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The Uses of Acetylacetone to Synthesize Pyridin-2-One Derivatives

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A SERIES of pyridin-2-one derivatives have been prepared from the reaction of acetyl acetone and cyanoacetohydrazide or dialkyl carbocyanohydrazodithioates as well as 2*H*-pyran-ones. Some reactions of the pyridin-2-one were also studied. The synthesized compounds were structurally characterized on the basis of UV, IR, ^{1}H NMR, ^{13}C NMR, mass spectrometry and elemental analyses.

Keywords: Pyridin-2-one, Cyanoacetohydrazide, Dialkyl carbocyanohydrazodithioates and 2*H*-pyran-ones.

The synthesis of pyridin-2-one derivatives is a continuing area of interest due to the number of biologically active molecules containing this moiety[1-5]. Natural compounds with this structure have emerged during the last ten years as potent antitumor, antibacterial activity[6,7], antifungal[8], antiinflammatory, analgesic, antipyfuztic[9], antiviral[10], psychotherapeutic[11] and evaluated as human rhinovirus (HRV) 3C-protease (3CP) inhibitors[12]. Moreover, pyridones are the key intermediates in the synthesis of the corresponding pyridines[13], they have been prepared by numerous methods[14]. Many literature sources describe more general approaches involving the condensation of unsaturated ketones with methylene active amides, using cyanoacetamide[15-19] or by the reaction of 2-pyrones with ammonia, amines as well as hydrazines [20].

Despite this large number of existing methods for the synthesis of 2-pyridones, we report here the synthesis of 4,6-disubstituted-2-pyridone derivatives and characterization of their structures by different spectral tools.

Experimental

Chemistry

All melting points were determined on a Stuart apparatus and the values given are uncorrected. IR spectra (KBr, cm^{-1}) were determined on a Perkin-Elmer 1430 spectrophotometer (Microanalysis Center, Alexandria University, Egypt). Electronic spectra were measured with a Perkin-Elmer Lambada 4B spectrophotometer (Microanalysis Center, Alexandria University, Egypt). ^{1}H NMR and^{13}C NMR spectra were recorded on Varian EM-390 at 90 MHz and Varian Gemini 300 MHz, operating at 75.50 MHz, respectively (Microanalysis Center, Alexandria University, Egypt)) using TMS as internal standard.

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Chemical shift values are recorded in ppm ondscale. Mass spectra were recorded at 70 eV with an AEL, MS-9 spectrometer (Microanalysis Center, Cairo University, Egypt). Elemental analyses were carried out at the Microanalysis Center, Cairo University, Egypt; found values were within±0.35% of the theoretical ones. Progress of the reactions was monitored using thin layer chromatography (TLC) sheets precoated with UV fluorescent silica gel Merck 60F 254 and was visualized using UV lamp.

1-Amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (2)

A solution of 2-isocyanoacetohydrazide (1) (11.5 g, 0.116 mol) in ethanol (100 ml) was gradually added to a solution of acetylacetone (11.6 g, 0.116 mol) in ethanol (50 ml) containing one drop of piperidine. After refluxing the reaction mixture for 10 min, and cooling, the separated product was filtered off, washed with ethanol and crystallized from ethanol.

Yield: 87 %; m.p.: 172–174 °C; UV (λ_{max} nm): MeOH, 395, 338, 224; (0.1 M) MeOH\$H_2SO_4$, 395, 338, 224; (0.1 M) MeOH\$NaOCH_3$, 395, 338, 224, 206; IR (KBr, cm^{-1}): 3283, 3201 (NH_2), 2218 (CN), 1621 (C=O); ^{1}H NMR (DMSO-d_6): δ 2.35 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 6.05 (s, 2H, NH_2, D_2O exchangeable), 6.25 (s, 1H, pyridine H-5); MS: *m/z* (%) 163 (M^+, 49.9). *Anal*. Calcd. for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75. Found: C, 58.62; H, 5.70; N, 26.01.

4,6-Dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (3)

A solution of 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (2) (2 g, 0.014 mol) in glacial acetic acid (8 ml) was treated dropwise with an aqueous solution of sodium nitrite (0.5 gm). The separated product was filtered off, washed with ethanol and crystallized from acetic acid.

Yield: 75 %; m.p.: 284–286 °C; UV (λ_{max} nm): MeOH, 395, 327, 237, 213; MeOH\$H_2SO_4$, 395, 327, 238, 213; MeOH\$NaOCH_3$, 395, 326, 246, 214;; IR (KBr, cm^{-1}): 3287 (NH), 2305 (CN), 1660 (C=O); ^{1}H NMR (DMSO-d_6): δ 2.24 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 6.05 (s, 1H, pyridine C-5), 12.14 (s, 1H, NH, D_2O exchangeable); MS: *m/z* (%) 148 (M^+, 55.9). *Anal*. Calcd. for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.63; H, 5.58; N, 18.78.

4,6-Dimethyl-5-nitro-2-oxo-1,2-dihydropyridine-3-carbonitrile (4)

A mixture of nitric (d 1.41; 3ml) and sulfuric (d 1.84; 3ml) acids in glacial acetic acid (10 ml) was gradually added to a solution of 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (2) (2 g, 0.014 mol) in glacial acetic acid (15 ml). The reaction mixture was warmed at 50°C for 15 min, then poured into cold water with stirring. The separated product was filtered washed with cold water, dried and crystallized from acetic acid.

Yield: 77 %; m.p.: 258–260 °C; UV (λ_{max} nm): MeOH, 390 (sh), 326, 232 (sh), 212; MeOH\$H_2SO_4$, 390 (sh), 327, 233, 209; MeOH\$NaOCH_3$, 370 (sh), 326, 239, 207; IR (KBr, cm^{-1}): 3288 (NH), 2228 (CN), 1654 (C=O); ^{1}H NMR

(DMSO-d_6): δ 2.32 (s, 6H, $2CH_3$), 10.22 (s, 1H, NH, D_2O exchangeable); MS: *m/z* (%) 193 (M^+, 24.1). *Anal*. Calcd. for $C_8H_7N_3O_3$: C, 49.74; H, 3.65; N, 21.75. Found: C, 49.52; H, 3.81; N, 22.01.

