3-(3,5-Dimethyl-1*H*-Pyrazol-1-yl)-3-Oxopropanenitrile as Precursor for Some New Mono-Heterocyclic and Bis-Heterocyclic Compounds

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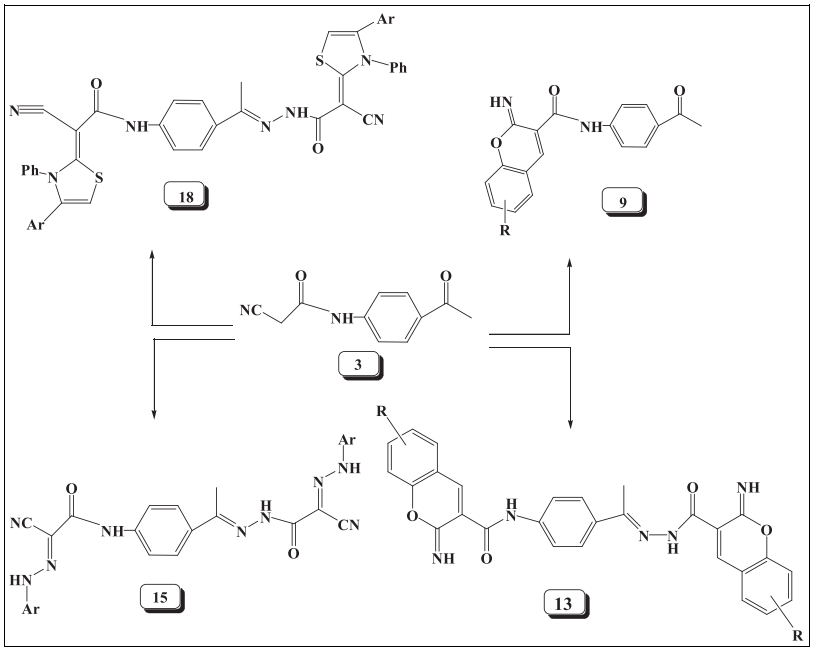


3-(3,5-Dimethyl-1 *H* -pyrazol-1-yl)-3-oxopropanenitrile **1** was used as a cyanoacetylating agent for synthesis of the acetanilide derivative **3**. Compound **3** was utilized as a key intermediate for the synthesis of some new mono-chromene and di-chromene derivatives **9** and **13**, the dihydrazo derivatives **15,** and the dithiazole derivatives **18** via the condensation with *o*-hydroxybenzaldehyde derivatives, the coupling with aryl diazonium salts, or the reaction with phenyl isothiocyanate in presence of KOH followed by phenacyl bromide derivatives respectively.

INTRODUCTION

In the last two decades, we have been involved in a program aiming to develop new simple procedures for the preparation of some new heterocyclic compounds of biological interest from laboratory available cheap starting materials [1–5].

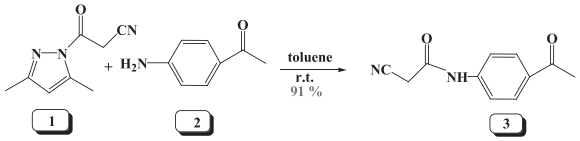
In the recent years, attention has been increasingly paid to the synthesis of novel mono-heterocyclic and bis-heterocyclic derivatives expected to exhibit various biological activities [6–14]. In the light of these data and in continuation of our program, we have recently reported the synthesis of some new bis-heterocyclic compounds of biological interest [15–17]. Because of the increasing demand on such compounds, it was decided to synthesize a new group of functionally substituted bis-chromenes and bis-thiazole derivatives. 4-Acetylcyanoacetanilide seemed a good precursor to fulfill our objective as a starting compound.

RESULTS AND DISCUSSION

The reaction of 3-(3,5-dimethyl-1 *H*-pyrazol-1-yl)-3-oxopropanenitrile **1** with 4-aminoacetophenone in refluxing toluene results in the displacement of the 3,5-dimethylpyrazole moiety from substrate **1** to give *N*-(4-acetyl-phenyl)-2-cyanoacetamide **3** (Scheme 1). The structure of the reaction product was confirmed on the basis of its spectral and analytical data. The IR spectrum of compound **3** showed intense absorption bands at $\nu_{stretch} = 3317$, 2257, 1710, and 1680 cm^{-1} due to NH, cyano group, and two carbonyl groups, respectively. The ^{1}H-NMR spectrum of **3** showed three singlet signals at $\delta = 2.6$, 3.95, and 10.6 ppm assignable to methyl, methylene, and amino NH protons, respectively beside two doublets (4H) of the aromatic protons. The mass spectrum of **3** showed a molecular ion peak at $m/z = 202$.

