenyl) diazenyl)-2,4-dimethylquinoline (XV)
Color: yellow, yield: 86 %, m.p.: 113-115 ^{o}C, M.W.: 330.21, Rf.: 0.81, IR (KBr, cm-1): 3078 (Ar-C-H) 1600 (C=O), 1521 (C=N), 1415 (C=C), 1303 (-N=N-) 1307 (-N=N-), 1184 (C-N), 1415 (C-CH_3), 769 (C-Cl). UV, λ_{max} (EtOH 60 %): 203, 241, 310, 357. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.43(S, 3H, CH_3), 3.35 (S, 3H, CH_3), 7.15 (d, 2H, H-Ar), 7.18 (d, 2H, H-Ar), 7.22 (s, 1H, CH quinoline), 7.47 (d, 1H, CH quinoline), 7.60 (d, 1H, CH quinoline). MS (EI, *m/z* (%)): 325.90 (M^+, 4.46), 314.03 (M^++1-$C_{16}H_{10}Cl_2N_3$, 4.44), 271.10 (M^++2 – $C_{15}H_{12}ClN_3$, 2.66), 111.00 (M^+-C_6H_4Cl, 33.27), 192.03 (M^+ -$C_9H_{11}ClN$, 5.35), 178.03 (M^+- $C_9H_7ClN_2$, 9.48).
(*E*)-3-((4-chlorophenyl) diazenyl)-2,4,6-trimethylquinoline (XVI)
Color: yellow, yield: 79 %, m.p.: 97-99 ^{o}C, M.W.: 309.80, Rf.: 0.79, IR (KBr, cm-1): 1650 (C=N), 1589 (C=C), 1172 (C-N), 1274 (-N=N-), 1431 (C-CH_3), 831 (C-Cl). UV, λ_{max} (EtOH 60 %): 205, 234, 334. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.36 (t, 6H, CH_3), 2.48 (S, 3H, CH_3), 7.17 (d, 2H, H-Ar), 7.18 (d, 2H, H-Ar), 7.40 – 7.43 (m, 3H, H -Ar), 7.52 (t, 1H, H-Ar), 7.68 (d, 1H, H-Ar). MS (EI, *m/z* (%)): 309.95 ([M^++2], 0.48), 308.95 ([M^++1], 0.34), 256.06 (M^+- $C_{14}H_{11}ClN_3$, 0.45), 120.05 ([m^++2], $C_7H_6N_3$, 100.00), 111.00 (M^+-C_6H_4Cl, 17.72), 99.00 (M^+ -C_5H_4Cl, 34.92), 92.05 ([M^++2] – C_7H_6, 49.79).

(*E*)-2,4-dimethyl-3-((4-sulfamoylphenyl) diazenyl) quinoline-6-sulfonamide (XVII)
Color: orange, yield: 51 %, m.p.: 222-224 ^{o}C, M.W.: 419.37, Rf.: 0.69, IR (KBr, cm-1): 1596 (C=N), 1514 (C=C), 1317 (-N=N-), 3342-3257 (NH_2), 1423 (C-CH_3), 1149 (Ar-C-N). UV, λ_{max} (EtOH 60 %): 209, 257, 363. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.45 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 6.85 (s, 4H, 2NH_2 sulfonamide), 7.73-7.79 (m, 4H, H-Ar), 7.68 (d, 1H, CH quinoline), 7.71 (d, 1H, CH quinoline), 7.85 (s, 1H, CH quinoline). MS (EI, *m/z* (%)): 418.06 (M^+), 403.05 ([M^++1], 1.58), 249.90 (M^++1, $C_{11}H_{11}N_3O_2S$, 9.77), 171.95 ([m^++1], $C_6H_6N_2O_2S$, 36.46), 236.00 ([M^++1], $C_{11}H_{11}N_2O_2S$, 2.01), 184.95 ([M^++1], $C_6H_6N_3O_2S$, 7.94), 250.90 (M^+ - $C_{11}H_{12}N_3O_2S$, 2.41).