1-(4-Hydroxypent-3-en-2-ylidene)amino)-4,6-dimethyl-2-oxo-1,2 dihydropyridine -3-carbonitrile (5)

A solution of 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (2) (1 g, 0.007 mol) in ethanol (10 ml) was added to a solution of acetylacetone (1.2 g, 0.012 mol) in ethanol (10 ml) acidified with acetic acid and the reaction mixture was refluxed for 10 hr. On cooling, the solid product was separated, filtered and crystallized from ethanol.

Yield: 79 %; m.p.: 146–148 °C; UV (λ_{max} nm): MeOH, 340, 284, 216; MeOH\$H_2SO_4$, 339, 270, 225; MeOH\$NaOCH_3$, 341 (sh), 302, 226 (sh), 205; IR (KBr, cm^{-1}): 3100 (CH aromatic), 2214 (CN), 1664 (C=O); ^{1}H NMR (DMSO-d_6): δ 1.61 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 5.35 (s, 1H, CH), 6.35 (s, 1H, pyridine H-5), 11.54 (s, 1H, OH, D_2O exchangeable); MS: *m/z* (%) 245 (M^+, 34.8). *Anal*. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.84; H, 6.32; N, 17.40.

General procedure for the synthesis of 6a,b

A solution of KOH (5.6 g, 0.2 mol) in methanol (100 ml) was gradually (10 min) added to a suspension of cyanoacetohydrazide (1) (9.9 g, 0.1 mol) in methanol (100 ml) with stirring at 0 °C, whereby the hydrazide completely dissolved. The reaction mixture was then treated dropwise (10 min) with CS_2 (7.6 g, 0.1 mol) at 0 °C. After complete addition of CS_2, the separated solid of potassium 2-(2-isocyanoacetyl)hydrazinecarbodithioate was filtered, washed with cold ethanol and dried (19 g, Yield: 84 %).

A suspension of the crude potassium 2-(2-isocyanoacetyl) hydrazinecarbodithioate (21 g, 0.09 mol) in methanol (100 ml) was gradually treated with stirring at 0 °C with an ethanolic solution of either methyl iodide (21.9 g, 0.186 mol) or ethyl iodide (24 g, 0.186 mol) in the course of 20 min. The reaction mixture was then kept overnight in the ice–chest with occasional shaking. The separated product was filtered and crystallized from methanol.

Dimethyl (2-isocyanoacetyl)carbonohydrazonodithioate (6a)

Yield: 79 %; m.p.: 127–129 °C; UV (λ_{max} nm): MeOH, 271, 227, 215 (sh); MeOH\$H_2SO_4$, 271, 244 (sh), 206; MeOH\$NaOCH_3$, 343, 273, 231, 207; IR (KBr, cm^{-1}): 3169 (NH), 3013 (CH aromatic), 2255 (CN), 1646 (C=O), 1572 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.43 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 3.85 (dd, 2H, J = 27.7 Hz, CH_2), 10.55 (s, 1H, NH, D_2O exchangeable); MS: *m/z* (%) 203 (M^+, 75.4). *Anal*. Calcd. for $C_6H_9N_3OS_2$: C, 35.45; H, 4.46; N, 20.67; S, 31.55. Found: C, 35.63; H, 4.71; N, 20.51; S, 31.33.

Diethyl (2-isocyanoacetyl)carbonohydrazonodithioate (6b)

Yield: 84 %; m.p.: 73–75 °C; UV (λ_{max} nm): MeOH, 275, 227, 212; MeOH\$H_2SO_4$, 275, 235 (sh), 206; MeOH\$NaOCH_3$, 343, 277, 235 (sh), 204; IR (KBr, cm^{-1}): 3173 (NH), 3089 (CH aromatic), 2255 (CN), 1682 (C=O), 1646 (C=N); ^{1}H NMR (DMSO-d_6): δ 1.35 (t, 6H, *J* = 7.0 Hz, $2CH_2$-$\underline{CH_3}$), 3.15 (q, 4H, *J* = 7.2 Hz, $2\underline{CH_2}$-CH_3), 3.91 (dd, 2H, *J* = 22.2 Hz, CH_2), 10.55 (br.s, 1H, NH, D_2O exchangeable);^{13}C NMR (DMSO-d_6): δ 13.8, 15.1, 24.4, 26.1, 26.7, 116.1, 158.2, 165.4; MS: *m/z* (%) 232 (M^{+1}, 100). *Anal*. Calcd. for $C_8H_{13}N_3OS_2$: C, 41.53; H, 5.66; N, 18.16; S, 27.72. Found: C, 41.32; H, 5.70; N, 18.27; S, 27.54.

General procedure for the synthesis of 7a,b

A solution of dimethyl (2-isocyanoacetyl)carbonohydrazonodithioate (6a) (1 g, 0.005 mol) in ethanol (10 ml) was refluxed for 30 min with an ethanolic solution of either benzaldhyde (0.5 ml, 0.005 mol) or benzil (1 g, 0.005 mol) containing one drop of piperidine. On cooling, the solid product was separated, filtered, washed with cold ethanol and crystallized from ethanol.

Dimethyl (2-cyano-3-phenylacryloyl)carbonohydrazonodithioate (7a)

Yield: 91 %; m.p.: 135–137 °C; UV (λ_{max} nm): MeOH, 307, 222 (sh), 205; MeOH\$H_2SO_4$, 308, 223 (sh), 205; MeOH\$NaOCH_3$, 366, 383, 209; IR (KBr, cm^{-1}): 3307 (NH), 3000 (CH aromatic), 2204 (CN), 1687 (C=O), C=N (1646); ^{1}H NMR (DMSO-d_6): δ 2.52 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 7.43–7.98 (m, 5H, Ar–H), 8.15 (s, 1H, $\underline{H}$C=C—), 10.62 (s, 1H, NH, D_2O exchangeable); MS: *m/z* (%) 291 (M^+, 14.9). *Anal*. Calcd. for $C_{13}H_{13}N_3OS_2$: C, 53.58; H, 4.50; N, 14.42; S, 22.01. Found: C, 53.74; H, 4.71; N, 14.72; S, 21.91

N'-(Bis(methylthio)methylene)-2-cyano-4-oxo-3,4-diphenylbut-2-enehydrazonic acid (7b)

