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4,6-Diacetylresorcinol in Heterocyclic Synthesis Part I: Vilsmeier-Haack Reactions of 4,6-Diacetylresorcinol and Its Schiff Bases and Hydrazones to Construct of New Linearly and Angularly Substituted Pyrano[3,2-*g*]chromenes

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Abstract

Application of Vilsmeier–Haack reaction on 4,6-diacetylresorcinol (**1**) leads to the formation of 4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarboxaldehyde (**2**) in good yield. The dicarboxaldehyde **2** was condensed with some carbon and nitrogen nucleophiles. Some aliphatic and aromatic Schiff bases of 4,6-diacetylresorcinol (**1**) were subjected to Vilsmeier–Haack reagent to afford 4,6-bis(alkyl/arylimino)-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehydes **10**, **14** and **15**. Wherever, treatment of some *bis*-hydrazones of 4,6-diacetylresorcinol **16-19** with Vilsmeier–Haack reagent afforded the corresponding 4,6-*bis*(pyrazole-3-yl-4-carboxaldehyde)resorcinols **20** and **21** which underwent oxidation with iodine to yield fused angularly polyheterocyclic systems **22** and **23**, respectively.

Keyword: 4,6-diacetylresorcinol, Vilsmeier-Haack reagent, pyrano[3,2-*g*]chromenes.

Introduction

The Vilsmeier–Haack reaction is a widely used method for the formylation of activated aromatic and heteroaromatic compounds [1,2]. The reactions of aliphatic substrates [3], particularly carbonyl compounds [4] with chloromethyleneiminium salts are highly versatile. They lead to multiple iminoalkylations in the presence of excess reagent and the resulting intermediates undergo cyclization to afford aromatic or heterocyclic compounds [5,6]. Multifunctional intermediates derived from these reactions (e.g., β-chloroenaldehydes) are subsequently exploited for the synthesis of functionalized heterocycles or other valuable target molecules [7,8]. Dibenzyl ketone on treatment with chloromethyleneiminium salt undergo multiple iminoalkylations followed by cyclization to afford 3,5-diphenyl-4H-pyran-4-one [9,10]. The reactions

of 2-hydroxyacetophenones with Vilsmeier-reagent also involve an iminoalkylation cyclization sequence, leading to the formation of 3-formylchromones [11-14].

The chromone and coumarin are found in the molecular structure of many important natural secondary metabolites [15,16] and compounds with high pharmacological activity [17,18]. The incorporation of a fused heterocyclic moiety in parent chromone and coumarin alters their properties and converts them into important derivatives [19,20]. Large numbers of heterocyclic fused with chromone and coumarin are used as drugs and dyes [21,22].

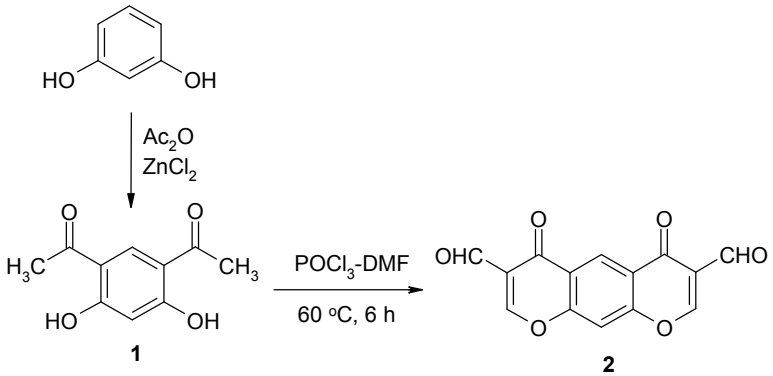
In our recent work we have demonstrated the utility of the Vilsmeier reagent in the synthesis of functionalized heterocyclic systems such as pyrazole, chromeno[4,3-c]pyrazole and chromeno[2,3-g]indazole [23]. Thus, as a continuation of our research interest in the synthesis of highly valuable heterocycles, we have prepared 4,6-diacetylresorcinol and its Schiff bases and hydrazones and examined their reactivity towards Vilsmeier Haack reagent. As a result, we report herein a facile and efficient synthesis of a fused heterocyclic moiety as 4-pyrone and 2-pyrone in parent chromone and coumarin which could be named as substituted linearly and angularly pyrano[3,2-*g*]chromenes by Vilsmeier-Haack reactions of the readily available 4,6-diacetylresorcinol and its Schiff bases and hydrazones.