(*E*)-6-bromo-3-((4-bromophenyl) diazenyl)-2,4-dimethylquinoline (XVIII)
Color: dark brown, yield: 90 %, m.p.: 163-165 ^{o}C, M.W.: 419.12, Rf.: 0.82, IR (KBr, cm-1): 3033 (Ar-C-H), 2918 (C-H), 1618 (C=N), 1494 (C=C), 1186 (C-N), 1236 (-N=N-), 622 (C-Br). UV, λ_{max} (EtOH 60 %): 206, 236. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.37 (s, 3H, CH_3), 2.87 (s, 3H, CH_3), 7.23 (q, 2H, H-Ar), 7.87 (q, 2H, H-Ar), 8.13-8.41 (q, 2H, CH quinoline), 9.14 (s, 1H, CH quinoline). MS (EI, *m/z* (%)): 420,00 (M^+, 2.64), 405.00 ([M^++4], $C_{16}H_{10}Br_2N_3$, 2.77), 342.00 ([M^++4], $C_{17}H_{13}BrN_3$, 3.32), 237.00 ([M^++4], $C_{11}H_9BrN$, 3.68), 186.00 ([M^++4], $C_6H_4BrN_2$, 7.13), 313.00 264.00 ([M^++2] – $C_{11}H_9BrN_3$, 2. 49), (M^+ -$C_{15}H_{12}BrN_3$, 5.22).

(*E*)-2, 4,6-trimethyl-3-(phenyldiazenyl)quinoline (XIX)
Color: yellow, yield: 78 %, m.p.: 261-263 ^{o}C, M.W.: 275.63, Rf.: 0.66, IR (KBr, cm-1): 3056 (Ar-C-H), 1637 (C=N), 1517 (C=C), 1190 (C-N), 1315 (-N=N-), 1438 (C-CH_3). UV, λ_{max} (EtOH 60 %): 203, 247, 363. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.31 (t, 6H, CH_3), 2.43 (s, 3H, CH_3), 7.03 (t, H, H-Ar), 7.49 (d, 2H, H-Ar), 7.25 (t, 2H, H -Ar), 7.51(m, 1H, 1H, CH quinoline), 7.58 (m, 1H, 1H, CH quinoline), 7.66 (t, 1H, 1H, CH quinoline). MS (EI, *m/z* (%)): 276.10 (M^+, 2.36), 262.10 ([M^++2]- $C_{17}H_{14}N_3$, 6.86), 224.00 ([M^++2], $C_{14}H_{12}N_3$, 2.71), 200,00 ([M^++2], $C_{12}H_{12}N_3$, 20.03), 77.05 (M^+ - C_6H_5, 76.24), 170.90 (M^+-$C_{12}H_{12}N$, 34.58), 91.05 (M^+ - C_6H_5N, 59.46), 105.05 ([M^+ - $C_6H_5N_2$, 35.27), 65.00 (M^+ - C_4H_3N, 100.00).

(*E*)-1-(2,4-dimethyl-3-(phenyldiazenyl) quinoline-6-yl) ethan-1-one (XX)