Yield: 92 %; m.p.: 198–200 °C; UV (λ_{max} nm): MeOH, 580, 387, 345, 292; MeOH\$H_2SO_4$, 580, 390, 345, 293; MeOH\$NaOCH_3$, 580, 390, 345, 290; IR (KBr, cm^{-1}): 3301 (NH), 3076 (CH aromatic), 2219 (CN), 1680, 1889 (2C=O), C=N (1592); ^{1}H NMR (DMSO-d_6): δ 2.11 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.21–7.64 (m, 10H, Ar–H), 7.90 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6): δ 19.8, 20.1, 98.6, 110.3, 119.3, 131.4, 132.9, 133.1, 135.0, 136.1, 137.6, 138.2, 142.9, 162.9, 173.1, 179.1; MS: *m/z* (%) 395 (M^+, 54.3). *Anal*. Calcd. for $C_{20}H_{17}N_3O_2S_2$: C, 60.74; H, 4.33; N, 10.62; S, 16.22. Found: C, 60.47; H, 4.60; N, 10.72; S, 15.94.

General procedure for the synthesis of 8a,b

when a solution of either 6a (2g, 0.01 mol) or 6b (5g, 0.02 mol) in methanol (20 ml) was treated with a methanolic solution of acetylacetone (0.79 g, 0.01

mol or 2.5 g, 0.02 mol) and two drops of piperidine. The reaction mixture was heated under reflux for 30 min. On cooling the solid product was separated, filtered, washed with cold methanol and crystallized from methanol.

Dimethyl (3-cyano-4,6-dimethyl-2-oxopyridin-1(2H)-yl) carbonimidodithioate (8a)

Yield: 84 %; m.p.: 184–186 °C; UV (λ_{max} nm): MeOH, 341, 225; MeOH\$H_2SO_4$, 341, 235; MeOH\$NaOCH_3$, 341, 225, 206; IR (KBr, cm^{-1}): 2953 (CH aromatic), 2215 (CN), 1645 (C=O), 1576 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.20 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.55 (s, 3H, S$\underline{CH_3}$), 2.65 (s, 3H, S$\underline{CH_3}$), 6.32 (s, 1H, pyridine H-5); ^{13}C NMR (DMSO-d_6): δ 13.9, 15.1, 18.5, 20.4, 99.7, 108.4, 116.4, 150.4, 155.4, 157.1, 180.1; MS: *m/z* (%) 268 (M^{+1}, 100). *Anal*. Calcd. for $C_{11}H_{13}N_3OS_2$: C, 49.41; H, 4.90; N, 15.72; S, 23.99. Found: C, 49.61; H, 5.12; N, 15.52; S, 23.78.

Diethyl (3-cyano-4,6-dimethyl-2-oxopyridin-1(2H)-yl) carbonimidodithioate (8b)

Yield: 78%; m.p.: 98–100 °C; UV (λ_{max} nm): MeOH, 342, 223; MeOH\$H_2SO_4$, 342, 237; MeOH\$NaOCH_3$, 342, 238, 206; IR (KBr, cm^{-1}): 2972 (CH aromatic), 2215 (CN), 1659 (C=O), 1587 (C=N); ^{1}H NMR (DMSO-d_6): δ 1.35 (t, 6H, *J* = 7.0 Hz, $2CH_2$-$\underline{CH_3}$), 2.20 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.15 (q, 4H, *J*= 7.2 Hz, $2\underline{CH_2}$-CH_3), 6.35 (s, 1H, pyridine H-5); MS: *m/z* (%) 295 (M^+, 55.3). *Anal*. Calcd. for $C_{13}H_{17}N_3OS_2$: C, 52.85; H, 5.80; N, 14.22; S, 21.71. Found: C, 52.62; H, 6.01; N, 14.50; S, 21.44.

Dimethyl (5-bromo-3-cyano-4,6-dimethyl-2-oxopyridin-1(2H)-yl) carbonimidodithioate (9)

A solution of bromine (3.2 g, 0.02 mol) in carbon tetrachloride (20 ml) was gradually added to a suspension of compound 7a (2.7 g, 0.01 mol) in CCl_4 (20 ml) with stirring for 1 hr at room temperature. The carbon tetrachloride solution was washed with water, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residual oily product solidified on treatment with ethanol and crystallized from ethanol.

Yield: 86 %; m.p.: 122–125 °C; UV (λ_{max} nm): MeOH, 352, 230; MeOH\$H_2SO_4$, 352, 232; MeOH\$NaOCH_3$, 352, 233; IR (KBr, cm^{-1}): 2929 (CH aromatic), 2220 (CN), 1665 (C=O), 1588 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.53 (s, 3H, S$\underline{CH_3}$), 2.61 (s, 3H, S$\underline{CH_3}$); MS: *m/z* (%) 346 (M^+, 12.7). *Anal*. Calcd. for $C_{11}H_{12}BrN_3OS_2$: C, 38.15; H, 3.49; Br, 23.08; N, 12.14; S, 18.52. Found: C, 38.41; H, 3.72; Br, 23.11; N, 12.01; S, 18.43

3-Bromo-4,6-diphenyl-2H-pyran-2-one (11a)

A suspension of 4,6-diphenyl-2*H*-pyran-2-one (10) (1.24 g, 0.005 mol) in chloroform (25 ml) was treated with a solution of bromine (0.265 g, 0.005 mol) in chloroform (8 ml) and the reaction mixture warmed for 15 min. The chloroform solution was then washed with water, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residual product was crystallized from benzene-n-hexane.

Yield: 85 %; m.p.: 128–130 °C; UV (λ_{max} nm): MeOH, 349, 254, 205; MeOH\$H_2SO_4$, 349, 254, 205; MeOH\$NaOCH_3$, 349, 254, 205; IR (KBr, cm^{-1}): 2945 (CH aromatic), 1723 (C=O); ^{1}H NMR (DMSO-d_6): δ 6.71 (s, 1H, pyran H-5), 7.41–7.87 (m, 10H, Ar–H); MS: *m/z* (%) 327 (M^+, 10.2). *Anal*. Calcd. for $C_{17}H_{11}BrO_2$: C, 62.41; H, 3.39; Br, 24.42. Found: C, 62.23; H, 3.70; Br, 24.12.