Grinding of compound **3** with the aromatic aldehydes **4a–d** in the presence of solid sodium hydroxide afforded

Scheme 1



the corresponding arylidene derivatives **6a–d** rather than chalcones **5a–d** (Scheme 2). The structure of isolated products **6a–d** was confirmed on the basis of their elemental analyses and spectroscopic data (IR, ^{1}H NMR, and MS). The IR spectrum of product **6b** taken as a typical example of the prepared series, showed absorption bands at $\nu_{stretch} = 3328$, 2218, 1705, and 1685 cm^{-1} corresponding to NH, CN, and CO groups, respectively. The ^{1}H-NMR spectrum of **6b** revealed the presence of two singlet signals assigned to the methyl and methoxy protons at $\delta = 2.60$ and 3.87 ppm, respectively. In addition, two singlet signals appeared at $\delta = 8.25$ and 10.57 ppm assigned for vinylic and NH protons. The mass spectrum together with the elemental analyses is in agreement with the proposed structure **6b** (Experimental and Scheme 2).

On the other hand, grinding of **3** with *o*-hydroxybenzaldehyde derivatives **7a–c** in presence of solid sodium hydroxide afforded yellow solid products of melting point above 300°C. The structure of these isolated products **9a–c** was established based on their elemental analyses and spectral data. For example, the IR spectra of the isolated products did not reveal absorption band near $\nu_{stretch} \approx 2200$ cm^{-1} assignable to cyano group and instead showed an absorption band near $\nu_{max} \approx 3290$ cm^{-1} attributable to NH groups. The ^{1}H-NMR spectra of the isolated products revealed a D_2O-exchangeable signal at $\delta \sim 10.15$ due to NH beside the other expected signals. The mass spectra together with the elemental analyses are in agreement with structures **9a–c** (Scheme 3).

Treatment of compound **3** with cyanoacetohydrazide **10** in refluxing dioxane afforded compound **11** (Scheme 4). The IR spectrum of compound **11** showed absorption bands at $\nu_{stretch} = 3325$, 3185, 2267, and 1674 cm^{-1} due to NH, CN, and the amide carbonyl groups, respectively. The ^{1}H-NMR spectrum of **11** showed singlet signals at $\delta = 2.23$, 3.91, 4.22, 10.41, and 10.97 ppm due to methyl, two methylene, and two NH protons, respectively, beside to the expected signals for aromatic protons. The mass spectrum of **11** showed a molecular ion peak at $m/z = 283$.

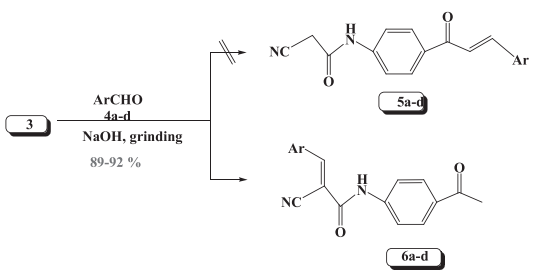
Refluxing compounds **11** with various aromatic aldehydes **4a–d** in 1:2 molar ratios in absolute ethanol containing few drops of piperidine gave the corresponding di-arylidene derivatives **12a–d** (Scheme 5). The structure of the isolated products **12a–d** was established based on their elemental analyses and spectral data. Thus, IR spectrum of the isolated product **12b** (for example) showed absorption band at $\nu_{stretch} = 2200$ cm^{-1} assignable to the cyano groups and an absorption band at $\nu_{stretch} = 3381$ cm^{-1} attributable to the NH group. Its ^{1}H-NMR spectrum revealed two singlet signals at $\delta = 2.34$ and 3.88 ppm due to the methyl and methoxy protons and other two singlets signals at $\delta = 8.16$ and 8.25 ppm due to the vinylic protons, respectively, in addition to D_2O-exchangeable signals at $\delta = 10.39$ and 11.0 ppm assignable to the amide protons, beside to the other expected signals for the aromatic protons. The mass spectra together with the elemental analyses are in agreement with structures **12**.

On the other hand, condensation of **11** with twofold excess of *o*-hydroxybenzaldehydes **7a–c** in absolute ethanol catalyzed by few drops of piperidine gave the colored products **13a–c** (Scheme 6). The structure of the isolated products was established on their elemental analyses and spectral data. For example, the IR spectrum of the isolated product **13a** showed absorption bands at $\nu_{stretch} = 3436$–3316, 1680, and 1659 cm^{-1} attributed to the NH and CO groups. Its ^{1}H-NMR spectrum revealed three D_2O-exchangeable signals at $\delta = 8.59$ (1H), 9.23 (1H), and 12.93 (2H) ppm attributable to the NH groups, in addition the other expected signals. The mass spectra together with the elemental analyses are in agreement with the proposed structures **13a–c**.

