Enaminones as Building Blocks in Heterocyclic Syntheses: A New Approach to Polyfunctionally Substituted Cyclohexenoazines

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A variety of polyfunctionally substituted condensed pyridines and pyrazolotetrahydroquinazolines have been synthesized utilizing cyclic enaminones as starting materials.

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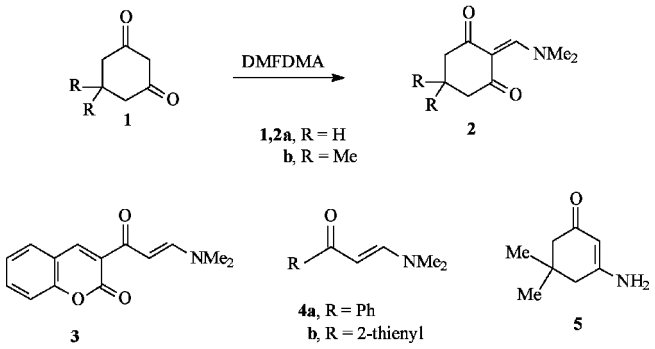
In conjunction to our previous interest in utilizing enaminones as building blocks for synthesis of polyfunctionally substituted heteroaromatics as potential agrochemicals or intermediates in dye and pharmaceutical industries [1-6], we report here our further results in this area. Thus enaminones **2a,b** were synthesized *via* condensation of **1a,b** with dimethylformamide dimethylacetal (DMFDMA) in refluxing xylene utilizing modified literature procedure [7]. The enaminones **3,4** were prepared following literature procedures [1,5,6] (Scheme1).

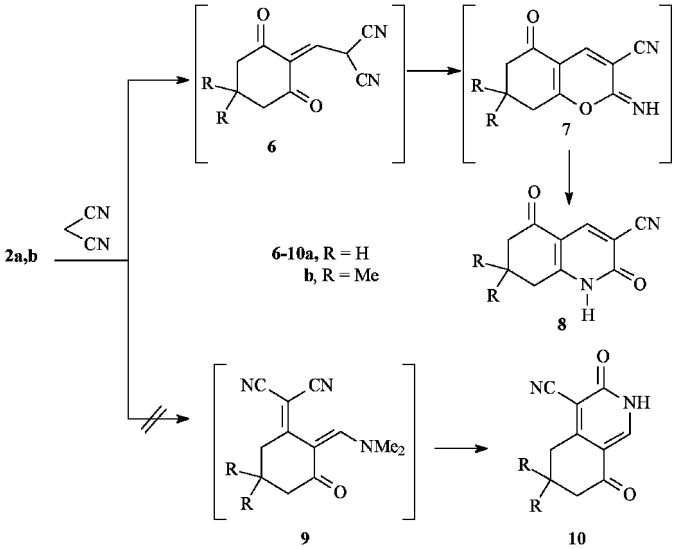
Scheme 1



The enaminones **2a,b** reacted with malononitrile in refluxing acetic acid and in presence of ammonium acetate to yield products of condensation *via* dimethylamine elimination. These may thus be formulated as **6-10**. Thus, initial Michael addition at the activated double bond can afford **6** that would then cyclise into **7** or isomerise into **8**. Alternatively, condensation of the carbonyl group in **2a,b** to the active methylene moiety would afford **9** that can then cyclise into **10** (Scheme 2). The acyclic compound **6** could be ruled out based on the ^{13}C NMR spectra that revealed the presence of only three sp^3 carbons at δ = 50.6 and 33.32 ppm for the two CH_2 and at δ = 28.44 ppm for the two equivalent CH_3 groups. Structure **8** is established for this reaction product as the HMBC spectra revealed correlation between the cyano function at δ = 116.47 and the singlet pyridyl-H in position 4 at δ = 8.33 ppm. The alternative structure **10** which could have resulted *via* initial condensation at the carbonyl function should display a correlation between the pyridyl-CH and the carbonyl function in position 7, which is not observed. Structure **7** was ruled out based on the stability of the reaction product on reflux in ethanol/hydrochloric acid solution, a condition that would lead to hydrolysis of the imine moiety in **7** or rearrangement into **8**.

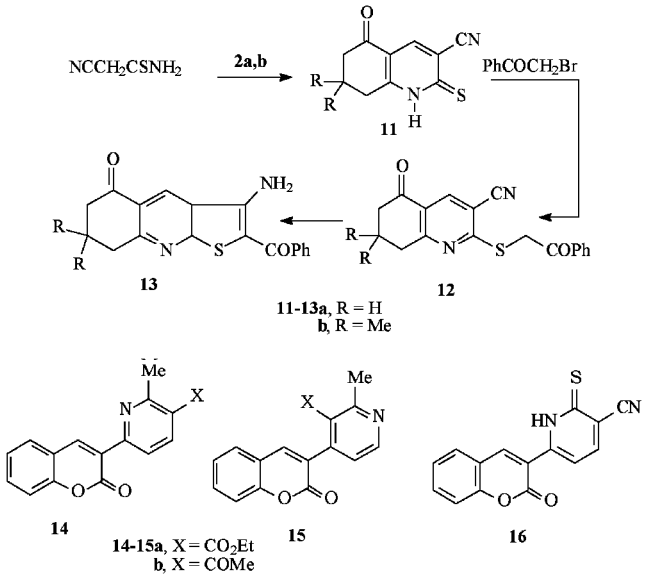
Similarly, reacting **2a,b** with cyanothioacetamide afforded **11a,b** in good yield. Structures **11a,b** were established for these reaction products based on analogy to the well established behavior of **2a,b** towards malononitrile. Compounds **11a,b** thus reacted with phenacyl bromide to yield the thienoquinolines **13a,b** probably formed *via* intermediacy of **12a,b** that could not be isolated. Ready

Scheme 2



formation of condensed thiophenes from reaction of 2-thioxopyridine-3-carbonitrile is a well-established route to pyridothiophenes that has been recently utilized by us for synthesis of benzotriazolylthienopyridines [8] (Scheme3).

