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Facile synthesis of functional heterocycles utilizing activated Benzylideneacetones

Hoda Sabry Othman[a], Khlood S. Abdel Zaher[a], Marwa M. Fouad[b], Galal A.M. Nawwar[a*]

[a]*Green Chemistry Department, National Research Centre, Giza, Egypt.*

[b]*Basic Science Department, Modern Academy for Engineering &Technology, Cairo, Egypt.*

Abstract

The utility of cinnamoylacetonitrile and chloroacetylcinnamates, as activated benzylideneacetones, in facile synthesis of difficulty accessible functional pyridines, furans and pyrans is presented here. Biomass-derived chemicals as furfural, gallic, benzoic, cinnamates, and acetone derivatives were used. The structures of all new synthesized compounds were confirmed on the basis of spectral analysis, IR, ^{1}H NMR, ^{13}C NMR, and MS spectroscopy.

Keywords: Benzylideneacetone, Biomass-derived chemicals, Ylide, Heterocycles.

1. Introduction

Biomass is the most dominant renewable source for chemical feedstocks. Valuation of biomass derived chemicals is a recent strategy worldwide to replace the use of petrochemicals. The climate change associated problems aggravated the need for such approach taken sustainability and environmental aspects into consideration. Finding such natural feedstocks will give the way for the production of various green active compounds. Benzylideneacetones represent an important class of propenones [1-4] which considered as good precursors for the synthesis of new compounds with wide spectrum biological activities. The chemically active functional groups in benzylideneacetone encourages scientists to its utilization in synthesis of new and difficulty accessible compounds.

Recently, Herrera's group succeeded to synthesize new derivatives of warfarin, one of the mostly used anticoagulants, from the reaction of benzylidineacetones and coumarins *via* Michael addition reaction [5]. In addition, Hua Yang *et al.* published the preparation of novel functionalized spirooxindoles in good to excellent chemical yields with good regioselectivities from 1,3-dipolar cycloaddition of isatins, benzylamine and benzylideneacetones [6]. Using sulfonamide organocatalyst, Miura's team reported the conjugate addition of dibenzylmalonate to different benzylideneacetone derivatives, affording the corresponding malonic acid alkyl ester derivatives in high yields with excellent enantioselectivities [7]. Regarding its biological activity, investigation of benzylideneacetone effect on the activity of mushroom tyrosinase revealed that benzylideneacetone could act as potent antityrosinase agent [8].

For further functionalization, activation of the methyl group in benzylideneacetone *via* substituting with additional functional groups in its specific structure arrangement (Fig **1**) enhances its synthetic versatility in heterocyclic synthesis as it has both nucleophilic and electrophilic sites. Also, it could act in pairs as a bidentate reagent affording several probabilities, the predominance of which depends on the reaction conditions and the other reactants. Moreover, versatility of these activated benzylideneacetones could be extended to form condensed heterocycles *via* the involvement of more than two centers in the reaction course.

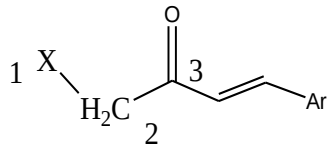

Fig.1: activated benzylideneacetones, X; electron-withdrawing group

In continuation to our pervious program directed to simple synthesis of small heterocylces with

*Corresponding author e-mail: gnawwar@yahoo.com.; (Galal A. M. Nawwar).

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anticipated biological activity [9-16], our current study concerns with benzylideneacetones as productive starting synthons, using biomass derived chemicals whenever possible.

2. Experimental:

General procedure for synthesis of 2-aryl-3-oxo-5-phenylpent-4-enenitrile (3a,b):

A solution of cinnamoacetonitrile (**1**) (1.7g; 0.01 mol) in 30 mL of dry benzene was stirred with sodium hydride (0.24g; 0.01 mol) at room temperature for 15 min. Each acid chloride, namely Furan-2-carbonyl chloride and 3,4,5-trimethoxy-benzoylchloride, (0.01 mol) was added to the stirred solution dropwise over a period of 15 min, followed by further stirring for 6hr and solvent evaporation. The residual oil was washed with 4N HCl and triturated with methanol to give the solid product, which filtered off and crystallized to afford compounds (**3**).

