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A New and Convenient Synthesis of 2-Imino-2*H*-pyrancarboxaldehydes from β-Ketoamides using Vilsmeier reagent

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Abstract

The synthesis of previously unreported 2-arylimino-2*H*-pyrancarboxaldehydes is achieved by the treatment of Vilsmeier reagent with *N*-arylacetoacetamides. 2-*N*-Alkyl and the parent 2-imino-2*H*-pyrancarboxaldehyde derivatives are synthesized from the corresponding acetoacetamide derivatives. A possible mechanism for the formation of 2-imino-2*H*-pyrancarboxaldehyde is discussed.

Keywords: iminium salts; ketoamides; Vilsmeier reagent.

Introduction

Synthetic chemists are concerned with increasingly sophisticated targets; there is a permanent demand to develop more and more novel synthetic routes able to target the ever increasing heterocyclic structures. Synthetic approaches to various substituted 2*H*-pyrans are of special interest and contemporary importance, because of the growing variety of 2*H*-pyran derivatives isolated from natural products[1-4]. Synthesis of parent 2*H*-pyrans has been difficult due to their valence isomerisation to cis 2,4-pentadienal[5]. However their derivatives have been synthesized by the cyclization of 1,3-dicarbonyl compounds using 2,3-dimethylbutenal and pyridine[6], 1,5-dicarbonyl compounds using HCl[7] and by the Diels-Alder reaction of ethyl pyruvates with 1-methoxy-1,3-butadiene[8]. Synthesis of the parent imino-2*H*-pyran and 2-arylimino-2*H*-pyrancarboxaldehyde from acetoacetamide derivatives has not yet been realised. Hence our objective of the present work is the synthesis of 2-arylimino-2*H*-pyrancarboxaldehydes from ß-ketoamides using the Vilsmeier reagent.

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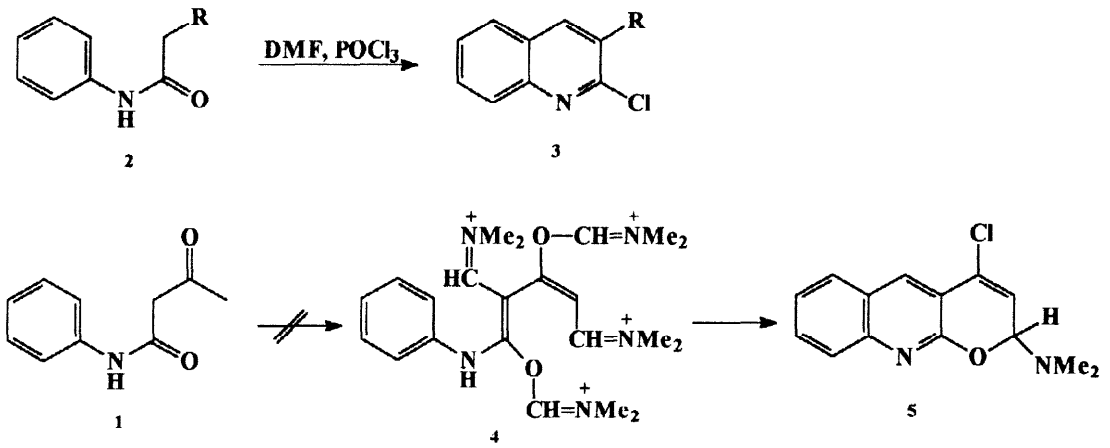
The halomethyleniminium salt derived from DMF and $POCl_3$ is a potential intermediate involved in the Vilsmeier-Haack-Arnold reaction. Halomethyleniminium salt has been extensively used for activated aromatic, hetero aromatic and fully conjugated systems[9,10]. The broad synthetic utility of this halomethyleniminium salt not restricted to formylation, but is also suitable for electrophilic substitutions followed by intramolecular cyclizations, producing various nitrogen and oxygen based heterocycles[11-15]. Recently our group have reported that the cyclization potential of this halomethyleniminium salt with various functional groups leads to heterocycles[16-20]. Previously *N*-phenylacetoacetamide has been cyclized under acidic condition leading to the formation of a quinoline derivative[21,22]. Although pyrancarboxaldehydes have been synthesized by treatment of 1,5-diketones with Vilsmeier reagent in our laboratory[23], the reaction of ß-ketoamides with the Vilsmeier reagent was not yet reported nor the synthesis of 2-imino-2*H*-pyran. This led us to undertake studies of Vilsmeier reagent with ß-ketoamides.