Scheme 3



Although enaminones **4a,b** have been recently reported to react smoothly with ethyl acetoacetate and acetylacetone in refluxing acetic acid and in presence of ammonium acetate [9,10], we failed to condense **2a,b** in similar manner with these reagents. However, enaminone **3** reacted smoothly with both reagents to yield products that were formulated as the pyridines **14a,b** and not isomeric **15a,b** based on ^{1}H NMR. Thus, ^{1}H NMR spectra of **14a** indicated pyridyl H-5 and H-4 as two doublets at δ = 7.68 ppm and 7.97 ppm with J = 8.2 Hz. If these were for H-3 and H-2 in **15**, one would expect J of 4-6 Hz [12].

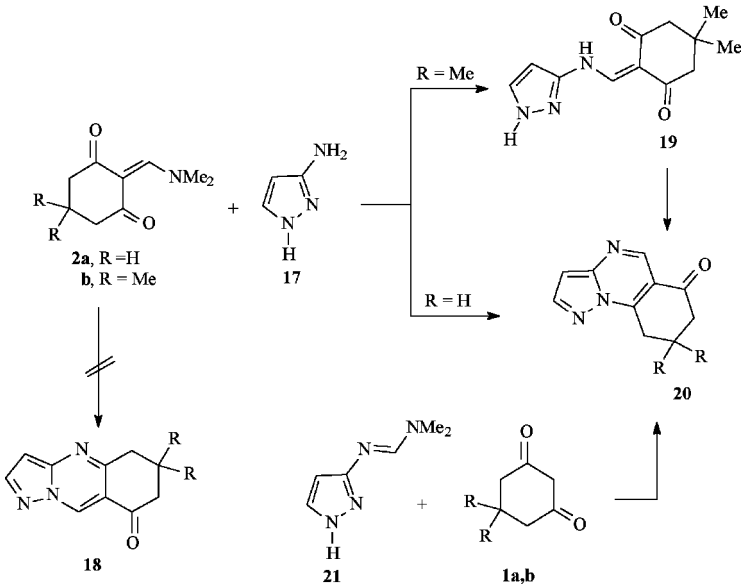
Reacting **3** with acetylacetone afforded **14b** based on observations similar to those discussed above. The reaction of **3** with cyanothioacetamide has afforded the pyridinthione **16** by similar sequence.

The reaction of heterocyclic amines with **4a,b** has been recently utilized by us for synthesis of azolopyrimidines [11-14]. Now we have found that **2a,b** also react with 3-amino-1*H*-pyrazole **17** to yield a pyrazolo[1,5-*a*]quinazoline derivatives that may be formulated as **18-20**. Structures **20a,b** were established by synthesizing them *via* the reaction of **21** with **1a,b**. In contrast to the behavior of **2a**, compound **2b** reacted with **17** to yield the enaminone **19** that cyclized further into **20** in refluxing DMF (Scheme 4).

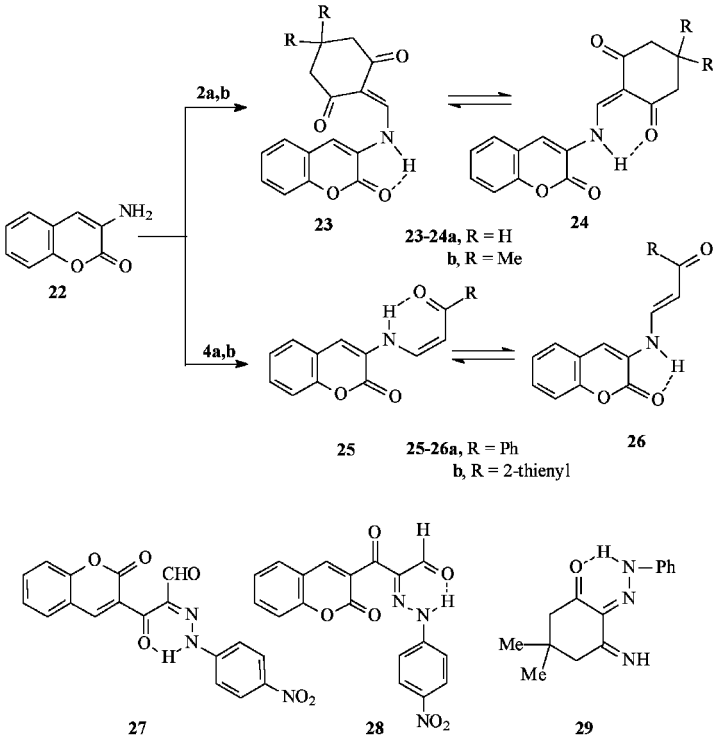
Compounds **2a,b** reacted with 3-aminocoumarine **22** to yield equilibrium mixture of enaminones **23a,b** and **24a,b**. Similar reaction of **4a,b** with **22** gave a mixture of the *Z*-and *E*- enaminones **25a,b** and **26a,b** in relative ratio 85:15 for **4a** and 80:20 for **4b**. The predominance of *Z* form for these products reflects the effect of hydrogen bonding in stabilizing this structure (Scheme 5). Trials to effect cyclisation of **23-26** into pyridine derivatives under diversity of cyclisation reaction conditions failed.