2-(furan-2-carbonyl)-3-oxo-5-phenylpent-4-enenitrile (3a):

Yellow crystals (THF); yield 65%; m.p 187-189ºC.
IR (KBr,cm^{-1}) υ: 1685, 1640 (2 CO), 2200 (CN). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 5.32 (s, 1H, methine H), 5.6 (m, 2H, furan H-3 and H-4), 6.92 (d, J_{HH}= 15 Hz, 1H, olefinic H), 7.2-7.9 (m, 6H, Ph and furan H-5), 8.10 (d, J_{HH}= 15Hz, 1H, olefinic H).Anal.Calcd. for $C_{16}H_{11}NO_3$ (265.3); C,72.44; H,4.18; N,5.28%; Found: C,72.28; H, 4.00; N 4.97%.

3-oxo-5-phenyl-2-(3,4,5-trimethoxybenzoyl)pent-4-enenitrile (3b):

Yellow crystals (Ethanol); yield 70%; m.p 191-193ºC.
IR (KBr,cm^{-1}) υ:, 1687, 1642 (2 CO), 2200 (CN). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 3.80-4.00 (9H, $3OCH_3$), 6.60 (d, J_{HH}= 15 Hz, 1H, olefinic H), 7.2-8.10 (m, 7H, Ph and gallate), 7.00 (d, J_{HH}= 15Hz, 1H, olefinic H), 12.70 (exchangeable 1H, OH, enol). m/z: 212(100%), 197(64%), 169(15%). Anal.Calcd. for $C_{21}H_{19}NO_5$ (365); C,69,03; H,5.24; N,3.83%; Found: C,68.99; H,5.01; N 3.61%.

General procedure for synthesis of 4-oxo-2-aryl-6-phenyl-4H-pyran-3-carbonitrile (4a,b):

The acyl derivatives (**3a,b**) were boiled each under reflux in 30 mL of acetic acid in the presence of 1mL trifluoroacetic acid for 5hr, followed by concentration of the reaction mixture, and then cooling. The formed precipitate, for each, was filtered off and crystallized to give (**4a,b**).

2-(furan-2-yl)-4-oxo-6-phenyl-4H-pyran-3-carbonitrile (4a):

Brown crystals (Ethanol); yield 70%; m.p 161-163ºC.
IR (KBr,cm^{-1}) υ: 1625 (CO), 2220 (CN). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 6.2 (2H, furan H-3 and H-4), 7.2-7.9 (m, 7H, Ph, furan H-5 and Pyrone H-5). Anal.Calcd. for $C_{16}H_9NO_3$ (263.2); C,72.99; H,3.44; N,5.32%; Found: C, 72.73; H, 3.25; N 5.01%.

4-oxo-6-phenyl-2-(3,4,5-trimethoxyphenyl)-4H-pyran-3-carbonitrile (4b):

Yellow crystals (Ethanol); yield 75%; m.p 181-183ºC.
IR (KBr,cm^{-1}) υ: 1628 (CO), 2220 (CN). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 3.80-4.00 (9H, $3OCH_3$), 6.60 (s, 1H, Pyrone H-5), 7.4-8.10 (m, 7H, Ph and gallate). m/z: 197(64%), 169(20%).^{13}CNMR (125 MHz, δppm, CDCl3): 56.3 (3C, $3OCH_3$), 103 (pyrone C-5),105.1(gallate C-2,C-6), 112 (pyrone C-3), 113(CN),126.6 (C_6H_5 C- 2, C-6), 127.7 (C_6H_5 C-4), 129 (gallate C-1), 129.3 (C_6H_5 C-3,C-5), 132.2(pyrone C-5), 132.4 (gallate C-4), 139.2(C_6H_5 C-1), 148.5 (gallate C-3,C-5), 168.9 (pyrone C-6), 178.0 (1C, CO), 180.0 (pyrone C-2). Anal.Calcd. for $C_{21}H_{17}NO_5$ (363); C,69.41; H,4.72; N,3.85%; Found: C, 69.20; H,4.51;N 3.62%.

