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Reactivity of Condensed Thiophenes in the Diels-Alder Reaction: The Reactivity of 3-Aminothieno [3,4:3`,4`] Benzo [*b*] Pyranone; 3-Aminothieno [3,4-*c*] Quinoline and of 5-Amino-7-Substituted Thieno [3,4-*d*] Pyridazinone Toward Electron-Poor Olefins and Acetylenes.

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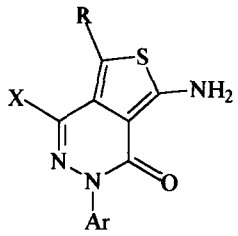
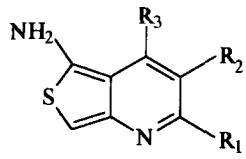
Abstract. The thieno [3,4:3`,4`] benzo [*b*] pyranone **(3b)** and the thieno [3,4-*c*] quinoline **(3c)** are prepared via reacting 4-methylcoumarin-3-carbonitrile **(9a)** and 4-methyl-2-oxo-1,2-dihydroquinolin-3-carbonitrile **(9b)** with elemental sulphur. Similarly the thieno [3,4:3`,4`] naphtho [1,2-*b*] pyran **(11)** is prepared from reaction of **(10)** and elemental sulphur. The condensed thiophenes **(3b,c)** and **(11)** react with a variety of electron-poor olefins to yield products of addition followed by hydrogen sulphide elimination. The reaction of **(3b,c)** and **(11)** with ethyl propiolate in refluxing dioxane/acetic acid mixture affords the condensed thiepins **(24a,c)** .The nature of product of reaction of **(3b,c)** and **(11)** with dimethyl acetylenedicarboxylate is dependent on applied reaction conditions. Thus the reaction of **(3b,c)** and **(11)** with dimethyl acetylenedicarboxylate in refluxing dioxane afforded condensed thiepins while at 250°C products of addition and desulfurization are obtained. Whereas thienopyridazinones **(1a,b)** react with ethyl acrylate and diethyl fumarate to yield thiadiazaacenaphthenones **(31a-c)** respectively, compounds **(1a,b)** react with N-phenylmaleimide to yield phthalazine **(32)**. The thienopyridazinone **(1c)** failed to react with the same reagents under similar conditions. Copyright © 1996 Elsevier Science Ltd

Thiophenes are known to be highly inactive as 4π electron components in the Diels-Alder type [4+2] cycloaddition[1-3]. However, Elnagdi et al[4-8] have shown that 5-aminothieno[3,4-*d*]pyridazinones **(1a,b)** and some thieno [3,4-*d*] pyridines **(2)** react readily with electron-poor olefins to yield [4+2] cycloadducts that decompose under reaction conditions via loss of hydrogen sulfide or elimination of hydrogen molecule to yield benzoazines[4-8]. Also Gronowitz and Dahlgren[9] have shown that benzo[*c*]thiophenes undergo ready 4+2 addition of dimethyl acetylenedicarboxylate to yield naphthalene derivatives. Recently, Döpp et al[10] have reported that thieno [3,4:3`,4`] benzo[*b*]pyranimine **(3a)** also adds diethyl fumarate and dimethyl acetylenedicarboxylate in Diels-Alder type reaction. While cycloadduct produced from reaction of **(3a)** with diethyl fumarate decomposed in a manner similar to that observed earlier by Elnagdi et al[8] for **(1a,b)** and **(2)** producing **(4)**, product of addition of **(3a)** to dimethyl acetylenedicarboxylate has rearranged into the thiepinobenzopyranone **(5).** We became thus interested to explore the behaviour of condensed thiophenes and to see whether a rearrangement into thiepins is a general reaction that can take place with other systems or with other reagents. Since participation of the imino function in **(4)** in addition reaction to the acetylene esters has resulted in the formation of mixtures of isomeric **(5)** that gave complex spectra which can not be used to exclude completely other possible structures for the formed thiepins, we have decided to work with

2-oxobenzopyranone and not with the imines. In the present paper we report synthetic approaches to several new condensed aminothiophenes as well as on their behaviour towards electron-poor olefins and acetylenes. Thus (**1a,b**) was prepared utilizing our newly reported synthetic approach[8]. Compound (**1c**) was prepared via coupling in situ generated 4-phenyl-3-oxobutanitrile (**6**) with benzenediazonium chloride and subsequent condensation of the produced phenylhydrazone (**7**) with ethyl cyanoacetate. The formed pyridazinone (**8**) then reacted readily with sulphur to yield (**1c**).