In this paper, we report a novel route to the synthesis of 2-imino-2*H*-pyrancarboxaldehydes from the reaction of *N*-phenylacetoacetamides with halomethyleniminium salt. The novelty of this synthetic route lies in the intramolecular cyclization of iminium salt by oxygen nucleophiles.

Results and Discussion

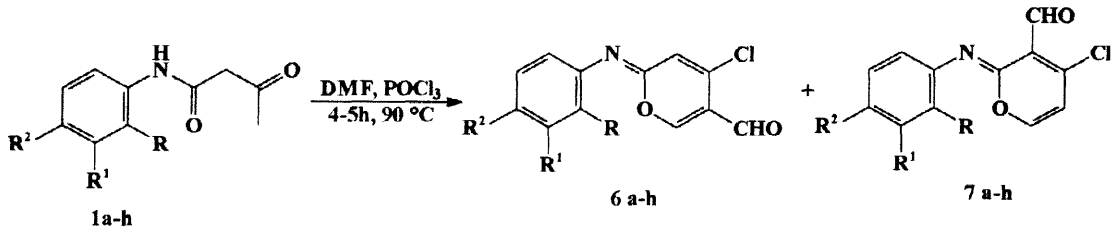
N-Arylacetoacetamides have been synthesized by treatment of aromatic amines with ethylacetoacetate[24]. Several examples of the synthesis of quinoline derivatives have been reported in the literature. The treatment of acylamide **2** with Vilsmeier reagent provided 2-chloro-3-substituted quinoline **3** in an efficient manner[25]. We have made an attempt to combine this strategy with Vilsmeier cyclization of *N*-phenylacetoacetamide to accomplish the synthesis of the pyran-fused quinoline **5** *via* the cascade cyclization of the intermediate **4** (Scheme 1), but the reaction did not proceed as anticipated.

Scheme 1



N-Phenylacetoacetamide **1a** (10 mmol) in DMF was added drop wise at 0°C to Vilsmeier reagent (8 equivalents) previously prepared from DMF and $POCl_3$ under stirred condition. The reaction mixture stirred at rt for 1 h and maintained at 90°C for 4-5 h on a water bath, cooled and neutralized with sodium acetate at 0°C. The crude solid was chromatographed to give regioisomeric 2-phenylimino-4-chloro-2*H*-pyran-5-carboxaldehyde **6a** and 2-phenylimino-4-chloro-2*H*-pyran-3-carboxaldehyde **7a** in 44% yield, in a ratio of 28:72. Similarly other substituted *N*-phenyl acetoacetamides also cyclized smoothly (Scheme 2 and Table 1).

Scheme 2



R=H,CH_3,OCH_3; R^1=H OR Cl; R^2=H,CH_3,OCH_3,Cl,Br

Table 1. Vilsmeier reaction products of *N*-phenylacetoacetamides with Vilsmeier reagent

S. No.	Substrate	Substituents			Product ratio[a,b]		Yield	m.p. (°C)	
	1	R	R^1	R^2	6 :	7	(%)	6	7
1	a	H	H	H	28	72	44	149-51	171-73
2	b	H	H	CH_3	50	50	50	172-74	154-55
3	c	H	H	OCH_3	60	40	40	158-59	127-28
4	d	H	H	Cl	48	52	55	193-95	201-03
5	e	H	H	Br	52	48	62	200	193-94
6	f	H	Cl	H	15	85	45	130-32	150-52
7	g	CH_3	H	H	60	40	40	104-06	171-73
8	h	OCH_3	H	H	40	60	40	86-88	120-22

a: All the products were duly characterised by ^1H NMR, ^{13}C NMR and IR spectroscopy, mass spectrometry and elemental analysis.

b: Product ratio is based on isolation by column chromatography.

The reaction of Vilsmeier reagent with activated methyl ketone leads to ß-chloro vinylaldehyde as an intermediate in a few cases [26,27]. We also pursued reaction conditions that would likely favour the formation of vinyl chloride and subsequent formylation. But GC-MS

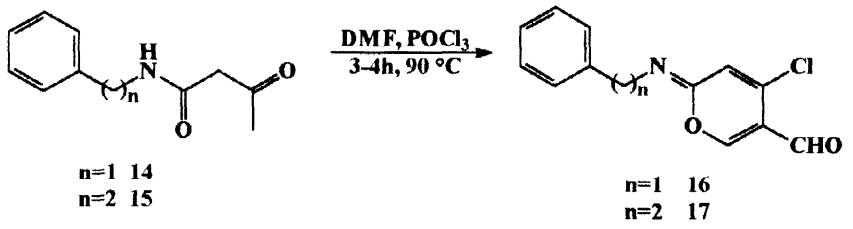
analysis showed clearly that neither of ß-chloro vinylaldehydes nor pyridine derivatives could be detected in the reaction mixtures, which were quenched with sodium acetate or ammonia or aromatic amines under a variety of the reaction conditions.

