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**Research Article**

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# Facile, Stepwise and Diversity Oriented Synthesis of 3-(2-Oxo-2H-Chromen-3-yl)-1-Phenyl-1*H*-Pyrazole-4-Carbaldehydes

**Devulapally Srikrishna* and Pramod Kumar Dubey**

*Department of Chemistry, Jawaharlal Nehru Technological University College of Engineering, Kukatpally, Hyderabad, Telangana, India*

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**ABSTRACT**

*3-Acetyl-2H-chromen-2-ones (1) when treated with phenylhydrazine in acetic acid gave 3-(1-(2-phenylhydrazono)ethyl)-2H-chromen-2-one (2) which on Vilsmeier-Haack formylation yielded the title compound, 3-(2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3). Alternatively, 3 could also be prepared in a stepwise manner by treating 1 with DMF-DMA to yield 3-(3-(dimethylamino)acryloyl)-2H-chromen-2-one (4) followed by reaction with phenylhydrazine leading to 3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one 5 and its subsequent treatment with the Vilsmeier-Haack reagent. Also, 3 could be prepared in an yet another alternative method by treating 2 with DMF-DMA to yield 5 followed by Vilsmeier-Haack formylation of the latter.*

**Keywords:** 3-acetyl-2*H*-chromen-2-ones; Phenylhydrazine; DMF-DMA; Pyrazoles; Vilsmeier-Haack reaction

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## INTRODUCTION

Coumarins are a family of naturally occurring lactones and have attracted interest in recent years because of their diverse pharmacological properties [1]. Coumarin derivatives have been reported to possess biological activities such as anti-HIV [2], anti-cancer [3], anti-inflammatory [4], antipsychotic [5] etc. Apart from these biological activities, coumarin derivatives are also known to exhibit a variety of applications such as florescent probes [6], polymers [7] etc. Pyrazole derivatives too have also attracted increasing attention of chemists and biologists due to their numerous biological activities, such as antimicrobial [8], anti-fungal [9], anti-bacterial [10], antiviral [11], analgesic [12] etc. Patel et al. reported [13] the reaction of acetophenone with phenylhydrazine in ethanol using a catalytic amount of acetic acid to yield the corresponding hydrazone which on Vilsmeier-Haack reaction gave 3-aryl-1-phenylpyrazole-4-carbaldehyde. Kumar et al. reported [14] the Vilsmeier-Haack reaction of acetophenone phenylhydrazones to yield corresponding 1,3-diphenyl-1*H*-pyrazole-4-carbaldehydes under heating at 50-60°C for 5-6 h. Abel et al. reported [15] the reaction of 3-acetyl-2*H*-chromen-2-one with DMF-DMA in xylene at reflux temperature to give the enaminone which on further reaction with phenylhydrazine resulted in the the formation of 3-(1-phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one. Similarly, Khadijah reported [16] the reaction of 3-acetyl-2*H*-benzo(g)chromen-2-one with DMF-DMA to yield 3-(3-(dimethylamino)acryloyl)-2*H*-benzo (g) chromen-2-one which on treatment with phenylhydrazine under microwave irradiation conditions resulted the corresponding pyrazole i.e., 3-(1-phenyl-1*H*-pyrazol-3-yl)-2*H*-benzo(g)chromen-2-one.

Holzer et al. reported [17] the Vilsmeier-Haack reaction of 3-(benzyloxy)-1-phenyl-1*H*-pyrazole to yield 3-(benzyloxy)-1-phenyl-1*H*-pyrazole-4-carbaldehyde in which the formylation occurred at the 4$^{th}$ position of the pyrazole ring. Similarly, Menegatti et al. reported [18] the synthesis of 1-(4-chlorophenyl)-1*H*-pyrazole-4-carbaldehyde on reaction of 1-(4-chlorophenyl)-1*H*-pyrazole with Vilsmeier-Haack reagent. Reddy et al. also reported [19] the Vilsmeier-Haack formylation of 3,5-dimethyl-1-phenyl-1*H*-pyrazole to yield 3,5-dimethyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde under refluxing conditions for 1 h. Prakash et al. reported [20] the Vilsmeier-

Haack reaction of 4-hydroxy-6-methyl-3-(1-phenyl-1*H*-pyrazol-3-yl)-2*H*-pyran-2-one to give the corresponding 4-formylated product i.e., 3-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde.
Based on the literature cited above and in continuation of our earlier work [21-24] on synthesis of oxygen-containing heterocycles of potential biological interest, the present work describes the design and synthesis of heterocyclic compounds bearing both the coumarin and pyrazole moieties in a single framework.

## EXPERIMENTAL SECTION

Melting points are uncorrected and were determined in open capillary tubes using hot sulphuric acid bath. TLC analyses were run on silica gel – G and visualization was done using UV lamp or Iodine. IR spectra were recorded using Perkin – Elmer 1700 spectrometer in KBr pellets. $^1$H NMR spectra were recorded in DMSO–$d_6$ with TMS as an internal standard using 400 MHz spectrometer. Mass spectra were recorded on Agilent-LCMS instrument under CI conditions and given by Q+1 values only.

**General Procedure for the Preparation of 2 from 1**
A mixture of 1 (5 mmol) and phenylhydrazine (5 mmol) and acetic acid (10 mL) was stirred at room temperature for 10 min. Then, the mixture was poured into ice-cold water (30 mL). The separated solid was filtered, washed with aqueous acetic acid (1:1, 2 x 5 mL) and dried. The crude product was recrystallized from suitable solvent to obtain pure 2.