Synthesis of 2-cinnamoyl-3-oxohex-4-enenitrile (6):

To a solution of 0.01 mole of cinnamoylacetonitrile (**1**) in dry tetrahydrofuran (20mL) in the presence of triethylamine (0.01 mol.), crotonyl chloride (0.01 mole in 15 mL dry tetrahydrofuran) was dropped over a period of 30min. Stirring was kept for further 2hr, and the reaction mixture was the filtered off. The solid obtained washed with water and crystallized.

Yellow crystals (Cyclohexane); yield 55%; m.p 147-149ºC.
IR (KBr,cm^{-1}) υ: 2200 (CN), 1680, 1665 (2CO).^{1}HNMR (500MHz, δppm, DMSO-d_6): 2.0 (dd,$J_{gem.}$=7Hz, $J_{vic.}$=2Hz, CH_3), 6.2 (s, 1H, CHCN), 6.80-7.50 (m, 9H, olefinicandPh). Anal.Calcd. for $C_{15}H_{13}NO_2$ (239); C,75.29; H,5.47; N,5.85%; Found: C,75.0; H, 5.20; N 5.40%.

Synthesis of 5-cinnamoyl-6-methoxy-2-methyl-2,3-dihydropyridin-4(1H)-one (7):

A steam of HCl gas was passed through a methanolic solution of (**6**) (0.01 mol. in 25 mL) for 30 min, followed by stirring the mixture for 96 hr at room temperature. The reaction mixture was then neutralized by potassium hydrogen carbonate, and the precipitated solid was filtered off, washed with water and crystallized.

White crystals (Methanol); yield 45%; m.p 164-166ºC.
IR (KBr,cm^{-1}) υ: 3400(OH), 3000-2800 (NH and ring stretching), 1690 (CO).^{1}HNMR(500MHz, δppm, DMSO-d_6): 1.2 (d,J=8Hz, 3H,CH_3), 3.0-3.2 (m, 2H, hydropyridine H-3), 4.1 (s, 3H, OCH_3), 5.2 (m,1H, hydropyridine H-2), 6.80 (d, J= 16 Hz, 1H, olefinic H), 7.0-7.5 (m, 7H,Ph, NH, OH), 7.9 (d, J= 16 Hz, 1H, olefinic H).^{13}CNMR (125 MHz, δppm, CDCl3): 21.9 (CH_3), 37.2 (pyridinone C-6), 48.3 (1C, OCH_3), 49.4(pyridinone C-5), 88.0 (pyridinone C-3), 126.2 (C_6H_5 C-2,C-6), 127.7 (C_6H_5 C-4), 128.2 (C_6H_5 C-3,C-5), 129.6 (olefinic C_α),132(C_6H_5 C-1), 149 (olefinic

C_β), 187 (cinnamoyl C=O), 192 (pyridinone C-2), 197 (pyridinone C=O). Anal.Calcd. for $C_{16}H_{17}NO_3$ (271.3); C,70.82; H,6.32; N,5.16%; Found: C,70.50; H, 6.00; N 4.90%.

Synthesis of 6-methoxy-2-phenyl-2,3-dihydropyridin-4(1H)-one (8):

A steam of HCl gas was passed through a methanolic solution of (**1**) (0.01 mole in 25 mL) for 30min and the solution was then refluxed for 96hr. After cooling, the formed precipitate was collected, washed with potassium hydrogen carbonate solution, then water and finally crystallized.