The present study is the first one for the direct synthesis and complete spectral chracterisation of 2-imino-2*H*-pyran carboxaldehydes from ß-keto amides using Vilsmeier reagent. A few reports are available regarding the synthesis and spectral characterisation of 2-arylimino-2*H*-pyran from cyclic pyrylium salt of 2*H*-pyrones[28-30]but not from cyclic intermediates.

Although an unambiguous mechanistic course for the reaction is premature, some speculations can be made at this stage on the intermediates involved in this reaction (Scheme 3). The terminal carbonyl group of *N*-phenyl acetoacetamide reacts with the chloromethyleniminium salt to yield chloro formyl derivative **8**. Before the intermediate **8** undergoes further reaction with another mole of reagent leading to diformyl derivatives, there will be two possible routes. In *route A* the carbonyl group undergoes O-formylation *via* the shift of H-atom from nitrogen giving intermediate **9**, which in turn undergoes further substitution at the terminal enamine to give intermediate **10**. The intermediate **10** undergoes intramolecular cyclization giving intermediate **11**. Hydrolysis of the cyclic intermediate **11** gives 2*H*-pyran-5-carboxaldehyde **6a** *via* loss of the dimethylamino group. In *route B*, the chloroformyl derivative **8** undergoes further substitution with halomethyleniminium salt giving intermediate **12** *via* the ketonic carbonyl group, which cyclizes spontaneously to give the intermediate **13**, followed by loss of the dimethylamino group resulting in the formation of **7a**.

In order to extend the scope of this reaction, we studied the synthesis of *N*-alkyl derivatives of 2*H*-pyrancarboxaldehydes. Accordingly, *N*-benylacetoacetamide **14** and *N*-(2-phenylethyl) acetoacetamide **15** were cyclized with Vilsmeier reagent at 90 °C to give the regioselective products 2-(*N*-benzyl)imino-4-chloro-2*H*-pyran-5-carboxaldehyde **16** and 2- (*N*-phenylethyl) imino-4-chloro-2*H*-pyran-5-carboxaldehyde **17** in 23 and 24 % yield respectively (Scheme 4). The formation of these regioisomeric products is probably due to the greater basicity of nitrogen which may favour the formation of intermediate **9** rather than that of intermediate **12**.