Results and Discussion

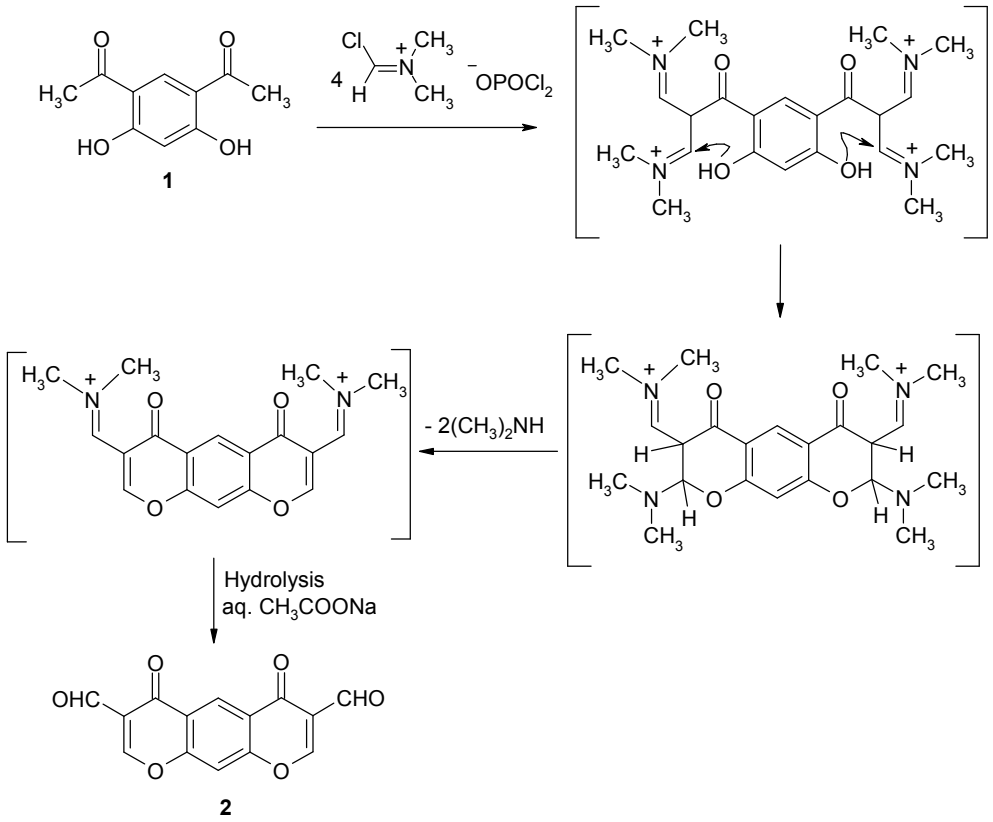
The Substrate **1** was prepared in excellent yield *via* acetylation of resorcinol with acetic anhydride in the presence of freshly fused zinc chloride according to the previously reported procedure (Scheme 1) [24].

Application of Vilsmeier-Haack reaction on 4,6-diacetylresorcinol (**1**) afforded 4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarboxaldehyde (**2**) in good yield (Scheme 1). It may be mentioned here that **2** was obtained by Mallaiah *et al* [25] in low yield. However, no full spectral characterization of the product was made. The proposed mechanism for the formation of **2** involved double formylation at each methyl group of **1**, followed by self cyclization then hydrolysis in basic medium [26] (Scheme 2). The IR spectrum of compound **2** showed three strong absorption bands at 1707, 1655 and 1625 cm^{-1} assignable to CHO, $C=O_{pyrone}$ and C=C functional groups, respectively. The ^{1}H-NMR spectrum of **2** exhibited singlet signal at δ 10.10 ppm for the formyl protons and the protons of the pyrone rings in position 2 resonated at δ 8.76 ppm. In addition, two singlets were present at δ 7.94 and 9.02 ppm

corresponding to the aromatic protons H−10 and H−5, respectively [27]. Furthermore, its mass spectrum of **2** revealed the molecular ion peak at *m/e* 270 (M^+).



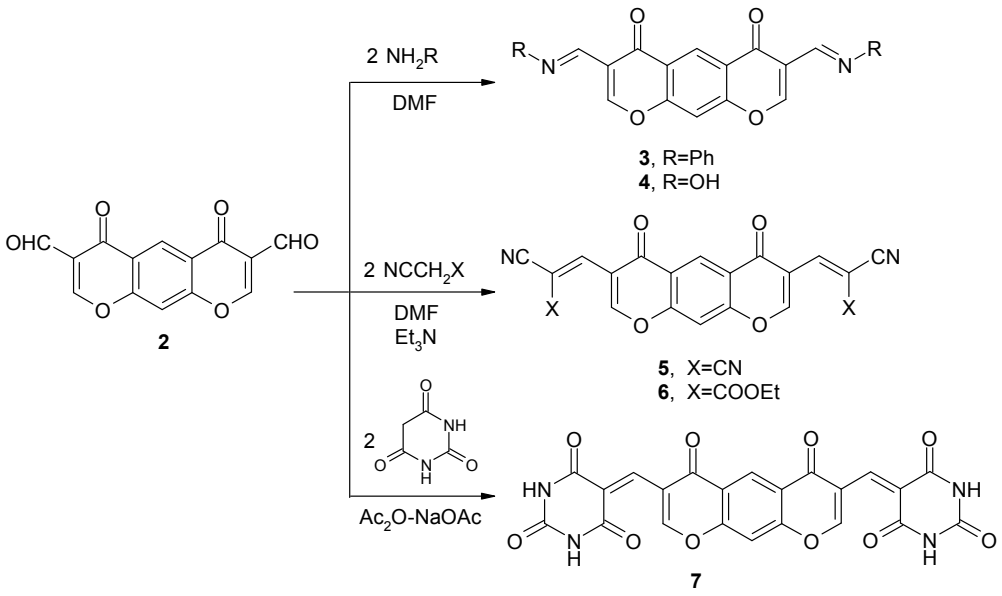
Scheme 1



Scheme 2

The chemical reactivity of 4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarboxaldehyde (**2**) was studied *via* its simple reactions with some carbon and

nitrogen nucleophiles. Thus, compound **2** was condensed with aniline and hydroxylamine hydrochloride in dry DMF to give quantitative yields of the corresponding *bis*-azomethine **3** and *bis*-oxime **4**, respectively (Scheme 3). The infrared spectra of **3** and **4** showed clearly disappearance of the aldehyde absorption band instead of new bands at δ 1594 and 1629 cm^{-1} for imino groups for them, respectively. ^{1}H-NMR spectrum of **4** showed the hydroxyl signal at δ 12.74 ppm in addition to the aromatic protons H−5 and H−10 at δ 8.89 and 7.48 ppm, respectively.