Yellow crystals (Methanol); yield 45%; m.p 207-209ºC

IR (KBr,cm^{-1}) υ: 3000-2800 (NH), 1685 (CO).^{1}HNMR(500MHz, δppm, DMSO-d_6): 3.31-3.3(m, 2H, hydropyridine CH_2), 4.0 (s, 3H, OCH_3), 5.5-5.6 (m, 1H, hydropyridine H-2), 6.8 (s, 1H, hydropyridine H-5), 7.5-7.6 (m,5H, C_6H_5). ^{13}CNMR (125MHz,δppm,CDCl3): 47.3(pyridinone C-5), 48.8 (OCH_3), 52.1 (pyridinone C-6), 126.3 (C_6H_5 C-4), 128.1 (C_6H_5 C-3,C-5), 129.1 (C_6H_5 C-2,C-6), 136.2 (pyridinone C-3), 142.4(C_6H_5 C-1), 165.2 (pyridinone C-2), 201.1(pyridinone C=O).Anal.Calcd. for $C_{12}H_{13}NO_2$(203); C,70.91; H,6.44; N,6.89%; Found: C,70.50; H, 6.10; N 6.60%.

Synthesis of 2-(2-bromopropanoyl)-3-hydroxy-5-phenylpenta-2,4-dienenitrile (10):

A stirred solution of (**1**) (0.01 mole) in dry benzene (30 mL) was treated with 2-bromo-propionyl bromide (0.01 mole) dropwise in the presence of sodium hydride (0.01mole). The reaction mixture was stirred for 6hr, followed by evaporation of the solvent. The oil residue washed with 4N HCl and triturated with methanol, then the obtained solid filtered off, and crystallized.

Yellow crystals (Cyclohexane); yield 75%; m.p 89-91ºC

IR (KBr,cm^{-1}) υ: 3200 (OH), 2230 (CN), 1670 (CO). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 2.1 (d, 3H, CH_3), 4.8 (d, H, CH-Br), 7.1-7.8 (m, 8H, phenyl-H, OH, oleifinic-H), 11.0 (s, H, OH). Anal.Calcd. for $C_{14}H_{12}BrNO_2$(305); C,61.58; H,3.97; N,4.63%; Found: C,60.99; H, 3.83; N 4.49%.

Synthesis of 5-methyl-4-oxo-2-styryl-4,5-dihydrofuran-3-carbonitrile (11):

Compound (**10**) was allowed to heat at 50ºC in ethanol in the presence of sodium ethoxide. The formed solid was then purified by methanol.

Yellow crystals (Methanol); yield 55%; m.p 122-124ºC

IR (KBr,cm^{-1}) υ: 2230 (CN), 1680 (CO).^{1}HNMR(500MHz, δppm, DMSO-d_6): 3.3 (d, 3H, CH_3), 7.1-7.8 (m, 7H, phenyl-H, olefinic-H), 11.8 (br, s, H, OH). Anal.Calcd. for $C_{14}H_{11}NO_2$ (225); C,71.48; H,4.68; N,5.95%; Found: C,71.00; H,4.21; N 6.08%.

General procedure for synthesis of 1-chloro-4-arylbut-3-en-2-one (15a,b):

To a solution of the free ylide (**13a**) in dry toluene, an appropriate aldehyde was added and the reaction mixture was heated under reflux for 4hr, followed by evaporation of the reaction solvent. The product was then extracted with petroleum ether.

1-chloro-4-phenylbut-3-en-2-one (15a):

Whitish crystals; yield 65%; m.p 96-98ºC

IR (KBr,cm^{-1}) υ: 3410 (CH, aromatic), 1625 (CO), 1602 (C=C).^{1}HNMR(500MHz, δppm, DMSO-d_6): 4.2 (CH_2), 7.0 (d, 1H, olefinic), 7.3-7.6 (m, 5H, C_6H_5), 7.7 (d, 1H, olefinic). Anal.Calcd. for $C_{10}H_9ClO$ (180.63); C, 66.49; H,5.02; Cl,19.63%; Found: C,66.26; H, 4.89; Cl,19.41%.

