SYNTHESIS OF SOME NOVEL THIAZOLE, AMINOTHIOPHENE, PYRIDINE, CHROMENE AND CHROMENOPYRIDINE DERIVATIVES

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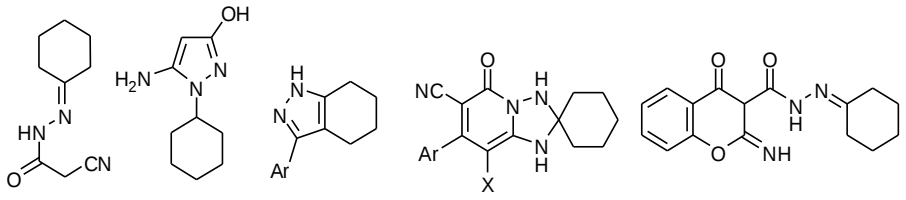
Abstract

The behavior of intermediate **7** towards some α-halogenated compounds has been investigated to synthesize some novel thiophene and thiazole derivatives **9, 11, 12, 14,** and **15**. Upon reacting 2-cyano-*N'*-(3, 4-dihydronaphthalen-1(*2H*)-ylidene) acetohydrazide **(6)** with acetylacetone, arylidenemalononitriles and/or $CH_3CHO/CH_2(CN)_2$ afforded 2-pyridone derivatives **16,17 and 21**. Treatment of compound **6** with DMF-DMA afforded *N,N*-dimethylaminomethylene derivative **22** which reacts with hydrazine hydrate to give α-tetraloneazine **(23)**. Cyclocondensation of **6** with *o*-hydroxyacetophenone, dibromosalicyaldehyde and/or 2-hydroxyna-phthaldehyde produced chromene derivatives **26**, **28a,b** and **29**.Treatment of **28a** with $CH_2(CN)_2$ gave chromeno[3,4-c]-pyridine derivative **31**.

Keywords: Thiophene; thiazole; thiazolidinone; 2-pyridones; chromenes; chromenopyridines.

Introduction

Cyanoacetic acid hydrazide is a versatile and convenient intermediate for the synthesis of many heterocyclic compounds [1-4]. It was found that, the cyclization of 2-cyano-*N'*-cyclohexylideneacetohydrazide **(1)** under different reaction conditions gave pyrazole **(2)**, *1H*- pyrazole **(3)** and spiro[cyclohexane-1,2-[1,2,4]triazolo[1,5-a]pyridine]-5'-(*1'H*)-one derive-atives **(4)** [5-7]. Also, refluxing **1** with salicyaldehyde afforded *N*-cyclohexylidene-2-imino-4-oxochromene-3-carbohydrazide **(5)** [8] (Fig. 1).



1 **2** **3** **4**; X = CN, CO_2Et, $CSNH_2$ **5**

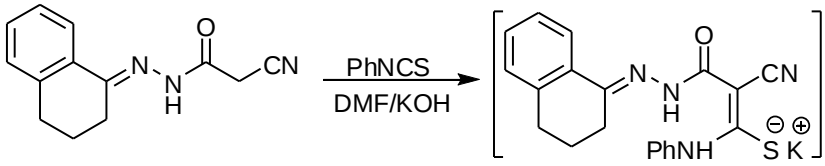
Fig. 1

As an extension of our efforts for the construction of hetercocyclic derivatives [9-17], the author reports herein the synthesis of thiazole , aminothiophene

derivatives, polyfunctionallized pyridine compounds, and chromeno pyridines starting with 2-cyano-*N'*-(3,4-dihydronaphthalen-1(2H)-ylidene) acetohydrazide **(6)** [18] through different chemical transformation reactions with varieties of electrophilic reagents under different reaction conditions.

Results and discussion

The reaction of 2-cyano-*N'*-(3, 4-dihydronaphthalen-1(*2H*)-ylidene) acetohydrazide **(6)** with phenyl isothiocyanate in DMF in the presence of potassium hydroxide at room temperature gave the non-isolable intermediate **7**, Equation 1.

