Utility of cyano-*N*-(2-oxo-1,2-dihydroindol-3-ylidene)acetohydrazide in the synthesis of novel heterocycles

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Cyano-*N*-(2-oxo-1,2-dihydroindol-3-ylidene)acetohydrazide was prepared by condensation of isatin with cyanoacetohydrazide in refluxing 1,4-dioxane. Subsequent reaction with a variety of electrophilic and nucleophilic reagents afforded novel heterocyclic compounds and spirooxoindoles. The IR, ^{1}H NMR and mass spectra of all the synthesised compounds are discussed.

Keywords: isatin, spirooxoindoles, thiazole and coumarin derivatives

Isatins are synthetically versatile substrates that display diverse biological and pharmacological properties.[1–5] It is an endogenous compound and reported to possess a wide range of central nervous system activities.[6,7] It has been reported that several compounds containing an isatin moiety possess antibacterial, antifungal, anticonvulsant, anti-inflammatory and anti-HIV activities.[8,9] Among several commercially available substituted hydrazines, cyanoacetohydrazide is a versatile and convenient intermediate for the synthesis of wide variety of heterocyclic compounds.[10,11]

As a continuation of our efforts[12–20] to identify new candidates that may be of value in designing new, potent, selective and less toxic antimicrobial agents, we report here the synthesis of some new heterocycles incorporating an indole moiety starting from cyanoacetohydrazide and isatin.

Results and discussion

It was claimed that the reaction of isatin with cyanoacetohydrazide in the presence of catalytic amount of triethylamine at room temperature yielded the corresponding *C*-condensation product **1**.[21]

Such a reaction in refluxing 1,4-dioxane afforded the *N*-condensation product which identified as 2-cyano-*N*′-(2-oxo-1,2-dihydroindol-3-ylidene) acetohydrazide **2** (Scheme 1).

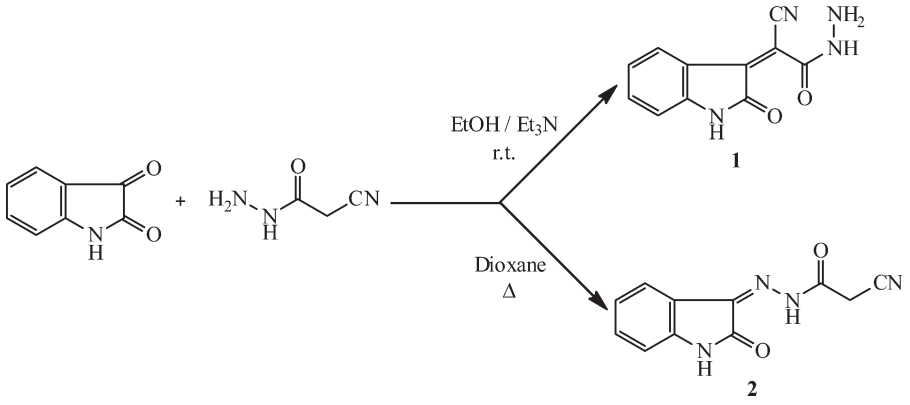
The structure of compound **2** was confirmed by IR, ^{1}H NMR, MS spectra and correct microanalysis (see Experimental). The mass spectrum showed the molecular ion at *m/z* 228 (12.8%).

Oxoindol-3-ylidene acetohydrazide **2** was expected to be a highly reactive compound. The carbonyl and cyano functions are suitably situated to enable reactions with common reagents to form a variety of heterocyclic compounds. Also, the active methylene of **2** can take part in condensation and substitution reactions. Thus, stirring **2** with salicylaldehyde (1:1 molar ratio) in 1,4-dioxane in the presence of a catalytic amount of piperidine at room temperature afforded an orange precipitate with molecular formula $C_{18}H_{11}N_3O_4$ (M = 333) which was identified as 2-oxo-*N*′-(2-oxoindolin-3-ylidene)-2*H*-chromene-3-carbohydrazide **3** (Scheme 2).

The structure **3** was substantiated from the correct analytical and spectroscopic data. The IR spectrum of **3** exhibited the stretching absorption bands for the NH group at 3151 cm^{-1} (br.), CO at 1736 and 1716 cm^{-1} and for the C=N group at 1620 cm^{-1} and was devoid of the stretching absorption band for nitrile group. The highest recorded peak in the mass spectrum of **3** at *m/z* 333 (1.97%) represents the molecular ion peak. The fragmentation pattern was in accord with the assigned structure (see Experimental).

The reaction of compound **2** with 1,3-diphenylpyrazole-4-carboxaldehyde in refluxing ethanol in the presence of aqueous potassium hydroxide (10%) afforded the condensation product **4**, the structure of which was confirmed from its spectroscopic data. Thus, ^{1}H NMR spectrum of **4** (DMSO-d_6) revealed the signals at δ 11.65 (br.s, 1H, NH, exchangeable with D_2O), 9.92 (s, 1H, NH, exchangeable with D_2O), 8.09 (s, 1H, olefinic proton) and 9.10–6.49 (m, 15H$_{arom.}$), which is in accord with the assigned structure. Moreover, the highest recorded peak at *m/z* 456 represents the radical cation [M-2]. Furthermore, the structure of **4** was chemically supported via hydrazinolysis in boiling *n-butanol* which yielded the pyrazole derivative **5** (Scheme 2).