The coupling reaction of **4a,b** with aromatic and heteroaromatic diazonium salts has been extensively utilized in recent years for synthesis of arylhydrazonopropanals that proved to be excellent starting materials for synthesis of polyfunctionally substituted pyridazines [6,15-17]. In this work, trials to couple **3** with benzenediazonium chloride failed. However, *p*-nitrobenzene diazonium chloride

Scheme 4



Scheme 5

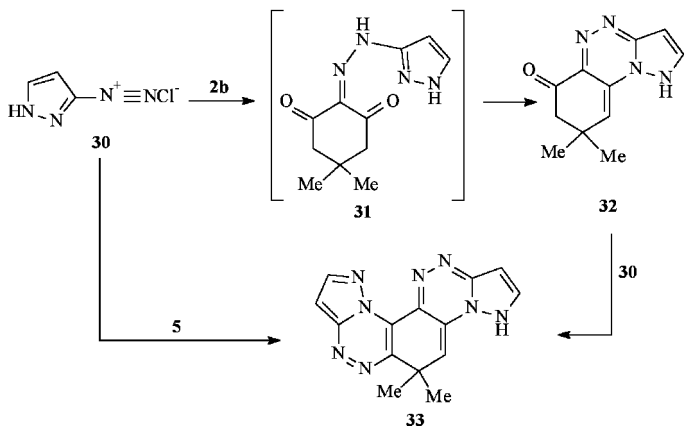


coupled readily with **3** to yield arylhydrazonopropanals that proved to exist as an equilibrium mixture of **27** and **28**. Thus, ^{1}H NMR showed two formyl signals at δ = 9.52 and 10.01 ppm of relative intensity 2:1. Also, two NH signals at δ = 12.93 and 14.01 ppm of the same relative intensities appeared. The downfield shift of formyl proton in the anti-form is a result of hydrogen bonding with the hydrazone NH as indicated in structure **28**. Thus the ^{1}H NMR spectra revealed signals at δ = 7.45-7.48 (m, 2H, coumarinyl-H), 7.66-7.67 (m, 2H, coumarinyl-H), 7.81 (d, 2H, *J* = 6.7 Hz, *p*-nitrophenyl-H), 8.01 (d, 2H, *J* = 9.2 Hz, *p*-nitrophenyl-H); 8.52 (s, 1H, coumarinyl H-4), 10.01 (s, 1H, CHO), 14.00 (br s, 1H, NH) for the anti-form **28** whereas signals at δ = 7.55-7.60 (m, 2H, coumarinyl-H), 7.67-7.80 (m, 2H, coumarinyl-H); 8.24 (d, 2H, *J* = 9.2 Hz, *p*-nitrophenyl-H), 8.32 (d, 2H, *J* = 9.2 Hz, *p*-nitrophenyl-H), 8.64 (s, 1H, coumarinyl H-4), 9.52 (s, 1H, CHO), 12.92 (br s, 1H, NH) revealed the syn-form **27**.

The enaminone **5** also coupled with benzene diazonium chloride to yield **29**. ^{1}H NMR of this reaction product indicates that it exists solely in the iminohydrazone form.

The enaminones **2a,b** failed to couple with aromatic diazonium salts however, compound **2b** coupled readily with diazotised heterocyclic amine **30** yielding a biscoupling product of molecular formula $C_{14}H_{12}N_8$ (MW = 292). This was formulated as **33** and is assumed to be formed *via* initial Japp Klingman type cleavage of the dimethylaminomethylene moiety in **2b** yielding **31** that cyclised into **32** and then coupled further with **30** to yield a hydrazone that cyclises into the final isolable product **33**. This same product was isolated on coupling **5** with **30** (Scheme 6).

Scheme 6



EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Shimadzu IR-740 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Ac-80 spectrometer with [$^2H_6$]DMSO as solvent (unless stated otherwise) and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on Gs/MS INCOS XL Finnigan MAT. Microanalyses were performed on LECO CHNS-932.

Analytical measurements were performed in Analab in Kuwait University, and Analytical data unit at Cairo University.

General Procedure for the Preparation of Compounds **2a,b** and **3**.

A suspension of each of cyclohexane-1,3-dione **1a**, 5,5-dimethylcyclohexane-1,3-dione **1b** (10 mmol) and 3-acetylbenzo[*b*]pyran-2-one (10 mmol) was treated with *N,N*-dimethylformamide dimethylacetal (1.46 g, 11 mmol) in xylene (20 ml). The reaction mixture was heated under reflux for 3 to 5 h. The solid product obtained upon cooling was recrystallized from the proper solvent.

2-Dimethylaminomethylenecyclohexan-1,3-dione (**2a**).

Compound **2a** was obtained as brown crystals in 60 % yield (1.0 g) from ($CHCl_3$/pet.ether); mp: 116°, Lit. mp. 114° [7] ; ir (KBr) ν_{max} = 1656 cm^{-1} (CO). MS (EI, 70 EV): *m/z* = 167 [M^+]. ^{1}H nmr (DMSO): δ = 1.77-1.80 (m, 2H, CH_2), 2.29 (t, 4H, *J* = 6.4 Hz, 2 CH_2), 3.02 (s, 3H, NCH_3), 3.39 (s, 3H, NCH_3), 7.99 (s, 1H, CH).