**3-(1-(2-Phenylhydrazono) ethyl)-2H-chromen-2-one (2a):**
Yield = 1.29 g (93%); mp 186-188°C (lit.[25] mp 188°C); IR (KBr): 1717 cm$^{-1}$ (strong, sharp, -CO of coumarin ring), 3380-3430 cm$^{-1}$ (broad, medium, -NH group); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.22 (s, 3H, -$CH_3$), 6.77-7.85 (m, 8H, Ar-H), 8.20 (s, 1H, Ar-H), 9.42 (s, 1H, -NH); HRMS calculated for $C_{17}H_{14}N_2O_2$ $(M+H)^+$: 279.1133, Found: 279.1131.

**6-Chloro-3-(1-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (2b):**
Yield = 1.32 g (85%); mp 132-134°C; IR (KBr): 1721 cm$^{-1}$ (strong, sharp, -CO of coumarin ring), 3309-3405 cm$^{-1}$ (broad, medium, -NH group); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.34 (s, 3H, -$CH_3$), 7.18-7.94 (m, 8H, Ar-H), 8.37 (s, 1H, Ar-H), 9.04 (s, 1H, -NH),; MS: m/z 313 ($M^+$+1).

**6-Bromo-3-(1-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (2c):**
Yield = 1.49 g (88%); mp 168-170°C; IR (KBr): 3335-3438 cm$^{-1}$ (broad, medium, -NH group), 1726 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.28 (s, 3H, -$CH_3$), 7.20-7.89 (m, 8H, Ar-H), 8.09 (s, 1H, Ar-H), 9.38 (s, 1H, -NH),; HRMS calculated for $C_{17}H_{13}BrN_2O_2$ $(M+H)^+$: 357.02386, Found: 357.02384.

**6-Nitro-3-(1-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (2d):**
Yield = 1.38 g (86%); mp 180-182°C; IR (KBr): 1732 cm$^{-1}$ (strong, sharp, -CO of coumarin ring), 3298-3402 cm$^{-1}$ (broad, medium, -NH group); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.08 (s, 3H, -$CH_3$), 7.20-8.25 (m, 8H, Ar-H), 8.82 (s, 1H, Ar-H), 9.11 (s, 1H, -NH),; MS: m/z 324 ($M.^+$+1).

**8-methoxy-3-(1-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (2e):**
Yield = 1.40 g (91%); mp 161-163°C (lit. [25] mp 163°C); IR (KBr): 1714 cm$^{-1}$ (strong, sharp, -CO of coumarin ring), 3330-3420 cm$^{-1}$ (broad, medium, -NH group); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.22 (s, 3H, -$CH_3$), 3.92 (s, 3H, -$OCH_3$), 6.77-7.40 (m, 8H, Ar-H), 8.17 (s, 1H, Ar-H), 9.44 (s, 1H, -NH); MS: m/z 309 ($M.^+$+1).

**General Procedure for Synthesis of 3 from 2**
To a cooled solution of DMF (25 mL) and $POCl_3$ (5 mL) at 0-5°C was added 2 (5 mmol). The reaction mixture was stirred at room temperature for 2-3 h. After completion of reaction, as indicated by the disappearance of starting materials on TLC, the mixture was poured into ice-cold water (30 mL). The separated solid was filtered, washed with water (2x15 mL) and dried to obtain crude 3. Recrystallization from a suitable solvent gave pure 3.

**3-(2-Oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3a):**
Yield = 1.37 g (87%); mp 212-214°C (lit. [25] mp 215-216°C); IR (KBr): 1716 cm$^{-1}$ (strong, sharp,-CO of aldehyde group), 1731 cm$^{-1}$ (strong, sharp,-CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 7.36-8.10 (m, 8H,

Ar-H), 8.46 (s, 1H, Ar-H), 9.27 (s, 1H, Ar-H), 9.97 (s, 1H, -CHO); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 114.8, 119.3, 119.9, 120.1, 123.4, 124.8, 127.8, 129.7, 132.6, 138.5, 142.8, 143.3, 146.4, 147.3, 159.0, 185.4; HRMS calculated for $C_{19}H_{12}N_2O_3$ $(M+H)^+$: 317.0926, Found: 317.0933.

**3-(6-Chloro-2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3b):**
Yield = 1.31 g (75%); mp 164-166°C; IR (KBr): 1710 cm$^{-1}$ (strong, sharp, -CO of aldehyde group), 1736 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 7.43-8.00 (m, 8H, Ar-H), 8.42 (s, 1H, Ar-H), 9.29 (s, 1H, Ar-H), 9.93 (s, 1H, -CHO); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 113.9, 118.6, 119.2, 121.3, 124.4, 124.9, 126.9, 129.5, 133.7, 137.6, 141.9, 142.8, 146.7, 147.8, 160.2, 187.1; Ms: m/z 351 ($M.^+$+1).

**3-(6-Bromo-2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3c):**
Yield = 1.55 g (79%); mp 223-225°C; IR (KBr): 1702 cm$^{-1}$ (strong, sharp, -CO of aldehyde group), 1733 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 7.46-8.40 (m, 8H, Ar-H), 8.76 (s, 1H, Ar-H), 9.24 (s, 1H, Ar-H), 9.74 (s, 1H, -CHO); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 113.6, 119.0, 119.4, 120.3, 122.9, 123.5, 127.1, 128.9, 132.7, 137.8, 141.8, 142.6, 145.7, 147.0, 158.5, 184.9; Ms: m/z 396 ($M.^+$+1).