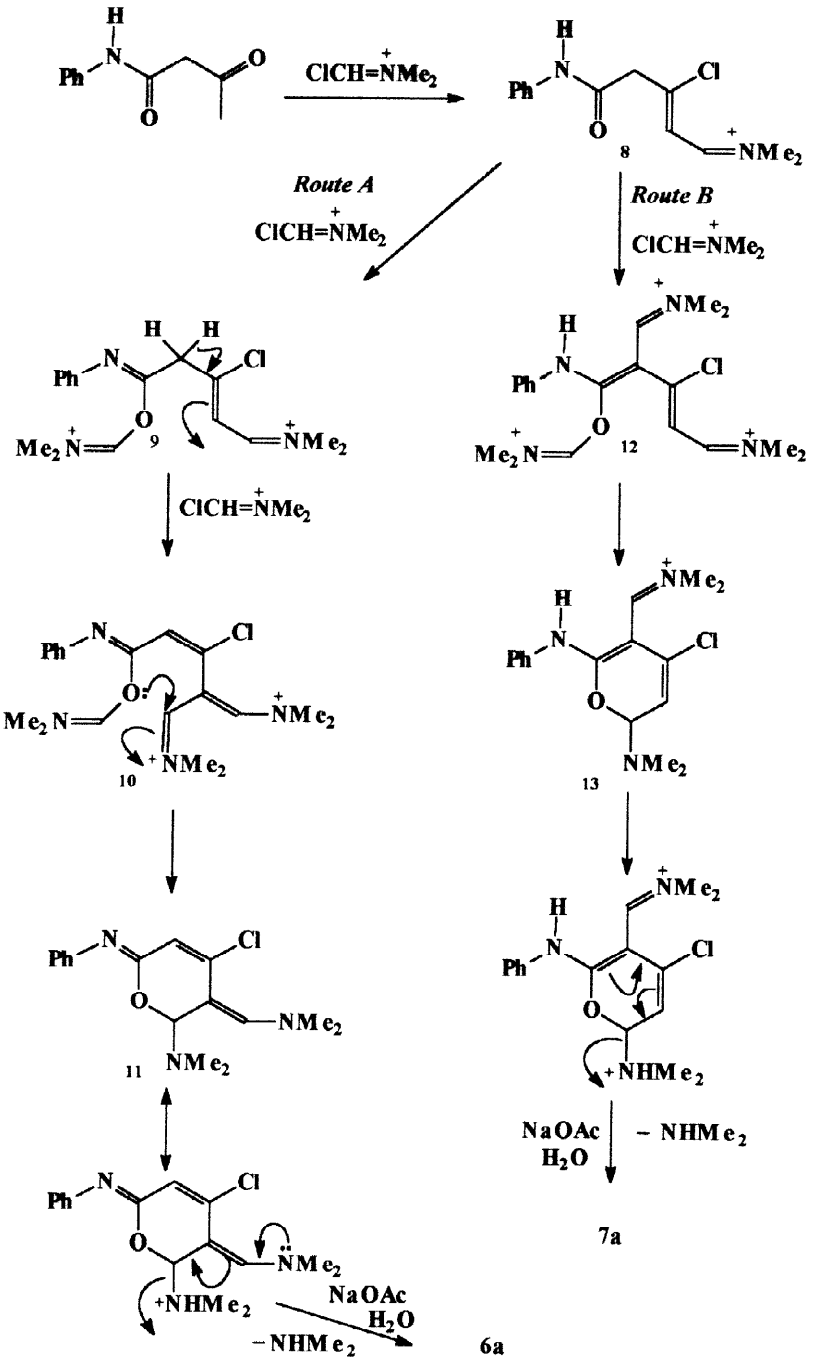
Scheme 4



n=1 14
n=2 15

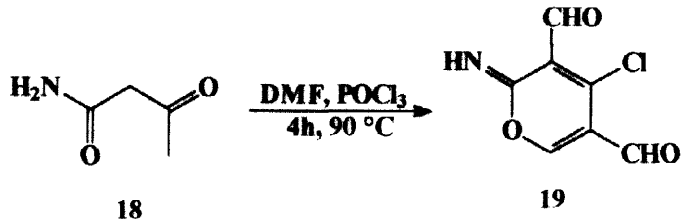
n=1 16
n=2 17

Scheme 3



The unsubstituted acetoacetamide **18** gave 2-imino-4-chloro-2*H*-pyran-3,5-dicarboxaldehyde **19** as the only product in 50 % yield (Scheme 5).

Scheme 5



18 **19**

In summary, we have shown that irrespective of the substitutions at the nitrogen atom, the *N*-aryl, *N*-alkyl or unsubstituted acetoacetamides are smoothly cyclized under Vilsmeier conditions to provide a novel and convenient route to the synthesis of 2-imino-2*H*-pyrancarboxaldehydes.

Experimental

Melting points were measured in capillary tubes and are uncorrected. Analytical thin layer chromatography was performed on precoated sheets of silica gel with 0.25 mm thickness containing PF 254 indicator (Merck, Darmstadt). Column chromatography was performed with silica gel (60-120 mesh, SD fine chemicals, Boisar).

Substituted acetoacetanilides were prepared following literature procedures[22]. Substituted aniline was slowly added to previously boiled ethylacetoacetate and refluxed further for 2-3 h. After cooling, the crude substituted acetoacetanilides were collected and recrystallised either in chloroform, acetic acid-water or ethanol. Similarly, *N*-(phenylmethyl) acetoacetamide and *N*-(2-phenylethyl)acetoacetamide were prepared.

General procedure for synthesis of 2-arylimino-2*H*-pyrancarboxaldehyde, alkylarylimino-2*H*-pyran carboxaldehyde and imino-2*H*- pyrancarboxaldehyde

Substituted *N*-phenylacetoacetamide (10 mmol) was dissolved in 5 mL of DMF and added dropwise to the Vilsmeier reagent prepared from DMF (7.8 mL) and $POCl_3$ (7.6 mL) in an ice bath over 20-30 min. The reaction mixture was stirred at room temperature for 1 h and maintained at 90 °C for 4 h. The resulting mixture was poured into ice water and neutralized with sodium acetate. The crude product was chromatographed to yield the products **6a-h** and **7a-h** .