3-Iodo-4,6-diphenyl-2H-pyran-2-one (11b)

A solution of iodine monochloride (0.4 g, 0.002 mol) in dry chloroform (10 ml) was gradually added to a solution of 4,6-diphenyl-2*H*-pyran-2-one (0.5 g, 0.002 mol) in dry chloroform (5ml) with stirring for 30 min at room temperature. The precipitated product was filtered and crystallized from ethanol.

Yield: 67 %; m.p.: 258–260 °C; IR (KBr, cm^{-1}): 2986 (CH aromatic), 1720 (C=O); ^{1}H NMR (DMSO-d_6): δ 6.82 (s, 1H, pyran H-5), 7.43–7.91 (m, 10H, Ar–H); MS: *m/z* (%) 374 (M^+, 100). *Anal*. Calcd. for $C_{17}H_{11}IO_2$: C, 54.57; H, 2.96. Found: C, 54.35; H, 2.81.

3-Nitro-4,6-diphenyl-2H-pyran-2-one (11c)

A mixture of nitric (d 1.41; 3 ml) and sulfuric (d 1.84; 3 ml) acids in glacial acetic acid (10 ml) was gradually added to a solution of 4,6-diphenyl-2*H*-pyran-2-one (10) (2 g, 0.08 mol) in glacial acetic acid (15 ml). The reaction mixture was warmed at 50°C for 15 min, cooled, poured into cold water with stirring. The separated product was filtered, washed with cold water, dried and crystallized from acetic acid.

Yield: 83 %; m.p.: 185–187 °C; IR (KBr, cm^{-1}): 2959 (CH aromatic), 1714 (C=O), 1534, 1340 (NO2); ^{1}H NMR (DMSO-d_6): δ 6.85 (s, 1H, pyran H-5), 7.41–7.98 (m, 10H, Ar–H); MS: *m/z* (%) 293 (M^+, 100). *Anal*. Calcd. for $C_{17}H_{11}NO_4$: C, 69.62; H, 3.78; N, 4.78. Found: C, 69.69; H, 4.01; N, 4.99.

1-Amino-4,6-diphenylpyridin-2(1H)-one (12)

A solution of 4,6-diphenyl-2*H*-pyran-2-one (10) (0.5 g, 0.002 mol) in ethanol (10 ml) was refluxed with 85% hydrazine hydrate (2 ml) for 1.5 hr. The reaction

mixture was then diluted with water, the separated product was filtered, washed with cold water, dried and crystallized from benzene-light petroleum (b.p. 60-80).

Yield: 58 %; m.p.: 163–165 °C; IR (KBr, cm^{-1}): 3268, 3195 (NH_2), 2945 (CH aromatic), 1645 (C=O); ^{1}H NMR (DMSO-d_6): δ 5.07 (br s, 2H, NH_2, D_2O exchangeable), 6.45 (d, 1H, *J* = 2.6 Hz, pyridine H-5), 6.86 (d, 1H, *J* = 2.6 Hz, pyridine H-3), 7.23–7.74 (m, 10H, Ar–H),; MS: *m/z* (%) 262 (M^+, 54.6). *Anal*. Calcd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.63; H, 5.17; N, 10.89.

4,6-Diphenylpyridin-2(1H)-one (13)

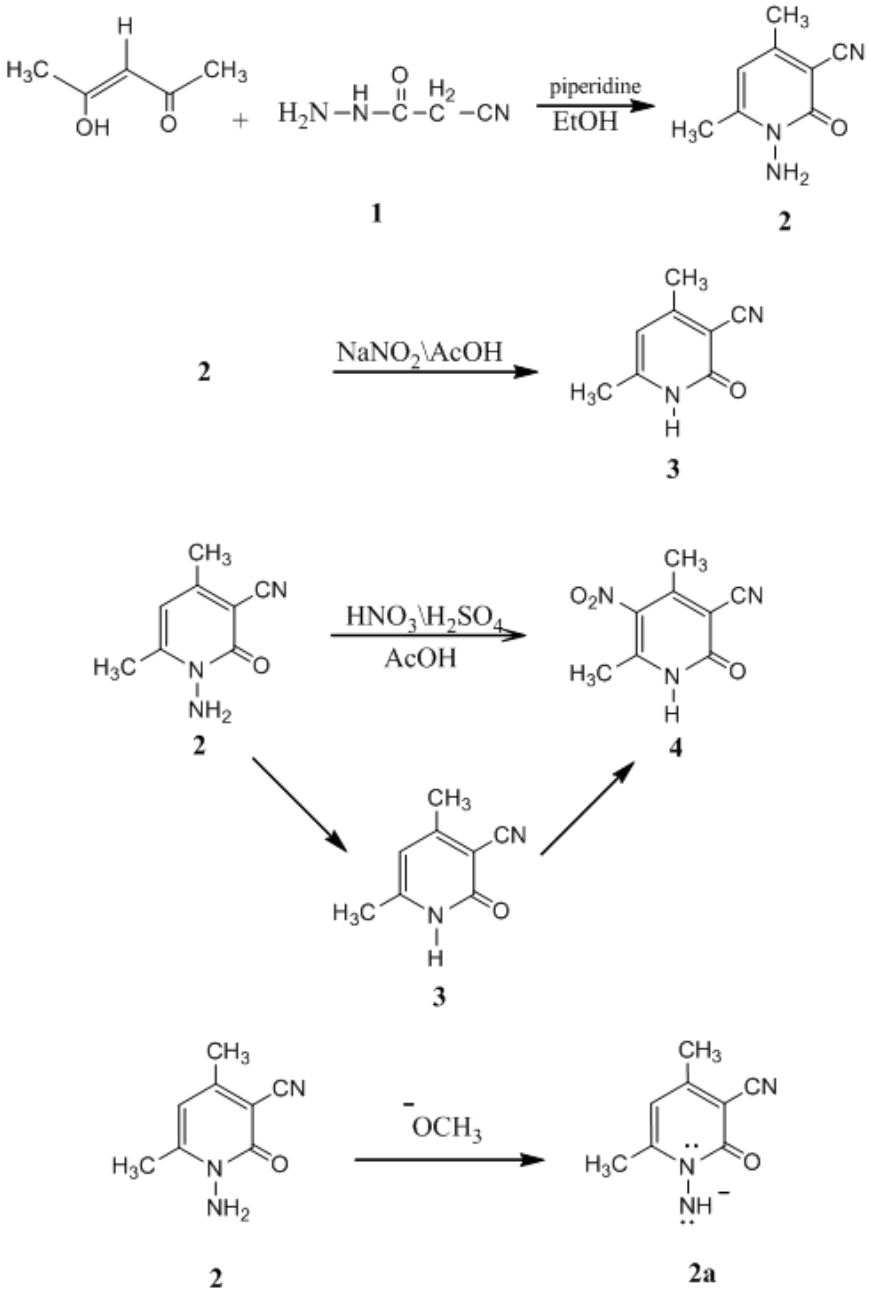
A solution of 1-amino-4,6-diphenylpyridin-2(1*H*)-one (12) (0.2 g, 0.0008 mol) in glacial acetic acid (8 ml) was treated dropwise with an aqueous solution of sodium nitrite (0.5 gm). The separated product was filtered off, washed with ethanol and crystallized from acetic acid.