Scheme 3

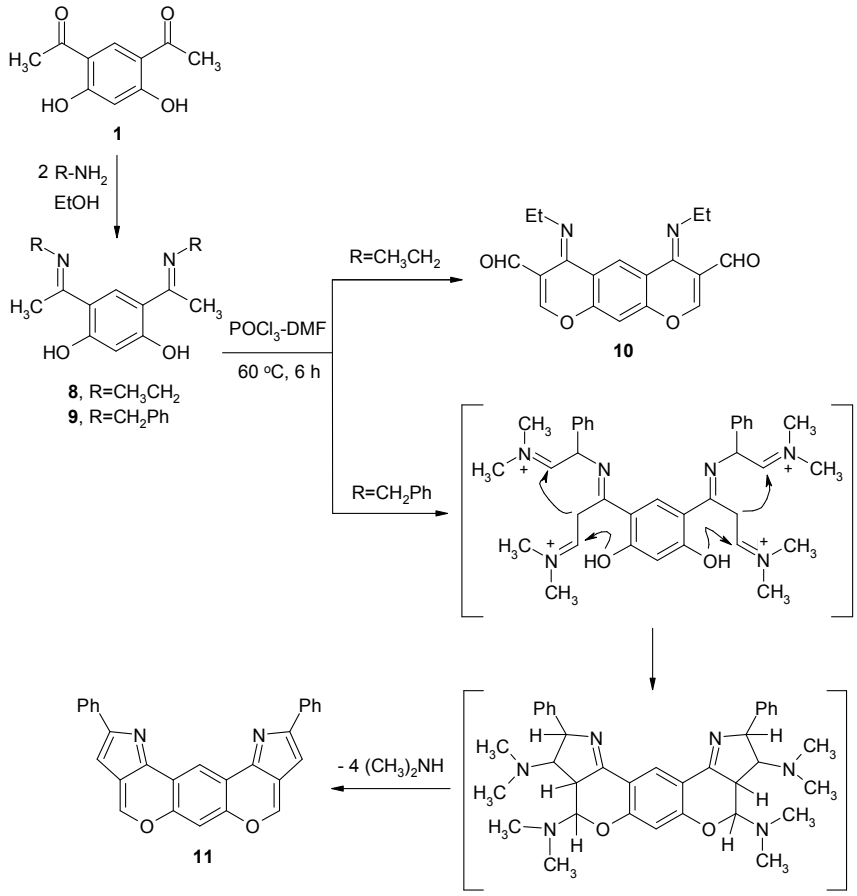
The Knoevenagel reaction of **2** with acyclic and cyclic active methylene groups has been reported as a synthetic route for the preparation of a wide variety of derivatives. Thus, the reaction of **2** with malononitrile and ethyl cyanoacetate in dry DMF containing few drops of triethylamine afforded 2,2'-[(4,6-dioxo-4*H*,6*H*-pyrano [3,2-*g*]chromene-3,7-diyl)dimethylylidene]dipropanedinitrile (**5**) and diethyl 3,3'-(4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-diyl)*bis*(2-cyanoprop-2-enoate) (**6**), respectively (Scheme 3). Similarly, condensation of **2** with barbaturic acid as cyclic active methylene in glacial acetic acid and fused sodium acetate yielded 5,5'-[(4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-diyl)dimethylylidene]dipyrimidine-2,4,6 (1*H*,3*H*, 5*H*)-trione (**7**) (Scheme 3). The assigned structures of **5**-**7** were confirmed by spectral data in addition to the correct elemental analysis. Their infrared spectra revealed a characteristic absorption band at region 2220-2192 cm^{-1} for nitrile groups in compounds **5** and **6**, in addition to the carbonyl groups of **6** and **7** appeared in

region 1635-1644 cm^{-1}. ^{1}H-NMR spectrum of **6** showed the ethoxy protons at δ 1.22 (CH_3) and 4.19 ppm (CH_2), while compound **7** revealed the NH protons as a broad signal at δ 11.50 ppm.

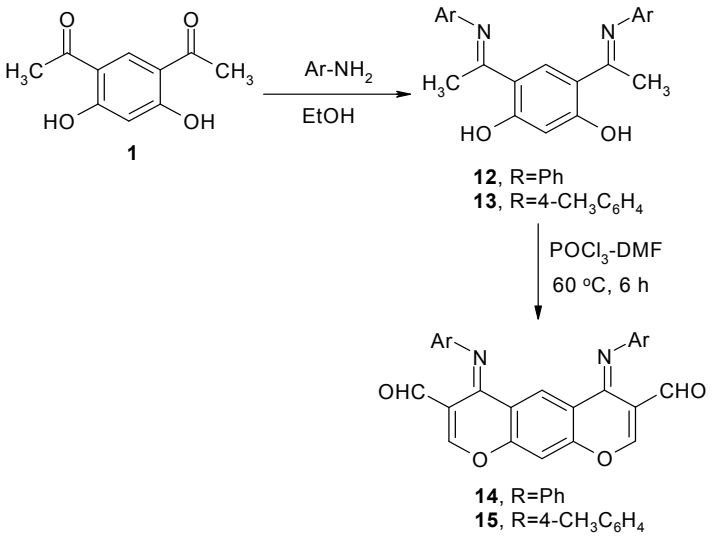
We selected some aliphatic and aromatic Schiff bases of 4,6-diacetylresorcinol as model compounds to examine their reaction behaviour under Vilsmeier-Haack conditions. Thus, treatment of 4,6-bis[1-(ethylimino)ethyl]resorcinol (**8**) and 4,6-bis[1-(benzylimino)ethyl]resorcinol (**9**) with Vilsmeier-Haack reagent afforded 4,6-bis(ethylimino)-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehyde (**10**) and 2,10-diphenylpyrano[3,2-*g*]chromeno[4,3-*b*:7,6-*b*]dipyrrole (**11**), respectively (Scheme 4). The proposed mechanism for the formation of **10** involved double formylation at each methyl group of acetyl groups **8**, followed by self cyclization then hydrolysis in basic medium as occurred in formation of **2** (Scheme 4). Also, the proposed mechanism for the formation of **11** involved monoformylation at each methyl and methylene groups **9**, followed by self cyclization then hydrolysis in basic medium (Scheme 4). The analytical and spectroscopic data proved the proposed structures of **10** and **11**. Their IR spectra revealed formyl group at 1704 cm^{-1} in compound **10** while it was absent in compound **11**. The ^{1}H-NMR spectrum of **10** showed the aldehydic protons at δ 10.08 ppm and ethyl group at δ 1.20 (CH_3) and 4.25 (CH_2). Furthermore, the ^{1}H-NMR spectrum of **11** did not show any aldehydic proton but showed the H−3 proton of pyrrole rings at δ 7.90 ppm which support the cyclization process. The mass spectra of compounds **10** and **11** showed prominent ion peaks M^+ at *m/z* 266 and 412, respectively.