2-Dimethylaminomethylene-5,5-dimethylcyclohexan-1,3-dione **2b**.

Compound **2b** was obtained as yellow crystals in 70 % yield (1.36 g) from ($CHCl_3$ / pet.ether) mp:
94 °, Lit. mp 94 °[7]. ir (KBr) ν_{max} = 1663 cm^{-1} (CO); MS (EI, 70 EV): *m/z* = 195 [M^+]. ^{1}H nmr (DMSO) δ = 0.96 (s, 6H, 2 CH_3), 2.21 (s, 4H, 2 CH_2), 3.04 (s, 3H, NCH_3), 3.38 (s, 3H, NCH_3), 7.95 (s, 1H, CH).

3-(3-Dimethylaminopropenoylcoumarine) (**3**).

Compound **3** was obtained as yellow crystals in 60 % yield (1.45 g) from ethanol; mp: 160°; ir (KBr) ν_{max} = 1717 and 1680 cm^{-1} (CO). MS (EI, 70 EV): m/z = 243 [M^+]. ^{1}H nmr (DMSO): δ = 2.99 (s, 3H, NCH_3), 3.19 (s, 3H, NCH_3), 6.31 (d, 1H, *J* = 12 Hz, vinyl 2-H), 7.28-7.37 (m, 2H, arom. H), 7.56-7.65 (m, 2H, arom. H), 7.94 (d, 1H, *J* = 12 Hz, vinyl 3-H), 8.61 (s, 1H, pyran 4-H).
Anal. Calcd. for $C_{14}H_{13}NO_3$ (243.25): C, 69.12; H, 5.39; N, 5.76. Found C, 69.33; H, 5.39; N, 5.69.

3-amino-5,5-dimethylcyclohex-2-enone (**5**).

A mixture of 5,5-dimethylcyclohexane-1,3-dione **1b** (1.4 g, 10 mmol), ammonium acetate (0.77 g, 10 mmol), acetic acid (0.6 ml, 10 mmol) was refluxed in toluene (20 ml) using Dean Stark apparatus for 5 to 6 h. The solvent was evaporated in vacuum, and the residual solid was crystallized from acetonitrile. Compound **5** was obtained as yellow crystals in 65 % yield (0.9 g); mp: 167 °; ir (KBr) ν_{max} = 2953 and 2890 (NH_2), 1684 cm^{-1} (CO). MS (EI, 70 EV): m/z = 139 [M^+]. ^{1}H nmr (DMSO): δ = 0.96 (s, 6H, 2 CH_3), 1.90 (s, 2H, CH_2), 2.12 (s, 2H, CH_2), 4.91 (s, 1H, olefenic-H), 6.84 (br s, 2H, NH_2).
Anal. Calcd. for $C_8H_{13}NO$ (139.19): C, 69.03; H, 9.41; N, 10.06. Found C, 69.29; H, 9.24; N, 10.21.

General Procedure for the Preparation of Compound **8a,b.**

A suspension of **2a,b** (1.67 g, 10 mmol), malononitrile (0.66 g, 10 mmol) and ammonium acetate (0.77 g, 10 mmol) was refluxed in acetonitrile (10 ml) for 2 h. The solvent was reduced to deposit a solid that was crystallized from acetonitrile.

2,5-Dioxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8a**).

Compound **8a** was obtained as brown crystals in 70 % yield (1.31 g); mp: 305°; ir (KBr) ν_{max} = 2952 (NH), 2230 (CN), 1686 and 1656 cm^{-1} (CO). MS (EI, 70 EV): m/z = 188 [M^+]. ^{1}H nmr (DMSO): δ = 1.98-2.05 (m, 2H, CH_2), 2.46 (t, 2H, *J* = 6.4 Hz, CH_2), 2.86 (t, 2H, *J* = 6.4 Hz, CH_2), 8.35 (s, 1H, H-4), 13.01 (br s, 1H, NH).
Anal. Calcd. for $C_{10}H_8N_2O_2$ (188.18): C, 63.82; H, 4.29; N, 14.89. Found C, 63.95; H, 4.37; N, 14.90.

7,7-Dimethyl-2,5-dioxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8b**).

Compound **8b** was obtained as white crystals in 75 % yield (1.62 g); mp: 327° ; ir (KBr) ν_{max} = 2953 (NH), 2230 (CN), 1668 cm^{-1} (CO). MS (EI, 70 EV): m/z = 216 [M^+]. ^{1}H nmr (DMSO): δ = 1.03 (s, 6H, 2 CH_3), 2.40 (s, 2H, CH_2), 2.80 (s, 2H, CH_2), 8.33 (s, 1H, H-4), 12.95 (br s, 1H, NH).
Anal. Calcd. for $C_{12}H_{12}N_2O_2$ (216.23): C, 66.65; H, 5.59; N, 12.96. Found C, 66.48; H, 5.55; N, 13.09.

General Procedure for the Preparation of Compounds **11a,b**.

A mixture of each of compound **2a,b** (1.67 g, 10 mmol) and cyanothioacetamide (1 g, 10 mmol) in ethanol 20 ml in the presence of few drops of triethylamine, was refluxed for 20 min. The solution was poured onto water containing drops of concentrated hydrochloric acid to deposit a solid that was collected by filtration and crystallized from proper solvent.

5-Oxo-2-thioxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (**11a**).