Yield: 59 %; m.p.: 208–210 °C; IR (KBr, cm^{-1}): 3110-3095 (NH), 2956 (CH aromatic), 1642 (C=O); ^{1}H NMR (DMSO-d_6): δ 5.47 (s, 1H, NH, D_2O exchangeable), 6.41 (d, 1H, *J* = 2.6 Hz, pyridine H-5), 6.82 (d, 1H, *J* = 2.6 Hz, pyridine H-3), 7.15–7.63 (m, 10H, Ar–H); MS: *m/z* (%) 247 (M^+, 35.1). *Anal*. Calcd. for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.32; H, 5.05; N, 5.44.

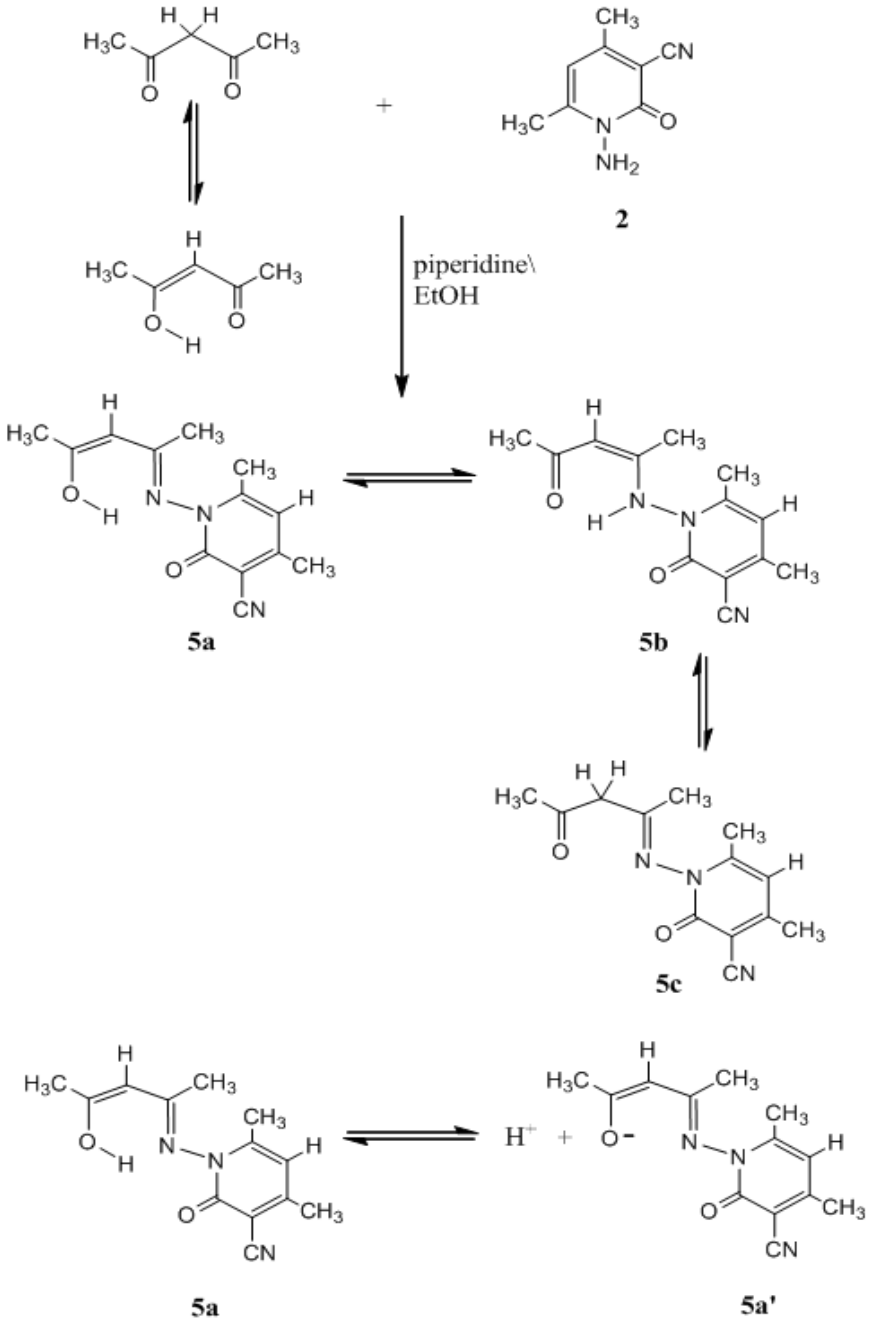
3-Nitro-4,6-diphenylpyridin-2(1H)-one (14)

A mixture of nitric (d 1.41; 3ml) and sulfuric (d 1.84; 3ml) acids in glacial acetic acid (10 ml) was gradually added to a solution of 4,6-diphenylpyridin-2(1*H*)-one (13) (2 g, 0.008 mol) in glacial acetic acid (10 ml). The reaction mixture was warmed at 50°C for 15 min, then poured into cold water with stirring. The separated product was filtered, washed with cold water, dried and crystallized from benzene.