On the other hand, the novel 4,6-bis(phenylimino)-4*H*,6*H*-pyrano[3,2-*g*] chromene-3,7-dicarbaldehyde (**14**) and 4,6-bis(4-methylphenylimino)-4*H*,6*H*-pyrano [3,2-*g*]chromene-3,7-dicarbaldehyde (**15**) were obtained from treatment of 4,6-bis[1-(phenylimino)ethyl]resorcinol (**12**) and 4,6-bis[1-(4-methylphenylimino)ethyl] resorcinol (**13**), respectively, with Vilsmeier-Haack reagent (Scheme 5). The proposed mechanism for the formation of **14** and **15** involved double formylation at each methyl group of acetyl groups **8**, followed by self cyclization then hydrolysis in basic medium as occurred in formation of **2**. The IR spectra of **14** and **15** showed the strong absorption bands at region 1690 and 1698 cm^{-1} assignable to CHO groups, respectively. Their ^{1}H-NMR spectra of **14** and **15** exhibited singlets at δ 10.20 and 10.11 ppm for the formyl protons and the protons of the pyrone rings in position 2

resonated at δ 8.51 and 9.07 ppm, respectively. Moreover, their mass spectral data revealed their molecular ion peaks at *m/e* 420 and 448, respectively.



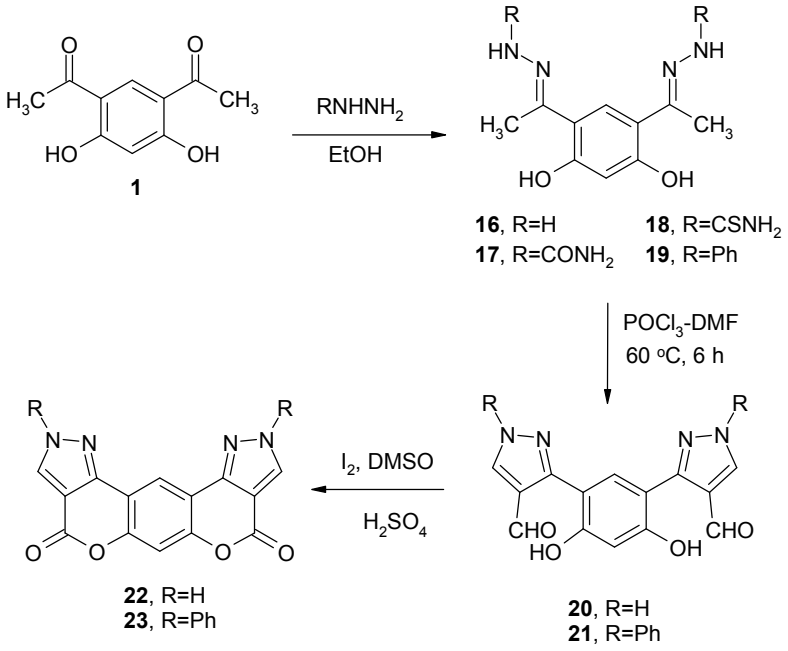
Scheme 4



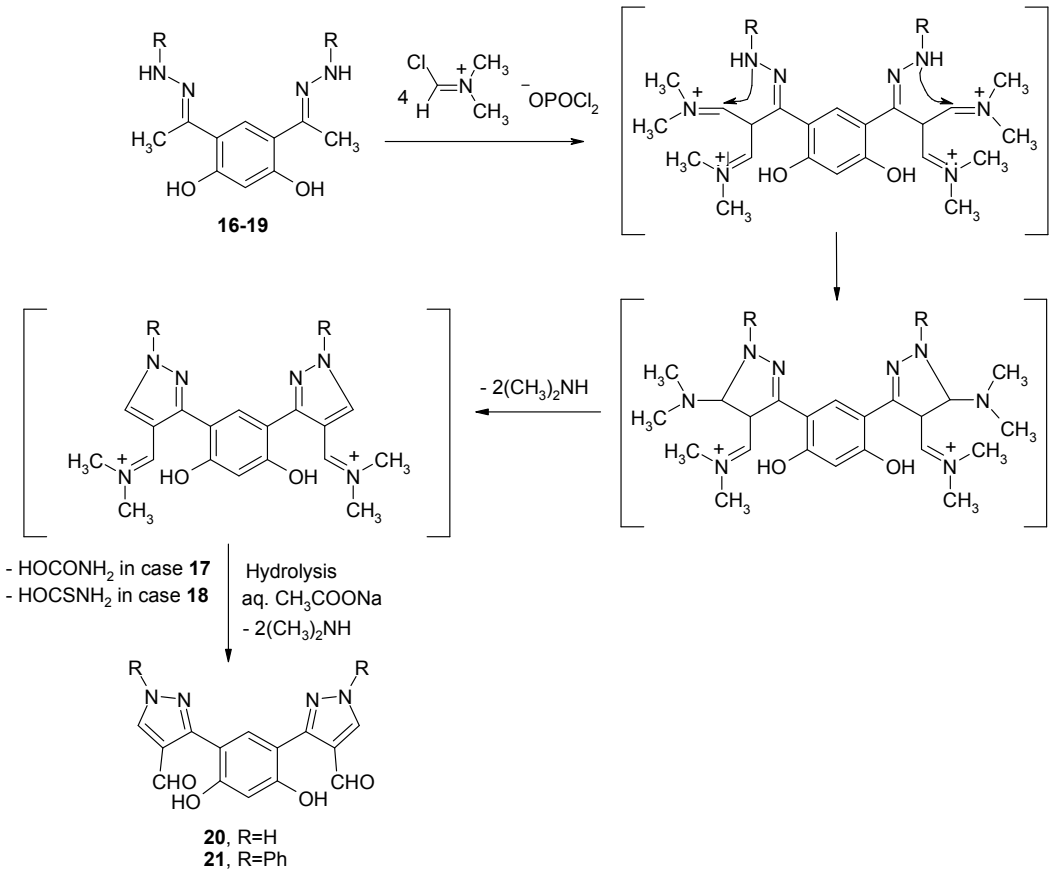
Scheme 5

The present work was also extended to apply the Vilsmeier-Haack reaction on some hydrazones of 4,6-diacetylresorcinol that led to new 4,6-bis(4-formylpyrazol-3-yl)resorcinol systems. Thus, the *bis*-hydrazone **16**, *bis*-semicarbazone **17** and *bis*-thiosemicarbazone **18** were treated with Vilsmeier reagent under the previous conditions afforded only one a light brown crystalline product namely, 4,6-*bis*(1*H*-4-formylpyrazole-3-yl)resorcinol (**20**) (Scheme 6) [28]. Formation of compound **20** involved double formylation at the methyl groups of **16**, **17** and **18** followed by nucleophilic attack of NH groups at $-CH=N^{+}(CH_3)_2$ moieties to eliminate two molecules of dimethylamine. The basic hydrolysis removes the amide and thioamide moiety to give the final product (Scheme 7). The spectral data of **20** recommended the proposed structure as its ^{1}H-NMR spectrum displayed a broad singlet (D_2O exchangeable) at δ 12.50 ppm due to NH and OH protons and singlet signal at δ 9.80 ppm indicated to the aldehydic protons. The H–5 protons of the formed pyrazole rings were also observed in ^{1}H-NMR spectrum at δ 8.41 ppm. Also, its IR spectrum showed very broad band at 3119 cm^{-1} due to NH and OH groups and aldehyde groups at 1692 cm^{-1}. Similarly, when the *bis*-phenylhydrazone **19** was subjected to Vilsmeier-Haack reagent gave 4,6-bis(4-formyl-1-phenyl-pyrazol-3-yl)resorcinol (**21**) (Scheme 6). The structure of **21** was proved by the analytical and spectroscopic data. For example, its ^{1}H-NMR spectrum displayed the aldehydic proton at δ 9.85 ppm while H-5 of pyrazole rings at δ 9.21 ppm, respectively. The mass spectrum of **21** recorded the molecular ion peak of **21** at *m/z* 450 (66%)