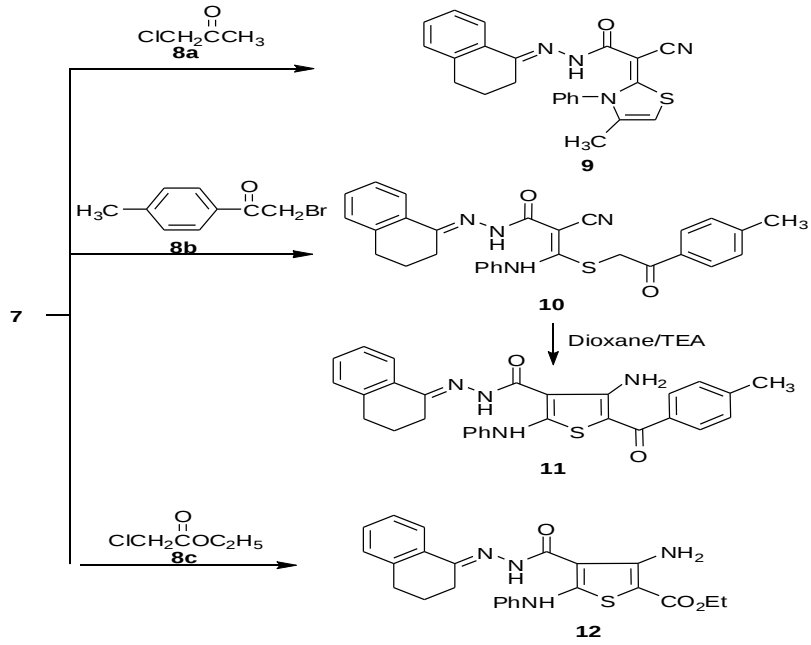


6 **7**

Equation 1

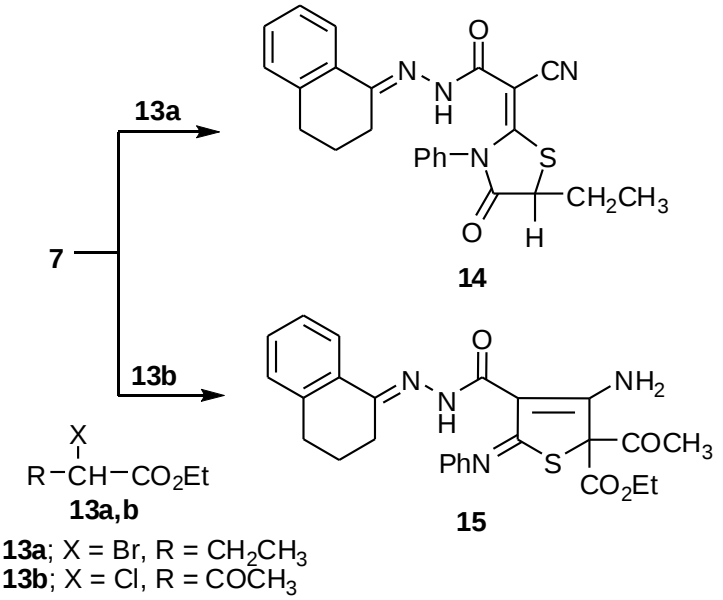
Treatment of the intermediate **7** with chloroacetone **(8a)** furnished the novel 4-methylthiazole derivative **9**. ^{1}HNMR spectrum of compound **9** revealed three singlets at δ 1.85, 6.96, and 9.93 corresponding to methyl, thiazole-H, and NH (disappeared after addition of D_2o), respectively. On the other hand, the reaction of **7** with 4-methylphenacyl bromide **(8b)** afforded a product **10** which was transformed into thiophene derivative **11** through intramolecular addition of methine carbanion to the nitrile function by refluxing in dioxane/TEA. The infrared spectrum of **10** revealed absorption bands at 3374 and 3256 cm^{-1} (2NH). Also, ^{1}H NMR spectrum of **10** in DMSO-d_6 exhibited a singlet at δ 4.09 ppm characteristic for CH_2 protons and two singlets at 9.20 and 12.82 ppm corresponding to two NH groups. The infrared spectrum of **11** showed disappeared of cyano group. The reaction of the intermediate **7** with ethyl chloroacetate **(8c)** at room temperature afforded tetrasubstituted thiophene derivative **12**, **Scheme 1**.

The infrared spectrum of compound **12** showed absorption bands of the two C=O groups at 1664, 1724 cm^{-1} in addition to NH, NH_2 and C=N groups. Mass spectrum of compound **12** revealed a molecular ion peak at m/z 448 (87.7%) and the base peak was found in the spectrum at m/z 243.



Scheme 1

Treatment of the non-isolable intermediate **7** with ethyl α-bromo butyrate **(13a)** at room temperature gave 4-thiazolidinone derivative **14, Scheme 2**. The ^{1}HNMR spectrum of **14** supports the proposed structure which reveals the presence of triplet CH proton at δ 4.30 ppm. The mass spectrum of compound **14** showed a molecular ion peak at m/z 430 and the base peak was found at m/z 243. The formation of **14** may be assumed to proceed through the initial alkylation followed by intramolecular cyclization via Dieckmann type reaction [19,20] with the elimination of ethanol molecule. When **7** was allowed to react with ethyl α-chloroacetoacetate **(13b)** a single product was formed which is formulated as 2,5-dihydrothiophene derivative **(15)**, **Scheme 2**. IR spectrum showed the absence of CN group and the presence of NH_2, NH&CO absorption bands. ^{1}HNMR spectrum (DMSO-d_6) showed two exchangeable signals at 6.7&10.42 ppm (NH_2,NH), singlet signal at 1.9 ppm ($COCH_3$). Its mass spectrum showed no molecular ion peak and a fragment at m/z 243 corresponding to a base peak and other peaks at m/z 474 (M-16) & 247.