**3-(6-Nitro-2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3d):**
Yield = 1.31 g (73%); mp 203-205°C; IR (KBr): 1711 cm$^{-1}$ (strong, sharp, -CO of aldehyde group), 1738 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 7.31-7.64 (m, 8H, Ar-H), 8.20 (s, 1H, Ar-H), 9.12 (s, 1H, Ar-H), 9.86 (s, 1H, -CHO); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 112.8, 118.4, 120.0, 120.7, 124.1, 124.8, 128.1, 129.9, 133.6, 137.9, 141.9, 144.0, 145.9, 148.1, 158.5, 185.1; Ms: m/z 362 ($M.^+$+1).

**3-(8-methoxy-2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde (3e):**
Yield = 1.24 g (72%); mp 242-244°C (lit.[25] mp. 240-241°C); IR (KBr): 1701 cm$^{-1}$ (strong, sharp, -CO of aldehyde group), 1739 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 3.94 (s, 3H, -$OCH_3$), 7.34-8.00 (m, 8H, Ar-H), 8.44 (s, 1H, Ar-H), 9.28 (s, 1H, Ar-H), 9.92 (s, 1H, -CHO); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 56.1, 114.5, 119.0, 119.5, 120.1, 123.6, 124.4, 127.9, 129.4, 132.5, 138.8, 142.9, 143.6, 146.3, 147.9, 159.5, 185.6; Ms: m/z 347 ($M.^+$+1).

**General Procedure for the Synthesis of 4 from 1**
A mixture of 1 (5 mmol) and DMF-DMA (5 mL) was heated at 100°C for 1 h. The reaction was monitored by TLC analysis. After the completion of reaction, the mixture was cooled to room temperature and then poured into ice-cold water (30 mL). The separated solid was filtered, washed with water (2 × 15 mL) and dried to obtain crude 4. The crude product upon recrystallization from a suitable solvent gave pure 4.

**3-(3-(Dimethylamino)acryloyl)-2H-chromen-2-one (4a):**
Yield = 1.03 g (85%); mp 164-166°C (lit.[15] mp 165°C); IR (KBr): 1704 cm$^{-1}$ (strong, sharp, -CO of acetyl group), 1721 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.95 (s, 3H, -$CH_3$), 3.15 (s, 3H, -$CH_3$), 5.88 (d, 1H, -CH=CH-$NMe_2$), 7.27-7.96 (m, 4H, Ar-H, 1H, -CH=CH-$NMe_2$ ), 8.45 (s, 1H, Ar-H), HRMS calculated for $C_{14}H_{13}NO_3$ $(M+H)^+$: 244.0973, Found: 244.1025.

**6-Chloro-3-(3-(dimethylamino)acryloyl)-2H-chromen-2-one (4b):**
Yield = 1.12 g (81%); mp 89-91°C; IR (KBr): 1702 cm$^{-1}$ (strong, sharp, -CO of acetyl group), 1730 cm$^{-1}$ (strong, sharp, -CO of coumarin ring),; $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.98 (s, 3H, -$CH_3$), 3.11 (s, 3H, -$CH_3$), 5.59 (d, 1H, -CH=CH-$NMe_2$), 7.25 (d, 1H, Ar-H), 7.48 (d, 1H, Ar-H), 7.61 (d, 1H, -CH=CH-$NMe_2$), 7.98 (s, 1H, Ar-H), 8.29 (s, 1H, Ar-H), Ms: m/z 278 ($M.^+$+1).

**6-Bromo-3-(3-(dimethylamino)acryloyl)-2H-chromen-2-one (4c):**
Yield = 1.25 g (78%); mp 152-154°C; IR (KBr): 1715 cm$^{-1}$ (strong, sharp, -CO of acetyl group), 1738 cm$^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.87 (s, 3H, -$CH_3$), 3.15 (s, 3H, -$CH_3$), 5.94 (d, 1H, -CH=CH-$NMe_2$), 7.41 (s, 1H, Ar-H), 7.80 (d, 2H, Ar-H), 8.13 (d, 1H, -CH=CH-$NMe_2$), 8.49 (s, 1H, Ar-H); Ms: m/z 323($M.^+$+1).

**6-Nitro-3-(3-(dimethylamino)acryloyl)-2H-chromen-2-one (4d):**
Yield = 1.05 g (73%); mp 131-133°C; IR (KBr): 1712 $cm^{-1}$ (strong, sharp, -CO of acetyl group), 1736 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.99 (s, 3H, -$CH_3$), 3.10 (s, 3H, -$CH_3$), 5.55 (d, 1H, -CH=CH-$NMe_2$), 7.22 (d, 1H, Ar-H), 7.39 (d, 1H, Ar-H), 7.56 (d, 1H, -CH=CH-$NMe_2$), 7.94 (s, 1H, Ar-H), 8.44 (s, 1H, Ar-H); Ms: m/z 289 ($M.^+$+1).

**3-(3-(Dimethylamino)acryloyl)-8-methoxy-2H-chromen-2-one (4e):**
Yield = 1.13 g (83%); mp 222-224°C; IR (KBr): 1724 $cm^{-1}$ (strong, sharp, -CO of acetyl group), 1739 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 2.87 (s, 3H, -$CH_3$), 3.15 (s, 3H, -$CH_3$), 3.92 (s, 3H, -$OCH_3$), 6.02 (d, 1H, -CH=CH-$NMe_2$), 7.28-7.41 (m, 3H, Ar-H), 7.75 (d, 1H, -CH=CH-$NMe_2$), 8.47 (s, 1H, -Ar-H), Ms: m/z 274 ($M.^+$+1).