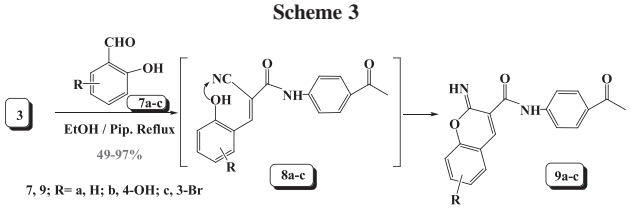
Compound **11** undergoes the coupling reaction with aryldiazonium chlorides **14a–d** (twofold excess) to afford the corresponding di-arylhydrazono derivatives **15a–d** (Scheme 7). The elemental analyses and spectral data of the products **15a–d** are in full agreement with their proposed structures (cf. Experimental).

The reaction of compound **11** with phenyl isothiocyanate in DMF in presence of KOH followed by the addition of the

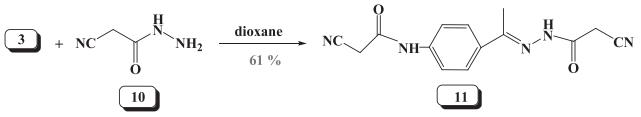
Scheme 2



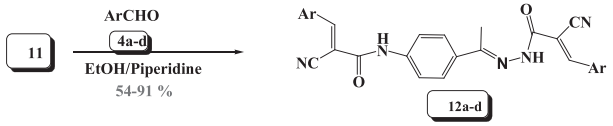
Scheme 3



Scheme 4

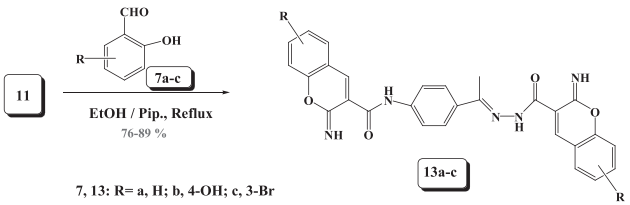


Scheme 5



4, 12: Ar=a, C_6H_5; b, 4-$MeOC_6H_4$; c, 4-ClC_6H_4; d, 2-Thienyl

Scheme 6



7, 13: R= a, H; b, 4-OH; c, 3-Br

phenacyl bromides **17a–c** to the reaction mixture led to the di-thiazole derivatives **18a–c** (Scheme 8). The analytical and spectral data for compounds **18a–c** are in full agreement with their proposed structures (cf. Experimental).

EXPERIMENTAL

Melting points were determined on an electrothermal (9100) apparatus (Kleinfeld, Gehrden, Germany) and are uncorrected. IR spectra were recorded as KBr pellets on a Nicolet 205 spectrophotometer (Nicolet, Madison, WI, USA). The ^{1}H-NMR spectra were taken on a Varian Gemini 300 MHz spectrometer (Varian Inc., Palo Alto, CA, USA) in DMSO-d_6 using TMS as internal standard, and chemical shifts are expressed in δ (ppm) values. Mass spectra were taken on a Shimadzu GCMS-GB 1000 PX (Shimadzu, Kyoto, Japan; 70 eV). Elemental analyses and spectral measurements were carried out by the microanalytical center at Cairo University and the analytical laboratory of the institute of organic chemistry, Technical University of Dresden, Germany. The starting compound **1** was prepared according to the reported literature [18].

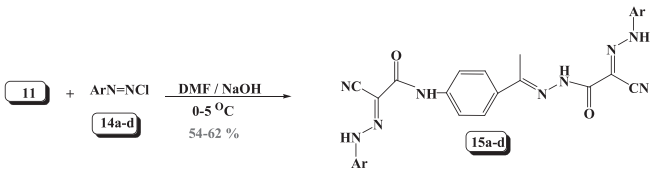
Synthesis of *N*-(4-acetylphenyl)-2-cyanoacetamide 3. To a hot solution of 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-oxopropanenitrile **1** (0.01 mol) in dry toluene (10 mL) was added 4-aminoacetophene (0.01 mol). The reaction mixture was refluxed until precipitation then left to cool. The solid precipitate so formed was collected by filtration and recrystallized from ethanol–dioxane mixture (1:1) as pale brown crystals, yield (91%), mp 225°C; $\nu_{stretch}$/cm^{-1} (KBr) 3317 (NH), 2257 (CN), 1710 and 1680 (CO); δ_H = 2.62 (s, 3H, CH_3), 3.95 (s, 2H, CH_2), 7.68–7.70 (dd, 2H, *J* = 1.8, 2.4 Hz, Ar), 7.93–7.95 (dd, 2H, *J* = 1,8, 2.4 Hz, Ar), 10.61 (s, 1H, NH). MS: *m*/*z* = 202 (27.9%), 190 (33.5%), 136 (40.7%), 69 (100%), 55 (63.5%). *Anal*. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.52; H, 5.1; N, 14.13%.