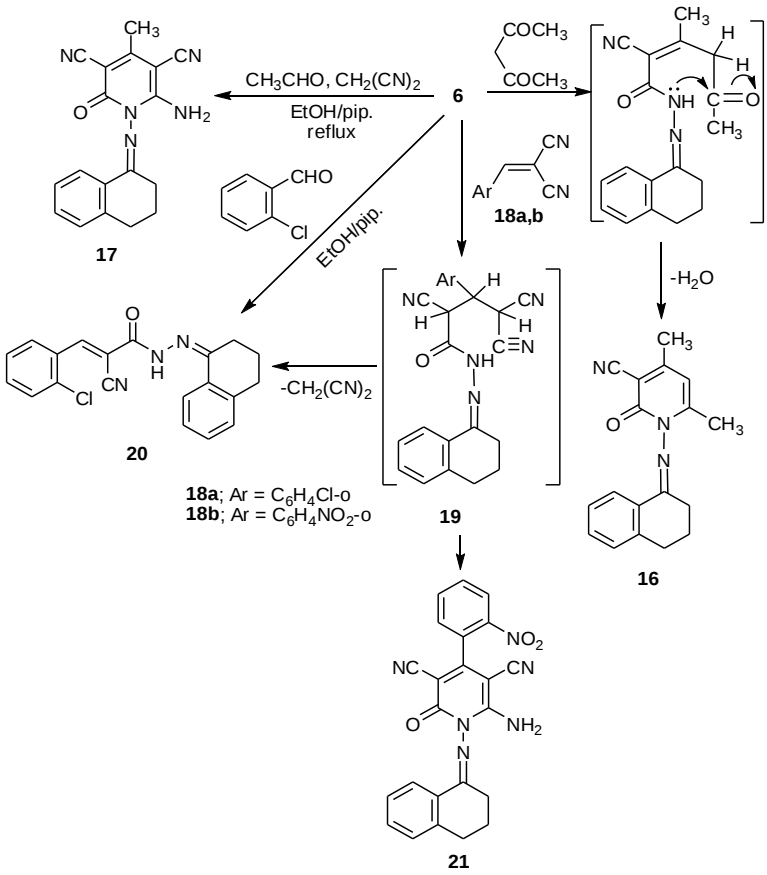
Scheme 2

A number of pyridine and aminopyridine derivatives are incorporated into variety of therapeutic drugs such as milirinon and possess a broad spectrum of biological activities [21-23]. Thus, cyclocondensation of **6** with acetylacetone in refluxing ethanol containing a catalytic amount of piperidine yielded regioselectively 1-(3,4-dihydronaphthalene-1(*2H*)-ylideneamino)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**16**) [24,25]. The infrared spectrum of compound **16** showed the disappearance of NH band. ^{1}HNMR spectrum revealed three singlets at δ 2.25, 2.37, 6.40 ppm assignable to two CH_3 groups and CH-pyridone.

The one-pot condensation of compound **6** with acetaldehyde and malononitrile (1 : 1: 1 molar ratio) at reflux temperature in ethanol in the presence of piperidine afforded the 2-pyridone derivative **17**, **Scheme 3**. The IR spectrum of **17** revealed the amino, nitrile and carbonyl stretching vibration bands at 3364, 3310, 2210 and 1674 cm^{-1}, respectively. In addition, ^{1}HNMR spectrum exhibited signals at δ 2.38, 8.16 corresponding to methyl and NH_2 protons. Mass spectrum of compound **17** exhibited the molecular ion peak at m/z 317 with a base peak at m/z 116. Refluxing **6** with arylidenemalononitriles **(18a,b)** in ethanol/piperidine gave acrolylhydrazide **20** and pyridine derivative **21**, respectively [26-28]. Formation of **20**&**21** may be explained to occur by addition of the methine carbanion of **6** to the activated double

bond of **18** forming Michael adduct **19** which undergoes spontaneous elimination of malononitrile to give **20** and/or intramolecular cyclization to afford **21**, respectively, **Scheme 3**.

Also, further support of **20** was achieved through the reaction of **6** with *o*-chlorobenzaldehyde in ethanol in the presence of a catalytic amount of piperidine (m.p.&m.m.p.). ^{1}HNMR spectra of compounds **20** and **21** showed the absence of the active methylene group and the presence of olefinic and NH_2 protons signals at δ 8.04 and 8.46 ppm, respectively.



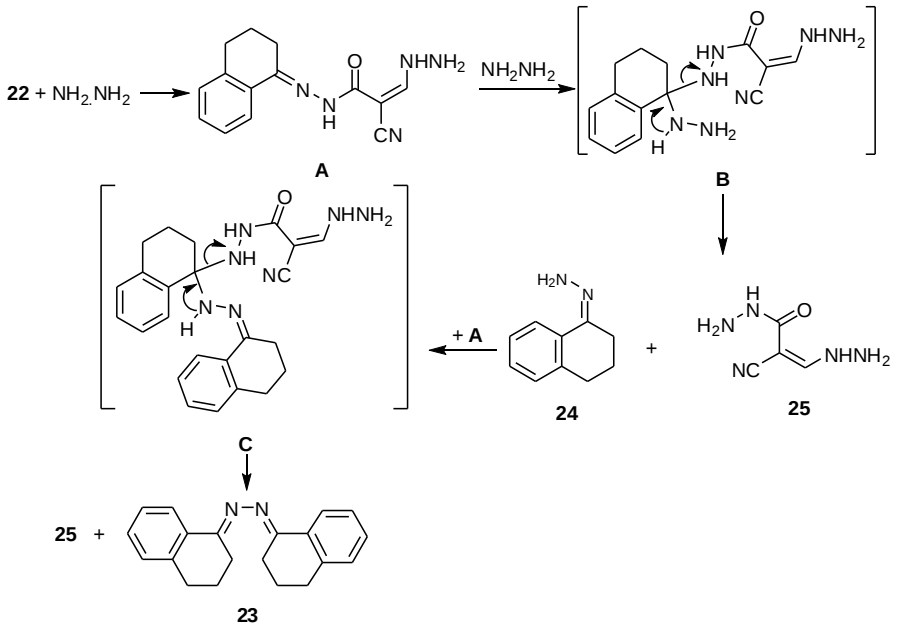
Scheme 3

Condensation of **6** with dimethylformamide-dimethylacetal (DMF-DMA) at reflux temperature in xylene afforded *N*,*N*-dimethylamino-methylene derivative **22**.