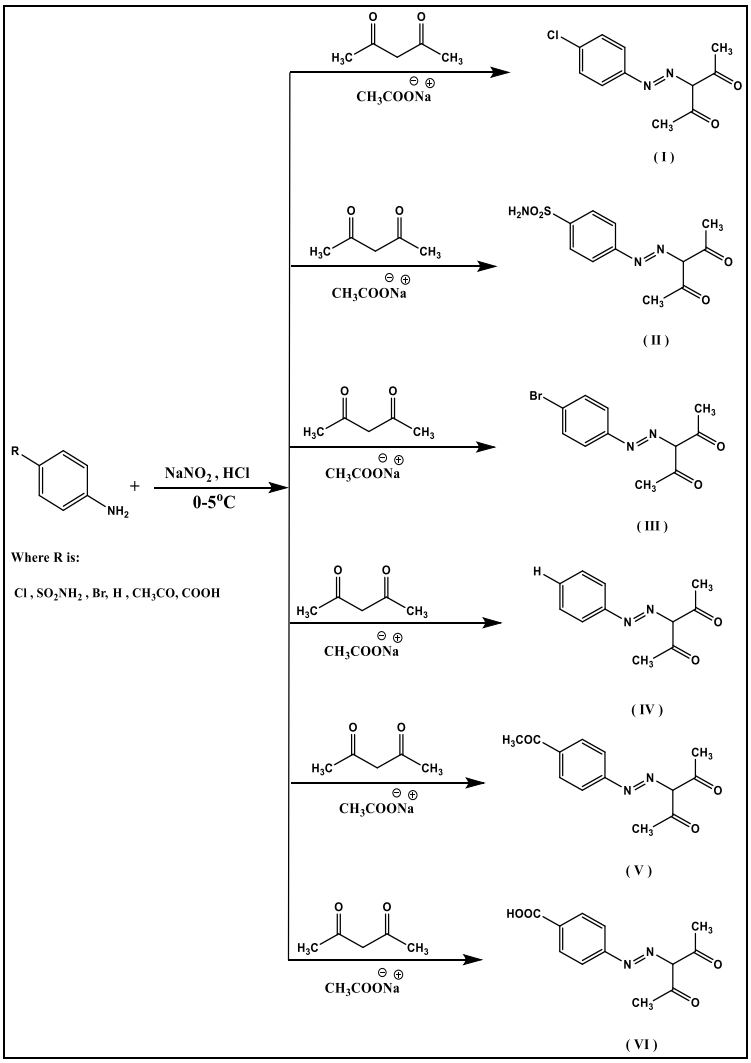
Color: green yellow, yield: 84 %, m.p.: 117-119 ^{o}C, M.W.: 303.37, Rf.: 0.75, IR (KBr, cm-1): 1645 (C=O), 1519 (C=N), 1420 (C=C), 1272 (-N=N-), 1176 (C-N), 1433 (C-CH_3). UV, λ_{max} (EtOH 60 %): 204, 235, 320. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.31 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.48 (s, 3H, -OCH_3), 7.48 (q, 2H, H-Ar), 7.50 (q, 2H, H-Ar), 7.63 (m, 2H, H-Ar), 7.64 (d, 1H, CH quinoline), 7.66 (d, 1H, CH quinoline), 7.68 (s, 1H, CH quinoline). MS (EI, m/z (%)): 303.00 (M^+), 304.00 ([M^++1], 1.15), 305.00 ([M^++1], 1.07), 237,00 ([M^++2]-$C_{15}H_{13}N_3$, 1.41), 146,00 ([M^++2]- $C_9H_8N_2$, 5.77), 95.05 ([M^++1] – C_6H_5N, 55.71), 120.05 (M+ - C_8H_6O, 100.00), 251.00 (M^+ - $C_{15}H_{13}N_3O$, 3.76), 185.00 (M^+-$C_{11}H_{11}N_3$, 2.48).

(*E*)-1-(-4-((6-acetyl-2,4-dimethylquinoline-3-yl) diazenyl) phenyl) ethan-1-one (XXI)