Compound 11a was obtained in 57 % yield (1.16 g) from ethanol/DMF; mp >350°; ir (KBr) ν_{max} = 2955 (NH), 2229 (CN), 1663 cm^{-1} (CO). MS (EI, 70 EV): m/z = 204 [M^+]. ^{1}H nmr (DMSO): δ = 2.01-2.07 (m, 2H, CH_2), 2.52 (t, 2H, *J* = 6.4 Hz, CH_2), 2.95 (t, 2H, *J* = 6.4 Hz, CH_2), 8.31 (s, 1H, H-4), 14.36 (br s, 1H, NH).
Anal. Calcd for $C_{10}H_8N_2OS$ (204.18): C, 58.82; H, 3.95; N, 13.72, S 15.68. Found C, 58.51; H, 3.67; N, 13.30; S, 15.34.

7,7-Dimethyl-5-oxo-2-thioxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (**11b**).

Compound **11b** was obtained in 83 % yield (1.92 g) from ethanol/dioxane; mp >350°; ir (KBr) ν_{max} = 3007 (NH), 2229(CN), 1670 cm^{-1} (CO). MS (EI, 70 EV): m/z = 232 [M^+]. ^{1}H nmr (DMSO): δ = 1.03 (s, 6H, 2 CH_3), 2.44 (s, 2H, CH_2), 2.91 (s, 2H, CH_2), 8.24 (s, 1H, H-4), 14.41 (br s, 1H, NH).
Anal. Calcd for $C_{12}H_{12}N_2OS$ (232.23): C, 62.06; H, 5.21; N, 12.06, S 13.79. Found C, 61.92; H, 5.07; N, 11.83; S, 13.00.

General Procedure for the Preparation of Compounds **13a,b**.

A mixture of each of compound **11a,b** (10 mmol) was refluxed with bromoacetophenone (1.99 g. 10 mmol) in DMF (10 ml) for 30 min. The solid formed was collected by filtration and crystallized from ethanol.

3-Amino-2-benzoyl-7,8-dihydro-6*H*-thieno[2,3-*b*]quinolin-5-one (**13a**).

Compound **13a** was obtained in 59 % yield (1.89 g) from chloroform; mp = 266°; ir: 1685 and 1646 (CO), 3420 cm^{-1} (NH_2). MS (EI, 70 EV): m/z = 322 [M^+]. ^{1}H nmr (DMSO): δ = 2.06 (t, 2H, *J* = 6.4 Hz, CH_2), 2.54 (m, 2H, CH_2), 2.92 (t, 2H, *J* = 6.4 Hz, CH_2), 7.37-7.39 (m, 1H, arom-H), 7.46-7.50 (m, 2H, arom-H), 8.04-8.06 (m, 2H, arom-H), 8.14 (s, 2H, NH_2 D_2O exchangeable), 8.91 (s, 1H, H-4).
Anal. Calcd for $C_{18}H_{14}N_2O_2S$ (322.31): C, 67.07; H, 4.38; N, 8.69, S 9.937. Found C, 66.71; H, 4.457; N, 8.98; S, 9.72.

3-Amino-2-benzoyl-7,7-dimethyl-7,8-dihydro-6*H*-thieno[2,3-*b*]-quinolin-5-one (**13b**).

Compound **13b** was obtained in 50 % yield (1.75 g); mp = 233°; ir: 1674 and 1646 (CO), 3396 cm^{-1} (NH_2). MS (EI, 70 EV): m/z = 350 [M^+]. ^1H nmr (DMSO): δ = 1.04 (s, 6H, CH_3), 2.62 (s, 2H, CH_2), 3.09 (s, 2H, CH_2), 7.52-7.59 (m, 3H, arom-H), 7.75-7.77 (m, 2H, arom-H), 8.60 (s, 2H, NH_2 D_2O exchangeable), 9.18 (s, 1H, H-4).

Anal. Calcd for $C_{20}H_{18}N_2O_2S$ (350.36): C, 68.56; H, 5.18; N, 8.00; S, 9.142. Found C, 68.12; H, 5.023; N, 8.39; S, 9.51.

General Procedure for the Preparation of Compounds **14a,b** and **16**.

To a stirred suspension of compound **3** (2.43 g, 10 mmol) and ammonium acetate (1 g), acetic acid (10 ml), each of acetylacetone (1.0 g, 10 mmol) and ethyl acetoacetate (1.3 g, 10 mmol) was added. The reaction mixtures were heated under reflux for 30 min, and then allowed to cool to room temperature. The solid products so obtained were collected by filtration, and crystallized from ethanol / dioxane.

Ethyl 2-methyl-6-(coumarin-3-yl)nicotinic acid ester (**14a**).

Compound **14a** was obtained in 69 % yield (2.10 g); mp.164°; ir: 1727 and 1677 cm^{-1} (CO). MS (EI, 70 EV): m/z = 309 [M^+]. ^1H nmr (DMSO) δ = 1.35 (t, 3H, *J* = 7.08 Hz, OCH_2CH_3), 2.81 (s, 3H, CH_3), 4.34 (q, 2H, *J* = 7.08 Hz, OCH_2CH_3), 7.40-7.48 (m, 2H, coumarinyl-H), 7.68 (d, 1H, *J* = 8.2 Hz, H-5), 7.97 (d, 1H, *J* = 8.2 Hz, H-4), 8.24-8.29 (m, 2H, coumarinyl-H), 8.94 (s, 1H, coumarinyl H-4).

Anal. Calcd for $C_{18}H_{15}NO_4$ (309.31): C, 69.89; H, 4.89; N, 4.53. Found C, 69.91; H, 4.93; N, 4.34.

3-(5-Acetyl-6-methylpyridin-2-yl)coumarin (**14b**).