1 a,Ar= Ph; R= Me; X= CO_2Me
b,Ar= 4-$CH_3OC_6H_4$; R=Me; X= CO_2Me
c,Ar= R= Ph; X= CN



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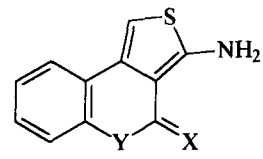
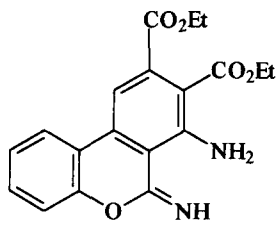


3 a,X=NH; Y=O
b,X=Y=O
c,X=O; Y=NH



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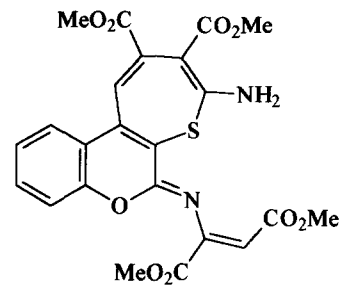

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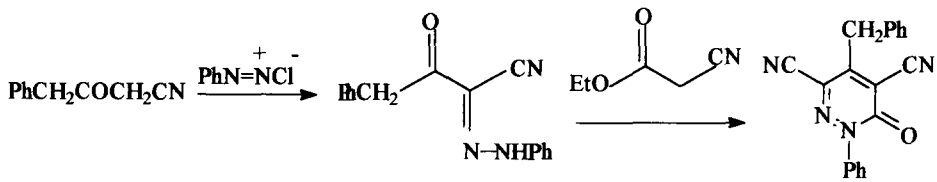
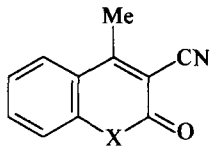
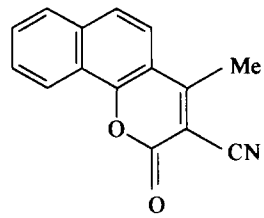


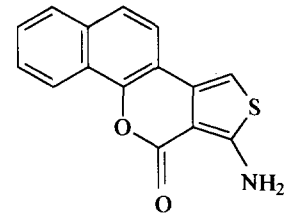
6 **7** **8**

Treatment of 2-hydroxyacetophenone with ethyl cyanoacetate produced (**9a**) . The latter compound reacted with sulphur in refluxing DMF/piperidine, affording thieno[3,4:3`,4`] benzo[*b*]pyran (**3b**) in good yield. Similarly condensing 2-aminoacetophenone with ethyl cyanoacetate produced (**9b**) which reacted with sulphur

to yield **(3c)**. In a similar way condensing 2-acetyl-1-naphthol with ethyl cyanoacetate gave **(10)** which reacted with elemental sulphur to yield **(11)**. The formation of **(3b,c)** and **(11)** from **(9a,b)** and **(10)** is further extension of our condensed thiophenes synthesis from alkylhetero-aromatic carbonitriles and sulphur .





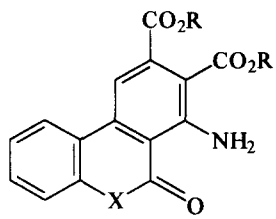


9 a,X=O
b,X=NH

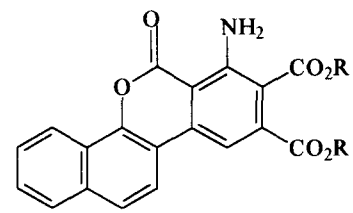
10

11

Compounds **(3b)** and **(11)** reacted with diethyl fumarate at 250°C to yield products of addition and hydrogen sulphide elimination which are formulated as **(12a)** and **(13a)** respectively.