1-chloro-4-(4-chlorophenyl)but-3-en-2-one(15b):

Yellow crystals; yield 65%; m.p 105-107ºC

IR (KBr,cm^{-1}) υ: 3411 (CH, aromatic), 1628 (CO), 1602 (C=C).^{1}HNMR(500MHz, δppm, DMSO-d_6): 4.2 (CH_2), 7.0 (d, 1H, olefinic), 7.3 (d, 2H, C_6H_4Cl), 7.5 (d, 2H, C_6H_4Cl), 7.7 (d, 1H, olefinic). m/z: 215 (M^+, 13%), 213 (20%), 166 (35%), 164 (100%), 137 (20%), 102 (15%). Anal.Calcd. for $C_{10}H_8Cl_2O$ (215); C,55.84; H,3.75; Cl,32.97%; Found: C,55.62; H,3.53; Cl,32.74%.

General procedure for synthesis of 5-amino-4,6,6,6-tetrachloro-1-arylhexa-1,4-dien-3-one(16a,b):

0.01 mole of cinnamoylchloromethyl or its para-chlorophenyl derivative, in dry cyclohexane (20 mL) and dry THF (20 mL), was treated with trichloroacetonitrile (0.01) in the presence of catalytic amount of TEA. The reaction mixture was refluxed for 3hr, followed by concentration and cooling. The precipitated solid (**16**) was then collected.

5-amino-4,6,6,6-tetrachloro-1-phenylhexa-1,4-dien-3-one(16a):

Yellow crystals (Cyclohexane); yield 60%; m.p 150-152ºC

IR (KBr,cm^{-1}) υ: 3250 (NH_2), 1680 (CO). ^{1}HNMR(500MHz, δppm, DMSO-d_6): 4.78(s,2H,NH_2), 7.0(d,1H,olefinic), 7.5 (d,1H, olefinic), 7.6-7.9 (m,5H,C_6H_5). Anal.Calcd. for$C_{12}H_9Cl_4NO$ (325); C,44.34; H, 2.79; Cl, 43.63%; N, 4.31; Found: C, 44.12; H, 2.56;Cl, 43.40%; N, 4.10.

5-amino-4,6,6,6-tetrachloro-1-(4-chlorophenyl)hexa-1,4-dien-3-one(16b):

Yellow crystals (Cyclohexane); yield 65%;m.p 154-156ºC

IR (KBr,cm^{-1}) υ: 3250 (NH_2), 1680 (CO). ^{1}HNMR (500MHz, δppm, DMSO-d_6): 5.8(s,2H,NH_2), 7.0 (d,1H,olefinic), 7.5 (d,2H, C_6H_4Cl),7.7(d,1H, olefinic),

7.6 (2H,C_6H_4Cl). Anal.Calcd. for $C_{12}H_8Cl_5NO$ (359.46);C,40.10;H, 2.24;Cl, 49.31 ; N,3.90%;Found: ,39.95; H, 2.01; Cl, 49.10 ; N,3.69%.

General procedure for synthesis of 3-chloro-6-aryl-2-(trichloromethyl) pyridin-4-ol (17a,b):

Compound (**16**) was refluxed in pyridine for 3hr, then poured on crushed ice, filtered and crystallized.

3-chloro-6-phenyl-2-(trichloromethyl)pyridin-4-ol (17a):

Brown crystals (Dioxan); yield55%; m.p 236-238ºC

IR (KBr,cm^{-1}) υ:3350 (OH), 1625 (C=N). ^{1}HNMR(500MHz, δppm, DMSO-d_6): 7.48-7.93 (m, 5H, C_6H_5), 8.26 (1H, pyridine H-5), 12.05 (s, 1H, OH). Anal.Calcd. for $C_{12}H_7Cl_4NO$ (323); C,44.62; H,2.18; Cl,43.90; N, 4.34%; Found: C,44.40; H,2.00; Cl,43.68; N, 4.12%.