The oxidation reaction of compounds **20** and **21** with iodine in dimethylsulfoxide [29] afforded the new fused angularly polyheterocyclic systems namely, pyrano[3,2-*g*]chromeno[4,3-*c*:7,6-*c*]dipyrazol-2,8-(4H)dione (**22**) and 2,10-diphenyl-pyrano[3,2-*g*]chromeno[4,3-*c*:7,6-*c*]dipyrazol-2,8-(4H)dione (**23**), respectively (Scheme 7). The absorption band of carbonyl groups appeared at xxxx and xxxx cm^{-1} in the IR spectra of **22** and **23**, respectively. Also, their structures were confirmed from ^{1}H-NMR spectrum by disappearance of protons OH and CHO in compounds **20** and **21** (See experimental section). Finally, the molecular ion peaks of **22** and **23** were recorded with accordance with their molecular formulas.



Scheme 6



Scheme 7

Conclusion

An efficient one-pot synthesis of 4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-dicarboxaldehyde (**2**) from 4,6-diacetylresorcinol in the presence of $POCl_3$ in DMF was achieved. This general protocol provides a novel and facile access to other substituted linearly and angularly pyrano[3,2-*g*]chromenes by sequential Vilsmeier-Haack reaction, intramolecular cyclization and aromatization reactions of Schiff bases and hydrazones of 4,6-diacetylresorcinol.

Experimental

The melting point was determined in an open capillary tube on a digital Stuart SMP-3 apparatus. Infrared spectra were measured on FTIR Nicolet IS10 spectrophotometer (cm^{-1}), using KBr disks. The ^1H NMR spectra were measured on Mercury-300BB (300 MHz), using DMSO-d_6 as a solvent and the chemical shifts δ downfield from TMS as an internal standard. The ^{13}C-NMR spectra could not be recorded for all these compounds due to their poor solubility in higher concentrations in common solvents. Mass spectra recorded on a Gas Chromatographic DI analysis Shimadzu instrument Q-2010 Plus at 70 eV. Elemental microanalyses were performed at microanalysis center in ministry of defense, Cairo, Egypt. The purity of the synthesized compounds was checked by thin layer chromatography (TLC). All the *bis*-Schiff bases, *bis*-hydrazones and *bis*-(thio)semicarbazones: **8** [30], **9** [31], **12** [32], **13** [32], **16** [33], **17** [34], **18** [34] and **19** [33] were prepared according to the reported procedures in the literature.