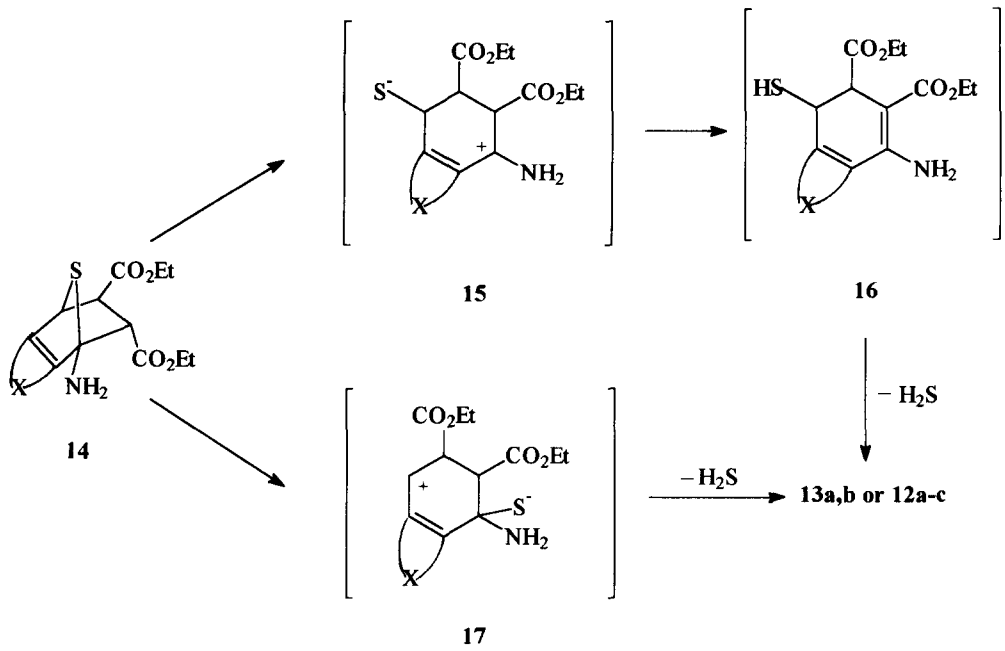
12 a,X=O; R=Et
b,X=O; R=Me
c,X=NH; R=Me



13 a, R=Et
b, R=Me

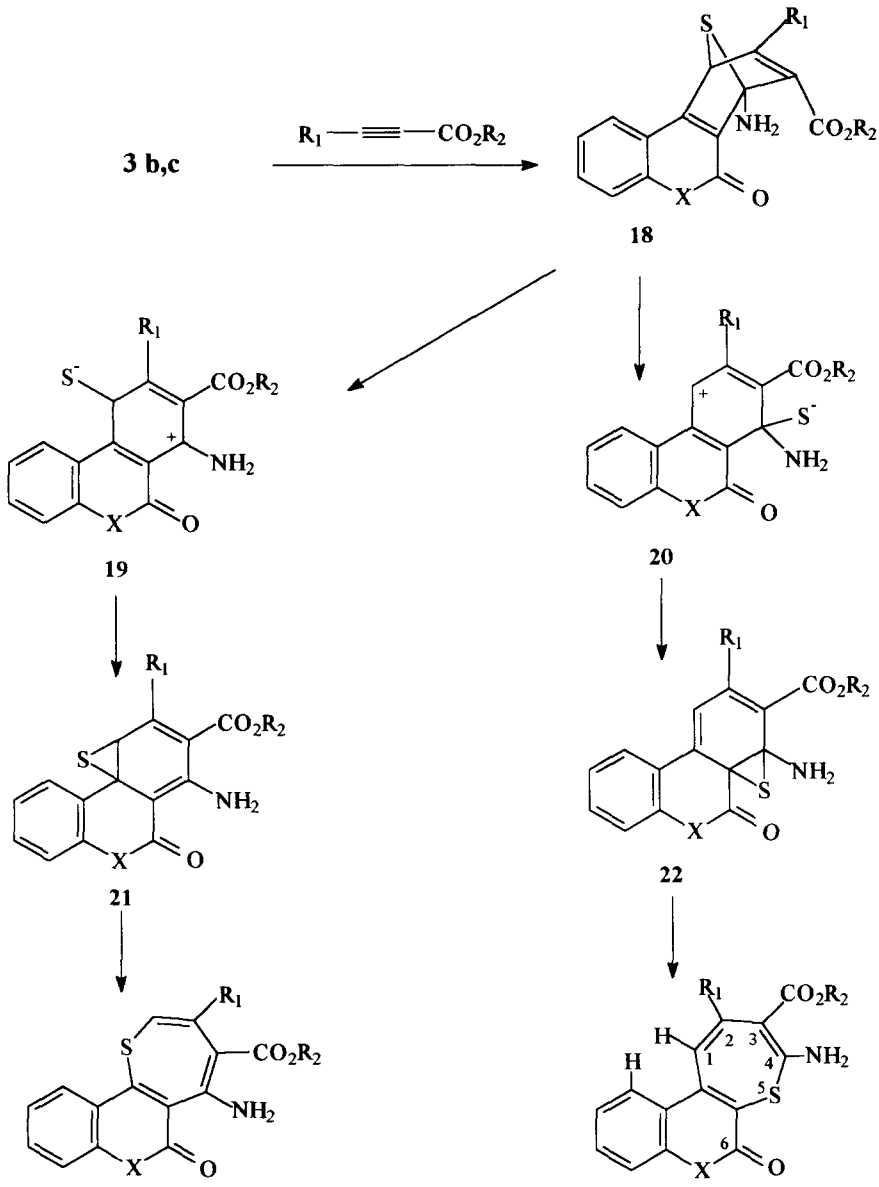
It is assumed that initially formed cycloadducts **(14)** first rearrange into either **(15)** or **(17)** and then transfer a proton yielding **(16)** that aromatize into final isolable products. Although intermediacy of **(15)** seems most likely as it is more stable than **(17)**, involvement of **(17)** cannot be ruled out, as adducts produced by Döpp et al[9] can rearrange only via similar intermediate into the isolated thiepins.

The reaction of **(3b,c)** with dimethyl acetylenedicarboxylate and with ethyl propiolate in refluxing dioxane has resulted in formation of 1:1 adducts. These can thus be formulated as cycloadducts **(18)** or isomers **(21-24)**. Thus ring opening of **(18)** would lead to **(19)** or **(20)**. Species **(19)** can then isomerise either to **(21)** or **(23)** while **(20)** can also give **(22)** or **(24)** .

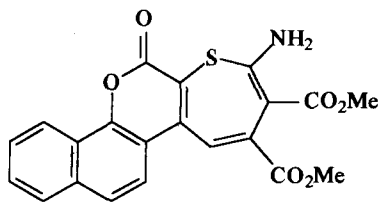


Structures **(18, 21 or 22)** were readily ruled out based on ^{13}C NMR of the products which revealed absence of signals for sp^3 carbons other than the two methoxy carbons. Stucture **(23)** was also excluded based on NOE difference experiments which has revealed structure **(24a)**. Thus, irradiation of the low field signal at δ 8.23 ppm in **(24a)** enhanced the doublet at δ 5.90 ppm as well as benzene ring protons at δ 7.93 ppm. When compounds **(24b,d)** were heated above their melting points in absence of a solvent for short period, compounds **(12b,c)** were obtained. The formation of **(12b,c)** from **(24b,d)** is assumed to occur via 6π-electrocyclization of **(24b,d)** to yield **(22)** which on desulphurization afforded **(12b,c)**. Similar to the behaviour of **(3b,c)**, compound **(11)** also reacted with dimethyl acetylenedicarboxylate in refluxing dioxane to yield the thiepin **(25)**. Although thiepins are predicted to have anti aromatic character[11] and are expected to undergo ready sulphur extrusion[12], reports on some annulated thiepins[13-16] have ascribed their thermal stability to delocalisation of the thiepin π-electrons into the π-electron system of annulated rings giving rise to azulene-like charge separated structures which is possible in our systems.