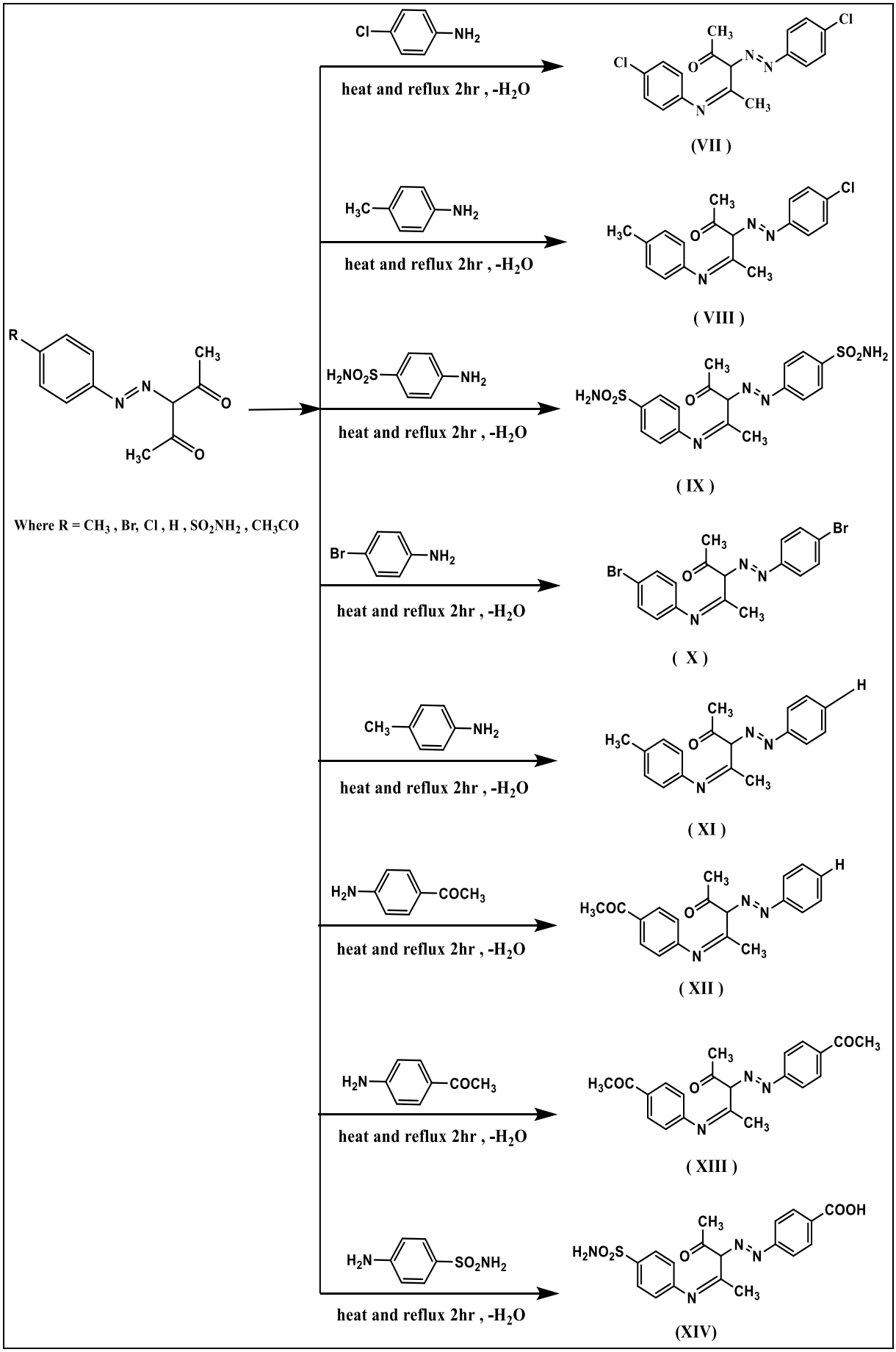
Color: brown, yield: 62 %, m.p.: 141-143 ^{o}C, M.W.: 345.40, Rf.: 0.69, Rf.: 0.83, IR (KBr, cm-1): 3997(Ar-C-H), 1674 (C=O), 1596 (C=N), 1504 (C=C), 1261 (-N=N-), 1153 (C-N), 1357 (C-CH_3). UV, λ_{max} (EtOH 60 %): 241, 271, 369. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.31 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.48 (s, 3H, -OCH_3), 7.59 (q, 2H, H-Ar), 7.64 (q, 2H, H-Ar), 7.95 (d, 1H, CH quinoline), 7.99 (d, 1H, CH quinoline), 8.00 (s, 1H, CH quinoline). MS (EI, m/z (%)): 345.00 ([M^+], 3.38), 346.00 ([M^++1], 3.04), 347.00 ([M^++2], 3.88), 149,05 ([M^++2]-$C_8H_7N_2O$, 14.96), 57,05 ([M^++1] -C_3H_4O, 100.00), 320.00 ([M^++1] -$C_{19}H_{17}N_3O_2$, 5.83), 160.00 ([M^++1]-$C_{10}H_9NO$, 9.80), 106.00 ([M^++1] -$C_6H_5N_2$, 53.51), 276.00 (M+ - $C_{17}H_{14}N_3O$, 5.54), 264.00 (M^+ - $C_{16}H_{14}N_3O$, 5.30).