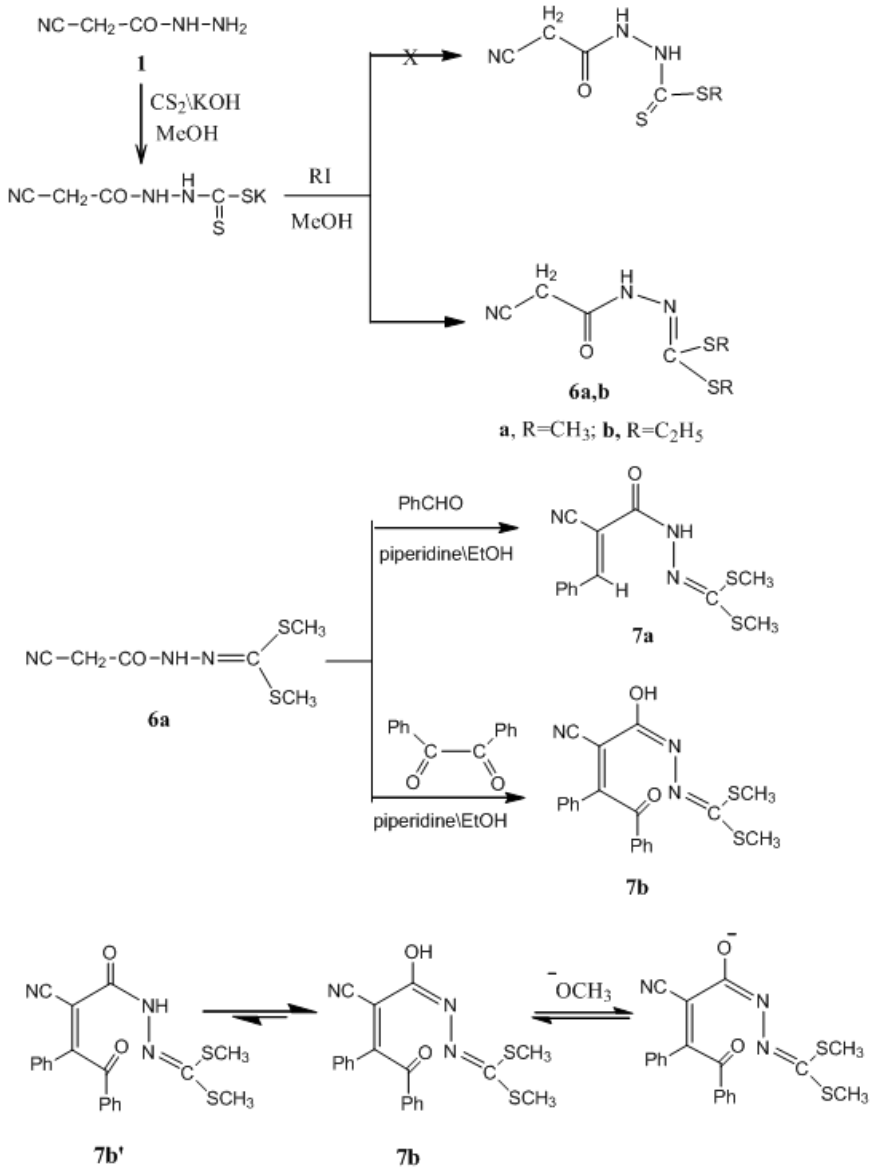
Yield: 81 %; m.p.: 254–256 °C; IR (KBr, cm^{-1}): 3150 (NH), 2928 (CH aromatic), 1670 (C=O), 1530, 1335 (NO_2); ^{1}H NMR (DMSO-d_6): δ 3.21 (s, 1H, NH, D_2O exchangeable), 6.56 (s, 1H, pyridine H-5), 7.43–7.81 (m, 10H, Ar–H); MS: *m/z* (%) 292 (M^+, 24.7). *Anal*. Calcd. for $C_{17}H_{12}N_2O_3$: 69.86; H, 4.14; N, 9.58. Found: 69.64; H, 4.32; N, 9.81.



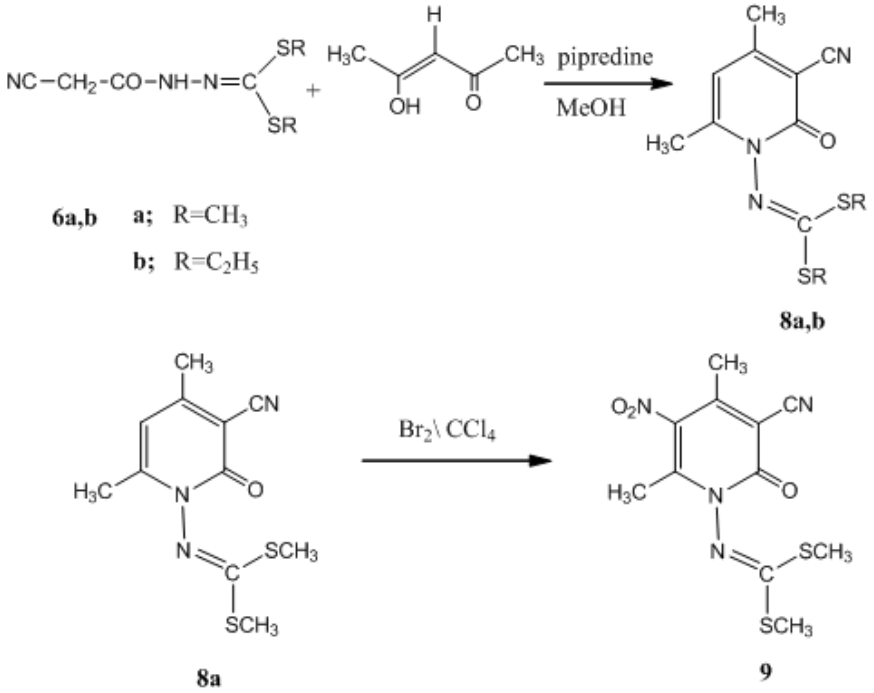
Scheme 1. synthesis of compounds 2-4.