When the reaction of **(3b)** and **(11)** was conducted at 250°C, the reaction produced **(12b)** and **(13b)** respectively via addition and desulfurization. Attempted preparation of **(12c)** similarly failed. We believe that thiepins **(24 and 25)** are intermediates in these reactions and that under reaction conditions they undergo electrocyclisations yielding **(22)** which are decomposed further into isolated products.



Similar to their behaviour toward diethyl fumarate compounds **(3b,c)** and **(11)** also added N-phenylmaleimide to yield **(26a,b)** and **(27)** respectively.



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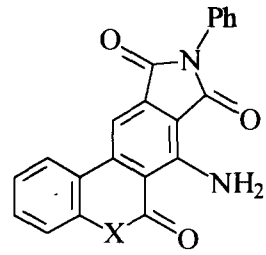
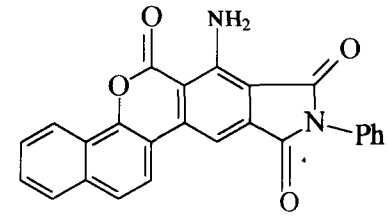


26 a, X=O
b,X=NH



27

Recently we have reported that **(1a)** reacts with acrylonitrile to yield the thiadiazaacenaphthenes **(31a)** whose structure was confirmed by X-ray crystallography[8]. Now we report that also **(1a)** reacts with ethyl acrylate and **(1b)** with diethyl fumarate to yield the thiadiazaacenaphthenes **(31b,c)**. These are formed via intermediacy of **(28)** that ring opens into **(30)** then lose a proton and cyclise into final isolable products via elimination of methoxide ion. It is thus confirmed that intermediates like **(29)** are not formed in reaction of **(1a,b)** with electron-poor olefins although the presence of methyl function renders such intermediate more stable than intermediate that led to products isolated by Döpp et al[10] as well as those obtained here. Fusion of **(1a)** with N-phenylmaleimide at 140°C produced the phthalazine **(32).** It seems that under such condition, loss of hydrogen sulphide and not methanol elimination is the predominating reaction pathway. Compound **(1c)** failed to react with either dimethyl acetylenedicarboxylate or with electron-poor olefins under a variety of conditions. Although the introduction of a phenyl substituent decreases the HOMO-LUMO energy of the system and thus is expected to increase reaction rate, also the phenyl substituent sterically hinders the approaching reagent.

In conclusion, amino condensed thiophenes are active as 4π electron systems. With acetylenes the formed cycloadducts undergo facile opening by cleavage of the C-4, sulphur bond to yield products whose structure depends upon the reagent and reaction conditions. These, when heated (~250°C), undergo sulphur elimination via initial electrocyclisation into condensed thiranes giving dibenzopyrans, benzoquinolines and benzonaphthopyrans. With olefins, the cycloadducts undergo ring opening and then lose hydrogen sulphide affording **(12-13).**

Acknowledgment:

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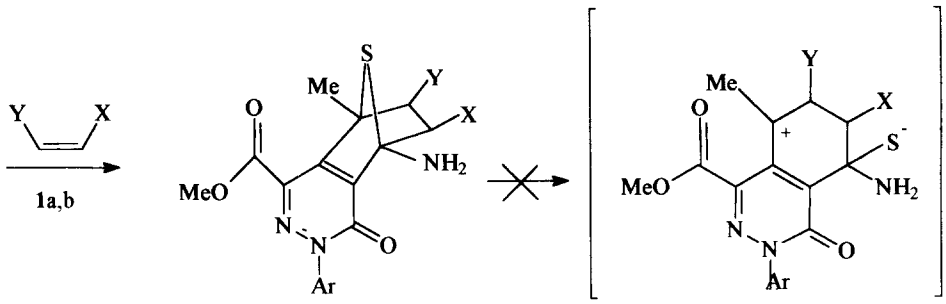
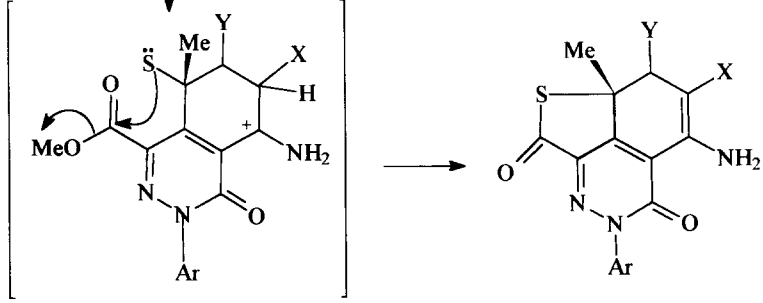