Synthesis of compounds 6a–d. A mixture of *N*-(4-acetyl-phenyl)-2-cyanoacetamide **3** (0.01 mol) and sodium hydroxide (0.01 mol) was ground in a mortar till complete mixing then the aromatic aldehyde **4a–d** were added with grinding for 24 hr. The reaction mixture was poured onto ice–water mixture acidified with concentrated hydrochloric acid. The solid products were collected by filtration, washed with water, and recrystallized from an ethanol–dioxane mixture (1:1).

***N*-(4-acetylphenyl)-2-cyano-3-phenylprop-2-enamide 6a**. Yellow crystals, yield (92%), mp 210°C; $\nu_{stretch}$/cm^{-1} (KBr) 3318 (NH), 2240 (CN), 1691 and 1580 (CO); δ_H = 2.56 (s, 3H, CH_3), 7.48-8.01 (m, 9H, Ar), 8.33 (s, 1H, CH), 10.74 (s, 1H, NH). *Anal*. Calcd for $C_{18}H_{14}N_2O_2$ (290.32): C, 74.47; H, 4.86; N, 9.65. Found: C, 74.66; H, 5.06; N, 9.89%.

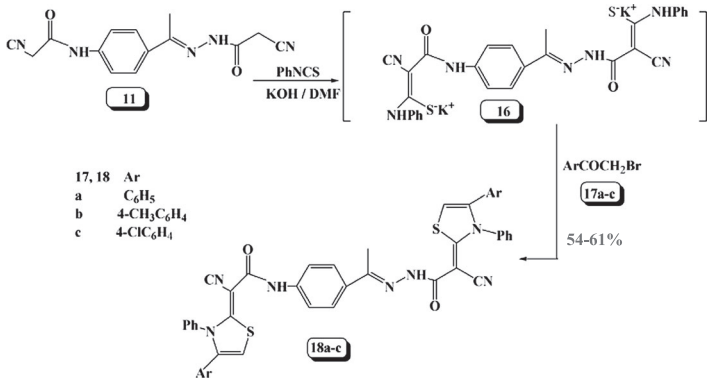
***N*-(4-acetylphenyl)-2-cyano-3-(4-methoxyphenyl)prop-2-enamide 6b**. Yellow crystals, yield (90%), mp 240°C; $\nu_{stretch}$/cm^{-1} (KBr) 3328 (NH), 2218 (CN), 1705 and

Scheme 7



14, 15 Ar= a, C_6H_5; b, 4-$CH_3C_6H_4$; c, 4-$CH_3OC_6H_4$; d, 4-ClC_6H_4

Scheme 8



1685 (CO); $\delta_H = 2.60$ (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 7.16–8.05 (m, 8H, Ar), 8.25 (s, 1H, CH), 10.57 (s, 1H, NH). *Anal*. Calcd for $C_{19}H_{16}N_2O_3$ (320.34): C, 71.24; H, 5.03; N, 8.74. Found: C, 71.45; H, 5.17; N, 9.05%.

N-(4-acetylphenyl)-3-(4-chlorophenyl)2-cyanoprop-2-enamide 6c. Whitish brown crystals, yield (91%), mp 254°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3330 (NH), 2260 (CN), 1710 and 1660 (CO); $\delta_H = 2.50$ (s, 3H, CH_3), 7.54–7.57 (dd, 2H, $J = 3.9$, 4.8 Hz, Ar), 7.66–7.69 (dd, 2H, $J = 3.9$, 4.8 Hz, Ar), 7.91–7.96 (m, 4H, Ar), 8.0 (s, 1H, CH), 10.61 (s, 1H, NH). *Anal*. Calcd for $C_{18}H_{13}ClN_2O_2$ (324.76): C, 66.57; H, 4.03; Cl, 10.92; N, 8.63. Found: C, 66.75; H, 4.21; Cl, 11.09; N, 8.87%.

N-(4-acetylphenyl)-2-cyano-3-(thiophen-2-yl)prop-2-enamide 6d. Brown crystals, yield (89%), mp 226°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3320 (NH), 2246 (CN), 1695 and 1650 (CO); $\delta_H = 2.53$ (s, 3H, CH_3), 7.05–7.83 (m, 7H, Ar), 8.91 (s, 1H, CH), 10.41 (s, 1H, NH). *Anal*. Calcd for $C_{16}H_{12}N_2O_2S$ (296.34): C, 64.85; H, 4.08; N, 9.45; S, 10.82. Found: C, 65.03; H, 4.28; N, 9.73; S, 11.12%.