Compound **14b** was obtained in 75 % yield (2.10 g); mp. 207°; ir: 1727 and 1681 cm^{-1} (CO). MS (EI, 70 EV): m/z = 279 [M^+]. ^1H nmr (DMSO): δ = 2.50 (s, 3H, $COCH_3$), 2.73 (s, 3H, CH_3), 7.37-7.44 (m, 2H, coumarinyl H), 7.64-7.68 (m, 1H, coumarinyl H), 7.93 (d, 1H, *J* = 8.5 Hz, coumarinyl H), 8.22 (d, 1H, *J* = 8.24 Hz, pyridyl H-3), 8.29 (d, 1H, *J* = 8.25 Hz, pyridyl H-4), 8.87 (s, 1 H, coumarinyl H-4).

Anal. Calcd for $C_{17}H_{13}NO_3$ (279.28): C, 73.11; H, 4.69; N, 5.02. Found C, 73.41; H, 4.70; N, 4.82.

6-(Coumarin-3-yl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile (**16**).

To a stirred suspension of compound **3** (2.43 g, 10 mmol) and ammonium acetate (1 g), acetic acid (10 ml), cyanothioacetamide (1.0 g, 10 mmol) was added. The reaction mixture was heated under reflux for 15 min, and then allowed to cool to room temperature. The solid product so obtained were collected by filtration, and crystallized from ethanol/dioxane. Compound 16 was obtained in 68 % yield (1.9 g); mp = 298°; ir: 3103 (NH), 2225 (CN), 1704 cm^{-1} (CO). MS (EI, 70 EV): m/z = 280 [M^+]. ^1H nmr (DMSO): δ = 7.22 (d, 1H, *J* = 7.70 Hz, coumarinyl H-8), 7.47 (t, 1H, *J* = 7.70 Hz, coumarinyl H-6), 7.52 (d, 1H, *J* = 8.28 Hz, pyridyl H-5), 7.77 (t, 1H, *J* = 7.70 Hz, coumarinyl H-7), 7.84 (d, 1H, *J* = 8.10 Hz, pyridyl H-4), 8.23 (d, 1H, *J* = 7.80 Hz, coumarinyl H-5), 8.64 (s, 1H, coumarinyl H-4), 14.10 (br s, 1H, NH).

Anal. Calcd for $C_{15}H_8N_2O_2S$ (280.23): C, 64.29; H, 2.88; N, 10.00; S, 11.44. Found C, 64.14; H, 3.07; N, 10.27; S, 11.32.

General Procedure for the Preparation of Compounds **19** and **20**.

To a suspension of **2a,b** (1.67 g, 10 mmol) in pyridine (10 ml), 3- aminopyrazole **17** (0.83 g, 10 mmol) was added and the reaction mixture was refluxed for 10 min. The solid formed was collected by filtration and crystallized in ethanol

5,5-Dimethyl-2-[(1*H*-pyrazol-3-ylamino)-methylene]-cyclohexane-1,3-dione (**19**).

Compound **19** was obtained in 71 % yield (1.65 g); mp 183°; ir: 2952 and 2869 (2 NH), 1668 cm^{-1} (CO). MS (EI, 70 EV): m/z = 233 [M^+]. ^1H nmr (DMSO): δ = 1.00 (s, 6H, CH_3), 2.33 (s, 2H, CH_2), 2.41 (s, 2H, CH_2), 6.47 (d, 1H, *J* = 2.0 Hz, pyrazolyl H-4), 7.76 (d, 1H, *J* = 2.0 Hz, pyrazolyl H-5), 8.53 (d, 1H, *J* = 12 Hz, CH), 12.53 (d, 1H, *J* = 16 Hz, NH), 12.80 (br s, 1H, NH).

Anal. Calcd. for $C_{12}H_{15}N_3O_2$ (233.26): C, 61.78; H, 6.48; N, 18.02. Found C, 62.10; H, 6.67; N, 18.32.

General Procedure for the Preparation of Compounds **20a,b**.

A suspension each of cyclohexane and 5,5-dimethylcyclohexane-1,3-dione (1.12 g, 10 mmol), in acetic acid (10 ml) was refluxed with enaminone of 3- aminopyrazole (1.38 g, 10 mmol) for 1.5 h. The solid formed was collected by filtration and crystallized in ethanol.

8,9-Dihydro-7*H*-pyrazolo[1,5-*a*]quinazolin-6-one (**20a**).

Compound **20a** was obtained as yellow crystals from ethanol in 50 % yield (0.93 g); mp = 182°; ir: 1676 cm^{-1} (CO). MS (EI, 70 EV): m/z = 187 [M^+]. ^1H nmr ($CDCl_3$): δ = 2.35-2.41 (m, 2H, CH_2), 2.74-2.77 (t, 2H, *J* = 6.4 Hz, CH_2), 3.50-3.54 (t, 2H, *J* = 6.4 Hz, CH_2), 6.82 (d, 1H, *J* = 2.16 Hz, pyrazolyl H-4), 8.29 (d, 1H, *J* = 2.16 Hz, pyrazolyl H-5), 9.03 (s, 1H, quinazolinyl H-5).

Anal. Calcd. for $C_{10}H_9N_3O$ (187.20): C, 64.16; H, 4.85; N, 22.45. Found C, 64.52; H, 4.85; N, 22.437.

8,8-Dimethyl-8,9-dihydro-7*H*-pyrazolo[1,5-*a*]quinazolin-6-one (**20b**).