1a,b

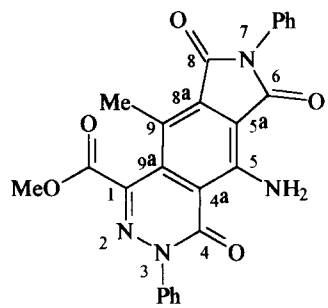
28

29



30

31 a, Y= H; X= CN, Ar = Ph
b, Y= H; X= CO_2Et, Ar = 4-$MeOC_6H_4$
c, Y= X= CO_2Et, Ar = Ph



32

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 [D_6] DMSO as solvent and TMS as internal standards; chemical shifts are reported in δ units (ppm). Mass spectra were measured on Gs/MS INCOS XL Finnigan MAT. Microanalysis were performed on LECO CHNS-932. Compounds (**1a,b**) were prepared following our recently published procedure[8].

3-Oxo-4-phenyl-2-phenylhydrazonobutanonitrile (7) : A solution of acetonitrile (4.1g, 0.1mol) in toluene (100 mL) was treated with ethyl phenylacetate (16.4g, 0.1mol), then sodium hydride was added (4.0g, 60%). The reaction mixture was refluxed for 1.5h then evaporated in vacuo. The remaining solid product was triturated with water, neutralized with hydrochloric acid and extracted with chloroform. Evaporation of the chloroform layer afforded an oily syrup which was dissolved in ethanol (100 mL) and treated with sodium acetate (10g), then gradually treated under stirring with a solution of benzendiazonium chloride (prepared from 9.3g,0.1mol of aniline and appropriate quantities of both hydrochloric acid and sodium nitrite as has been described earlier[8]). The solid product, so formed, was collected by filtration and crystallized from ethanol. Compound **7** was obtained as yellow crystals from ethanol (70%); m.p.137°C; **IR:** 3235 (NH), 2205 (CN) and 1681cm^{-1} (CO). **^{1}H NMR:** δ 4.20 (s, 2H, CH_2), 7.27-7.56 (m, 10H, 2Ar-H) and 12.30 ppm (br, 1H, NH); .Anal. Calcd. for $C_{16}H_{13}N_3O$ (263.29) : C,72.98; H,4.98; N,15.96. Found: C,72.97;H,5.04; N,15.99.

4-Benzyl-1,6-dihydro-6-oxo-1-phenylpyridazine-3,5-dicarbonitrile (8) : A mixture of **7** (2.63g, 0.01mol), ethyl cyanoacetate (1.13g, 0.01mol), ammonium acetate (3.0g) and acetic acid (0.6 mL) was heated with stirring at 200°C for half an hour, then left to cool and triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from ethanol. Compound **8** was obtained as yellow crystals (70%) m.p. 212°C, **IR:** 2225(CN) and 1673 cm^{-1} (ring CO). **^{1}H NMR:** δ 4.27 (s, 2H, CH_2), 7.39-7.57 ppm (m, 10H, 2Ar-H); **^{13}C NMR:** δ 151.78 (C-6), 139.69 (C-3), 134.22 (C-4), 133.26, 129.80, 129.04, 128.62, 127.80, 126.98, 125.51 and 121.64 (ring carbons), 115.07 and 113.08 (2CN) and 112.55 (C-5); **MS:** m/z (EI) 313 (M+1); Anal. Calcd. for $C_{19}H_{12}N_4O$ (312.32) : C,73.06; H,3.87; N,17.94. Found: C,73.10; H,4.10; N,17.74.