The ^{1}HNMR spectrum of compound **22** revealed two singlets at δ 3.21 and 7.84 ppm corresponding to $N(CH_3)_2$ and CH-methine, respectively. Its mass spectrum showed a molecular ion peak at m/z 282 (7.6%) together with a base peak at m/z 123. Treatment of **22** with hydrazine hydrate at reflux temperature in ethanol afforded unexpected α-tetraloneazine **(23)**, **Scheme 4**. Its infrared spectrum showed the absence of NH, C≡N and C=O groups. The ^{1}HNMR spectrum of compound **23** in DMSO-d_6 showed the absence of *N*,*N*-dimethyl moiety, NH and CH-methine protons. In addition, the structure of **23** was supported by its mass spectrum which revealed a molecular ion peak at m/z 288 and M/2 at m/z 144 together with a base peak at m/z 116.

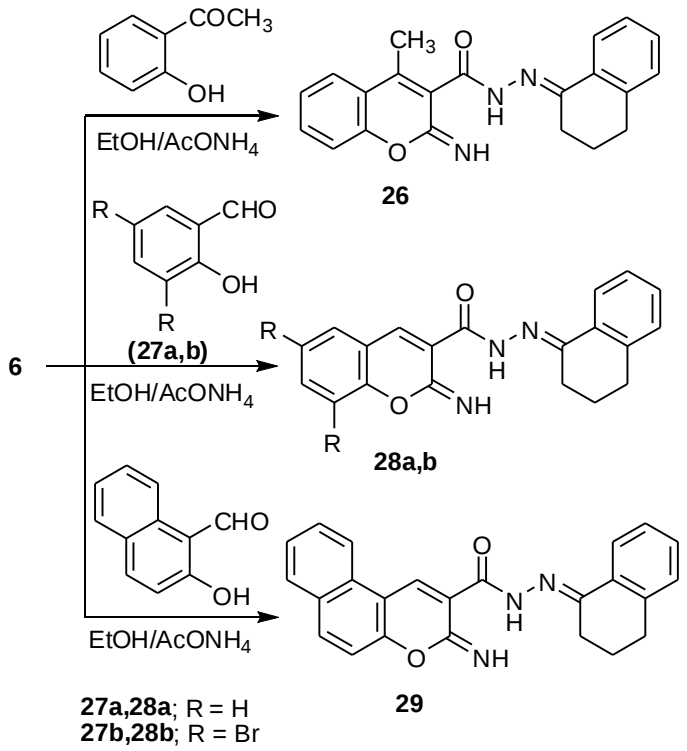
Scheme 4

A possible pathway for this reaction is believed to involve two steps. The first step is the nucleophilic substitution of dimethylamino by hydrazine to give the intermediate A, while the second step involves the addition of hydrazine molecule to the azomethine group of A to give the hydrazine intermediate B which readily rearranges to non-isolable β-hydrazino-α-cyanoacrolylhydrazide **25** and α-tetralone hydrazine **24**. It is possible that **24** may undergo a nucleophilic addition to azomethine moiety of A to give the intermediate C which finally rearranges into **25** and α-tetraloneazine **23**, **Scheme 5**.



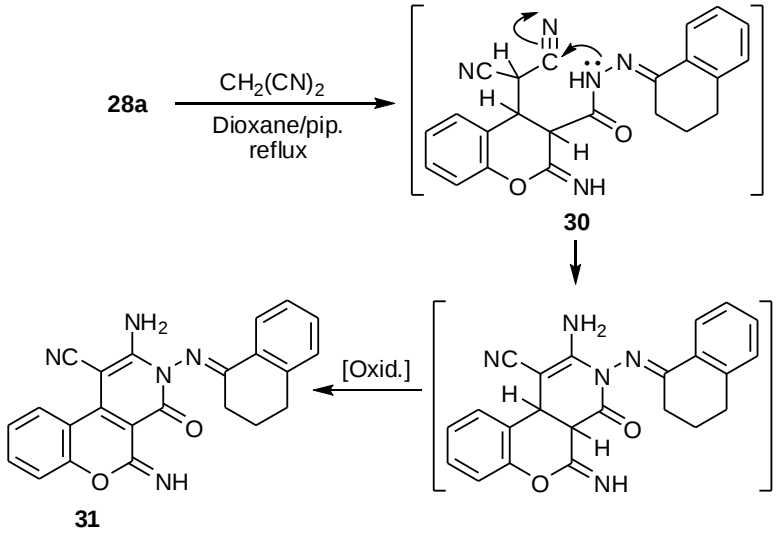
Scheme 5

The reaction of **6** with *o*-hydroxyacetophenone afforded 4-methyl 2-iminochromene-3-carbohydrazide derivative **26**. ^{1}HNMR spectrum of **26** revealed a singlet at δ 2.51 due to CH_3 group and two singlets at 12.9 and 13.48 corresponding to two NH groups. On the other hand, Knoevenagel cyclocondensation of compound **6** with *o*-phenolic aldehydes **27a,b** in refluxing ethanolic ammonium acetate furnished 2-iminochromenes **28a,b** and 2-iminobenzo[f]chromene derivative **29**, respectively, Scheme 6. The structure of **28b** and **29** was established through analytical and spectral data. The absence of the nitrile group in the infrared spectrum of **28b** and **29** confirmed the cyclization process. ^{1}HNMR spectra of compounds **28b** and **29** revealed a singlet chromene-H-4 at δ 8.56 and a singlet benzochromene-H-4 at 9.22 ppm, respectively.