Synthesis of compounds 2, 10, 11, 14, 15, 20 and 21: General procedure for Vilsmeier-Haack reaction of 4,6-diacetylresorcinol 1, *bis*-Schiff bases 8, 9, 12, 13 and *bis*-hydrazones 16-19.

The Vilsmeier reagent was prepared by adding $POCl_3$ (60 mmol, 6 mL) dropwise to ice-cold dry DMF (30 mL) whilst stirring. The mixture was then stirred for 10–15 min at 0 °C. Each one of the compounds **1**, **8**, **9**, **12**, **13** and **16-19** (10 mmol) was added as a solution in DMF (10 mL) to the above Vilsmeier reagent. Then the mixture was heated to 60-70 °C and stirred for 6 h. The reaction mixture was cooled and poured into crushed ice and 3 g of sodium acetate was added under constant manual stirring. The reaction mixture was kept aside overnight. The resulting precipitate was filtered off and crystallization from DMF to give the corresponding products **2**, **10**, **11**, **14**, **15**, **20** and **21**, respectively.

***4,6-Dioxo-4H,6H-pyrano[3,2-g]chromene-3,7-dicarboxaldehyde (2)*:** Brown solid; yield 81%; m.p. > 300 ^{o}C. IR (KBr, cm^{-1}): 3064 (C−H$_{arom}$), 1707 (CHO), 1655 (C=O$_{pyrone}$), 1625 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 7.94 (s, 1H, H−10), 8.76 (s, 2H, H−2), 9.02 (s, 1H, H−5), 10.10 (s, 2H, CHO). MS (*m/z*, I %): 270 (M^{+}, 1.3%), 269 (1), 242 (100), 214 (56), 188 (15), 160 (16), 116 (9), 102 (13), 53 (53). Anal. Calcd for $C_{14}H_6O_6$ (270.20): C, 62.23; H, 2.24. Found: C, 61.88; H, 2.23.

***4,6-Bis(ethylimino)-4H,6H-pyrano[3,2-g]chromene-3,7-dicarbaldehyde (10)*:** Brown solid; yield 61%; m.p. > 300 ^{o}C. IR (KBr, cm^{-1}): 3064 (C−H$_{arom}$), 2930 (C−H$_{aliph}$), 1704 (CHO), 1655 (C=N), 1624 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 1.20 (t, 6H, CH$_3$), 4.25 (br, 4H, CH$_2$), 8.27 (s, 1H, H−10), 8.80 (s, 2H, H−2), 9.01 (s, 1H, H−5), 10.08 (s, 2H, CHO). MS (*m/z*, I %): 266 (M−2Et, 42%), 257 (46), 228 (62), 203 (50), 170 (62), 138 (58), 122 (67), 91 (47), 80 (90), 64 (100), 50 (89). Anal. Calcd for $C_{18}H_{16}N_2O_4$ (324.34): C, 66.66; H, 4.97; N, 8.64. Found: C, 66.86; H, 4.75; N, 8.33.

***2,10-Diphenylpyrano[3,2-g]chromeno[4,3-b:7,6-b]dipyrrole (11)*:** Brown solid; yield 90%; m.p. > 300 ^{o}C. IR (KBr, cm^{-1}): 3045 (C−H$_{arom}$), 1625 (C=N), 1590 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 7.20−7.60 (m, 11H, Ph−H and H−10), 7.90 (s, 1H, H−3$_{pyrrole}$), 8.24 (s, 2H, H−2), 8.34 (s, 1H, H−5). MS (*m/z*, I %): 412 (M^{+}, 4%), 399 (25), 347 (35), 301 (38), 281 (71), 213 (30), 172 (24), 133 (37), 105 (44), 93 (84), 87 (29), 69 (100), 50 (19). Anal. Calcd for $C_{28}H_{16}N_2O_2$ (412.45): C, 81.54; H, 3.91; N, 6.79. Found: C, 80.24; H, 3.60; N, 7.02.

***4,6-Bis(phenylimino)-4H,6H-pyrano[3,2-g]chromene-3,7-dicarbaldehyde (14)*:** Light brown solid; yield 86%; m.p. > 300 ^{o}C. IR (KBr, cm^{-1}): 3060 (C−H$_{arom}$), 1690 (CHO), 1653 (C=N), 1616 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 7.40−7.90 (m, 10H, Ph−H), 7.95 (s, 1H, H−10), 8.14 (s, 2H, H−5), 8.51 (s, 1H, H−2), 10.20 (s, 2H, CHO). MS (*m/z*, I %): 420 (M^{+}, 5%), 419 (12), 413 (18), 365 (77), 331 (25), 315 (94), 287 (53), 227 (47), 171 (42), 133 (36), 121 (99), 98 (100), 86 (61), 65 (28). Anal. Calcd for $C_{26}H_{16}N_2O_4$ (420.43): C, 74.28; H, 3.84; N, 6.66. Found: C, 73.97; H, 3.59; N, 6.92.

***4,6-Bis(4-methylphenylimino)-4H,6H-pyrano[3,2-g]chromene-3,7-dicarbaldehyde (15)*:** Buff solid; yield 83%; m.p. > 300 ^{o}C. IR (KBr, cm^{-1}): 3072 (C−H$_{arom}$), 2900 (C−H$_{aliph}$), 1698 (CHO), 1654 (C=N), 1616 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 2.50 (s, 6H, CH$_3$), 7.64, 7.67 (d, 4H, *J* =8.7, Ar−H), 7.94 (s, 1H, H−10), 8.04, 8.07 (d, 4H, *J* =8.7, Ar−H), 8.86 (s, 2H, H−5), 9.07 (s, 1H, H-2), 10.11 (s, 2H, CHO). MS (*m/z*, I %): 448 (M^{+}, 0.2%), 447 (0.17), 408 (1), 395 (1), 339 (0.4), 299 (1), 271 (2), 236 (5),

208 (3), 180 (2), 129 (24), 97 (32), 73 (100), 57 (66). Anal. Calcd for $C_{28}H_{20}N_2O_4$ (448.48): C, 74.99; H, 4.50; N, 6.25. Found: C, 74.65; H, 4.24; N, 6.43.