5-Amino-3,4-dihydro-3,7-diphenyl-4-oxo-thieno[3,4-*d*]pyridazine-1-carbonitrile (1c) : A suspension of compound **8** (3.12g, 0.01mol), in dioxane (10 mL) was treated with elemental sulphur (0.32g, 0.01mol) and piperidine (0.2 mL). The reaction mixture was refluxed for 4h, then poured onto water, the solid product, so formed, was collected by filtration and crystallized from the proper solvent. Compound **1c** was obtained as red crystals from dioxane (82%) m.p. 220°C; **IR:** 3400 and 3295 (NH_2), 2220(CN) and 1656 cm^{-1} (ring CO). **^{1}H NMR:** δ 7.40-7.50 (m, 10H, 2Ar-H) and 7.88 ppm (br, 2H, NH_2); **^{13}C NMR:** δ 162.85 (C-4), 157.85 (C-1), 140.24 (C-5), 130.59, 129.99, 128.68, 128.23, 127.98, 127.32, 125.51 and 121.29 (ring carbons),119.14 (C-

7), 118.28 (CN), 113.37 (C-4a) and 104.84 (C-7a); **MS:** m/z (EI) 345 (M+1); Anal. Calcd. for $C_{19}H_{12}N_4OS$ (344.32) : C,66.27; H,3.51; N,16.27; S,9.29. Found: C,66.56; H,3.70; N,15.97; S,9.22.

General procedure for the preparation of (9a,b) and (10): A mixture of ethyl cyanoacetate (1.13g, 0.01mol) and ammonium acetate (5g) was treated with either of o-hydroxyacetophenone, o-aminoacetophenone or 2-acetyl-1-naphthol (0.01mol). The reaction mixture was heated at 220°C for 15min, left to cool and then triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from the proper solvent.

4-Methyl-2-oxo-benzo[*b*]pyran-3-carbonitrile (9a) : Compound **9a** was obtained as yellow crystals from dioxane (80%); m.p. 197°C; **IR:** 2220(CN) and 1714cm^{-1} (ring CO). **^{1}H NMR :** δ 2.73 (s, 3H, CH_3) and 7.41-8.05 ppm (m, 4H, Ar-H) ;**^{13}C NMR:** δ 164.14 (C-2), 161.15 (C-8a), 157.27 (C-4a), 153.99 (C-4), 135.82 (C-7), 127.61 (C-6), 126.03 (C-5), 119.15 (C-8), 117.71 (CN), 102.50 (C-3) and 18.28 (CH_3); **MS:** m/z (EI) 185 (M^+); Anal. Calcd. for $C_{11}H_7NO_2$ (185.18):C,71.34; H,3.80; N,7.56. Found: C,71.36; H,3.83; N,7.55.

4-Methyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile (9b): Compound **9b** was obtained as white crystals from dimethylformamide (78%) m.p. 320°C; **IR:** , 3465 (NH), 2210(CN) and 1648 cm^{-1} (ring CO). **^{1}H NMR:** δ 2.71 (s, 3H, CH_3), 7.28-7.93 (m, 5H, Ar-H) and 12.20 ppm (br, 1H, NH); **^{13}C NMR:** δ 158.87 (C-2), 158.80 (C-8a), 139.43 (C-4), 133.96 (C-4a), 126.75 (C-7), 123.16 (C-5), 118.36 (C-6), 116.47 (C-8), 115.86 (CN), 106.35 (C-3) and 18.47 (CH_3); **MS:** m/z (EI) 184 (M^+); Anal. Calcd. for $C_{11}H_8N_2O$ (184.19) : C,71.73; H,4.37; N,15.20. Found: C,71.78; H,4.37; N,15.27.

4-Methyl-2-oxo-naphtho[1,2-*b*]pyran-3-carbonitrile (10) : Compound **10** was obtained as light green crystals from dimethylformamide (70%) m.p. 280°C; **IR:** 2220 (CN) and 1724 cm^{-1} (ring CO). **^{1}H NMR:** δ 2.81 (s, 3H, CH_3) and 7.79-8.04 ppm (m, 6H, Ar-H); **^{13}C NMR:** δ 163.47 (C-2); 161.33 (C-10b); 136.47, 130.59, 128.42, 128.40, 128.27, 125.40, 122.77, 121.63, 121.36 (ring carbons), 119.92 (CN), 114.90 (C-4), 110.90 (C-3) and 18.75 (CH_3); **MS:** m/z (EI) 235 (M^+); Anal. Calcd. for $C_{15}H_9NO_2$ (235.24): C,76.58; H,3.85; N,5.95.Found: C,76.96; H,3.95; N,5.73.