Scheme 6

The reactivity of **28a** [18] towards malononitrile under reflux in dioxane in the presence of piperidine was investigated; where by the novel chromeno[3,4-c]pyridine derivative **31** was obtained**, Scheme 7**. Mass spectrum of **31** revealed a molecular ion peak at m/z 395 (2.02%) with a base peak at m/z 300. The formation of **31** may be assumed to proceed via the Michael addition of malononitrile carbanion to C_3-C_4 double bond in **28a** to yield the acyclic Michael adduct **30** followed by intramolecular cyclization and dehydrogenation under reaction conditions.



Scheme 7

In conclusion, it is clear that the behaviour of 2-cyano-*N′*-cyclohexylideneacetohydrazide towards some electrophilic reagents is totally different than the behaviour of 2-cyano-*N′*-(3,4-dihydronaphthalen-1(*2H*)-ylidene)acetohydrazide towards the same reagents under similar reaction conditions.

Experimental

All melting points are uncorrected. IR spectra (KBr) were measured on Shimadzu 440 spectrometer, ^{1}H NMR spectra were obtained in DMSO on a Varian Gemini 200 MHz spectrometer using TMS as internal standard; chemical shifts are reported as (ppm). Mass spectra were obtained on GCMS\QP 1000 Ex mass spectrometer at 70 ev. Elemental analyses were carried out at the Microanalytical Center, Faculty of Science Cairo University, Egypt.

*Preparation of compounds **9**, **10**,**11**,**12**, **14**,and **15**: General procedure:* To a suspension of finely powdered potassium hydroxide (100 mmol) in dry dimethylformamide (15 ml) at 0ºC, the cyanoacetic acid hydrazide deri-vative (**6**, 100 mmol) and then phenyl isothiocyanate (100 mmol) were added in portions. The reaction mixture was stirred at room temperature for 3h and then treated with α-halogenated compound (100 mmol) and left at room temperature for 24 h, then it was poured into ice/water and acidified with HCl. The resulting precipitate was filtered off, dried and recrystallized from the proper solvent**.**

2-Cyano-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-2-(4-methyl-3-phenyl-thiazol-2(3H)-ylidene)acetohydrazide (**9**, $C_{23}H_{20}N_4OS$).

Yield 65%; brown crystals (dioxane); mp 180-182°C; IR (KBr): $\bar{\nu}$ 3236 (NH), 2178 (C≡N), 1670 (C=O), 1602 (C=N) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.85 (s, 3H, CH_3), 2.01 (p, 2H, CH_2), 2.57-2.94 (m, 4H, $2CH_2$), 6.96 (s, 1H, thiazole-H), 7.22-7.93 (m, 9H, Ar-H), 9.93 (s, 1H, NH-exchangeable with D_2O). Anal. Calcd. for $C_{23}H_{20}N_4OS$ (400): C, 69.00; H, 5.00; N, 14.00. Found: C, 68.90; H, 4.79; N, 13.95.

2-Cyano-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-3-(2-oxo-2-p-tolyleth-ylthio)-3-(phenylamino)acrylohydrazide (**10**, $C_{29}H_{26}N_4O_2S$).

Yield 63%; yellow crystals (ethanol); mp 215-217°C; IR (KBr): $\bar{\nu}$ 3374, 3256 (2NH), 3067 (CH-arom.), 2932 (CH-aliph.), 2182 (C≡N), 1650 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.79 (p, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.55 (t, 2H, CH_2), 2.70 (t, 2H, CH_2), 4.09 (s, 2H, CH_2), 7.07-7.40 (m, 12H, Ar-H), 8.06 (d, 1H, Ar-H), 9.20, 12.82 (2s, 2H, 2NH-exchangeable with D_2O). Anal. Calcd. for $C_{29}H_{26}N_4O_2S$ (494): C, 70.44; H, 5.26; N, 11.33. Found: C, 70.39; H, 5.20; N, 11.20.

4-Amino-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-5-(4-methylbenzoyl)-2-(phenylamino)thiophene-3-carbohydrazide (**11**, $C_{29}H_{26}N_4O_2S$).

Yield 68%; brown crystals (dioxane); mp 240-242°C (decomp.); IR (KBr): $\bar{\nu}$ 3338, 3200, 3192 (NH_2/NH), 2928 (CH-aliph,), 1652 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.80 (hump, 2H, CH_2), 2.34 (s, 3H, CH_3), 2.67 (t, 2H, CH_2), 2.71 (t, 2H, CH_2), 7.09-7.96 (m, 14H, Ar-H, NH_2-exchangeable with D_2O), 8.01 (d, 1H, Ar-H), 9.94, 10.51 (2s, 2H, 2NH-exchangeable with D_2O) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): δ 21.2, 22.9,24.3,30.2, 95.6, 105.2, 117.1, 122.2, 124.3, 127.6, 128.5, 129.4, 129.9, 131.5, 131.8, 135.7, 137.6, 139.5, 143.1, 147.4, 163.4, 170.6, 186.4 ppm. Anal. Calcd. for $C_{29}H_{26}N_4O_2S$ (494): C, 70.44; H, 5.26; N, 11.33. Found: C, 70.20; H, 5.30; N, 11.10.