**General Procedure for the Preparation of 5 from 4**
A mixture of 4 (5 mmol), phenylhydrazine (5 mmol) and acetic acid (20 mL) was stirred at room temperature for about 30 min. After the completion of the reaction, as indicated by TLC, the mixture was poured into ice-cold water (30 mL). The separated solid was filtered, washed with water (2 × 20 mL) and dried to obtain crude 5. The crude product was recrystallized from a suitable solvent to obtain pure 5.

**3-(1-Phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one (5a):**
Yield = 1.21 g (84%); mp 133-135°C(lit.[15] mp 135°C); IR (KBr): 1736 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 6.76 (d, 1H, Ar-H), 7.28-7.72 (m, 9H, Ar-H), 7.86 (d, 1H, Ar-H), 8.20 (s, 1H, Ar-H); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 114.8, 119.3, 119.9, 120.1, 123.4, 124.8, 127.8, 129.7, 132.6, 138.5, 142.8, 143.3, 146.4, 147.3, 159.0; HRMS calculated for $C_{18}H_{12}N_2O_2$ $(M+H)^+$: 289.0977, Found: 289.0966.

**6-Chloro-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one (5b):**
Yield = 1.17 g (73%); mp 111-113°C; IR (KBr): 1728 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$-TMS): δ 6.79-7.74 (m, 9H, Ar-H), 7.88 (s, 1H, Ar-H), 8.23 (s, 1H, Ar-H); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 111.3, 115.8, 119.0, 120.6, 124.8, 126.1, 127.3, 128.4, 128.9, 130.2, 137.5, 140.7, 145.8, 152.8, 160.2; Ms: m/z 323 ($M.^+$+1).

**6-Bromo-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one (5c):**
Yield = 1.40 g (77%); mp 220-222°C; IR (KBr): 1714 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 6.68-7.64 (m, 9H, Ar-H), 7.91 (s, 1H, Ar-H), 8.45 (s, 1H, Ar-H); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 109.9, 115.9, 118.6, 120.4, 124.5, 126.5, 128.5, 128.9, 129.3, 130.2, 139.9, 142.1, 146.5, 152.7, 161.3; Ms: m/z 368 ($M.^+$+1).

**6-Nitro-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one (5d):**
Yield = 1.16 g (70%); mp 99-101°C; IR (KBr): 1717 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 6.84-7.59 (m, 9H, Ar-H), 7.74 (s, 1H, Ar-H), 8.33 (s, 1H, Ar-H); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 111.1, 115.2, 118.9, 120.5, 124.8, 126.5, 127.1, 128.2, 128.8, 129.4, 137.8, 142.0, 147.3, 152.8, 161.4; Ms: m/z 334 ($M.^+$+1).

**8-Methoxy-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one (5e):**
Yield = 1.28 g (81%); mp 164-166°C; IR (KBr): 1723 $cm^{-1}$ (strong, sharp, -CO of coumarin ring); $^1$H-NMR (400 MHz, DMSO-$d_6$/TMS): δ 3.90 (s, 3H, -$OCH_3$), 6.75-7.81 (m, 10H, Ar-H), 8.17 (s, 1H, Ar-H); $^{13}$C-NMR (100 MHz, DMSO-$d_6$/TMS): 110.9, 115.6, 119.4, 121.2, 125.3, 126.2, 126.8, 128.0, 128.7, 130.2, 137.9, 142.2, 147.1, 152.6, 162.3; Ms: m/z 319 ($M.^+$+1).

**General Procedure for the Synthesis of 5 from 2**
A mixture of 2 (5 mM), DMF-DMA (5 mmol) and dioxane (20 mL) was heated at 100°C for about 3-4 h. The reaction was monitored by TLC analysis. After the completion of reaction, the mixture was cooled to room temperature and poured into ice-cold water (30 mL). The separated solid was filtered, washed with water (2 x 10 mL) and dried. The crude product was recrystallized from a suitable solvent to yield pure 5.

**5a:** Yield = 0.88 g (61%);
**5b:** Yield = 0.95 g (59%);
**5c:** Yield = 1.04 g (57%);
**5d:** Yield = 0.89 g (54%);
**5e:** Yield = 0.82 g (52%)

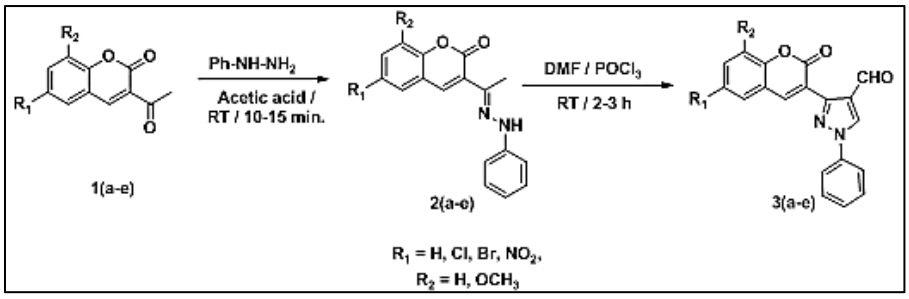
**General Method for the Synthesis of 3 from 5**

To a mixture of DMF (25 mL) and $POCl_3$ (5 mL) cooled in an ice-bath at 0-5°C and was added 3 (5 mmol). Then the reaction mixture was allowed to room temperature and then it was maintained at 60°C in an oil-bath for 3-4 h. The completion of the reaction was checked by TLC for disappearance of starting material. After completion of the reaction, the mixture was poured into ice-cold water (30 mL). The separated solid was filtered, washed with water (2 x 20 mL) and dried to obtain a crude product. The latter was recrystallized from a suitable solvent to obtain pure 3.