Compound **20b** was obtained as yellow crystals from ethanol in 50 % yield (1.07 g); mp = 142°; ir: 1679 cm^{-1} (CO). MS (EI, 70 EV): m/z = 215 [M^+]. ^1H nmr (DMSO): δ = 1.14 (s, 6H, CH_3), 2.50 (s, 2H, CH_2), 2.59 (s, 2H, CH_2), 6.91 (d, 1H, *J* = 2.16 Hz, pyrazolyl H-4), 8.46 (d, 1H, *J* = 2.16 Hz, pyrazolyl H-5), 8.84 (s, 1H, quinazolinyl H-5).

Anal. Calcd. for $C_{12}H_{13}N_3O$ (215.25): C, 66.95; H, 6.09; N, 19.52. Found C, 66.161; H, 6.029; N, 19.46.

General Procedure for the Preparation of Compounds **23-24a,b**.

A mixture of aminocoumarine **22** (1.61 g, 10 mmol) and **2a,b** (1.67 g, 10 mmol) was refluxed in acetic acid for 1 h. The solution was allowed to cool and the solid obtained was crystallized in ethanol/dioxane.

2-[(Coumarin-3-ylamino)-methylene]cyclohexane-1,3-dione **23-24a**.

Compounds **23,24a** were obtained as yellow crystals in 35 % yield (1.03 g); mp = 202°; ir: 2968 (NH), 1725 and 1666 cm^{-1} (CO). MS (EI, 70 EV): m/z = 283 [M^+]. ^1H nmr (DMSO): δ = 1.90-1.96 (m, 2H, CH_2), 2.48 (t, 4H, *J* = 6.4 Hz, 2 CH_2), 7.41 (t, 1H, *J* = 7.68 Hz, coumarinyl H-6), 7.47 (d, 1H, *J* = 7.68 Hz, coumarinyl H-8), 7.58 (t, 1H, *J* = 7.68 Hz, coumarinyl H-7), 7.73 (d, 1H, *J* = 7.80 Hz, coumarinyl H-5), 8.42 (s, 1H,

coumarinyl H-4), 8.60 (d, 1H, *J* = 12.8 Hz, methylene-H), 12.64 (br s, 1H, NH).

Anal. Calcd for $C_{16}H_{13}NO_4$ (283.27): C, 67.84; H, 4.63; N, 4.95. Found C, 67.23; H, 4.6; N, 5.057.

5,5-Dimethyl-2-[(coumarin-3-ylamino)-methylene]cyclohexane-1,3-dione (**24b**).

Compound **24b** was obtained as yellow crystals in 75 % yield (2.33 g); mp = 256°; ir 2954 (NH), 1708 and 1668 cm^{-1} (CO). MS (EI, 70 EV): m/z = 311 [M^+]. ^1H nmr (DMSO): δ = 1.01 (s, 6H, 2 CH_3), 2.08 (s, 2H, CH_2), 2.41 (s, 2H, CH_2), 7.41 (t, 1H, *J* = 7.68 Hz, coumarinyl H-6), 7.46 (d, 1H, *J* = 7.68 Hz, coumarinyl H-8), 7.58 (t, 1H, *J* = 7.68 Hz, coumarinyl H-7), 7.73 (d, 1H, *J* = 7.80 Hz, coumarinyl H-5), 8.40 (s, 1H, coumarinyl H-4), 8.60 (d, 1H, *J* = 12.8 Hz, methylene-H), 12.00 (br s, 1H, NH).

Anal. Calcd for $C_{18}H_{17}NO_4$ (311.32): C, 69.44; H, 5.50; N, 4.50. Found C, 69.50; H, 5.35; N, 4.64.

General Procedure for the Preparation of Compounds **25 a,b**.

A mixture of aminocoumarine **22** (1.61g, 10 mmol) and **4a,b** (10 mmol) was refluxed in pyridine for 4 hrs. The solution was allowed to cool and the solid obtained was crystallized in ethanol/dioxane.

3-(3-Oxo-3-phenylpropenylamino)coumarine (**25a**).

Compound **25a** was obtained in 70 % yield (2.03 g) as yellow crystals; mp = 243°; ir: 2963 (NH), 1715 and 1638 cm^{-1} (CO). MS (EI, 70 EV): m/z = 291 [M^+]. ^1H nmr (DMSO): δ = 6.40 (d, 0.85 H, *J* = 8 Hz, H-2 in E form), 6.95 (d, 0.15H, *J* = 16 Hz, H-2 in *Z* form), 7.34-7.87 (m, 9H, arom-H), 7.98 (s, 1H, coumarinyl H-4), 8.02 (d, 0.85 H, *J* = 8 Hz, H-1 in *E* form), 8.09 (d, 0.15H, *J* = 16 Hz, H-1 in Z form), 11.95 (d, 1H, *J* = 12.4 Hz, NH).

Anal. Calcd for $C_{18}H_{13}NO_3$ (291.29): C, 74.21; H, 4.5; N, 4.81. Found C, 74.13; H, 4.427; N, 4.861.

3-(3-Oxo-3-thien-2-yl-propenylamino)coumarine (**25b**).

Compound **25b** was obtained in 30 % yield (0.89 g) as yellow crystals; mp = 254°; ir: 2967 (NH), 1712 cm^{-1} (CO). MS (EI, 70 EV): m/z = 297 [M^+]. ^1H nmr (DMSO): δ = 6.30 (d, 0.85 H, *J* = 8 Hz, H-2 in *E* form), 6.84 (d, 0.15H, *J* = 16 Hz, H-2 in *Z* form), 7.22-7.85 (m, 7H, arom-H), 7.93 (s, 1H, coumarinyl H-4), 7.98 (d, 0.85H, *J* = 8 Hz, H-1 in *E* form), 8.01(d, 0.15H, *J* = 16 Hz, H-1 in *Z* form), 11.64 (d, 1H, *J* = 12.5 Hz, NH).