The IR spectrum of **5** showed one stretching absorption band for the carbonyl group at 1705 cm^{-1} together with ν_{NH} at 3200, 3134 cm^{-1} and devoid of the stretching absorption band



Scheme 1

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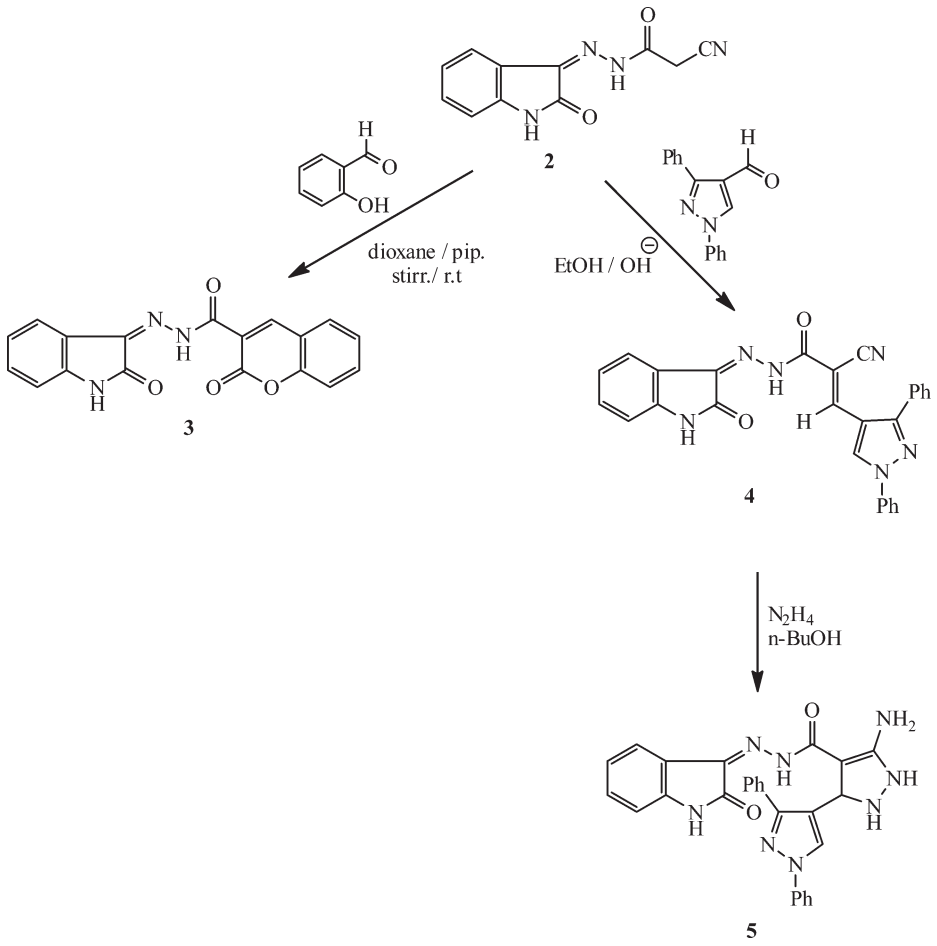


Scheme 2

for the nitrile group. The EI-MS fragmentation was consistent with the proposed structure and revealed the molecular ion peak at *m/z* 490 (23%) which upon loss of the isatin moiety, followed by hydrogen abstraction yielded the radical cation at *m/z* 346 (89.6%). The base peak at *m/z* 77 represents the phenyl cation.

The reactivity of the hydrazide **2** toward isothiocyanates was investigated. Thus, when compound **2** was allowed to react with phenyl isothiocyanate in the presence of potassium hydroxide in DMF at room temperature followed by *in situ* treatment with ethyl iodide, the novel ketene *N*,*S*-acetal **6** was obtained. Subsequent reaction of **6** with hydrazine hydrate in refluxing ethanol gave the sulfur free compound which was characterised as the amino pyrazole derivative **7** (Scheme 3).

The structure of **6** was established on the basis of its elemental analysis and spectral data. The mass spectrum revealed a molecular ion peak at *m/z* 391 (12.7%).

IR spectrum of the aminopyrazole derivative **7** was devoid of a $\nu_{C\equiv N}$ absorption and exhibited bands at 3358, 3250, 3158 cm^{-1} (NH, NH_2), 1685 cm^{-1} (C=O) and 1658 cm^{-1} (C=N). The mass spectrum showed a molecular ion peak at *m/z* 361 (35.5%) in agreement with its molecular formula $C_{18}H_{15}N_7O_2$.

Formation of the aminopyrazole derivative **7** is presumed to proceed via Michael addition of the hydrazinoamino group to the ethylenic bond side chain in **6** with elimination of the ethylthio group followed by intramolecular cyclisation at the cyano group (Scheme 4).

Upon stirring compound **2** with phenyl isothiocyanate in the presence of potassium hydroxide in DMF followed by addition of ethyl chloroacetate cycloalkylation occurred to afford the 1,3-thiazolidinone derivative **8** (Scheme 3).

The structure **8** was confirmed from the microanalytical and spectroscopic data. The IR spectrum of **8** displayed a ν_{NH} band (broad) centred at 3182 cm^{-1}, with $\nu_{C\equiv N}$ at 2205 cm^{-1}, ν_{CO} (thiazolidinone) at 1723 cm^{-1} and ν_{CO} (α,β-unsaturated amide) at 1680 cm^{-1}. The ^{1}H NMR spectrum (DMSO-d_6) exhibited signals characterstic for three types of protons, in agreement with the assigned structure. Furthermore, the mass spectrum revealed the molecular ion peak at *m/z* 406 (M+3, 35.7%).