***4,6-Bis(1H-4-formylpyrazole-3-yl)resorcinol (20)*:** Light brown solid; yield 73%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3119 (br, OH, NH), 1692 (CHO), 1632 (C=N). ^1H-NMR (δ ppm, DMSO-d_6): 6.42 (s, 1H, H−$2_{resorcinol}$), 7.95 (s, 1H, H−$2_{resorcinol}$), 8.41 (s, 2H, H−$2_{pyrazole}$), 9.80 (brs, 2H, CHO), 12.50 (br, 4H, OH and NH exchangeable with D_2O). MS (*m/z*, I %): 298 (M^+, 60%), 280 (55), 247 (95), 219 (80), 208 (77), 195 (100), 165 (72), 147 (83), 90 (78), 75 (77), 51 (58). Anal. Calcd for $C_{14}H_{10}N_4O_4$ (298.26): C, 56.38; H, 3.38; N, 18.78. Found: C, 56.12; H, 3.69; N, 18.81.

***4,6-Bis(4-formyl-1-phenyl-pyrazol-3-yl)resorcinol (21)*:**Yellow solid; yield 78%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3114 (br, OH), 1678 (CHO), 1620 (C=N), 1597 (C=C). ^1H-NMR (δ ppm, DMSO-d_6): 6.70 (s, 1H, H−$2_{resorcinol}$), 7.36−7.71 (m, 10H, Ph−H), 7.96 (s, 1H, H−$5_{resorcinol}$), 9.21 (s, 2H, H−$5_{pyrazole}$), 9.85 (brs, 2H, CHO), 12.40 (br, 2H, OH exchangeable with D_2O). MS (*m/z*, I %): 450 (M^+, 66%), 413 (77), 389 (67), 349 (96), 323 (75), 289 (81), 265 (82), 234 (66), 200 (89), 172 (77), 150 (81), 126 (100), 102 (84), 73 (94), 57 (79). Anal. Calcd for $C_{26}H_{18}N_4O_4$ (450.46): C, 69.33; H, 4.03; N, 12.44. Found: C, 68.96; H, 4.37; N, 12.11.

Synthesis of compounds 3 and 4: General procedure for condensation of 2 with nitrogen nucleopiles:

A mixture of compound **2** (2.5 mmol, 0.67 g) and freshly distillated aniline and/or hydroxylamine hydrochloride (5 mmol) in dry dimethylformamide (25 ml) was heated under reflux for 6 h. The formed precipitates after cooling, were filtered off and crystallization from dimethylformamide to give the products **3** and **4**, respectively.

3,7-Bis[(phenylimino)methyl]-4H,6H-pyrano[3,2-g]chromene-4,6-dione (3): Light brown solid; yield 66%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3055 (C−H_{arom}), 1663 (C=O_{pyrone}), 1594 (C=N)**.** ^1H-NMR (δ ppm, DMSO-d_6): 6.46−6.54 (m, 4H, Ph−H), 6.98 (d, 4H, *J*=7.2 Hz, Ph−H), 7.31 (t, 2H, *J* =7.8 Hz, Ph−H), 7.56 (s, 1H, H−10), 7.94 (s, 2H, CH=N), 8.26 (s, 2H, H−2), 8.80 (s, 1H, H−5). MS (*m/z*, I %): 420 (M^+, 1.4%), 404 (1), 379 (1), 341 (1), 264 (2), 239 (5), 223 (1), 163 (1), 130 (1), 93 (100), 66 (25). Anal. Calcd for $C_{26}H_{16}N_2O_6$ (420.43): C, 74.28; H, 3.84; N, 6.66. Found: C, 74.45; H, 4.17; N, 6.60.

***3,7-Bis[(hydroxyimino)methyl]-4H,6H-pyrano[3,2-g]chromene-4,6-dione (4)*:** Deep red solid; yield 61%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3397 (br, OH), 1650 (C=O_{pyrone}), 1629 (C=N). ^1H-NMR (δ ppm, DMSO-d_6): 7.48 (s, 1H, H−10), 7.95 (s, 2H, CH=N),

8.41 (s, 2H, H−2), 8.89 (s, 1H, H−5), 12.74 (brs, 2H, OH exchangeable with D_2O). MS (*m/z*, I %): 300 (M^+, 0.12%), 296 (2), 261 (2), 212 (6), 157 (4), 128 (2), 109 (6), 80 (100), 66 (11)**.** Anal. Calcd for $C_{14}H_8N_2O_6$ (300.23): C, 56.01; H, 2.69; N, 9.33. Found: C, 55.74; H, 2.53; N, 8.97.

Synthesis of compounds 5 and 6: General procedure for condensation of 2 with acyclic carbon nucleopiles:

A mixture of compound **2** (2.5 mmol, 0.67 g) and malononitrile and/or ethyl cyanoacetate (5 mmol) in dry dimethylformamide (25 ml) containing few drops of triethylamine, was heated under reflux for 6 h. The formed precipitates after cooling, were filtered off and crystallization from dimethylformamide to give the products **5** and **6**, respectively.