Synthesis of compounds 9a–c. A mixture of compound **3** (0.01 mol) and sodium hydroxide (0.01 mol) was ground in a mortar till complete mixing, then the *o*-hydroxybenzaldehyde derivatives **7a–c** were added with grinding for 24 hr. Finally, the reaction mixture was poured onto ice–water mixture acidified with concentrated hydrochloric acid. The solid product was collected by filtration, washed with water and recrystallized from dimethylformamide (DMF).

N-(4-Acetylphenyl)-2-imino-2H-chromene-3-carboxamide 9a. Brown crystals, yield (49%), mp > 300°C; $\nu_{stretch.}/cm^{-1}$ (KBr) 3190 (NH), 1702 and 1661 (CO); $\delta_H = 3.20$ (s, 3H, CH_3), 6.78–7.98 (m, 8H, Ar), 8.0 (s, 1H, CH), 8.90 (s, 1H, NH), 10.90 (s, 1H, NH). *Anal*. Calcd for $C_{18}H_{14}N_2O_3$ (306.32): C, 70.58; H, 4.61; N, 9.15. Found: C, 70.76; H, 4.81; N, 9.43%.

N-(4-Acetylphenyl)-7-hydroxy-2-imino-2H-chromene-3-carboxamide 9b. Brown crystals, yield (67%), mp > 300°C; $\nu_{stretch.}/cm^{-1}$ (KBr) 3439 (OH), 3290 (NH), 1697 and 1653 (CO); $\delta_H = 3.28$ (s, 3H, CH_3), 6.66–8.22 (m, 7H, Ar), 8.0 (s, 1H, CH), 9.54 (s, 1H, NH), 10.21 (s, 1H, NH); 11.50 (s, 1H, OH). *Anal*. Calcd for $C_{18}H_{14}N_2O_4$ (322.31): C, 67.07; H, 4.38; N, 8.69. Found: C, 67.26; H, 4.56; N, 8.42%.

N-(4-Acetylphenyl)-8-bromo-2-imino-2H-chromene-3-carboxamide 9c. Yellowish brown crystals, yield (97%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3200 (NH), 1705 and 1662 (CO); $\delta_H = 3.25$ (s, 3H, CH_3), 6.81–8.06 (m, 7H, Ar), 8.23 (s, 1H, CH), 9.52 (s, 1H, NH), 10.22 (s, 1H, NH). *Anal*. Calcd for $C_{18}H_{13}BrN_2O_3$ (385.21): C, 56.12; H, 3.40; Br, 20.74; N, 7.27. Found: C, 56.32; H, 3.59; Br, 20.91; N, 7.51%.

Synthesis of 2-cyano-*N*-(4-(1-(2-(2-cyanoacetyl) hydrazinylidene)ethyl)-phenyl)-acetamide 11. Compound **3** (0.01 mol) was refluxed with cyanoacetic acid hydrazide (0.01 mol) in dry dioxane for 7 h. The solid so formed was collected by filtration, washed with ethanol, and recrystallized from ethanol–dioxane mixture (1:1) as pale brown crystals, yield (61%), mp 250°C; $\nu_{stretch.}/cm^{-1}$ (KBr) 3326 and 3185 (NH), 2268 (CN), 1674 and 1600 (CO); $\delta_H = 2.23$ (s, 3H, CH_3), 3.91 (s, 2H, CH_2), 4.22 (s, 2H, CH_2), 7.57–7.81 (dd, 4H, $J = 8.4$, 8.7 Hz, Ar), 10.41 (s, 1H, NH), 10.97 (s, 1H, NH). MS: $m/z = 283$ (M^+, 64.5%), 243 (50.4%), 216 (47.5%), 215 (55.3%), 186 (33.3%), 174 (48.2%), 146 (42.6%), 119 (69.5%), 118 (84.4%), 107 (34.8%), 91 (79.4%), 90 (42.6%), 68 (100%), 65 (87.9%), 64 (49.6%), 63 (44.0%). *Anal*. Calcd for $C_{14}H_{13}N_5O_2$: C, 59.36; H, 4.63; N, 24.72. Found: C, 59.55; H, 4.80; N, 24.96%.

Synthesis of compounds 12a–d. A mixture of compound **11** (0.01 mol) with the aromatic aldehydes **4a–d** (0.02 mol) was refluxed in ethanol in presence of few drops of piperidine for 2 h. The solid so formed was collected by filtration, washed with ethanol, and recrystallized from ethanol–dioxane mixture.