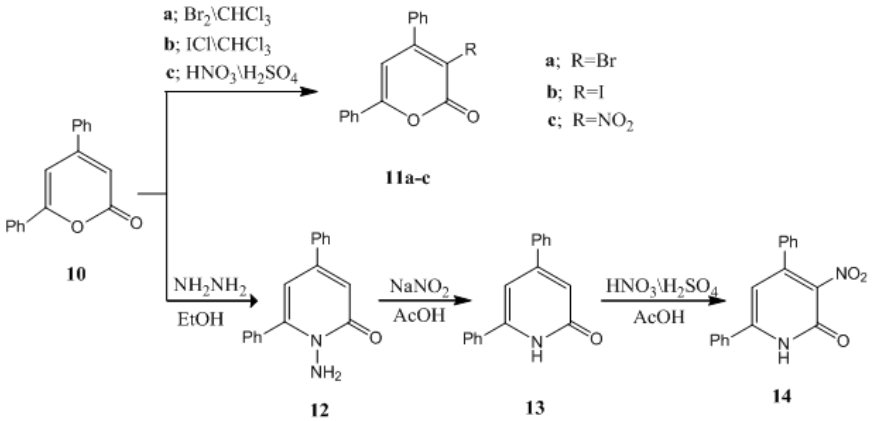
Scheme 2. Synthesis of compound 5.



Scheme 3. Synthesis of compounds 6a,b and 7a,b.



Scheme 4. Synthesis of compounds 8a,b and 9.



Scheme 5. Synthesis of compounds 11a-c; 12-14.

Results and Discussion

In the present investigation, some 2-pyridones containing a cyano group were synthesized. 1-Amino-3 cyano-4,6-dimethyl-2-pyridone (2) was prepared by the reaction of acetylacetone and 2-isocyanoacetohydrazide (1) in the presence of piperidine[21]. The structure of compound 2 was confirmed through

the study of its spectral data and elemental analysis. The ^{1}H NMR spectrum showed the presence of two singlets at δ 2.35 and 2.45 ppm ($2CH_3$) beside another two singlets at δ 6.05 and 6.25 for NH_2 (D_2O exchangeable) and pyridine H-5, respectively. Moreover, the electronic spectrum of compound 2 was recorded in MeOH, MeOH\$H_2SO_4$ (0.1 M) and MeOH\$NaOCH_3$ (0.1M). The spectrum in neutral and acidic solution solutions was characterized by the presence of three absorption maxima at 395, 338 and 224 nm. However, in basic medium, the spectrum showed a new band at 206 nm. This may be explained by assuming deprotonation of the NH_2 giving the anion 2a (Scheme1).

4,6-Dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (3) was obtained by nitrous acid deamination of 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (2), which was found to be completely identical to an authentic sample prepared by the condensation of acetylacetone and cyanoacetamide [21].

Nitration of compound 2 with the conventional nitrating mixture [conc. HNO_3\H_2SO_4 (1:1)] resulted only in the isolation of the deaminated product 4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (3). However, prolonged treatment of compound 2 with the nitrating mixture led to the formation of 3-cyano-4,6-dimethyl-5-nitro-2-oxo-1,2-dihydropyridine-3-carbonitrile (4) which was also formed from the reaction of compound 3 with the nitrating mixture (Scheme 1). The presence of one singlet at δ 2.32 ppm corresponding to six protons ($2CH_3$) beside another singlet at δ 10.22 ppm for NH (D_2O exchangeable) with the absence of pyridine H-5 signal in the ^{1}H NMR spectrum, proved the formation of compound 4.

Condensation of compound 2 with acetylacetone afforded compound 5 which could be represented by any of the three possible tautomeric forms 5a, 5b or 5c [22,23] (Scheme 2). The structure of compound 5 was confirmed through the study of its spectral data and elemental analysis. Thus, the ^{1}H NMR spectrum of compound 5 showed the presence of four singlets at δ 1.61, 1.74, 2.44 and 2.62 ppm corresponding to the presence of four CH_3 groups. Also, the presence of signal at δ 5.35 ppm for C-H proton of the acetylacetone moiety and 11.54 (OH, D_2O exchangeable) ppm supported that the condensation product 5 exist in the enol-imine structure 5a[23]. Moreover, the electronic spectrum of compound 5 was recorded in MeOH, MeOH\$H_2SO_4$ (0.1 M) and MeOH\$NaOCH_3$ (0.1M) (Fig. 1) (see the experimental section) showed the presence of two isobestic points at 272 and 238 nm., a fact that denotes the presence of an acid-base equilibrium. A comparison of the spectra revealed that the band at 284 nm in the neutral species becomes more intense in basic medium and diminishes in acid solution which confirmed that compound 5 exists in the enol-imine structure 5a. The latter compound exists in equilibrium in the neutral solution. In acidic solution the form 5a predominates, while the anion 5a' is the predominant form in the basic medium (Scheme 2).

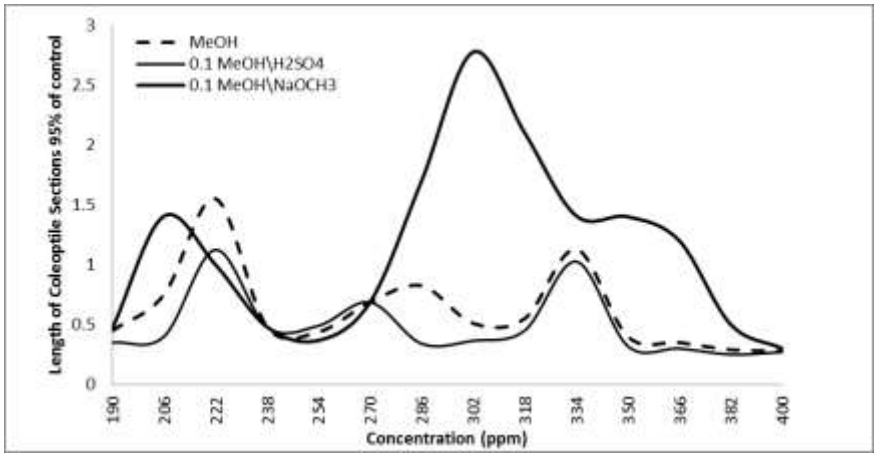


Fig. 1. Electronic spectrum of compound 5.