**3a:** Yield = 1.09 g (69%);
**3b:** Yield = 1.08 g (62%);
**3c:** Yield = 1.14 g (58%);
**3d:** Yield = 1.17 g (65%);
**3e:** Yield = 1.04 g (60%)

## RESULTS AND DISCUSSION

Commercially available salicylaldehydes were treated with ethyl acetoacetate in triethanolamine containing a catalytic amount of L-proline at room temperature for 30 min to yield 3-acetyl-2H-chromen-2-ones (1) [24]. The latter, on treatment with phenylhydrazine in acetic acid at RT for 10-15 min resulted in the formation of (3-(1-(2-phenylhydrazono)ethyl)-2*H*-chromen-2-ones (2). 2 on Vilsmeier-Haack reaction at room temperature for 2-3 h yielded the title compounds 3-(2-oxo-2*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehydes (3) (Scheme 1).

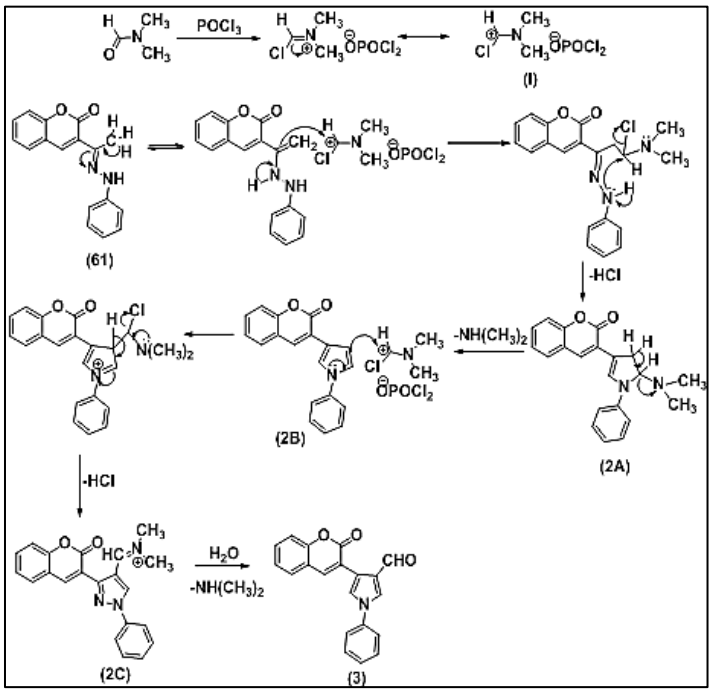



**Scheme 1: Synthesis of 3-(2-oxo-2*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehydes**

A plausible mechanism for the formation of 3 from 2 was studied and explained. Reaction between DMF and $POCl_3$ forms the Vilsmeier-Haack complex I, which initially attacks the phenylhydrazone (2) and subsequently losses a molecule of HCl, followed by initiation of cyclization via an internal nucleophilic attack of -NH group to provide an intermediate (2A). 2A then losses a molecule of dimethylamine ($NHMe_2$) to give the pyrazole derivative (2B). This pyrazole 2B then undergoes electrophilic substitution with another molecule of Vilsmeier-Haack reagent to give an iminium salt (2C) which is further hydrolyzed to give the corresponding 4-formyl pyrazole 3 (Scheme 2).

The reaction conditions and physical data of the compounds 2(a-e) and 3(a-e) are recorded in Table 1.

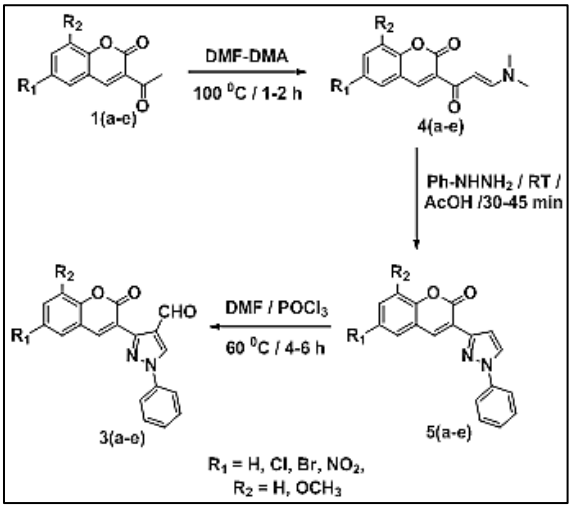
Alternatively, the compound 3a could also be prepared in a stepwise manner. Thus, 3-acetyl-2*H*-chromen-2-one (1a, i.e., 1, $R_1$=$R_2$=H) was heated to 100°C with N,N-dimethylformamide dimethyl acetal (DMF-DMA) under solvent free conditions to yield 3-(3-(dimethylamino)acryloyl)-2*H*-chromen-2-one (4a i.e., 4, $R_1$=$R_2$=H) which on reaction with phenylhydrazine led to the formation of 3-(1-phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (5a i.e., 5, $R_1$=$R_2$=H). Further, 5a, on Vilsmeier-Haack reaction, resulted in the formation of 3-(2-oxo-2*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (3a i.e., 3, $R_1$=$R_2$=H). This route of preparation of 3a from 1a by reaction with DMF-DMA followed by phenylhydrazine and Vilsmeier-Haack formylation was found to be a general one and was extended to other derivatives of 1 (Scheme 3). A probable mechanism for the formation of 5 from 4 involves the nucleophilic addition reaction between 4 and phenylhydrazine followed by removal of a water molecule and subsequent cyclization to give the pyrazole 5. The structures of all the products have been established on the basis of their spectral data. (Please see the experimental section) (Tables 2 and 3).