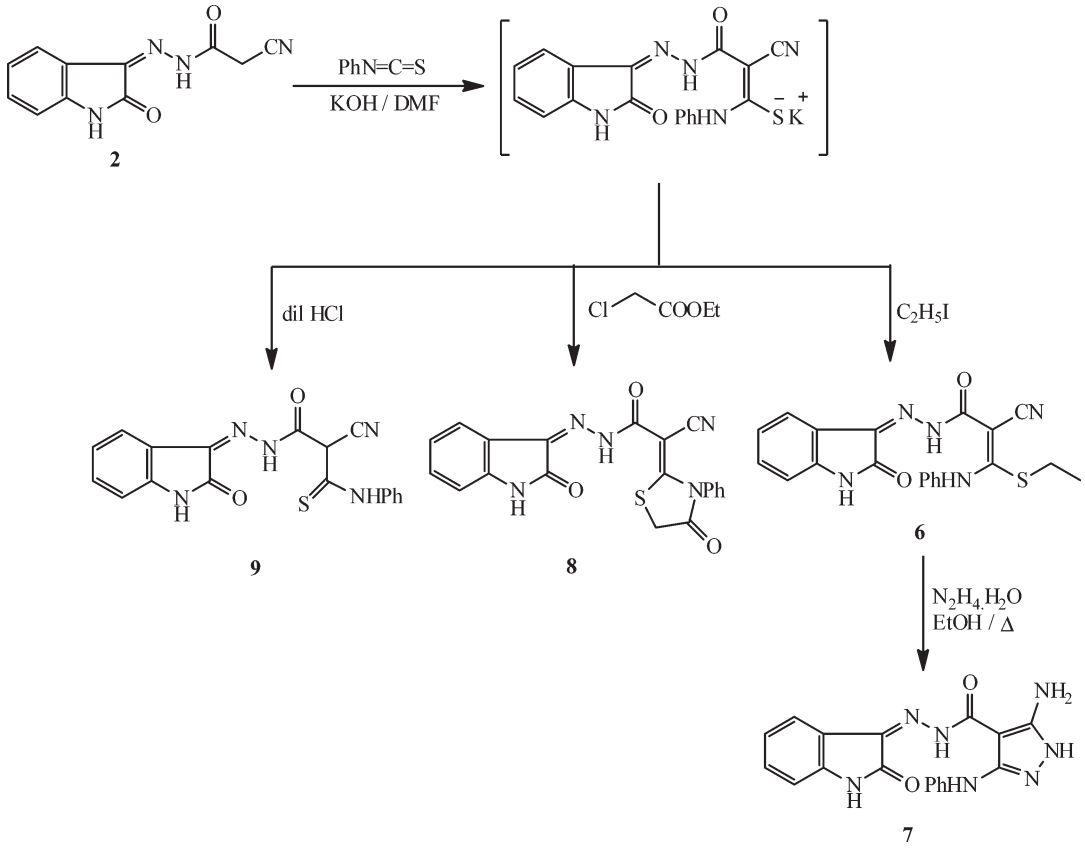
Compound **9** was obtained in good yield upon treatment of **2** with phenyl isothiocyanate in KOH/DMF followed by acidification with dilute HCl. The microanalytical and spectroscopic data were in agreement with the proposed structure **9**.

Treatment of compound **2** with elemental sulfur and phenyl isothiocyanate in refluxing ethanol in the presence of a catalytic amount of triethylamine afforded the 2-thioxothiazolidin-5-carbohydrazide **10** (Scheme 5). The structure **10** was substantiated from the microanalytical and spectroscopic data.

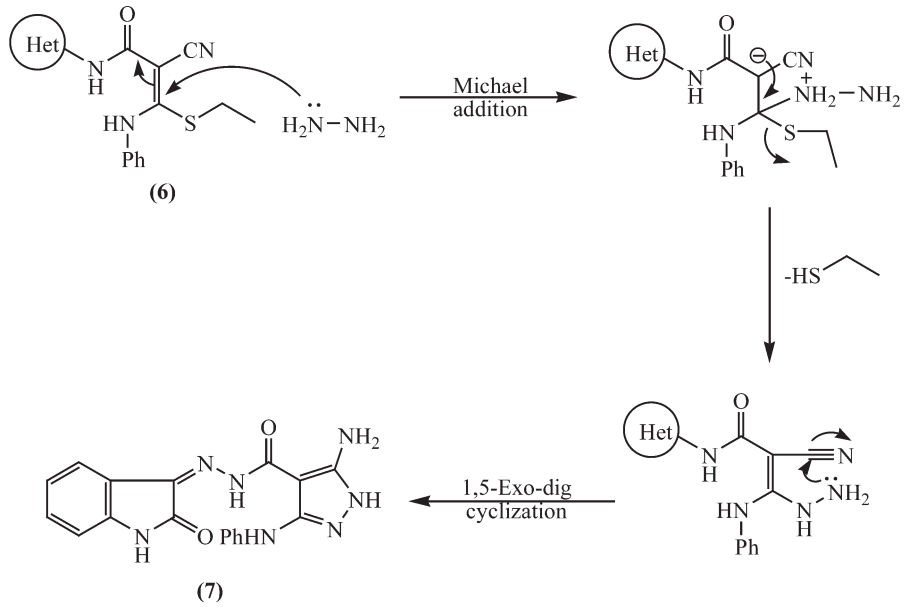
Refluxing compound **2** with 3,4-dimethoxycinnamonitrile in boiling 1,4-dioxane in the presence of triethylamine followed by acidification with dilute acetic acid afforded the 2′,5-dioxo-3,5-dihydro-1*H*-spiro{[1,2,4]triazolo[1,5-*a*]pyridine-2,3′-indoline}-6,8-dicarbonitrile **11**. The IR, ^{1}H NMR and mass spectra of **11** were in consistent with the assigned structure.

The reaction of **2** with an arylidenemalononitrile appeared to proceed via Michael addition to give the adduct **A** which undergoes two cyclisation processes and dehydrogenation to afford the spiro compound **11** (Scheme 6).