Ethyl 3-amino-4-(2-(3,4-dihydronaphthalen-1(2H)-ylidene)hydrazinecar-bonyl)-5-(phenylamino)thiophene-2-carboxylate (**12**, $C_{24}H_{24}N_4O_3S$).

Yield 61%; brown crystals (dioxane); mp 220-222°C; IR (KBr): $\bar{\nu}$ 3340, 3260, 3200 (NH_2/NH), 1724, 1664 (C=O), 1600 (C=N) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.22 (t, 3H, CH_3), 1.81 (m, 2H, CH_2), 2.62 (t, 2H, CH_2), 2.72 (t, 2H, CH_2),

4.17 (q, 2H, CH_2), 6.71 (s, 2H, NH_2-exchangeable with D_2O), 7.07-7.40 (m, 8H, Ar-H), 8.04 (d, 1H, Ar-H), 9.98, 10.42 (2s, 2H, 2NH-exchangeable with D_2O). MS (EI): *m/z* (%) 448 (M^+, 87.7), 304 (2.8), 261 (2.4), 243 (100), 144 (40.4), 116 (37.9), 90 (11.3), 52 (13.2). Anal. Calcd. for $C_{24}H_{24}N_4O_3S$ (448): C, 64.28; H, 5.35; N, 12.50. Found: C, 64.20; H, 5.20; N, 12.35.

2-Cyano-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-2-(5-ethyl-4-oxo-3-phenylthiazolidin-2-ylidene)acetohydrazide (**14**, $C_{24}H_{22}N_4O_2S$).

Yield 61%; brown crystals (dioxane); mp 240-242°C; IR (KBr): $\overline{\nu}$ 3376 (NH), 2924 (CH-aliph.), 2189 (C≡N), 1734, 1674 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.03 (t, 3H, CH_3), 1.79 (p, 2H, CH_2), 1.99 (m, 2H, CH_2), 2.57 (t, 2H, CH_2), 2.72 (t, 2H, CH_2), 4.31 (t, 1H, CH), 7.17-7.56 (m, 8H, Ar-H), 8.02 (d, 1H, Ar-H), 9.97 (s, 1H, NH-exchangeable with D_2O). MS (EI): *m/z* (%) 430 (M^+, 15.3), 271 (32), 243 (100), 159 (4.9), 116 (14.4), 90 (3.4), 52 (9.5). Anal. Calcd. for $C_{24}H_{22}N_4O_2S$ (430): C, 66.97; H, 5.11; N, 13.02. Found: C, 66.60; H, 5.00; N, 12.80.

Ethyl 2-acetyl-3-amino-4-(-2-(3,4-dihydronaphthalen-1(2H)ylidene)hydrazinecarbonyl)-5-(phenylimino)-2,5-dihydro-thiophene-2-carboxylate (**15**, $C_{26}H_{26}N_4O_4S$).

Yield 69%; brown crystals (dioxane); mp 260-262°C; IR (KBr): $\overline{\nu}$ 3330, 3221, 3146 (NH_2/NH), 2934 (CH-aliph.), 1705, 1662 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.22 (t, 3H, CH_3), 1.81 (p, 2H, CH_2), 1.90 (s, 3H, $COCH_3$), 2.66 (t, 2H, CH_2), 2.72 (t, 2H, CH_2), 4.15 (q, 2H, CH_2), 6.71 (s, 2H, NH_2-exchangeable with D_2O), 7.07-7.40 (m, 8H, Ar-H), 8.02 (d, 1H, Ar-H), 10.42 (s, 1H, NH-exchangeable with D_2O). MS (EI): *m/z* (%) 474 (M^+-NH_2, 0.7), 451 (0.8), 450 (7.5), 447 (3.2), 243 (100), 242 (56.3), 116 (27.5), 100 (3.3), 90 (7.1), 78 (13.5), 52 (9.1). Anal. Calcd. for $C_{26}H_{26}N_4O_4S$ (490): C, 63.67; H, 5.30; N, 11.42. Found: C, 63.50; H, 5.10; N, 11.25.

1-(3,4-Dihydronaphthalen-1(2H)-ylideneamino)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**16**, $C_{18}H_{17}N_3O$). Equimolar amounts of **6** (100 mmol) and acetylacetone (100 mmol) with piperidine (10 mmol) in refluxing ethanol (50 ml) for 1h and then allowed to cool. The solid product was collected and recrystallized as brown crystals from acetic acid to give **16**.

Yield: 69%, m.p. 225-227°C; IR (KBr): $\bar{\nu}$ 3072 (CH-arom.), 2942 (CH-aliph.), 2216 (C≡N), 1656 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.83 (p, 2H, CH_2), 2.25 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.43 (t, 2H, CH_2), 2.88 (t, 2H, CH_2), 6.40 (s, 1H, CH-pyridine), 7.32-7.52 (m, 3H, Ar-H), 8.19 (d, 1H, Ar-H). Anal. Calcd. for $C_{18}H_{17}N_3O$ (291): C, 74.22; H, 5.84; N, 14.43. Found: C, 74.10; H, 5.60; N, 14.20.