2-Phenylimino-4-chloro-2H-pyran-5-carboxaldehyde (6a) and 2-Phenylimino-4-chloro-2H-pyran-3-carboxaldehyde (7a)

The title compounds were synthesized from *N*-phenylacetoacetamide (1.77 g, 10 mmol) according to the general procedure. The crude products were chromatographed (90:10 petroleum ether : ethyl acetate) to afford yellow solid of **6a** (0.28 g ,12 %). m.p. 149-151°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (s, 1H, C<u>H</u>O), 8.16 (s, 1H, OC<u>H</u>=C), 7.54-7.44 (m, 3H, Ph), 7.37-7.30 (m, 2H, Ph), 6.70 (s, 1H, C<u>H</u>=CCl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.66, 160.38, 146.38, 143.87, 138.90, 129.64, 129.60, 126.13, 119.84, 114.68; IR (KBr) 2925, 2850, 1696, 1661, 1518, 1408, 1340, 1282, 815, 745, 698 cm^{-1}.MS *m/z* 233(M^+), 235(M+2); Anal. Calcd for $C_{12}H_8ClNO_2$ C, 61.69; H, 3.45; N, 5.99; Found C, 61.99; H, 3.48; N, 6.03; and yellow solid of **7a** (0.75 g, 32 %). m.p. 171- 173°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.36 (s, 1H ,C<u>H</u>O), 7.53-7.43 (m, 4H, OC<u>H</u>=C and Ph), 7.35-7.33 (m, 2H, Ph), 6.37 (d, 1H, *J* = 7.2 Hz, OCH=C<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.40, 161.41, 150.49, 141.72, 139.10, 129.61, 129.38, 126.21, 122.06, 109.58; IR (KBr) 2859, 2766, 1702, 1645, 1515, 1457, 762, 695 cm^{-1}; MS *m/z* 233(M^+); Anal. Calcd for $C_{12}H_8ClNO_2$ C, 61.69; H, 3.45; N, 5.99 Found C, 61.87; H, 3.50; N, 6.03.

2-(4-Methylphenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6b) and 2-(4-Methylphenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7b)

The title compounds were synthesized from *N*-(4-methylphenyl)acetoacetamide (1.99 g, 10 mmol) according to the general procedure. The crude products were chromatographed (85:15 petroleum ether : ethyl acetate) to afford colourless needles of **6b** (0.62 g, 25 %). m.p. 172-174°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.04 (s, 1H, C<u>H</u>O), 8.14 (s, 1H, OC<u>H</u>=C), 7.32 (d, 2H, *J* = 8.4 Hz, Ar), 7.20 (d, 2H, *J* = 8.4 Hz, Ar), 6.68 (s, 1H, C<u>H</u>=CCl), 2.39(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.70, 160.41, 146.23, 144.00, 140.17, 136.57, 130.20, 125.84, 119.75, 114.60, 21.16;IR (KBr) 1694 cm^{-1}; MS *m/z* 247 (M^+); Anal. Calcd for $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.06; N, 5.65; Found C, 63.34; H, 4.08; N, 5.67 and light yellow solid of **7b** (0.62 g, 25 %). m.p. 55 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.36 (s, 1H, C<u>H</u>O), 7.45 (d, 1H, *J* = 7.5 Hz, OC<u>H</u>=C), 7.32 (d, 2H, *J* = 8.2 Hz, Ar), 7.18 (d, 2H, *J* = 8.2 Hz, Ar), 6.36 (d, 1H, *J* = 7.1 Hz, OCH=C<u>H</u>), 2.36 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.46, 161.34, 146.33, 138.71, 129.60, 126.41, 119.67, 118.49, 114.70, 109.32,21.10; IR (KBr) 2766, 1702 cm^{-1}; MS *m/z* 247(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.06; N, 5.65; Found C, 63.24; H, 4.16; N, 5.78.