2-Cyano-N-(4-{1-[(2-cyano-3-phenyl-acryloyl)-hydrazono]-ethyl}-phenyl)-3-phenylacrylamide 12a. Yellow crystals, yield (82%), mp 235°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3355 (NH), 2208 (CN), 1678 and 1598 (CO); $\delta_H = 2.29$ (s, 3H, CH_3), 7.59–8.02 (m, 15H, Ar and CH), 8.23 (s, 1H, CH), 8.29

(s, 1H, NH), 10.55 (s, 1H, NH). MS: $m/z = 459$ (M^+, 11.1%), 371 (17%), 370 (10.1%), 303 (15%), 274 (10.4%), 156 (100%), 155 (37.8%), 127 (10.8%), 128 (92.3%), 102 (28.8%), 91 (24.6%), 77 (52.7%). *Anal*. Calcd for $C_{28}H_{21}N_5O_2$: C, 73.19; H, 4.61; N, 15.24. Found: C, 73.37; H, 4.79; N, 15.50%.

2-Cyano-N-[4-(1-{[2-cyano-3-(4-methoxy-phenyl)-acryloyl]-hydrazono}-ethyl)-phenyl]-3-(4-methoxy-phenyl)acrylamide 12b. Yellow crystals, yield (91%), mp 268°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3381 (NH), 2201 (CN), 1687 and 1580 (CO); $\delta_H = 2.34$ (s, 3H, CH_3), 3.88 (s, 6H, $2OCH_3$), 7.15 (s, 1H, NH), 7.19–8.07 (m, 12H, Ar), 8.16 (s, 1H, CH), 8.25 (s, 1H, CH), 10.42 (s, 1H, NH). MS: $m/z = 519$ (M^+, 17.2%), 518 (M^+-1; 20.7%), 504 (24.1%), 392 (20.7%), 286 (55.2%), 338 (24.1%), 243 (20.7%), 188 (20.7%), 186 (100%), 184 (44.8%), 158 (51.7%), 147 (34.5%), 128 (27.6%), 98 (34.5%), 96 (37.9%). *Anal*. Calcd for $C_{30}H_{25}N_5O_4$: C, 69.35; H, 4.85; N, 13.48. Found: C, 69.53; H, 5.04; N, 13.74%.

3-(4-Chloro-phenyl)-N-[4-(1-{[3-(4-chloro-phenyl)-2-cyano-acryloyl]-hydrazono}-ethyl)-phenyl]-2-cyanoacrylamide 12c. Yellow crystals, yield (54%), mp 273°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3374 (NH), 2202 (CN), 1682 and 1573 (CO); $\delta_H = 2.32$ (s, 3H, CH_3), 7.23 (s, 1H, CH), 7.46–8.01 (m, 12H, Ar), 8.20 (s, 1H, CH), 8.34 (s, 1H, NH), 10.62 (s, 1H, NH). *Anal*. Calcd for $C_{28}H_{19}Cl_2N_5O_2$ (528.39): C, 63.65; H, 3.62; Cl, 13.42; N, 13.25. Found: C, 63.83; H, 3.81; Cl, 13.61; N, 13.51%.

2-Cyano-N-(4-{1-[(2-cyano-3-thiophen-2-yl-acryloyl)-hydrazono]-ethyl}-phenyl)-3-thiophen-2-yl-acrylamide 12d. Yellowish green crystals, yield (70%), mp 253°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3376 (NH), 2210 (CN), 1698 and 1584 (CO); $\delta_H = 2.27$ (s, 3H, CH_3), 7.32 (s, 1H, CH), 7.51–7.82 (m, 10H, Ar), 8.35 (s, 1H, CH), 8.51 (s, 1H, NH), 10.73 (s, 1H, NH). *Anal*. Calcd for $C_{24}H_{17}N_5O_2S_2$ (471.55): C, 61.13; H, 3.63; N, 14.85; S, 13.60. Found: C, 61.31; H, 3.81; N, 15.09; S, 13.94%.

Synthesis of compounds 13a–c. A mixture of compound **11** (0.01 mol) with the *o*-hydroxybenzaldehyde derivatives **7a–c** (0.02 mol) was refluxed in ethanol in presence of few drops piperidine for 6 h. The solid products so formed were collected by filtration, washed with ethanol, and recrystallized from dimethylformamide (DMF).

2-Imino-N-(4-(1-(2-(2-imino-2H-chromene-3-carbonyl) hydrazono)-ethyl) phenyl)-2H-chromene-3-carboxamide 13a. Yellow crystals, yield (89%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3436–3316 (NH), 1680 and 1659 (CO); $\delta_H = 3.29$ (s, 3H, CH_3), 7.26–7.86 (m, 12H, Ar), 8.55 (s, 2H, 2CH), 8.59 (s, 1H, NH), 9.23 (s, 1H, NH), 12.93 (s, 2H, 2NH),. *Anal*. Calcd for $C_{28}H_{21}N_5O_4$ (491.50): C, 68.42; H, 4.31; N, 14.25. Found: C, 68.62; H, 4.50; N, 14.51%.