6-Amino-1-(3,4-dihydronaphthalen-1(2H)-ylideneamino)-4-methyl-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (**17**, $C_{18}H_{15}N_5O$). A mixture of **6** (100 mmol), acetaldehyde (100 mmol) and malononitrile (100 mmol) in ethanol (30 ml) containing piperidine (10 mmol) was refluxed for 3h. The solid product produced was filtered then recrystallized from dioxane to give **17**.

Yield: 69%, m.p. 286-288°C; IR (KBr): $\bar{\nu}$ 3364, 3310 (NH_2), 2932 (CH-aliph.), 2210 (C≡N), 1674 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.79 (p, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.49 (t, 2H, CH_2), 2.86 (t, 2H, CH_2), 7.19-7.54 (m, 3H, Ar-H), 8.16 (s, 2H, NH_2-exchangeable with D_2O) 8.26 (d, 1H, Ar-H) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): δ 13.1,23.2,28.4,31.2, 68.2, 117.1, 118.2, 123.2,126.4, 128.7, 129.3, 131.1, 137.0, 144.3, 157.2, 159.1, 167.1 ppm; *m/z* (%) 317 (M^+, 30), 289 (30), 144 (73.3), 116 (100), 90 (60), 52 (20). Anal. Calcd. for $C_{18}H_{15}N_5O$ (317): C, 68.13; H, 4.73; N, 22.08. Found: C, 68.00; H, 4.55; N, 21.90.

*3-(2-Chlorophenyl)-2-cyano-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-acrylohydrazide (***20**, $C_{20}H_{16}ClN_3O$*).*

A mixture of **6** (100 mmol), *o*-chlorobenzaldehyde (100 mmol) and piperidine (10 mmol) in ethanol (30 ml) was refluxed for 1h. The solid product which obtained on hot was collected, filtered off and recrystallized from acetic acid to give **20**.

Yield: 80%; mp 218-220°C; IR (KBr): $\bar{\nu}$ 3180 (NH), 3076 (CH-arom.), 2942 (CH-aliph.), 2270 (C≡N), 1684 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.78-1.86 (m, 2H, CH_2), 2.58-2.62 (m, 2H, CH_2), 2.71-2.75 (m, 2H, CH_2), 7.17-8.02 (m, 8H, Ar-H), 8.04 (s, 1H, CH-methylidene), 10.95 (s, 1H, NH-exchangeable with D_2O). Anal. Calcd. for $C_{20}H_{16}ClN_3O$ (349.5): C, 68.66; H, 4.57; N, 12.01. Found: C, 68.50; H, 4.45; N, 11.88.

6-Amino-1-(3,4-dihydronaphthalen-1(2H)-ylideneamino)-4-(2-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (**21**, $C_{23}H_{16}N_6O_3$). A mixture of **6** (100 mmol) and the *o*-nitrobenzylidene-malononitrile (100 mmol) in ethanol (30 ml) was

treated with piperidine (10 mmol) and the reaction mixture was refluxed for 3h. The solid product which produced on heating was filtered and recrystallized from acetic acid to give **21**.

Yield: 70%; mp295-297°C; IR (KBr): $\bar{\nu}$ 3398, 3282 (NH_2), 2212 (C≡N), 1666 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.83-1.90 (m, 2H, CH_2), 2.46-2.61 (m, 2H, CH_2), 2.90-2.92 (m, 2H, CH_2), 7.34-8.46 (m, 10H, Ar-H + NH_2-exchangeable with D_2O). Anal. Calcd. for $C_{23}H_{16}N_6O_3$ (424): C, 65.09; H, 3.77; N, 19.81. Found: C, 64.78; H, 3.55; N, 19.60.

2-Cyano-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-3-(dimethylamino)-acrylohydrazide (**22**, $C_{16}H_{18}N_4O$).To a solution of hydrazone derivative **(6)** (100 mmol) in m-xylene, dimethylformamide-dimethylacetal (DMF-DMA) (100 mmol) was added and the reaction mixture was refluxed for 2h. The solid product which produced on heating was filtered and recrystallized from dioxane to give **22**.

Yield: 65%; mp 160-162°C; IR (KBr): $\bar{\nu}$ 3372 (NH), 3012 (CH-arom.), 2932, 2856 (CH-aliph.), 2178 (C≡N), 1674 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.83 (p, 2H, CH_2), 2.61 (t, 2H, CH_2), 2.73 (t, 2H, CH_2), 3.21 (s, 6H, $2CH_3$), 7.15-7.26 (m, 3H, Ar-H), 7.84 (s, 1H, CH), 8.12 (d, 1H, Ar-H), 9.59 (s, 1H, NH-exchangeable with D_2O). MS (EI): *m/z* (%) 282 (M^+, 7.6), 161 (2.9), 91 (3), 80 (16.4), 53 (7.8). Anal. Calcd. for $C_{16}H_{18}N_4O$ (282): C, 68.08; H, 6.38; N, 19.85. Found: C, 68.00; H, 6.18; N, 19.75.

1,2-Bis(3,4-dihydronaphthalen-1(2H)-ylidene)hydrazine (**23**, $C_{20}H_{20}N_2$). A mixture of compound **22**(100 mmol) and hydrazine hydrate (100 mmol) in ethanol (30 cm^3) was refluxed for 3h. The solid product which obtained on hot was filtered off and recrystallized from acetic acid to give **23**.