2-(4-Methoxyphenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6c) and 2-(4-Methoxyphenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7c)

The title compounds were synthesized from *N*-(4-methoxyphenyl)acetoacetamide (2.07 g, 10 mmol) according to the general procedure. The crude products were chromatographed (90:10

petroleum ether : ethyl acetate) to afford light yellow solid of **6c** (0.64 g, 24 %). m.p. 158-159 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (s, 1H, C<u>H</u>O), 8.15 (s, 1H, OC<u>H</u>=C), 7.23 (d, 2H, *J* = 6.0 Hz, Ar), 6.96 (d, 2H, *J* = 6.0 Hz, Ar), 6.66 (s, 1H, C<u>H</u>=CCl), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.81, 160.20, 146.35, 144.13, 138.27, 131.60, 127.44, 120.06, 114.60, 107.80, 55.63; IR (KBr) 1700 cm^{-1} ; MS *m/z* 263(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_3$ C, 59.21; H, 3.82; N, 5.31; Found C, 59.24; H, 3.90; N, 5.38; and yellow solid of **7c** (0.42 g, 16 %). m.p. 127-128 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.35 (s, 1H, C<u>H</u>O), 7.48 (d, 1H, *J* = 7.5 Hz, OC<u>H</u>=C), 7.22 (d, 2H, *J* = 6.3 Hz, Ar), 6.95 (d, 2H, *J* = 6.9 Hz, Ar), 6.35 (d, 1H, *J* = 7.5 Hz, OCH=C<u>H</u>), 3.81 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.52, 161.65, 142.07, 138.21, 131.75, 127.21, 121.80, 119.62, 114.67, 109.41, 55.35; IR (KBr) 2859, 1703 cm^{-1} ; MS *m/z* 263(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_3$ C, 59.21;H, 3.82; N, 5.3; Found C, 59.12; H, 4.08; N, 5.07.

2-(4-Chlorophenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6d) and 2-(4-Chlorophenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7d)

The title compounds were synthesized from *N*-(4-chlorophenyl)acetoacetamide (2.11 g, 10 mmol) according to the general procedure. The crude products were chromatographed (80:20 petroleum ether : ethyl acetate) to afford as colourless solid of **6d** (0.69 g, 26 %). m.p.193-195 °C;^{1}H NMR (300 MHz, $CDCl_3$) δ 10.06 (s, 1H, C<u>H</u>O), 8.12 (s, 1H, OC<u>H</u>=C), 7.48 (d, 2H, *J* = 8.4 Hz, Ar), 7.26 (d, 2H, *J* = 9.3 Hz, Ar), 6.70 (s, 1H, C<u>H</u>=CCl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.65, 160.23, 146.63, 143.39, 137.23, 135.75, 129.84, 127.56, 119.91, 114.90; IR (KBr) 2860, 1704 cm^{-1}; MS *m/z* 267(M^+); Anal. Calcd for $C_{12}H_7Cl_2NO_2$ C, 53.76; H, 2.63; N, 5.22; Found C, 53.59; H, 2.61; N, 5.25; and yellow solid of **7d** (0.77 g, 29 %). m.p. 201-203 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ10.30 (s, 1H, C<u>H</u>O), 7.50-7.45 (m, 3H, OC<u>H</u>=C and Ar), 7.32-7.29 (m, 2H, Ar), 6.40 (d, 1H, *J* = 7.2 Hz, OCH=C<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.22, 161.23, 147.01, 143.73, 141.26, 135.27, 129.89, 127.60, 118.27, 109.92; IR (KBr)1701 cm^{-1};MS *m/z* 267(M^+); Anal. Calcd for $C_{12}H_7Cl_2NO_2$ C, 53.76; H, 2.63 N, 5.22; Found C, 54.07; H, 2.84; N, 5.21.

2-(4-Bromophenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6e) and 2-(4-Bromophenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7e)

The title compounds were synthesized from *N*-(4-bromophenyl)acetoacetamide (2.55 g, 10 mmol) according to the general procedure.The crude products were chromatographed (85:15 petroleum ether : ethyl acetate) to afford light yellow solid of **6e** (0.99 g, 32 %). m.p. 200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.06 (s, 1H, C<u>H</u>O), 8.13 (s, 1H, OC<u>H</u>=C), 7.64 (d, 2H, *J* = 8.7 Hz, Ar), 7.23 (d, 2H, *J* = 8.7 Hz, Ar), 6.71 (s, 1H, C<u>H</u>=CCl);^{13}C NMR (75 MHz, $CDCl_3$) δ 185.66, 160.42, 143.31, 137.72, 132.54, 128.51, 127.10, 123.78,120.84, 118.99; IR (KBr) 1694 cm^{-1}; MS *m/z* 311(M^+,); Anal. Calcd for $C_{12}H_7BrClNO_2$ C, 46.11; H, 2.26; N, 4.48; Found C, 46.33; H, 2.30;

N, 4.45; and light yellow solid of **7e** (0.94 g, 30 %). m.p. 193-194 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.30 (s, 1H, CHO), 7.65-7.56 (m, 3H, OCH=C and Ar), 7.46-7.42 (m, 1H, Ar), 7.24-7.19 (m, 1H, Ar), 6.39 (d, 1H, *J* = 7.2 Hz, OCH=CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.49, 160.40, 142.51, 132.17, 128.99, 127.21, 124.82, 122.82, 119.24, 109.23; IR (KBr) 2766, 1706; cm^{-1}; MS *m/z* 311(M^+); Anal. Calcd for $C_{12}H_7BrClNO_2$ C, 46.11; H, 2.26; N, 4.48; Found C, 46.50; H, 2.23; N, 4.53.