3-chloro-6-(4-chlorophenyl)-2-(trichloromethyl) pyridin-4-ol (17b):

Brownish crystals (Dioxan); yield 63%;m.p251-253ºC

IR (KBr,cm^{-1}) υ: 3419 (CH, aromatic), 1627(C=N).^{1}HNMR(500MHz,δppm,DMSO-d_6): 7.48-7.93 (m, 4H, C_6H_4Cl), 8.26 (1H, pyridine H-5), 12.05 (s, 1H, OH). ^{13}CNMR (125MHz, δppm, CDCl3): 87.3(1C, CCl_3), 115.3 (pyridine C-3), 123.0 (pyridine C-5), 126.8 (C_6H_5 C-2,C-6), 129 (C_6H_5 C-3,C-5), 132 (C_6H_5 C-4), 138.1(C_6H_5 C-1), 157 (pyridine C-6), 159.9 (pyridine C-2), 166.1(pyridine C-4). Anal.Calcd. for $C_{12}H_6Cl_5NO$ (357.45); C,40.32; H,1.69; Cl,49.59; N, 3.92%; Found: C,40.10; H,1.47; Cl,49.37; N, 3.70%.

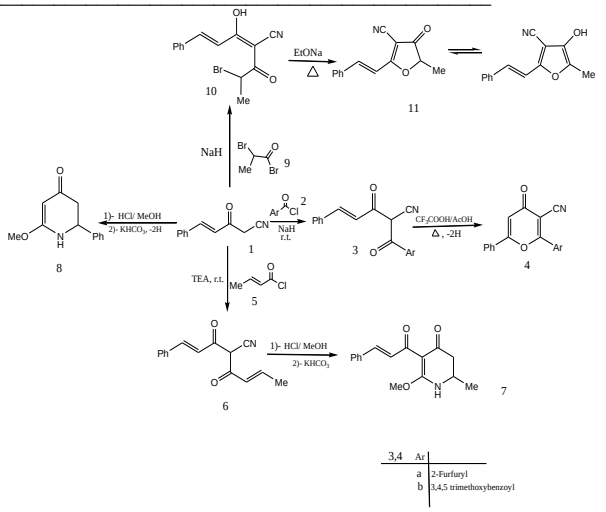
Synthesis of methyl 3-(3-hydroxypyridin-2-yl) acrylate (19):

To a solution of the free ylide (**13b**) in dry toluene, 3-Hydroxy-pyridine-2-carbaldehyde was added and the reaction mixture was heated under reflux, followed by solvent evaporation and extraction of the product with cyclohexane.

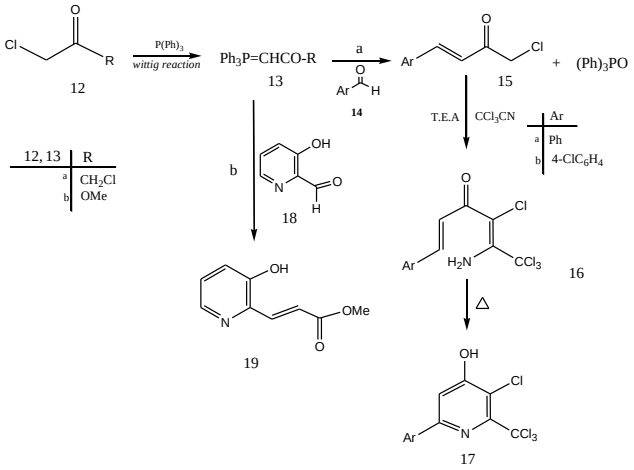
Yellow crystals (Cyclohexane); yield73%; m.p 66-68ºC