Anal. Calcd for $C_{16}H_{11}NO_3S$ (297.26): C, 64.64; H, 3.73; N, 4.71; S, 10.774. Found C, 64.67; H, 3.785; N, 4.835; S, 10.68.

2-[(4-Nitrophenyl)-hydrazono]-3-oxo-3-(coumarin-3-yl)-propionaldehyde (**27**).

Compound **3** (10 mmol) was dissolved in ethanol (20 ml) and treated with sodium acetate (1.23 g, 15 mmol), then gradually treated under stirring with a solution of *p*-nitrobenzenediazonium chloride prepared from *p*-nitroaniline and (10 mmol) and the appropriate quantities of both hydrochloric acid and sodium nitrite. The solid product, so formed, was collected by filtration and crystallized from ethanol/dioxane. Compound **27** was obtained in 45 % yield (1.65 g) as red crystals; mp = 209°; ir: 3086 (NH), 1724 and 1685 cm^{-1} (CO). MS (EI, 70 EV): m/z = 365 [M^+]. ^1H nmr (DMSO): δ = 7.45-7.48 (m, 2 (1/3)H, coumarinyl-H), 7.55-7.60 (m, 2 (2/3)H, coumarinyl-H), 7.66-7.67 (m, 2 (1/3)H, coumarinyl-H), 7.67-7.80 (m, 2 (2/3)H, coumarinyl-H), 7.81 (d, 2 (1/3)H, *J* = 6.7 Hz, p-nitrophenyl-H), 8.01 (d, 2 (1/3)H, *J* = 9.2 Hz, p-nitrophenyl-H), 8.24 (d, 2 (2/3)H, *J* = 9.2 Hz, p-nitrophenyl-H); 8.32 (d, 2 (2/3)H, *J* = 9.2 Hz, p-nitrophenyl-H); 8.52 (s, 1 (1/3)H, coumarinyl H-4); 8.64 (s, 1 (2/3)H, coumarinyl H-4), 9.52 (s, 1 (2/3)H, CHO), 10.01 (s, 1 (1/3)H, CHO), 12.92 (br s, 1 (2/3)H, NH); 14.00 (br s, 1 (1/3)H, NH).

Anal. Calcd for $C_{18}H_{11}N_3O_6$ (365.29): C, 59.18; H, 3.04; N, 11.5. Found C, 59.50; H, 3.35; N, 11.66.

Amino-5,5-dimethyl-2-(phenylhydrazono)-cyclohex-3-enone (**29**).

Compound **5** (10 mmol) was dissolved in ethanol (20 ml) and treated with sodium acetate (1.23 g, 15 mmol), then gradually treated under stirring with a solution of benzenediazonium chloride prepared from aniline and (10 mmol) and the appropriate quantities of both hydrochloric acid and sodium nitrite. The solid product, so formed, was collected by filtration and crystallized from ethanol. Compound **29** was obtained in 80 % yield (1.94 g); mp = 226°; ir: 3151 and 3026 (NH_2), 2953 (NH), 1620 cm^{-1} (CO). MS (EI, 70 EV): m/z = 243 [M^+]. ^1H nmr (DMSO): δ = 1.04 (s, 6H, 2CH_3), 2.33 (s, 2H, CH_2), 2.62 (s, 2H, CH_2), 7.29-7.33 (m, 1H, arom-H), 7.43-7.47 (m, 2H, arom-H), 7.68 (m, 2H, arom-H), 8.95 (br s, 1H, NH), 11.42 (br s, 1H, NH).

Anal. Calcd. for $C_{14}H_{17}N_3O$ (243.30): C, 69.11; H, 7.04; N, 17.27. Found C, 69.12; H, 6.97; N, 17.21.

3*H*-6,6-Dimethyldipyrazolo[5,1-*c*:5',1'-*c*']benzo[1,2-*e*:4,3-*e*']di-1,2,4-triazine (**33**).

Each of compound **2b**, 5 (10 mmol) was dissolved in ethanol (20 ml) and treated with sodium acetate (1.23 g, 15 mmol), then gradually treated under stirring with a solution of pyrazolyldiazonium chloride (prepared from 3-aminopyrazol (10 mmol) and the appropriate quantities of both hydrochloric acid and sodium nitrite as has been described earlier ref.) The solid formed was collected by filtration and crystallized from ethanol/dioxane. Compound 33 was obtained in 80 % yield (2.33 g); mp >350°; ir: 3207 cm^{-1} (NH). MS (EI, 70 EV): m/z = 292 [M^+]. ^1H nmr (DMSO): δ = 1.71 (s, 6H, 2CH_3), 5.83 (s, 1H, CH), 5.97 (d, 1H, *J* = 1.92 Hz, pyrazolyl-H), 7.45 (d, 1H, *J* = 2.54 Hz, pyrazolyl-H), 7.72 (d, 1H, *J* = 1.9 Hz, pyrazolyl-H), 8.52 (d, 1H, *J* = 2.54 Hz, pyrazolyl-H), 10.50 (s, 1H, NH).

Anal. Calcd. For $C_{14}H_{12}N_8$ (292.30): C, 57.52; H, 4.14; N, 38.34. Found C, 57.40; H, 4.22; N, 37.76.

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