The reaction of compound **2** with nucleophilic reagents such as hydrazine, carbon nucleophiles and thioglycolic acid have been investigated. Thus, hydrazinolysis of **2** with hydrazine



Scheme 3

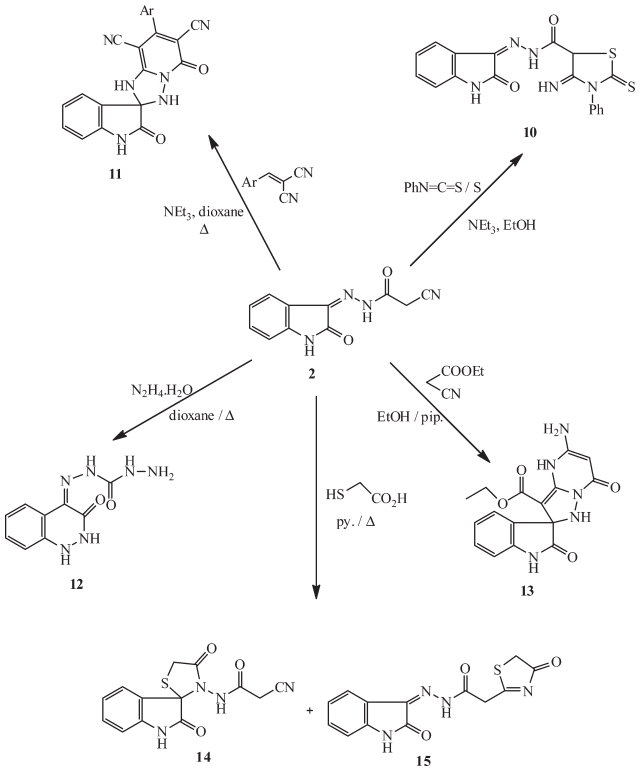


Scheme 4

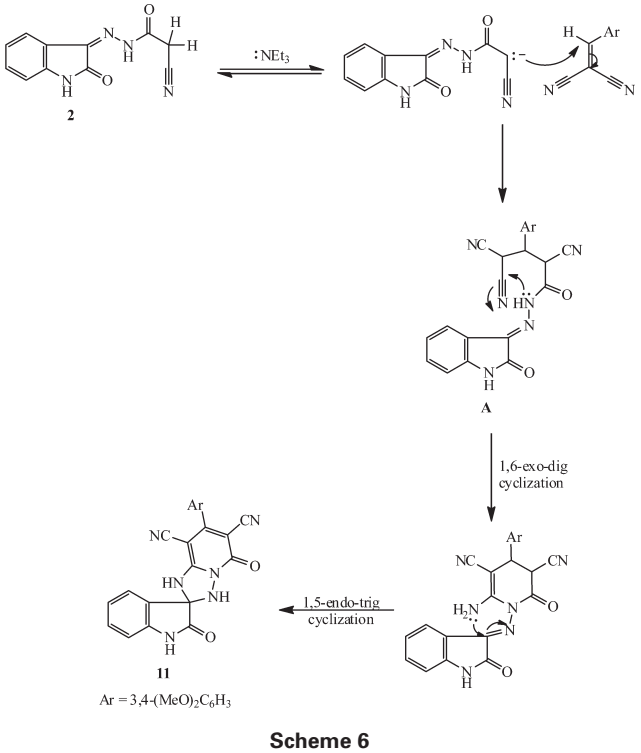
hydrate (80%) in boiling 1,4-dioxane furnished a compound with molecular formula $C_9H_{10}N_6O_2$ [M = 234 (33.3%)] which was identified using the spectral data as the cinnoline derivative **12** (Scheme 5). The evolution of ammonia during the course of reaction and the absence of the absorption band for the nitrile group in the IR spectrum suggests the following pathway (Scheme 7):

The reaction of **2** with the anion derived from ethyl cyanoacetate in the presence of piperidine in boiling ethanol afforded the spiropyrazolo[1,5-*a*]pyrimidine oxoindole derivative **13** (Scheme 5). The structure **13** was confirmed by the microanalytical and spectroscopic data. Thus, the IR spectrum of **13** displayed $\nu_{NH2,NH}$ at 3358, 3260, 3157 cm^{-1}, $\nu_{CO(ester)}$ at 1685 cm^{-1} (chelated H-bonding), ν_{CO} at 1658 cm^{-1} and was devoid of the stretching absorption band for the C≡N group. The mass spectrum of **13** showed the molecular ion peak at *m/z* 341 (46.7%).

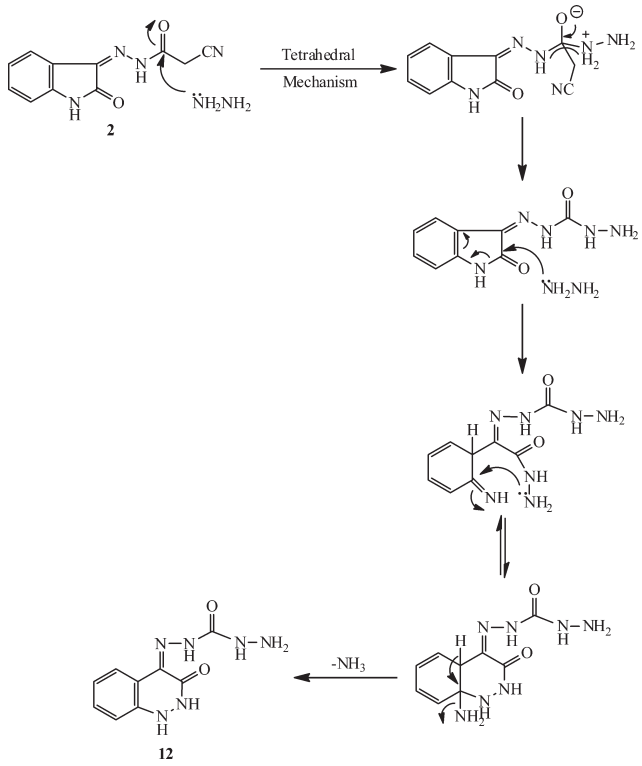
Furthermore, ^{1}H NMR spectrum (DMSO-d_6) revealed the presence of five protons attributable to 5NH at δ 10.65 (s, 1H, exchangeable with D_2O), 10.5 (s, 1H, exchangeable with D_2O),