(*E*)-4-((2,4-dimethyl-6-sulfamoylquinoline-3-yl) diazenyl) benzoic acid (XXII)

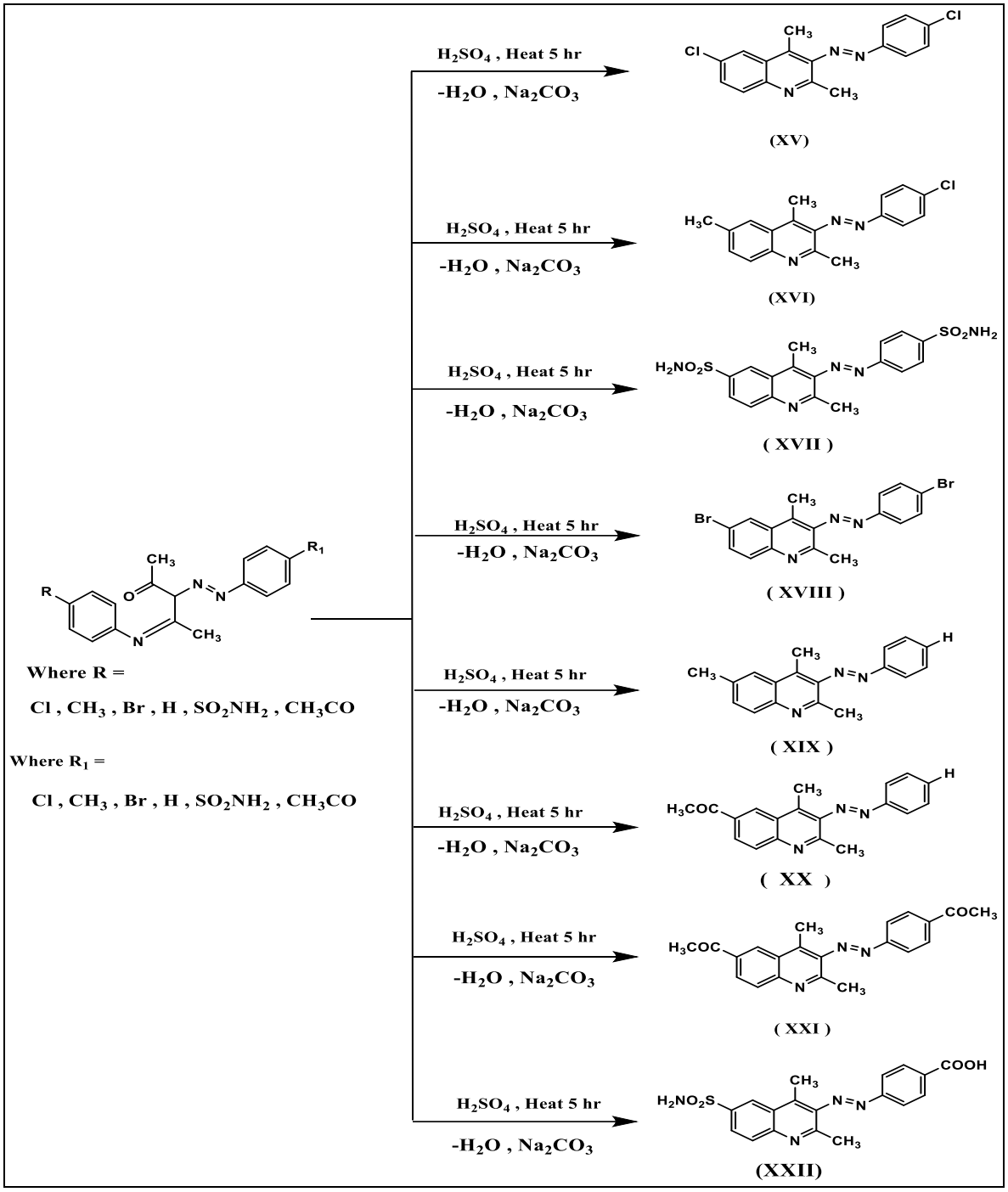
Color: pall brown, yield: 89 %, m.p.: 170-173 ^{o}C, M.W.: 384.41, Rf.: 0.69, Rf.: 0.78, IR (KBr, cm-1): 1600 (C=O), 1552 (C=N), 1512 (C=C), 1309 (-N=N-), 1151 (C-N), 1392 (C-CH_3), 3369-3269 (NH_2), 1095 (S=O), 3461 (O-H). UV, λ_{max} (EtOH 60 %): 209, 260, 366. ^{1}H NMR (300 MHz, DMSO, δ, ppm): 2.31(s, 3H, CH_3), 2.43 (s, 3H, CH_3), 5.78 (s, 2H, NH_2), 7.73-7.09 (d, 2H, H-Ar), 7.27 (d, 2H, H-Ar), 7.44 (d, 1H, CH quinoline), 7.48 (d, 1H, CH quinoline), 7.84 (s, 1H, CH quinoline), 8.94 (s, 1H, COOH). MS (EI, *m/z* (%)): 384.08 (M^+), 307.00 ([M^++2], $C_{13}H_{11}N_3O_4$ 1.39), 316.95 ([M^++2], $C_{17}H_{15}N_4O_2S$, 2.54), 307.00 ([M^++2] – $C_{13}H_{11}N_3O_4S$, 1.39), 289.00 ([M^++1], $C_{13}H_{12}N_4O_2S$, 1.16), 189.00 ([M^++1] - $C_{10}H_8N_2O_2$, 32.78), 264.00 ([M^++1], $C_{11}H_{11}N_4O_2S$, 32.78).