2-(3-Chlorophenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6f) and 2-(3-Chlorophenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7f)

The title compounds were synthesized from *N*-(3-chlorophenyl)acetoacetamide (2.11 g, 10 mmol) according to the general procedure. The crude products were chromatographed (90:10 petroleum ether : ethyl acetate) to afford yellow solid of **6f** (0.19 g, 7 %). m.p. 130-133°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.07 (s, 1H, CHO), 8.13 (s, 1H, OCH=C),7.47-7.45 (m, 2H, Ar), 7.37 (s, 1H, Ar), 7.26-7.22 (m, 1H, Ar), 6.72 (s, 1H, CH=CCl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.61, 160.37, 146.66, 143.29, 139.70, 135.33, 130.66, 129.97, 126.70, 124.50, 119.98, 114.89; IR (KBr)2850, 1694 cm^{-1}; MS *m/z* 267(M^+); Anal. Calcd for $C_{12}H_7Cl_2NO_2$ C, 53.76 H, 2.63; N, 5.22; Found C, 54.00; H, 2.66; N, 5.28; and colourless solid of **7f** (1.04 g, 39%). m.p. 150-152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.35 (s, 1H, CHO), 7.50-7.38 (m, 4H, OCH=C and Ar), 7.27-7.24 (m, 1H, Ar), 6.39 (d, 1H, *J* = 7.5 Hz, OCH=CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.45, 160.73, 150.22, 145.15, 140.45, 139.24, 134.59, 130.17, 129.05, 126.91, 123.66, 109.23; IR (KBr) 2771, 1690 cm^{-1}; MS *m/z* 267(M^+); Anal. Calcd for $C_{12}H_7Cl_2NO_2$ C, 53.76; H, 2.63; N, 5.22; Found C, 53.96; H, 2.60; N, 5.27.

2-(2-Methylphenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6g) and 2-(2-Methylphenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7g)

The title compounds were synthesized from *N*-(2-methylphenyl)acetoacetamide (1.91 g, 10 mmol) according to the general procedure. The crude products wereas chromatographed (85:15 petroleum ether : ethyl acetate) to afford light yellow solid of **6g** (0.59 g, 24 % yield). m.p. 171-173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (s, 1H, CHO), 8.05 (s, 1H, OCH=C), 7.41-7.29 (m, 3H, Ar), 7.13 (d, 1H, *J* = 7.5 Hz, Ar), 6.71 (s, 1H, CH=CCl), 2.12 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.68, 160.14, 146.49, 144.04, 138.16, 134.58, 131.36, 127.39, 126.68, 119.81, 114.58, 21.61; IR (KBr)1690 cm^{-1}; MS *m/z* 247(M^+) Anal. Calcd for $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.07; N, 5.66; Found C, 63.19; H, 4.11; N, 5.60; and yellow solid of **7g** (0.40 g, 16 %). m.p. 104-106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.30 (s, 1H, CHO), 7.43-7.29 (m, 4H, OCH=C and Ar), 7.15 (d, 1H, *J* = 7.5 Hz, Ar), 6.38 (d, 1H, *J* = 7.2 Hz, OCH=CH), 2.13 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.51, 161.26, 150.41, 148.62, 141.93, 134.70, 131.36, 129.87, 127.36, 126.74,

109.52, 21.55; IR (KBr) 2840, 1690 cm^{-1}; MS *m/z* 247(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.07; N, 5.66; Found C, 62.98; H, 4.10; N, 5.64.