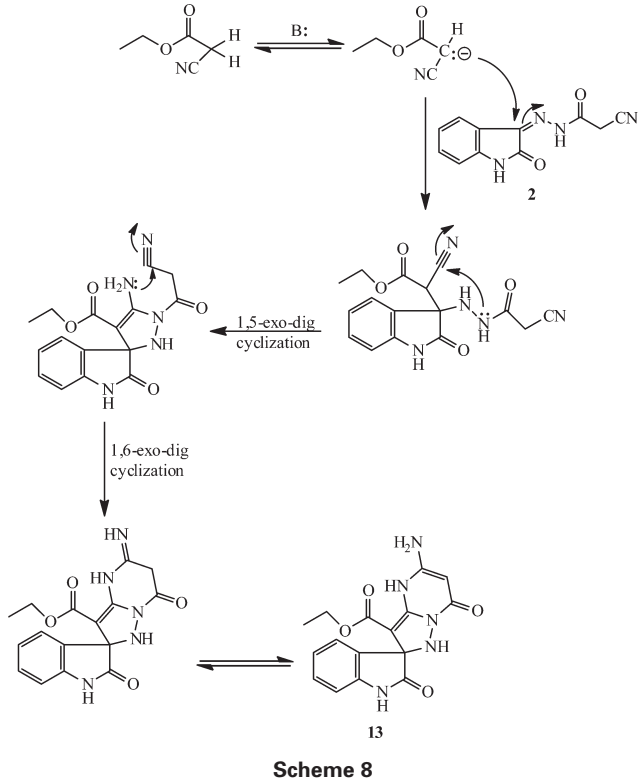
Scheme 5



Scheme 6



Scheme 7



Scheme 8

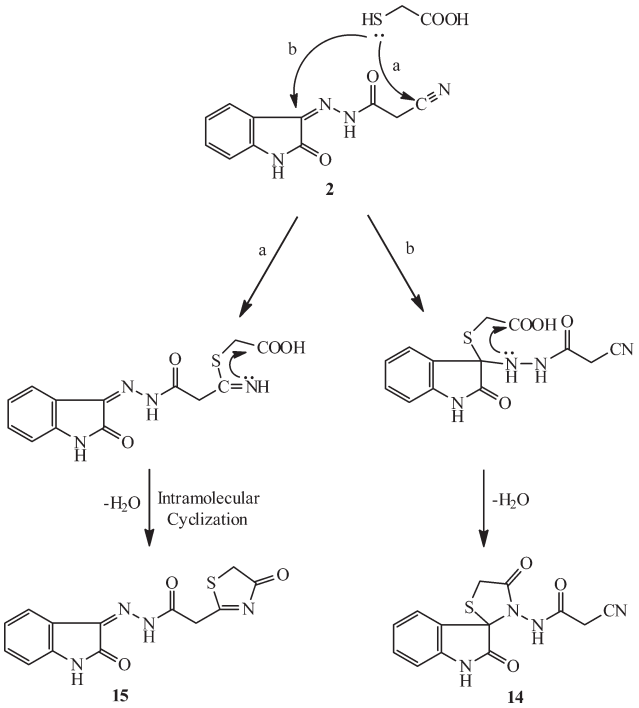
9.5–9.4 (d, 2H, exchangeable with D_2O), 8.7 (s, 1H, exchangeable with D_2O), 7.36–6.84 (m, $4H_{arom.}$), 4.27–4.20 (q, 2H, J = 6.5 Hz), 2.51 (s, 1H) and 1.057–1.005 (t, 3H, J = 6.5 Hz). The reaction can be rationalised as shown in Scheme 8.

The reaction of the hydrazide **2** with thioglycolic acid in refluxing pyridine afforded two isomeric products at (*m/z* 302) which were identified as **14** and **15**. The structure of compounds **14** and **15** were confirmed by microanalytical and spectroscopic data.

The formation of **14** and **15** from **2** is summarised in Scheme 9.

Experimental

Melting points are uncorrected and were measured using an electric melting point apparatus (G-K). The IR spectra were recorded on a Pye-Unicam SP1200 spectrophotometer using KBr discs. The ^{1}H NMR spectra were determined on a Varian GEMINI 300 MHz NMR spectrophotometer using $CDCl_3$ or DMSO-d_6 as solvent with TMS as



Scheme 9

an internal standard. The elemental analyses were carried out in the Faculty of Science, Ain Shams University. MS were recorded on Shimadzu GC-MS QP1000EX instrument in the Microanalytical Laboratory, Cairo University. The monitoring of the progress of all reactions was carried out by TLC.

*2-Cyano-*N′*-(2-oxo-1,2-dihydroindol-3-ylidene)acetohydrazide* (**2**): A mixture of isatin (1.47 g, 0.01 mol) and cyanoacetohydrazide (0.99 g, 0.01 mole) in 1,4-dioxane (20 mL) was warmed for 5 min. The yellow solid which separated after slow evaporation was collected by filtration and then recrystallised from 1,4-dioxane to give **2** as yellow crystals; m.p. 241–243 °C, yield 97%. IR (ν/cm^{-1}): 3262, 3211, 3135 (NH), 2259 (C≡N), 1735, 1701 (C=O), 1608 (C=N). MS *m/z* (%): 228 (M^{+}; 12.8), 160 (44.8), 132 (83.3), 104 (84.7), 77 (100). ^{1}H NMR (DMSO-d_6) δ (ppm): 11.62 (s, 1H, NH, exchangeable with D_2O), 10.8 (s, 1H, NH, exchangeable with D_2O), 8.08–6.8 (m, 4H$_{arom.}$), 4.32 (s, 2H, CH_2). Anal. Calcd for $C_{11}H_8N_4O_2$ (228.21): C, 57.89; H, 3.53; N, 24.55. Found: C, 57.87; H, 3.55; N, 24.52%.