Scheme 1: chemical structure of (*E*)-3-((4-substitutedphenyl) diazenylpentane-2, 4-dione (I-VI)



Scheme 2: chemical structure of (Z)-3-((E)-(4-substituted phenyl) diazenyl)-4-((4-substituted phenyl) imino)pentan-2-one (VII – XIV)



Scheme 3: chemical structure of (*E*)-6-substituted-3-((4-substitutedphenyl) Diazenyl)-2,4-dimethylquinoline derivatives (XV – XXII)

Result and Discussion

The objective of the present study is to have synthesized quinoline derivatives by Combs reaction in three steps. The first step involves diazonium coupling reaction which is generally considered to proceed with an intermediate formation of (*E*)-3-((4-substitutedphenyl)diazenyl pentane-2,4-dione derivatives (I-VI) (Scheme 1), then condensation to a (*Z*)-3-((*E*)-(4-substituted phenyl) diazenyl)-4-((4-substitutedphenyl)imino)pentan-2-one derivatives (VII-XIV) (Scheme 2) followed by elimination of a water molecule and cyclisation of the resulting by the heating and elimination of water in present Sulphuric acid to afford final compounds (*E*)-6-substituted-3-((4-substitutedphenyl)diazenyl)-2,4-dimethyl quinoline derivatives (XV-XXII) (Scheme 3).

The starting product structure of quinoline in this study has been synthesized by combs reaction which is treatment *p*-substituted aniline with acetyl acetone in presence of sodium nitrite, sodium acetate, hydrochloric acid and ethanol to yielded (*E*)-3-((4-substitutedphenyl)diazenyl pentane-2,4-dione derivatives (I-VI) (Scheme 1) (Thakare *et al.*, 2012) [10].

The (*Z*)-3-((*E*)-(4-substituted phenyl) diazenyl)-4-((4-substituted phenyl) imino) pentan-2-one derivatives (VII-XIV)) where obtained in good yields by condensation of the (*E*)-3-((4-substitutedphenyl)diazenyl pentane-2,4-dione derivatives (I-VI) with 4-substitutedaniline in present Calcium Sulphate, heat and dissolved mixture in

ether (Scheme 2). The treatment of (Z)-3-((E)-(4-substituted phenyl) diazenyl)-4-((4-substituted phenyl) imino) pentan-2-one derivatives (VII-XIV) with the Sulphuric acid in base medium (Na_2CO_3) as Catalyst to yielded the final compounds (*E*)-6-substituted-3-((4-substituted phenyl) diazenyl)-2,4-dimethyl quinoline derivatives (XV-XXII) (Scheme 3).

The structure of the above compounds (I -XIV) Scheme 1 and 2 was mentioned by TLC and confirmed by IR spectral data, but the structure of compounds (XV-XXII) Scheme 3 were confirmed by analytical spectral data IR, UV, NMR, MS spectra. The spectrum formation of compounds I, II, III, IV, V and VI (Scheme 1) was confirmed by the peak at ~3350 cm^{-1} in IR spectrum which is due to the NH stretching of hydrazinylidene. A band at ~1670 cm^{-1} is due to C=O stretch of the ketone group, the band for C=N in diazenyl group show at ~1580 cm^{-1}, the C=C of aromatic group appeared in ~1480 cm^{-1}, the C-Cl group appeared in ~769 cm^{-1}, and the C-Br group appeared in ~622 cm^{-1}.