2-(2-Methoxyphenyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (6h) and 2-(2-Methoxyphenyl)imino-4-chloro-2H-pyran-3-carboxaldehyde (7h)

The title compounds were synthesized from *N*-(2-methoxyphenyl)acetoacetamide (2.07 g , 10 mmol) according to the general procedure. The crude products were chromatographed (80:20 petroleum ether : ethyl acetate) to afford light red solid of **6h** (0.63 g, 24 %). m.p. 86-88 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 9.93 (s, 1H, CHO), 7.97 (s, 1H, OCH=C), 7.37 (t, 1H, *J* = 6 Hz), 7.14 (d, 1H, *J* = 6.6 Hz, Ar), 6.79 (d, 2H, *J* = 7.2 Hz, Ar), 6.62 (s, 1H, CH=CCl), 3.70 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.74, 162.89, 153.68, 145.49, 131.26, 127.32, 127.31, 120.84, 119.54, 114.43, 112.26, 55.61; IR (KBr)1691 cm^{-1}; MS *m/z* 263(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_3$ C, 59.22; H, 3.82; N, 5.31; Found C, 58.96; H, 3.86; N, 5.33; and colourless solid of **7h** (0.42 g, 16 %). m.p. 120-22 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 10.30 (s, 1H, CHO), 7.45-7.30 (m, 4H, OCH=C and Ar), 7.15 (d, 1H, *J* = 7.5 Hz, Ar), 6.40 (d,1H, *J* = 7.4 Hz, OCH=CH), 3.70 (s,3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.49, 150.42, 147.96, 140.92, 133.72, 131.30, 129.87, 127.30, 126.16, 119.26, 109.60, 55.65; IR (KBr) 2769, 1695; cm^{-1}; MS *m/z* 263(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_3$: C, 59.22; H, 3.82; N, 5.31; Found C, 59.43; H, 3.86; N, 5.28.

2-(Phenylmethyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (16)

The title compound was synthesized from *N*-(phenylmethyl)acetoacetamide (1.91 g, 10 mmol) according to the general procedure. The crude product was chromatographed (85:15 petroleum ether : ethyl acetate) to afford colourless solid of **16** (0.57 g, 23 %). m.p. 90-92 °C;^1H NMR (300 MHz, $CDCl_3$) δ 9.97 (s, 1H, CHO), 8.11 (s, 1H, OCH=C), 7.35-7.23 (m, 5H, Ph), 6.63 (s, 1H, CH=CCl), 5.12 (s,2H, CH_2Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.67, 162.21, 146.15, 143.10, 134.49, 129.21, 128.62, 128.45, 119.28, 114.75, 52.76; IR (KBr) 2860, 1680 cm^{-1}; MS *m/z* 247(M^+); Anal. Calcd for $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.07; N, 5.66; Found C, 62.75; H, 4.12; N, 5.67.

2-(2-Phenylethyl)imino-4-chloro-2H-pyran-5-carboxaldehyde (17)

The title compound was synthesized from *N*-(2-phenylethyl) acetoacetamide (2.05 g, 10 mmol) according to the general procedure. The crude product was chromatographed (85:15 petroleum ether : ethyl acetate) to afford yellow solid of **17** (0.63 g, 24 %). m.p. 92-93 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 9.98 (s, 1H, CHO), 7.69 (s, 1H, OCH=C), 7.30-7.08 (m, 5H, Ph), 6.60(s, 1H, CH=CCl), 4.16 (t, 2H, *J* = 7.2 Hz, CH_2N), 3.02 (t, 2H, *J* = 7.2 Hz, CH_2Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.84, 160.00, 145.53, 142.95, 135.92, 128.26, 128.12, 126.57, 118.34, 113.39, 51.70, 34.14; IR (KBr) 2858, 1675 cm^{-1}; MS *m/z* 261(M^+); Anal. Calcd for $C_{14}H_{12}ClNO_2$ C, 64.25; H, 4.62;

N, 5.35; Found C, 64.01; H, 4.70; N,5.39.

4-Chloro-2-imino-2H-pyran-3,5-carboxaldehyde (19)

The title compound was synthesized from acetoacetamide (1.01 g, 10 mmol) according to the general procedure. The crude product was chromatographed (90:10 petroleum ether : ethyl acetate) to afford colourless solid of **19** (0.75 g, 50 %). m.p. 88-90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.49 (s, 1H, C<u>H</u>O), 10.43 (s, 1H, C<u>H</u>O), 8.89 (s, 1H, OC<u>H</u>=C); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.80, 186.59, 157.26, 152.70, 148.51, 127.80, 127.26; IR (KBr) 3231, 2881, 1711, 1683 cm^{-1}; MS *m/z*150(M^+); Anal. Calcd for $C_7H_4ClNO_3$ C, 45.31; H, 2.17; N, 7.55; Found C, 45.50; H, 2.12; N, 7.51.

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