*2-Oxo-*N′*-(2-oxoindolin-3-ylidene)-2*H*-chromene-3-carbohydrazide* (**3**): A mixture of **2** (1.0 g, 4.4 mmol) and salicylaldehyde (0.467 mL, 4.4 mmol) in 1,4-dioxane (20 mL) in the presence of piperidine (0.5 mL) was stirred at room temperature for 3 h. The reaction mixture was poured onto ice and acidified with dilute acetic acid. The precipitated solid was filtered off, washed several times with cold water and then recrystallised from toluene to give **3** as orange crystals; m.p. 218–220 °C, yield 65%. IR (ν/cm^{-1}): 3151 (br., NH), 1736, 1716 (C=O), 1620 (C=N). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.9 (s, 1H, NH, exchangeable with D_2O), 9.8 (s, 1H, NH, exchangeable with D_2O), 8.4–7.0 (m, 8H$_{arom.}$), 6.7 (s, 1H). MS *m/z* (%): 333 (M^{+}; 1.97), 265 (35.29), 237 (91.97), 145 (20.12), 18 (100), 91 (34.99), 90 (38.24), 565 (60.97). Anal. Calcd for $C_{18}H_{11}N_3O_4$ (333.3): C, 64.86; H, 3.33; N, 12.61. Found: C, 64.88; H, 3.20; N, 12.43%.

*2-Cyano-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)-*N′*-(2-oxoindolin-3-ylidene)acrylohydrazide* (**4**): To a solution of **2** (1.0 g, 4.4 mmol) in 10% ethanolic KOH (10 mL) and 1,3-diphenylpyrazole-4-carboxaldehyde (1.09 g, 4.4 mmol) was added. The reaction mixture was heated under reflux for 1 h and then allowed to cool. The precipitate that formed was collected by filtration, washed with ethanol, dried and recrystallised from EtOH–DMF (1:1) to give **4** as orange crystals; m.p. 292–293 °C, yield 97%. IR (ν/cm^{-1}): 3424 (br.), 3164 (w), 2206 (C≡N), 1701 (C=O). MS *m/z* (%): 456 (M-2; 4). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.45 (br.s, 1H, NH, exchangeable with D_2O), 9.92 (s, 1H, NH, exchangeable with D_2O), 8.09 (s, 1H, olefinic proton), 9.1–6.49 (m, 15H$_{arom.}$). Anal. Calcd for $C_{27}H_{18}N_6O_2$ (458.47): C, 70.73; H, 3.96; N, 18.33. Found: C, 70.70; H, 3.88; N, 18.15%.

*5-Amino-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)-*N′*-(2-oxoindolin-3-ylidene)-1*H*-pyrazole-4-carbohydrazide* (**5**): A mixture of **4** (1.0 g, 2.2 mmol) and hydrazine hydrate 80% (0.01 mol) in *n-butanol* (20 mL) was heated under reflux for 3 h. After evaporation of the solvent in *vacuo*, the solid obtained was collected by filtration and recrystallised from petroleum ether (b.p. 60–80 °C) to give **5** as buff crystals; m.p. 182–183 °C, yield 36%. IR (ν/cm^{-1}): 3200, 3134 (w) (NH), 1705 (C=O). MS *m/z* (%): 490 (M^{+}; 23), 346 (89.6), 77 (100). Anal. Calcd for $C_{27}H_{22}N_8O_2$ (490.52): C, 66.11; H, 4.52; N, 22.84. Found: C, 66.05; H, 4.35; N, 22.92.

*2-Cyano-3-(ethylthio)-*N′*-(2-oxoindolin-3-ylidene)-3-(phenylamino) acrylohydrazide* (**6**): To a stirred solution of potassium hydroxide (0.56 g, 0.01 mol) in *N,N*-dimethylformamide (20 mL) was added compound **2** (2.28 g, 0.01 mol). After the mixture was stirred for 30 min., phenyl isothiocyanate (1.2 mL, 0.01 mol) was added. Stirring was continued at room temperature for 12 h and then ethyl iodide (0.62 mL, 0.01 mol) was added and stirring was continued for additional 6 h. The separated product was filtered off, washed several times with cold water and recrystallised from toluene to give **6** as light green crystals; m.p. 248–249 °C, yield 48%. IR (ν/cm^{-1}): 3200, 3145 (NH), 2195 (C≡N), 1697 (C=O), 1640 (C=N). MS *m/z* (%): 391 (M^{+}; 12.7), 330 (70.2), 231 (43.3), 203 (64.7), 169 (38.6), 161 (58.1), 77 (100). ^{1}H NMR (DMSO-d_6) δ (ppm): 13.53 (s, 1H, NH, exchangeable with D_2O), 12.06 (s, 1H, NH, exchangeable with D_2O), 11.27 (s, 1H, NH, exchangeable with D_2O), 7.54–6.93 (m, 9H$_{arom.}$), 2.7–2.6 (q, 2H, *J* =7.2 Hz), 1.14–1.10 (t, 3H, *J* = 7.5 Hz). Anal. Calcd for $C_{20}H_{17}N_5O_2S$ (391.45): C, 61.37; H, 4.38; N, 17.89; S, 8.19. Found: C, 61.25; H, 4.14; N, 17.67; S, 8.22%.

*5-Amino-*N′*-(2-oxoindolin-3-ylidene)-3-(phenylamino)-1*H*-pyrazole-4-carbohydrazide* (**7**): A mixture of **6** (1.0 g, 2.56 mmol) and hydrazine hydrate 80% (5 mmol) in ethanol (20 mL) was heated under reflux for 4 h. After evaporation of the solvent *in vacuo*, the solid obtained was collected and recrystallised from ethanol to give **7** as brown crystals; m.p. 223–224 °C, yield 77%. IR (ν/cm^{-1}): 3358, 3250, 3158 (NH, NH_2), 1685 (C=O), 1658 (C=N). ^{1}H NMR (DMSO-d_6) δ (ppm): 11.4 (s, 1H, NH, exchangeable with D_2O), 10.1 (s, 1H, NH, exchangeable with D_2O), 9.4 (br.s, 1H, NH, exchangeable with D_2O), 8.7 (br.s, 1H, NH, exchangeable with D_2O), 8.3–7.0 (m, 9H$_{arom.}$), 5.7 (br.s, 2H, NH_2, exchangeable with D_2O). MS *m/z* (%): 361 (M^{+}; 35.5), 259 (52.9), 231 (47.1), 160 (23.5), 55 (100). Anal. Calcd for $C_{18}H_{15}N_7O_2$ (361.36): C, 59.83; H, 4.18; N, 27.13. Found: C, 59.65; H, 4.20; N, 27.36%.