In the present investigation compound 2 failed to react with carbon disulfide and methyl iodide[24,25]. Therefore, a new synthetic strategy had to be adopted by the introduction of the sulfur moiety to the cyanoacetohydrazide 1 before condensation with acetylacetone. However, when cyanoacetohydrazide 1 was subjected to the standard carbodithioation experimental condition[24,25], the only isolated product was shown to be dialkyl (2-isocyanoacetyl) carbonohydrazonodithioate (6a,b; R= CH_3, C_2H_5) by using 2 moles of each of KOH and alkyl iodide. The novel products 6a,b (R= CH_3, C_2H_5) were characterized through a study of their spectral data, together with some condensation reactions with simple carbonyl and α-dicarbonyl compounds.(Scheme 3). Thus, the ^{1}H NMR spectrum of compound 6b (as an example) showed the presence of triplet and quartet at δ 1.35 and 3.15 ppm corresponding to the $2CH_3$ and $2CH_2$ protons of the two ethyl groups. The two protons of the active methylene group being magnetically nonequivalent showing double doublet at δ 3.91 ppm beside a broad singlet at δ 10.55 ppm for NH group (D_2O exchangeable). Moreover, ^{13}C NMR spectrum showed δ: 13.8, 15.1 ($2CH_3$), 24.4, 26.1, 26.7 (3 CH_2), 116.2 (CN), 158.1 (C=N), 165.4 (CO).

Condensation of 6a with either benzaldhyde or benzil afforded the condensation products 7a,b. The ^{1}H NMR spectrum of 7b (as an example) showed the presence of two methyl signals at δ 2.11 and 2.42 ppm, together with multiplet at δ 7.21–7.64 ppm corresponding to the ten aromatic protons. The singlet at δ 7.90 ppm may be attributed to the OH proton of the enol-imine form 7b (R=CH_3), a behavior often characterizing such systems [23] . At the time being, ^{13}C NMR spectrum revealed δ: 19.8, 20.1 ($2CH_3$), 119.3 (CN), 162.9 (C=N), 173.1, 179.1 (2CO). A further elucidation of the structure of compound 7b was achieved through a study of its electronic spectrum in MeOH, MeOH\$H_2SO_4$ (0.1 M) and MeOH\$NaOCH_3$ (0.1M) (see the experimental section). The UV spectrum is characterized by the appearance of four absorption maxima at 580, 387, 245 and 282 nm which were not affected neither in acidic nor in basic

media. This phenomenon could only be explained by assuming the predominance of the enol-imine form (7b) rather than the keto-imine (7b') in the neutral solution (Scheme 3)

2 - Oxopyridin -1 (2*H*) -yl) carbonimidodithioate derivatives 8a,b were synthesized from the reaction of 6a,b with acetylacetone in the presence of piperidine as a base. The ^{1}H NMR spectrum for 8a (as an example) exhibited the presence of four methyl groups' singlets at δ 2.20, 2.35, 2.55 and 2.65 ppm beside another singlet at δ 6.32 ppm corresponding to pyridine H-5. In addition, the ^{13}C NMR spectrum showed δ 13.9, 15.1, 18.5, 20.4 ($4CH_3$), 116.4 (CN), 157.1 (C=N), 180.1 (CO).

It was reported that the S-CH_3 group could be substituted with halogen[26]. However, treatment of compound 8a with $Br_2\backslash CCl_4$ led to the introduction of bromine at the five position of the 2-pyridone ring giving compound 9. The ^{1}H NMR spectrum of compound 9 was almost identical with that of 8a, except for the disappearance of the C-5 proton signal (Scheme 4).

A well-established route for the synthesis of 2-pyridones involves the reaction of 2*H*-pyran-2-ones with ammonia, amines as well as hydrazines[20] Therefore, in the present work a series of 3-substituted 4,6-diphenyl-2*H*-pyran-2-one (11a-c) were prepared from 4,6-diphenyl-2*H*-pyran-2-one (10). The structure of 11a-c was in agreement with their spectral data and elemental analyses (see experimental section). 3-Substituted 4,6-diphenyl-2*H*-pyran-2-one (11a-c) failed to react with hydrazine hydrate and only resinous product was formed which could not be identified. Only, 4,6-diphenyl-2*H*-pyran-2-one (10) reacted with hydrazine hydrate and afforded 1-amino-4,6-diphenylpyridin-2(1*H*)-one (12). The structure of the latter compound was confirmed on the basis of its spectral data and elemental analysis. The ^{1}H NMR spectrum of compound 12 exhibited two doublets (J = 2.6 Hz) at δ 6.45 and 6.86 ppm due to long rang coupling between C-5 and C-3 protons, respectively. Also, the presence of broad singlet at δ 5.07 ppm (D_2O exchangeable) for NH_2 protons beside multiplet corresponding to the ten aromatic protons at δ 7.23–7.74 ppm. Deamination of compound 12 with sodium nitrite in glacial acetic acid afforded 4,6-Diphenylpyridin-2(1*H*)-one (13)[27]. Finally, 3-nitro-4,6-diphenylpyridin-2(1*H*)-one (14) was prepared from the nitration of compound 13 using the conventional nitrating mixture [conc. $HNO_3\backslash H_2SO_4$ (1:1)]. The structure of the latter compound was confirmed through the study of its spectral data and elemental analysis (Scheme 5).

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استخدام الأسيتيل اسيتون فى تحضير مشتقات بيريدين 2-اون

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فى هذا البحث تم تحضير سلسلة من مشتقات بيريدين 2-اون من خلال تفاعل الأسيتيل اسيتون مع سيانواسيتوهيدرازيد او ثنائى الكيل كاربوسيانوهيدرازودای ثيووات و كذلك--*2H* بيران-اون. كذلك تم معالجة بعض تفاعلات بيريدين 2-اون . تم التعرف على التركيب الكيميائى لكل المركبات المحضرة باستخدام الطرق الطيفية (اطياف الأشعة فوق البنفسجية ، تحت الحمراء، الرنين النووى المغناطيسى ^{1}H NMR و (^{13}C NMR) وكذلك طيف الكتلة و التحاليل الدقيقة لكل من الكربون، الهيدروجين، النيتروجين و الكبريت.