7-Hydroxy-N-(4-(1-(2-(7-hydroxy-2-imino-2H-chromene-3-carbonyl)-hydrazono)-ethyl)phenyl)-2-imino-2H-chromene-3-carboxamide 13b. Yellow crystals, yield (83%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3423 (OH), 3320–3184 (NH), 1673 and 1595 (CO); $\delta_H = 3.30$ (s, 3H, CH_3), 6.60 (s, 2H, OH), 6.74 (s, 1H, CH), 7.57–7.89 (m, 10H, Ar), 8.48 (s, 1H, CH), 8.50 (s, 1H, NH), 9.03 (s,1H, NH), 10.43 (s, 1H, NH), 13.52 (s, 1H, NH). *Anal*. Calcd for $C_{28}H_{21}N_5O_6$ (523.50): C, 64.24; H, 4.04; N, 13.38. Found: C, 64.24; H, 4.16; N, 13.66%.

8-bromo-N-(4-(1-(2-(8-bromo-2-imino-2H-chromene-3-carbonyl)-hydrazono)-ethyl)-phenyl)-2-imino-2H-chromene-3-carboxamide 13c. Yellow crystals, yield (76%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3410–3315 (NH), 1681 and 1660 (CO); $\delta_H = 3.29$ (s, 3H, CH_3), 7.08–7.97 (m, 11H, Ar and CH), 8.50 (s, 1H, CH), 8.80 (s, 1H, NH), 9.50 (s, 1H, NH), 10.50 (s, 1H, NH), 13.44 (s, 1H, NH). *Anal*. Calcd for $C_{28}H_{19}Br_2N_5O_4$ (649.29): C, 51.80; H, 2.95; Br, 24.61; N, 10.79. Found: C, 51.61; H, 3.13; Br, 24.91; N, 11.04%.

Synthesis of 2-(2-(1-(4-(2-cyano-2-(2-arylhydrazono)-acetamido)-phenyl)-ethylidene)-hydrazinyl)-2-oxo-*N*'-arylacetohydrazonoyl cyanides 15a–d: (General procedure). To a cold solution of compound **11** (0.01 mol), dissolved in the least amount of pyridine (10 ml) were added dropwise at 0–5°C the aryldiazonium salts **14a–d** (0.02 mol). The solid products so formed were collected by filtration and recrystallized from dioxane–ethanol mixture.

2-Cyano-N-[4-(1-{[2-cyano-2-(phenyl-hydrazono)-acetyl]-hydrazono}-ethyl)-phenyl]-2-(phenyl-hydrazono)-acetamide 15a. Brown crystals, yield (58%), mp 280°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3350–3200 (NH), 2250 (CN), 1678 (CO); $\delta_H = 2.32$ (s, 3H, CH_3), 6.81–7.35 (m, 12H, Ar and 2NH), 7.68–7.81 (m, 4H, Ar), 10.25 (s, 1H, NH), 10.94 (s, 1H, NH). *Anal*. Calcd for $C_{26}H_{21}N_9O_2$ (491.50): C, 63.54; H, 4.31; N, 26.65. Found: C, 63.72; H, 4.49; N, 25.89%.

2-Cyano-N-[4-(1-{[2-cyano-2-(4-methylphenyl-hydrazono)-acetyl]-hydrazono}-ethyl)-phenyl]-2-(4-methylphenyl-hydrazono)-acetamide 15b. Brown crystals, yield (58%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3361–3198 (NH), 2258 (CN), 1722 (CO); $\delta_H = 2.31$ (s, 3H, CH_3), 2.42 (s, 6H, $2CH_3$), 7.03–7.46 (m, 10H, Ar and 2NH), 7.51–8.13 (m, 4H, Ar), 10.30 (s, 1H, NH), 10.96 (s, 1H, NH). *Anal*. Calcd for $C_{28}H_{25}N_9O_2$ (51956): C, 64.73; H, 4.85; N, 24.26. Found: C, 64.91; H, 5.05; N, 24.55%.

2-Cyano-N-[4-(1-{[2-cyano-2-(4-methoxyphenyl-hydrazono)-acetyl]-hydrazono}-ethyl)-phenyl]-2-(4-methoxyphenyl-hydrazono)-acetamide 15c. Brown crystals, yield (54%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3351–3228 (NH), 2261 (CN), 1730 (CO); $\delta_H = 2.34$ (s, 3H, CH_3), 3.87 (s, 6H, $2OCH_3$), 7.11–7.53 (m, 10H, Ar and 2NH), 7.71–8.33 (m, 4H, Ar), 10.38 (s, 1H, NH), 11.03 (s, 1H, NH). *Anal*. Calcd for $C_{28}H_{25}N_9O_4$ (551.56): C, 60.97; H, 4.57; N, 22.86. Found: C, 60.79; H, 4.76; N, 22.61%.