*2-Cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)-*N′*-(2-oxoindolin-3-ylidene)acetohydrazide* (**8**): To a stirred solution of potassium hydroxide (0.56 g, 0.01 mol) in *N,N*-dimethylformamide (20 mL) was added compound **2** (2.28 g, 0.01 mol). After the mixture was stirred for 30 min., phenyl isothiocyanate (1.2 mL, 0.01 mol) was added to the resulting mixture. Stirring was continued at room temperature for 12 h and then ethyl chloroacetate (1.07 mL, 0.01 mol) was added and stirring was continued for additional 6 h. The reaction mixture was acidified with cold dilute acetic acid. The separated solid was filtered off, washed several times with cold water and recrystallised from ethanol to give **8** as dark brown crystals; m.p. 204–206 °C, yield 85%. IR (ν /cm^{-1}): 3182 (br.), 2205 (C≡N), 1723 (C=O$_{thiazolidinone}$), 1680 (C=O$_{α,β\text{-unsaturated amide}}$). MS *m/z* (%): 406 (M+3; 35.7), 322 (64.3), 99 (42.9), 55 (100). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.78 (s, 1H, NH, exchangeable with D_2O), 10.37 (s, 1H, NH, exchangeable with D_2O), 8.15–6.78 (m, 9H$_{arom.}$), 3.45 (s, 2H). Anal. Calcd for $C_{20}H_{13}N_5O_3S$ (403.41): C, 59.55; H, 3.25; N, 17.36; S, 7.96. Found: C, 59.53; H, 3.27; N, 17.40; S, 7.93%.

*2-Cyano-*N′*-(2-oxoindolin-3-ylidene)-3-(phenylamino)-3-thioxopropanehydrazide* (**9**): To a stirred solution of potassium hydroxide (0.56 g, 0.01 mol) in *N,N*-dimethylformamide (20 mL) was added compound **2** (2.28 g, 0.01 mol). After the mixture was stirred for 30 min., phenyl isothiocyanate (1.2 mL, 0.01 mol) was added to the resulting mixture. Stirring was continued at room temperature for 12 h. The reaction mixture was acidified with cold dilute HCl. The solid product that separated was filtered, washed with water and recrystallised from ethanol to give **9** as green crystals; m.p. 226–228 °C, yield 67%. IR (υ/cm^{-1}): 3218 (br.s) (NH), 2177 (C≡N), 1712 (C=O), 1617 (C=N), 1343 (C=S). ^{1}H NMR (DMSO-d_6) δ (ppm): 11.6 (s, 1H, NH, exchangeable with D_2O), 10.0 (s, 1H, NH, exchangeable with D_2O), 8.8–7.1 (m, 10H$_{arom.}$+NH), 3.3 (s, 1H).MS *m/z* (%): 336 (M^{+}–HCN, 24.7), 227 (12.6), 160 (31.3), 77 (100). Anal. Calcd for $C_{18}H_{13}N_5O_2S$ (363.39): C, 59.49; H, 3.61; N, 19.27; S, 8.82. Found: C, 59.21; H, 3.36; N, 19.45; S, 8.60%.

*4-Imino-*N′*-(2-oxoindolin-3-ylidene)-3-phenyl-2-thioxothiazolidin-5-carbohydrazide* (**10**): To a solution of compound **2** (2.28 g, 0.01 mol) in ethanol (15 mL) containing triethylamine (0.5 mL), elemental sulfur (0.32 g, 0.01 mol) and phenyl isothiocyanate (1.35 mL, 0.01 mol) were added. The reaction mixture was heated at 60 °C for 2 h with continuous stirring. After cooling, the reaction mixture was acidified with cold dilute acetic acid. The precipitated solid was filtered off, washed several times with cold water and recrystallised from toluene to give **10** as reddish brown crystals; m.p. 208–209 °C, yield 79%. IR (ν/cm^{-1}): 3413, 3238 (br.s) (NH), 1699 (C=O), 1624 (C=N), 1364 (C=S). ^{1}H NMR ($CDCl_3$) δ (ppm): 11.2 (s, 1H, NH, exchangeable with D_2O), 9.9 (s, 1H, NH, exchangeable with D_2O), 8.6–7.0 (m, 9H$_{arom.}$), 3.7 (br.s, 2H, exchangeable with D_2O). MS *m/z* (%): 395 (M$^+$; 35.4), 235 (76.3), 207 (15.7), 161 (70.7), 135 (36.9), 104 (51.1), 77 (100). Anal. Calcd for $C_{18}H_{13}N_5O_2S_2$ (395.46): C, 54.67; H, 3.31; N, 17.71; S, 16.22. Found: C, 54.47; H, 3.29; N, 17.96; S, 16.25%.

*7-(3,4-Dimethoxyphenyl)-2′,5-dioxo-3,5-dihydro-1*H*-spiro[[1,2,4]triazolo[1,5-*a*]pyridine-2,3′-indoline]-6,8-dicarbonitrile* (**11**): A mixture of **2** (1.0 g, 4.4 mmol) and 2-(3,4-dimethoxybenzylidene)malononitrile (0.94 g, 4.4 mol) in 1,4-dioxane (25 mL) in the presence of triethylamine (0.5 mL) was heated under reflux for 3 h. the reaction mixture was concentrated and acidified with cold dilute acetic acid. The solid which separated out was filtered off, washed several times with cold water and recrystallised from ethanol to give **11** as brown crystals; m.p. 188–190 °C, yield 71%. IR (ν/cm^{-1}): 3428 (NH), 2209 (C≡N), 1699 (C=O). ^{1}H NMR ($CDCl_3$) δ (ppm): 11.4 (s, 1H, NH, exchangeable with D_2O), 9.9 (s, 1H, NH, exchangeable with D_2O), 8.7 (s, 1H, NH, exchangeable with D_2O), 8.2–6.9 (m, 7H$_{arom.}$), 3.89 (s, 6H, 2OMe). MS *m/z* (%): 412 (M–CO, 26.1), 252 (17.4), 216 (39.1), 119 (56.5), 92 (52.2), 51 (100). Anal. Calcd for $C_{23}H_{16}N_6O_4$ (440.41): C, 62.72; H, 3.66; N, 19.08. Found: C, 62.37; H, 3.46; N, 19.11%.