2,2'-[(4,6-Bioxo-4H,6H-pyrano[3,2-g]chromene-3,7-diyl)dimethylylidene]dipropane-dinitrile (5)**:** Brown solid; yield 70%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3058 ($C-H_{arom}$), 2220, 2192 (2 C≡N), 1654 ($C=O_{pyrone}$). ^{1}H-NMR (δ ppm, DMSO-d_6): 7.12 (s, 2H, CH=C), 7.47 (s, 1H, H−10), 8.32 (s, 2H, H−2), 8.50 (s, 1H, H−5). MS (*m/z*, I %): 366 (M^+, 7%), 351 (23), 309 (24), 256 (27), 210 (19), 160 (54), 129 (40), 96 (39), 82 (100), 64 (74), 57 (63). Anal. Calcd for $C_{20}H_6N_4O_4$ (366.30): C, 65.58; H, 1.65; N, 15.30. Found: C, 65.84; H, 1.98; N, 15.67.

Diethyl 3,3'-(4,6-dioxo-4H,6H-pyrano[3,2-g]chromene-3,7-diyl)bis(2-cyanoprop-2-enoate) (6)**:** Brown solid; yield 55%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3066 ($C-H_{arom}$), 2928 ($C-H_{aliph}$), 2200 (C≡N), 1733 ($C=O_{ester}$), 1635 ($C=O_{pyrone}$). ^{1}H-NMR (δ ppm, DMSO-d_6): 1.22 (t, 6H, *J* =6.9 Hz, CH_3), 4.19 (q, 4H, *J* =6.9 Hz, CH_2), 7.53 (s, 2H, CH=C), 7.88 (s, 1H, H−10), 8.07 (s, 2H, H−2), 8.34 (s, 1H, H−5). MS (*m/z*, I %): 460 (M^+, 2 %), 424 (41), 407 (40), 338 (57), 283 (90), 255 (47), 189 (90), 163 (56), 148 (66), 122 (100), 95 (86), 64 (73), 55 (46). Anal. Calcd for $C_{24}H_{16}N_2O_8$ (460.40): C, 62.61; H, 3.50; N, 6.08. Found: C, 62.51; H, 3.43; N, 6.31.

Synthesis of 5,5'-[(4,6-dioxo-4*H*,6*H*-pyrano[3,2-*g*]chromene-3,7-diyl)dimethyl-ylidene]dipyrimidine-2,4,6 (1*H*,3*H*, 5*H*)-trione (7)

A mixture of compound **2** (2.5 mmol, 0.67 g) and barbaturic acid (5 mmol, 0.32 g) in glacial acetic acid (25 ml) and fused sodium acetate (2 g), was heated under reflux for 6 h. The reaction mixture was cooled and poured into crushed ice and kept under constant manual stirring for 1 h. The resulting precipitate was filtered off, washed with water several times and crystallized from dimethylformamide to give the product **7**. Deep red solid; yield 60%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 3283, 3202 (br, 2 NH),

1707 (3 $C=O_{pyrimidinetrione}$), 1644 ($C=O_{pyrone}$). ^{1}H-NMR (δ ppm, DMSO-d_6): 6.94 (s, 2H, CH=C), 7.94 (s, 1H, H−10), 8.35 (s, 2H, H−2), 8.55 (s, 1H, H−5), 11.50 (brs, 4H, NH exchangeable with D_2O). MS (*m/z*, I %): 490 (M^+, 3%), 478 (4), 449 (9), 392 (7), 368 (21), 313 (10), 264 (12), 239 (18), 197 (6), 185 (7), 149 (11), 123 (16), 109 (35), 97 (30), 83 (38), 71 (65), 57 (100). Anal. Calcd for $C_{22}H_{10}N_4O_{10}$ (490.35): C, 53.89; H, 2.06; N, 11.43. Found: C, 53.55; H, 2.41; N, 11.52.

Synthesis of compounds 22 and 23: General procedure for oxidation of 20 and 21 with iodine:

To a solution of each **20** and **21** (2.5 mmol) in dimethylsulfoxide (15 ml), iodine (10 mol %) and 4-5 drops of concentrated sulfuric acid was added. The reaction mixture was heated at 120 ^oC for 10 h. The contents were cooled to room temperature and poured into ice-cooled water. The separated solids were filtered and washed with diluted sodium thiosulphate solution. Finally, the obtained products were crystallized from dimethylformamide to give the products **22** and **23**, respectively.

***Pyrano[3,2-g]chromeno[4,3-c:7,6-c]dipyrazol-2,8-(4H)dione (22)**:* Light brown solid; yield 59%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 1712 (C=O), 1612 (C=N), 1595 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 6.74 (s, 1H, H−10), 8.81 (s, 1H, H−5), 8.98 (s, 2H, $H-5_{pyrazole}$), 10.12 (brs, 2H, NH exchangeable with D_2O). Anal. Calcd for $C_{14}H_6N_4O_4$ (294.23): C, 57.15; H, 2.06; N, 19.04. Found: C, 56.83; H, 1.69; N, 18.74.

***2,10-Diphenylpyrano[3,2-g]chromeno[4,3-c:7,6-c]dipyrazol-2,8-(4H)dione (23)**:* Light brown solid; yield 62%; m.p. > 300 ^oC. IR (KBr, cm^{-1}): 1718 (C=O), 1615 (C=N), 1596 (C=C). ^{1}H-NMR (δ ppm, DMSO-d_6): 6.77 (s, 1H, H−10), 7.43−8.08 (m, 10H, Ph−H), 8.36 (s, 1H, H−5), 9.16 (s, 2H, $H-5_{pyrazole}$). Anal. Calcd for $C_{26}H_{14}N_4O_4$ (446.43): C, 69.95; H, 3.16; N, 12.55. Found: C, 69.57; H, 2.86; N, 12.19.

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