The structure of all (*Z*)-3-((*E*)-(4-substituted phenyl) diazenyl)-4-((4-substituted phenyl) imino) pentan-2-one derivatives (VII-XIV) (Scheme 2) were confirmed by using FT-IR spectroscopy. It showed several characteristic sharp bands in the IR region, where the bands in the range between 1644-1665 cm^{-1} indicated the appearance of the carbonyl C=O group of the formed ketone, which was conjugated to hydrogen bond. The absorption bands at 1460-1578 cm^{-1} due the aromatic C=C group.

The IR Spectra of (*E*)-6-substituted-3-((4-substitutedphenyl)diazenyl)-2,4-dimethyl quinoline (XIV-XXI) (Scheme 3) was confirmed by the peak at ~3200 cm^{-1} in IR spectrum which is due to the aromatic C-H, The band for C=N in aromatic ring show at ~1580 cm^{-1}, the C=C of aromatic group appeared in ~1480 cm^{-1}, the C-Cl group appeared in ~880 cm^{-1}, and the C-Br group appeared in ~780 cm^{-1}, and the band –N=N– in diazenyl group showed in ~1167 cm^{-1}.

Ultra violet spectroscopy (UV) is the technique provides information about compounds with conjugated double bonds. The UV-V is spectra of Synthesis of (*E*)-6-substituted-3-((4-substituted phenyl)diazenyl)-2,4-dimethylquinoline (XV – XXII) recorded in 60% ethanol. The λ max values of all synthesized compounds are absorption band positions broadly lie between 234 – 366 nm assignable to π -π* transitions due to the conjugated in quinoline moiety.

^{1}HNMR tool of the NMR technique used in structure determination of the unknown molecules. It give information abuot the number, and the megantic environment of the each protone found the unknown molecule. The results were in δ value (ppm), on which the resonance of the protone in DMSO, all compounds have the same structure but defferent in the substetuent (R, R_1). The ^{1}HNMR spectera of the synthesized quinoline derivatives (XV-XXII). All synthesized compounds (XV, XVI, XVII, XVIII, XIX, XX, XXI, XXII) have three protone of methyl group (-CH_3) appeared as single (s) peak at the 2.31 – 2.87 ppm, and their aromatic protone in defferent invironment were apeared at exepted region and the bound of them was tabulated in table (2.20). Compounds (XV, XVII, XVIII, XIX, XX, XXI, XXII) appeared CH- quinoline protone as single, doupled, multiplied between range (7.99 – 9.14) ppm.

XX, XXI compounds exhibit two single (s) peak at 2.53 ppm and 2.51 ppm charasterctic of acetyl group (CH_3CO- link with aromatic ring. Six protons of three amino group ($3NH_2$) attached to XVII and XXII observed as single peak at 5.78 – 6. 85 ppm. Compound XVII have one proton of carboxylic acid group (-COOH) which is appeared as single (s) peak at 8.94 ppm. Mass spectra of all synthesized compounds (XV- XXII) appear peaks [M^+], [M^++1], [M^++2], [M+3] and [M+4] and these were consistent with product structures. The M+1 and M+2 isotopes peaks was observed in compounds (XVII - XXII). M+1 occur due to the presence of isotopes ^{2}H, ^{13}C. M+2 the isotope peak of one halogen atom (Cl) in compounds (XVI). Compounds XV, XVIII showing M+4 isotopes peak due to these compounds have two halogen atoms (Cl or Br).

Conclusion

Quinoline its very importance heterocyclic compound established literature review in the biological activity, and their derivatives considerable subject of many research studies used to build other compounds due their wide prevalence biological activities. In this manuscript, we have synthesized of some new (*E*)-6-substituted-3-((4-substitutedphenyl)diazenyl)-2,4-dimethyl quinoline derivatives as the gist with good synthesized. The identities of synthesized compounds used spectral data such as (IR, UV, ^{1}HNMR, and mass spectroscopy). The importance of such study lies synthesis of (*E*)-3-((4-substituted phenyl) diazenyl pentane-2,4-dione derivatives (I-VI) (Scheme 1) which could be helpful chemist to synthesis other heterocyclic compounds have many importance.

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