**Scheme 2: Plausible mechanism for the formation of 3 from 2**

**Table 1: Reaction conditions, yield and physical data of compounds 2(a-e) and 3(a-e)**

| S.No | Substrate | Reagent | Reaction Condition | Product obtained | Yield (%) |
|---|---|---|---|---|---|
| 1 | 1a: $R_1$=H, $R_2$=H | $PhNHNH_2$ | RT/ 10 min | 2a: $R_1$=H, $R_2$=H | 93 |
| 2 | 1b: $R_1$=Cl, $R_2$=H | $PhNHNH_2$ | RT/ 15 min | 2b: $R_1$=Cl, $R_2$=H | 85 |
| 3 | 1c: $R_1$=Br, $R_2$=H | $PhNHNH_2$ | RT/ 12 min | 2c: $R_1$=Br, $R_2$=H | 88 |
| 4 | 1d: $R_1$=$NO_2$, $R_2$=H | $PhNHNH_2$ | RT/ 10 min | 2d: $R_1$=$NO_2$, $R_2$=H | 86 |
| 5 | 1e: $R_1$=H, $R_2$=$OCH_3$ | $PhNHNH_2$ | RT/ 15 min | 2e: $R_1$=H, $R_2$=$OCH_3$ | 91 |
| 6 | 2a: $R_1$=H, $R_2$=H | DMF+$POCl_3$ | RT/ 2h | 3a: $R_1$=H, $R_2$=H | 87 |
| 7 | 2b: $R_1$=Cl, $R_2$=H | DMF+$POCl_3$ | RT/ 2½ h | 3b: $R_1$=Cl, $R_2$=H | 75 |
| 8 | 2c: $R_1$=Br, $R_2$=H | DMF+$POCl_3$ | RT/ 2h | 3c: $R_1$=Br, $R_2$=H | 79 |
| 9 | 2d: $R_1$=$NO_2$, $R_2$=H | DMF+$POCl_3$ | RT/ 3h | 3d: $R_1$=$NO_2$, $R_2$=H | 73 |
| 10 | 2e: $R_1$=H, $R_2$=$OCH_3$ | DMF+$POCl_3$ | RT/ 2½ h | 3e: $R_1$=H, $R_2$=$OCH_3$ | 72 |

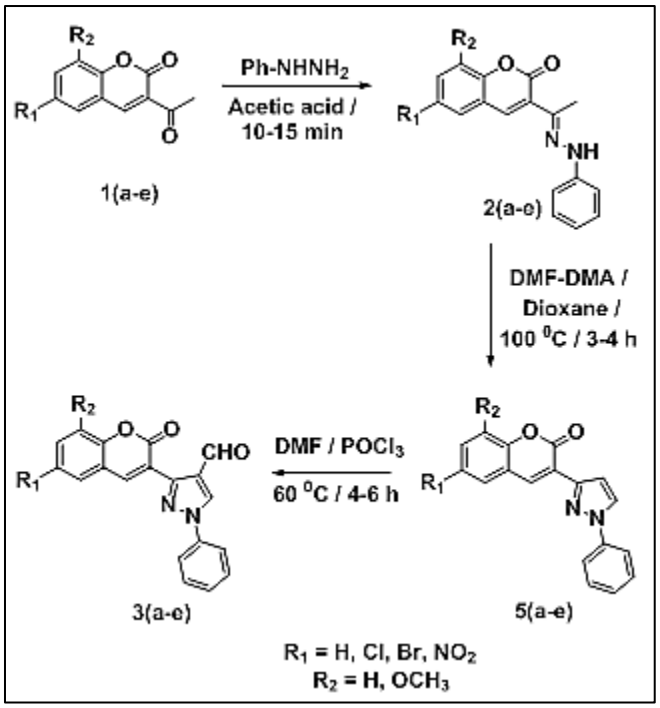


**Scheme 3: Synthesis of 3 from 1 by reaction with DMF-DMA followed by phenylhydrazine and VHF reaction**

**Table 2: Reaction conditions, yield and physical data of compounds 4(a-e), 5(a-e) and 3(a-e) that were prepared in Scheme 3**