IR (KBr,cm^{-1}) υ: 3350 (OH), 1705(CO).^{1}HNMR(500MHz, δppm, DMSO-d_6): 3.75 (3H, OMe), 7.40 (d, 1H, olefinic), 6.90 (d,1H, H-4), 7.90 (d,1H, H-6), 8.20 (d, 1H, olefinic), 7.30 (t, 1H, H-5), 11.77 (s, 1H, OH)

m/z: 277 (M^+, 10%), 277 (20%), 148 (18%), 120 (100%), 92 (20%), 65 (10%). Anal.Calcd. for $C_9H_9NO_3$ (179.17); C,60.33; H,5.06; N, 7.82%; Found: C,60.11; H,4.84; N, 7.60%.



Scheme 1



Scheme 2

3. Results and Discussion:

Cinnamoylacetonitrile (**1**) was allowed to react with acid chlorides (**2**), namely Furan-2-carbonyl chloride and 3,4,5-trimethoxy-benzoylchloride, in the presence of sodium hydride to afford compounds (**3a,b**) (Scheme **1**), which could be cyclized to the corresponding pyranones after reflux in acetic acid in the presence of trifluoroacetic acid (**4a,b**). It is assumed that compounds (**4a,b**) were formed *via* initial self-cyclization of the enol form of (**3**) with subsequent oxidation under reaction conditions of the formed hydropyran intermediate. Assigning the chemical structure of all compounds was based on the spectral data.

For compounds (**3**), ^{1}HNMR spectrum showed the methane signal at δ 5.31 ppm, beside two one proton doublets at δ 6.94 and δ 8.10 ppm (J=15Hz), attributed to the olefinic protons. Also, IR spectrum showed two carbonyl absorptions at υ ~ 1680 and 1650 cm^{-1}, in

addition to another signal at 2200 cm^{-1} attributed to the cyano group.

For compounds (**4**), the ^{1}HNMR spectrum revealed absence of the two parent olefinic protons. ^{13}CNMR exhibited presence of signals at ~ δ 56 ppm attributed to carbons of the three methoxy groups. Presence of one signal at δ178 ppm for one carbonyl group and another signal at δ113 ppm for cyano group could be also detected. C-5 and C-6 of 4H-pyrone ring appeared at δ 103 and 168 ppm, respectively. IR showed only one carbonyl absorption at υ 1625 cm^{-1} and cyano absorption at υ 2220cm^{-1}. This data became in accordance with the previously reported phenyl analogue, which prepared *via* another reaction pathway [17].

In addition, reaction of cinnamoylacetonitrile (**1**) with crotonyl chloride (**5**) in the presence of triethylamine resulted in formation of its *C*-crotonyl derivative (**6**), which after treating with methanolic HCl afforded 2-methyldihyropyridine derivative (**7**). *C*-crotonyl derivative (**6**) showed IR cyano absorption at υ 2200 cm^{-1}, and two carbonyl absorptions at υ 1680 and 1665 cm^{-1}. Its ^{1}HNMR spectrum revealed presence of a double doublet at δ 2.0 ppm (J=7 Hz, J=2Hz) attributed to the allyl methyl protons. Moreover, its mass spectrum gave a molecular formula compatible with $C_{15}H_{13}NO_2$ (m/z 239). However, compound (**7**) showed absence of the cyano group absorption and appearance of NH and ring stretching absorptions at 3000, 2800cm^{-1}. Its ^{1}HNMR spectrum revealed signals at δ 1.2 (3H), 3.0-3.2 (2H), and 5.2 (1H) ppm, beside the OCH_3 protons singlet at δ 4.1 ppm. In addition, its ^{13}CNMR showed appearance of a signal at δ 48.3 ppm attributed to the carbon of one methoxy group. Methyl carbon was also detected at δ 21.9 ppm. The presence of the characteristic signals of cinnamoyl olefinic carbons at 159 and 129.6 ppm [18] became in accordance with the suggested structure.