2-[(4-Chloro-phenyl)-hydrazono]-N-{4-[1-({2-[(4-chloro-phenyl)-hydrazonpo]-2-cyanoacetyl}-ydrazono)-ethyl]-phenyl}-2-cyanoacetamide 15d. Brown crystals, yield (62%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3348–3210 (NH), 2253

(CN), 1728 (CO); $\delta_H = 2.33$ (s, 3H, CH_3), 7.08–7.49 (m, 10H, Ar and 2NH), 7.68–8.21 (m, 4H, Ar), 10.35 (s, 1H, NH), 10.98 (s, 1H, NH). *Anal*. Calcd for $C_{26}H_{19}Cl_2N_9O_2$ (560.39): C, 55.72; H, 3.42; Cl, 12.65; N, 22.49. Found: C, 55.91; H, 3.22; Cl, 12.86; N, 22.74%.

Synthesis of the compounds 18a–c. Equimolar amounts of compound **11** (0.01 mol) and potassium hydroxide (0.02 mol) in dimethylformamide (DMF; 10 ml) were stirred at room temperature till complete dissolution of potassium hydroxide followed by the addition of phenyl isothiocyanate (0.02 mol) with stirring for 1 h. Finally, phenacyl bromides **17a–c** (0.02 mol) were added with stirring for more 1 h. The solid products so formed were collected by filtration and recrystallized from dioxane–ethanol mixture (1:1).

2-Cyano-N-[4-(1-{[2-cyano-2-(3,4-diphenyl-3H-thiazol-2-ylidene)-acetyl]-hydrazono}-ethyl)-phenyl]-2-(3,4-diphenyl-3H-thiazol-2-ylidene)-acetamide 18a. Brown crystals, yield (54%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3315–3208 (NH), 2220 (CN), 1630 (CO); $\delta_H = 2.32$ (s, 3H, CH_3), 6.73 (s, 1H, CH), 6.81–7.71 (m, 21H, Ar and CH), 7.75–7.81 (m, 4H, Ar), 10.18 (s, 1H, NH), 10.8 (s, 1H, NH). *Anal*. Calcd for $C_{44}H_{31}N_7O_2S_2$ (753.89): C, 70.10; H, 4.14; N, 13.01; S, 8.51. Found: C, 70.30; H, 4.32; N, 13.25; S, 8.75%.

2-Cyano-N-[4-(1-{[2-cyano-2-(3-phenyl-4-(4-methylphenyl) thiazol-2(3H)-ylidene)-acetyl]-hydrazono}-ethyl)phenyl]-2-(3-phenyl-4-(4-methylphenyl)-thiazol-2(3H)-ylidene)-acetamide 18b. Brown crystals, yield (61%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3338–3222 (NH), 2238 (CN), 1723 (CO); $\delta_H = 2.29$ (s, 3H, CH_3), 2.38 (s, 6H, $2CH_3$), 7.012 (s, 1H, CH), 7.24–7.87 (m, 19H, Ar and CH), 8.03–8.79 (m, 4H, Ar), 10.45 (s, 1H, NH), 10.91 (s, 1H, NH). *Anal*. Calcd for $C_{46}H_{35}N_7O_2S_2$ (781.95): C, 70.66; H, 4.51; N, 12.54; S, 8.20. Found: C, 70.84; H, 4.32; N, 12.78; S, 8.41%.

2-[4-(4-Chlorophenyl)-3-phenylthiazol-2(3H)-ylidene)-N-{4-[1-({2-[4-(4-chloro-phenyl)-3-phenylthiazol-2(3H)-ylidene]-2-cyanoacetyl}-hydrazono)-ethyl)phenyl)-2-cyanoacetamide 18c. Brown crystals, yield (59%), mp > 300°C; $\nu_{stretch}/cm^{-1}$ (KBr) 3321–3207 (NH), 2228 (CN), 1718 (CO); $\delta_H = 2.31$ (s, 3H, CH_3), 6.81 (s, 1H, CH), 6.87–7.93 (m, 19H, Ar and CH), 8.02–8.97 (m, 4H, Ar), 10.28 (s, 1H, NH), 10.87 (s, 1H, NH). *Anal*. Calcd for $C_{44}H_{29}Cl_2N_7O_2S_2$ (822.78): C, 64.23; H, 3.55; Cl, 8.62; N, 11.92; S, 7.79. Found: C, 64.41; H, 3.72; Cl, 8.82; N, 12.17; S, 8.01%.

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