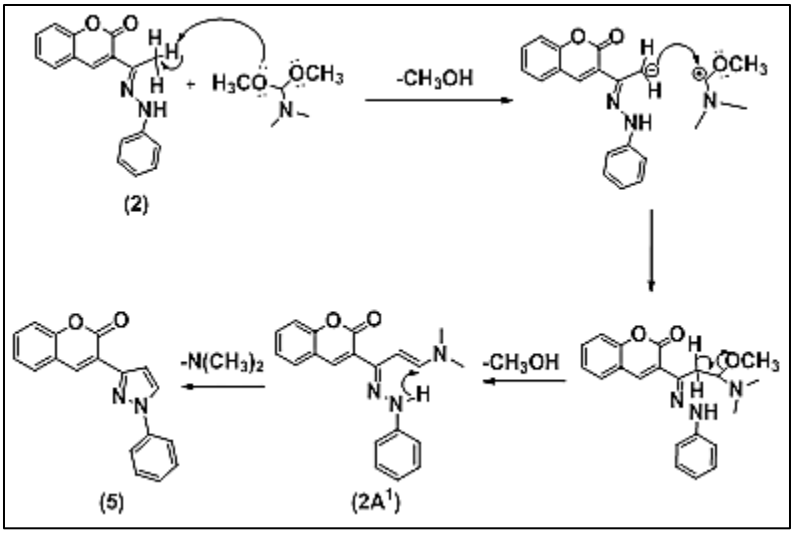
| S.No | Substrate | Reagent | Reaction Condition | Product obtained | Yield (%) |
|---|---|---|---|---|---|
| 1 | 1a: $R_1$=H, $R_2$=H | DMF-DMA | 100°C / 1 h | 4a: $R_1$=H, $R_2$=H | 85 |
| 2 | 1b: $R_1$=Cl, $R_2$=H | DMF-DMA | 100°C / 2 h | 4b: $R_1$=Cl, $R_2$=H | 81 |
| 3 | 1c: $R_1$=Br, $R_2$=H | DMF-DMA | 100°C / 1 h | 4c: $R_1$=Br, $R_2$=H | 78 |
| 4 | 1d: $R_1$=$NO_2$, $R_2$=H | DMF-DMA | 100°C / 1 h | 4d: $R_1$=$NO_2$, $R_2$=H | 73 |
| 5 | 1e: $R_1$=H, $R_2$=$OCH_3$ | DMF-DMA | 100°C / 2 h | 4e: $R_1$=H, $R_2$=$OCH_3$ | 83 |
| 6 | 4a: $R_1$=H, $R_2$=H | $PhNHNH_2$ | RT / 35 min | 5a: $R_1$=H, $R_2$=H | 84 |
| 7 | 4b: $R_1$=Cl, $R_2$=H | $PhNHNH_2$ | RT / 45 min | 5b: $R_1$=Cl, $R_2$=H | 73 |
| 8 | 4c: $R_1$=Br, $R_2$=H | $PhNHNH_2$ | RT / 35 min | 5c: $R_1$=Br, $R_2$=H | 77 |
| 9 | 4d: $R_1$=$NO_2$, $R_2$=H | $PhNHNH_2$ | RT / 30 min | 5d: $R_1$=$NO_2$, $R_2$=H | 70 |
| 10 | 4e: $R_1$=H, $R_2$=$OCH_3$ | $PhNHNH_2$ | RT / 40 min | 5e: $R_1$=H, $R_2$=$OCH_3$ | 81 |
| 11 | 5a: $R_1$=H, $R_2$=H | DMF+$POCl_3$ | 55-60°C / 4 h | 3a: $R_1$=H, $R_2$=H | 69 |
| 12 | 5b: $R_1$=Cl, $R_2$=H | DMF+$POCl_3$ | 55-60°C / 5 ½ h | 3b: $R_1$=Cl, $R_2$=H | 62 |
| 13 | 5c: $R_1$=Br, $R_2$=H | DMF+$POCl_3$ | 55-60°C / 5 h | 3c: $R_1$=Br, $R_2$=H | 58 |
| 14 | 5d: $R_1$=$NO_2$, $R_2$=H | DMF+$POCl_3$ | 55-60°C / 6 h | 3d: $R_1$=$NO_2$, $R_2$=H | 65 |
| 15 | 5e: $R_1$=H, $R_2$=$OCH_3$ | DMF+$POCl_3$ | 55-60°C / 4 ½ h | 3e: $R_1$=H, $R_2$=$OCH_3$ | 60 |

In an yet another alternative approach, 3-acetyl-2*H*-chromen-2-one (1a i.e., 1, $R_1$=$R_2$=H), when treated with phenylhydrazine in acetic acid at room temperature for 10 min resulted in the formation of (3-(1-(2-phenylhydrazono)ethyl)-2*H*-chromen-2-one (2a i.e., 2, $R_1$=$R_2$=H). The latter on reaction with DMF-DMA in dioxane at 100°C for 3-4 h, yielded 3-(1-phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (5a i.e., 5, $R_1$=$R_2$=H) which on Vilsmeier-Haack reaction gave the title compound 3a (3, $R_1$=$R_2$=H). This route of preparation of 3a from 1a by reaction with phenylhydrazine followed by DMF-DMA was found to be a general one and was extended to other derivatives of 1 (Scheme 4). All these products were compared with the products that were prepared in earlier routes (Schemes 1 and 3) and were found to be identical in all respects with mp, mmp and co-TLC.




**Scheme 4: Synthesis of 3 from 1 by reaction with phenylhydrazine followed by DMF-DMA and VHF reaction**

A plausible mechanism for the formation of **5** from 2 is shown in Scheme 5. In this, the reaction between DMF-DMA and 2 results in the loss of two molecules of methanol in two steps to give an intermediate $2A^1$ which undergoes cyclization to result in the formation of pyrazole 5. The overall yield for the formation of **3** from each route has been calculated and is shown in Tables 4-6.