Via the same manner, when cinnamoacetonitrile (**1**) itself treated with methanolic HCl, a new product with 2H-pyridine structure (**8**) was obtained. It is suggested that formation of dihydropyridines **7** and **8** occurred due to formation of the reactive imidates *via* methanolysis of nitrile group (Pinner reaction) [19], followed by subsequent self-cyclization, as illustrated in Fig (**2**).

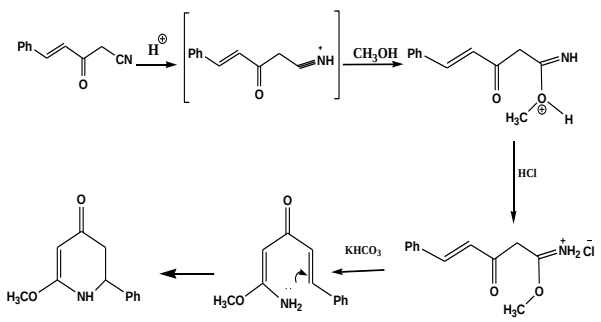


Fig.2: Formation of dihydropyridines **7**and **8** *via* pinner reaction

From ^{13}CNMR spectrum of compound 8, it could be noticed the absence of CN signal, and presence of carbon of methoxy group with signal at δ 48.8 ppm. C-5 and C-6 of dihydropyridine ring appeared at δ 47 and 52 ppm, respectively.

Furthermore, cinnamoylacetonitrile (**1**) reacted with 2-bromo-proionyl bromide (**9**) at room temperature in the presence of sodium hydride to afford adduct (**10**), the structure of which was based on its spectral data. Its ^{1}HNMR spectrum showed presence of doublet signal at 2.1 attributed to the methyl group, another doublet signal at δ 4.8 for CH-Br proton, as well as a D_2O exchangeable signal for enol-hydroxyl proton at δ 11.0 ppm. IR showed absorptions at 2230, and 1670 cm^{-1}attributed to cyano and carbonyl groups, respectively. Adduct (**10**) could be cyclized to furan derivative (**11**), under heating at 50°C, *via* elimination of hydrogen bromide [20].

Another method to prepare active benzylideneacetone derivatives was achieved *via* formation of the 1,3-dichloroacetone ylide (**13a**) with subsequent condensation with appropriate aldehydes (**14**) (Scheme **2**). Structures of these activated benzylideneacetones (**15a,b**) were given based on their spectral data and their chemical behavior. Thus, when the newly synthesized benzylideneacetones (**15**) treated with trichloroacetonitrile, the expected enaminoketones (**16**) were obtained in good yields.

^{1}HNMR spectrum of **16**, exemplified by (**16a**), revealed presence of a D_2O singlet at δ 5.7 ppm attributed to the 2H of the amino group, and two proton doublets at δ 7.0 and δ 7.7 ppm attributed to the olefinic protons. These along with the absence of the active methylene protons detected in the parent compound **15** as singlet at δ 4.2ppm.The formed enaminoketones underwent self-cyclization involving the amino nucleophile and the olefinic Michael receptor center affording the dihydropyridine intermediate which underwent readily oxidation under reaction conditions to give the final isolable hydroxyl pyridines (**17**).^{13}CNMR spectrum of compound (**17b**) showed appearance of a signal at δ 87.3 ppm attributed to carbon of CCl_3. In addition, C-5 and C-6 of pyridine ring appeared at δ 123 and 157 ppm, respectively.

Methyl cinnamate hetero-analogue (**19**) utilizing ylide (**13b**) was synthesized successfully and its structure was interpreted based on its spectral, elemental data and chemical behavior. It is worthy to mention that in an attempt to prepare its corresponding cinnamonitrile *via* reacting with acetonitrile, the previously reported [21] pyridocoumarin obtained instead of the desired cinnamonitrile.

4. Statements and Declarations:

There are no conflicts of interest to declare.

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