Yield: 55%; mp 280-282°C; IR (KBr): $\bar{\nu}$ 3062 (CH-arom.), 2934 (CH-aliph.), 1602 (C=N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.83 (p, 4H, $2CH_2$), 2.67 (t, 4H, $2CH_2$), 2.79 (t, 4H, $2CH_2$), 7.21-7.35 (m, 6H, Ar-H), 8.15 (d, 2H, Ar-H). MS (EI): *m/z* (%) 288 (M^+, 40.5), 144 (83.8), 116 (100), 115 (100), 90 (29.7), 52 (16.2). Anal. Calcd. for $C_{20}H_{20}N_2$ (288): C, 83.33; H, 6.94; N, 9.72. Found: C, 83.20; H, 6.90; N, 9.60.

*Synthesis of 2H-chromene derivatives **26**, **28b** and **29** : General procedure:* A mixture of compound **6** (100 mmol), *o*-hydroxyacetophenone (100 mmol) and/or

appropriate aldehyde (3,5-dibromosalicyaldehyde, 2-hydroxynaphthaldehyde) and ammonium acetate (10 mmol) in ethanol (30 ml) was refluxed for 3h. The solid product which produced on heating was collected and recrystallized from dioxane to furnish **26, 28b** and **29**.

N'-(3,4-Dihydronaphthalen-1(2H)-ylidene)-2-imino-4-methyl-2H-chromene-3-carbohydrazide (**26**, $C_{21}H_{19}N_3O_2$).

Yield: 65%; mp 275-277°C; IR (KBr): $\overline{\nu}$ 3400 (NH), 2932 (CH-aliph.), 1640 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.88 (p, 2H, CH_2), 2.50 (s, 3H, CH_3), 2.58 (t, 2H, CH_2), 2.80 (t, 2H, CH_2), 6.91-7.77 (m, 7H, Ar-H), 8.32 (d, 1H, Ar-H), 12.9, 13.48 (2s, 2H, 2NH-exchangeable with D_2O). ^{13}C NMR (50 MHz, DMSO-d_6): δ 20.9, 22.4, 23.2, 30.6, 109.4,115.3, 116.1, 122.2, 126.6, 126.1, 128.8, 129.5, 130.6, 132.7, 133.6, 139.5, 146.8, 149.4, 155.2, 159.4, 170.8 ppm. Anal. Calcd. for $C_{21}H_{19}N_3O_2$ (345): C, 73.04; H, 5.50; N, 12.17. Found: C, 72.90; H, 5.35; N, 12.24.

6,8-Dibromo-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-2-imino-2H-chromene-3-carbohydrazide (**28b**, $C_{20}H_{15}Br_2N_3O_2$).

Yield: 60%; mp 250-251°C; IR (KBr): $\overline{\nu}$ 3316 (NH), 2934 (CH-aliph.), 1676 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.89 (p, 2H, CH_2), 2.63 (t, 2H, CH_2), 2.77 (t, 2H, CH_2), 7.19-8.10 (m, 6H, Ar-H), 8.56 (s, 1H, chromene H-4), 9.38, 13.40 (2s, 2H, 2NH-exchangeable with D_2O). Anal. Calcd. for $C_{20}H_{15}Br_2N_3O_2$ (489): C, 49.07; H, 3.06; N, 8.58. Found: C, 48.87; H, 2.90; N, 8.45.

N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-3-imino-3H-benzo[f]chromene-2-carbohydrazide (**29**, $C_{24}H_{19}N_3O_2$).

Yield: 60%; mp 296-298°C; IR (KBr): $\overline{\nu}$ 3324 (NH), 2930 (CH-aliph.), 1682 (C=O) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 1.92 (p, 2H, CH_2), 2.49 (t, 2H, CH_2), 2.78 (t, 2H, CH_2), 7.24-8.64 (m, 10H, Ar-H), 9.22 (s, 1H, benzochromene H-4), 9.26, 13.53 (2s, 2H, 2NH-exchangeable with D_2O). Anal. Calcd. for $C_{24}H_{19}N_3O_2$ (381): C, 75.59; H, 4.98; N, 11.02. Found: C, 75.40; H, 4.85; N, 10.90.

2-Amino-3-(3,4-dihydronaphthalen-1(2H)-ylideneamino)-5-imino-4-oxo-4,5-dihydro-3H-chromeno[3,4-c]pyridine-1-carbonitrile (**31**, $C_{23}H_{17}N_5O_2$). A mixture of **28a** (100 mmol), malononitrile (100 mmol) and piperidine (10 mmol) in dioxane (30 ml) was heated under reflux for 3h. The solid product which produced on heating was collected by filtration and recrystallized from dimethylformamide.

Yield: 60%; mp >300°C; IR (KBr): $\bar{\nu}$ 3436, 3342 (NH_2), 3186 (NH), 2202 (C≡N), 1662 cm^{-1} (C=O). MS (EI): *m/z* (%) 395 (M^+, 2.02), 300 (100), 155 (28.3), 139 (7.2), 99 (35.7), 81 (15.5). Anal. Calcd. for $C_{23}H_{17}N_5O_2$ (395): C, 69.87; H, 4.30; N, 17.72. Found: C, 69.65; H, 4.10; N, 17.60.

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