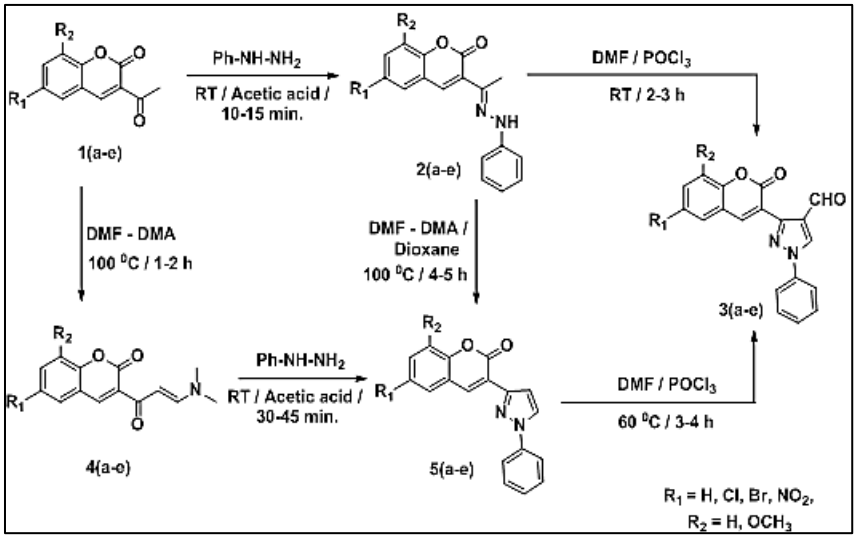



**Scheme 5: Plausible mechanism for the formation of 5 from 2**

**Table 3: Reaction conditions and physical data of compounds 5(a-e) obtained by the reaction of 2(a-e) with DMF-DMA**

| S.No | Substrate | Reagent | Reaction Condition | Product obtained | Yield (%) |
|---|---|---|---|---|---|
| 1 | 2a: $R_1$=H, $R_2$=H | DMF-DMA | 100°C / 3 ½ h | 5a: $R_1$=H, $R_2$=H | 61 |
| 2 | 2b: $R_1$=Cl, $R_2$=H | DMF-DMA | 100°C / 4 h | 5b: $R_1$=Cl, $R_2$=H | 59 |
| 3 | 2c: $R_1$=Br, $R_2$=H | DMF-DMA | 100°C / 3 h | 5c: $R_1$=Br, $R_2$=H | 57 |
| 4 | 2d: $R_1$=$NO_2$, $R_2$=H | DMF-DMA | 100°C / 3 h | 5d: $R_1$=$NO_2$, $R_2$=H | 54 |
| 5 | 2e: $R_1$=H, $R_2$=$OCH_3$ | DMF-DMA | 100°C / 4 h | 5e: $R_1$=H, $R_2$=$OCH_3$ | 52 |

All the above three routes (Schemes 1, 3 and 4) for the preparation of coumarinyl-pyrazole-aldehydes are nicely depicted in a single overall Scheme 6.




**Scheme 6: Overall scheme for the preparation of 3**

**Table 4: Overall yield for formation of 3 via the sequence 1→2→3**

| S. No. | Yield of 2 (from 1) | Yield of 3 (from 2) | Overall yield of 3 (from 1) |
|---|---|---|---|
| 1 | 2a: 93 | 3a: 87 | 3a: 81 |
| 2 | 2b: 85 | 3b: 75 | 3b: 64 |
| 3 | 2c: 88 | 3c: 79 | 3c: 70 |
| 4 | 2d: 86 | 3d: 73 | 3d: 68 |
| 5 | 2e: 91 | 3e: 72 | 3e: 66 |

**Table 5: Overall yield for formation of 3 via the sequence 1→4→5→3**

| S. No. | Yield of 4 (from 1) | Yield of 5 (from 4) | Yield of 3 (from 5) | Overall yield of 3 (from 1) |
|---|---|---|---|---|
| 1 | 4a: 85 | 5a: 84 | 3a: 69 | 3a: 49 |
| 2 | 4b: 81 | 5b: 73 | 3b: 62 | 3b: 37 |
| 3 | 4c: 78 | 5c: 77 | 3c: 58 | 3c: 35 |
| 4 | 4d: 73 | 5d: 70 | 3d: 65 | 3d: 33 |
| 5 | 4e: 83 | 5e: 81 | 3e: 60 | 3e: 40 |

**Table 6: Overall yield for formation of 3 via the sequence 1→2→5→3**

| S. No. | Yield of 2 (from 1) | Yield of 5 (from 2) | Yield of 3 (from 5) | Overall yield of 3 (from 1) |
|---|---|---|---|---|
| 1 | 2a: 93 | 5a: 61 | 3a: 69 | 3a: 39 |
| 2 | 2b: 85 | 5b: 59 | 3b: 62 | 3b: 31 |
| 3 | 2c: 88 | 5c: 57 | 3c: 58 | 3c: 29 |
| 4 | 2d: 86 | 5d: 54 | 3d: 65 | 3d: 30 |
| 5 | 2e: 91 | 5e: 52 | 3e: 60 | 3e: 28 |

## CONCLUSION

In conclusion, we have developed facile and stepwise methods for the synthesis of 3-(2-oxo-2H-chromen-3-yl)-1-phenyl-1H-pyrazole-4-carbaldehydes (3) starting from 3-acetyl-2H-chromen-2-one (1) in three different sequences. Out of these three methods, synthesis of 3 via sequence 1→2→3 seems to be the best method in terms of overall yield and purity of the final product as well as when simplicity of the method is considered. Although, the yields of the final product 3 in sequence 1→4→5→3 and sequence 1→2→5→3 are considerably less when compared to the sequence 1→2→3, we have successfully demonstrated two additional stepwise methods. Structures of all the prepared compounds were well established by spectral and analytical methods.

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