*1-(3-Oxo-2,3-dihydrocinnolin-4(1*H*)-ylidene)carbonohydrazide* (**12**): A mixture of **2** (1.0 g, 4.4 mmol) and hydrazine hydrate 80% (0.01 mol) in 1,4-dioxane (20 mL) was heated under reflux for 2 h. the solid formed after cooling was collected by filtration and recrystallised from ethanol to give **12** as pale green crystals; m.p. 244–246 °C, yield 72%. IR (ν/cm^{-1}): 3358 (s), 3154 (br.) (NH), 1686, 1656 (C=O). MS *m/z* (%): 234 (M$^+$; 33.3), 132 (20.5), 105 (43.6), 91 (56.4), 51 (100). Anal. Calcd for $C_9H_{10}N_6O_2$ (234.21): C, 46.15; H, 4.30; N, 35.88. Found: C, 46.38; H, 4.18; N, 35.68.

*Ethyl 5′-amino-2,7′-dioxo-4′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,5-*a*]pyrimidine]-3′-carboxylate* (**13**): To a solution of compound **2** (1.0 g, 4.4 mmol) in ethanol (20 mL) containing piperidine (0.5 mL), ethyl cyanoacetate (0.49 g, 4.4 mmol) was added. The reaction mixture was heated under reflux for 3 h, then poured on ice and acidified with dilute acetic acid. The precipitated solid was filtered off, washed several times with cold water and recrystallised from ethanol to give **13** as brown crystals; m.p. 212–214 °C, yield 32%. IR (ν/cm^{-1}): 3358, 3260, 3157 (NH$_2$, NH), 1685 (C=O$_{ester}$, chelated H-bonding), 1658 (C=O). MS *m/z* (%): 341 (M$^+$; 46.7). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.65 (s, 1H, NH, exchangeable with D_2O), 10.5 (s, 1H, NH, exchangeable with D_2O), 9.50–9.40 (d, 2H, NH$_2$, exchangeable with D_2O), 8.70 (s, 1H, NH, exchangeable with D_2O),7.36–6.84 (m, 4H$_{arom.}$), 4.27–4.20 (q, 2H, *J* = 6.5 Hz), 2.51 (s, 1H), 1.03 (t, 3H, *J* = 6.5 Hz). Anal. Calcd for $C_{16}H_{15}N_5O_4$ (341.32): C, 56.30; H, 4.43; N, 20.52. Found: C, 56.12; H, 4.40; N, 20.45%.

*2-Cyano-*N*-(2,4′-dioxospiro[indoline-3,2′-thiazolidine]-3′-yl)acetamide* (**14**) and *2-(4-oxo-4,5-dihydrothiazol-2-yl)-*N′*-(2-oxoindolin-3-ylidene)acetohydrazide* (**15**): A mixture of compound **2** (1.0 g, 4.4 mmol) and thioglycolic acid (0.3 mL, 4.4 mmol) in dry pyridine (20 mL) was heated under reflux for 3 h. after cooling the reaction mixture was poured on ice cold acetic acid. The separated solid was filtered off, washed several times with cold water and recrystallised from toluene to give **14**. The remaining solid product which was insoluble in toluene was recrystallised from 1,4-dioxane to give **15**.

14: Yellow crystals; m.p. 200–202 °C, yield 19%. IR (ν/cm^{-1}): 3201 (NH), 2262 (C≡N), 1725, 1696, 1619 (C=O). MS *m/z* (%): 302 (M$^+$; 8.8), 259 (12.5), 230 (48.0), 160 (71.3), 132 (100), 104 (77.5). ^{1}H NMR (DMSO-d_6) δ (ppm): 12.63 (s, 1H, enolic OH, exchangeable with D_2O), 11.33 (s, 1H, NH, exchangeable with D_2O), 7.54 (d, 1H, *J* = 7.5 Hz), 7.39 (dd, 1H, *J* = 6.3 Hz; *J* = 4.5 Hz), 7.11 (dd, 1H, *J* = 7.8 Hz; *J* = 7.5 Hz), 6.94 (d, 1H, *J* = 8.4 Hz), 4.41 (s, 2H), 4.21 (s, 1H). Anal. Calcd for $C_{13}H_{10}N_4O_3S$ (302.31): C, 51.65; H, 3.33; N, 18.53; S, 10.61. Found: C, 51.62; H, 3.32; N, 18.50; S, 10.64%.

15: Brown crystals; m.p. 272–274 °C, yield 58%. IR (ν/cm^{-1}): 3438, 3176 (NH), 1699, 1660 (C=O), 1620 (C=N). MS *m/z* (%): 302 (M$^+$; 15.5), 161 (100), 142 (56.7), 132 (10.7), 114 (29.6), 104 (28.4), 86 (28.4). ^{1}H NMR (DMSO-d_6) δ (ppm): 12.44 (br.s, 1H, enolic OH, exchangeable with D_2O), 11.76 (s, 1H, NH, exchangeable with D_2O), 11.20 (s, 1H, NH, exchangeable with D_2O), 7.46 (d, 1H, *J* = 7.2 Hz), 7.34 (d, 1H, *J* = 7.8 Hz), 7.09 (d, 1H, *J* = 7.8 Hz), 6.93 (d, 1H, *J* = 7.8 Hz), 3.80 (s, 2H), 3.29 (s, 1H). Anal. Calcd for $C_{13}H_{10}N_4O_3S$ (302.31): C, 51.65; H, 3.33; N, 18.53; S, 10.61. Found: C, 51.62; H, 3.31; N, 18.55; S, 10.64%.

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