Reaction of (9a,b) and (10) with elemental sulphur: A solution of each of **9a,b** and of **10** (0.01mol) in dimethyl formamide (10 mL) was treated with elemental sulphur (0.32g, 0.01mol) and piperidine (0.2 mL). The reaction mixture was refluxed for 4h, then poured into water, the solid product, so formed, was collected by filtration and crystallized from dioxane / ethanol mixture.

3-Aminothieno[3,4:3`,4`]benzo[*b*]pyran-4-one 3b: Compound **3b** was obtained as brown crystals (86%) m.p. 250°C; **IR:** 3445 and 3335 (NH_2) and 1682 cm^{-1} (ring CO). **^{1}H NMR :** δ 6.89 (s, 1H, 1-H) and 7.10-7.94

ppm (m, 6H, Ar-H and NH_2); **^{13}C NMR:** δ 166.80 (C-4), 151.27 (C-5a), 131.18 (C-3), 129.38 (C-9a), 124.50 (C-7), 124.30 (C-9), 124.03 (C-1), 118.30 (C-8), 117.27 (C-6), 98.50 (C-3a) and 97.66 (C-9b); **MS:** m/z (EI) 217 (M^+); Anal. Calcd. for $C_{11}H_7NO_2S$: C,60.81; H,3.24; N,6.44; S,14.75. Found: C,60.89; H,3.45; N,6.39; S,14.69.

3-Amino-4,5-dihydrothieno[3,4-*c*]quinolin-4-one (3c) : Compound **3c** was obtained as gray crystals (83%); m.p. 258°C; **IR:** 3405 and 3290 (NH_2) and 1635 cm^{-1} (ring CO).[1] **H NMR :** δ 6.79 (s, 1H, 1-H) , 7.02-7.76 (m, 4H, Ar-H), 7.85 (br, 2H, NH_2) and 10.40 ppm (br, 1H, NH); **^{13}C NMR:** δ 163.73 (C-4), 160.88 (C-5a), 138.44 (C-3), 134.68 (C-9a), 129.56 (C-7), 128.48 (C-9), 125.58 (C-8), 121.88 (C-6), 117.84 (C-1), 105.79 (C-3a) and 103.96 (C-9b); **MS:** m/z (EI) 216 (M^+);Anal. Calcd. for $C_{11}H_8N_2OS$ (216.26) : C,61.10; H,3.72; N,12.95.Found: C,61.60; H,3.81; N,12.93.

3-Aminothieno[3,4:3`,4`]naphtho[*b*]pyran-2-one (11) : Compound **11** was obtained as brown crystals (82%) m.p. 302°C; **IR:**3400and 3280 (NH_2) and 1668 cm^{-1} (ring CO).[1] **H NMR :** δ 6.96 (s, 1H, 1-H) and 7.49-8.33 (m, 6H, Ar-H) and 10.42 ppm (br, 2H, NH_2); **^{13}C NMR:** δ 165.95 (C-2), 157.96 (C-11b), 145.03 (C-3), 132.62 (C-5), 130.77, 127.22, 126.28, 128.23, 122.63, 120.64, 120.31 and 112.45 (ring carbons), 97.44 (C-5a) and 96.96 (C-2a); **MS:** m/z (EI) 267 (M^+); Anal. Calcd. for $C_{15}H_9NO_2S$ (267.30): C,67.40; H,3.39; N,5.24; S,11.99. Found: C,66.96; H,3.76; N,5.15; S,12.27.

Reaction of (3b,c) and (11) with electron-poor olefins and acetylenes:

a) At 250°C: A mixture of each of **3b** and **11** (0.01 mol) and diethyl fumarate or dimethyl acetylenedicarboxylate (0.01 mol) was heated at 250°C for 20 min. The reaction mixture was left to cool, then triturated with dioxane and precipitated by adding ethanol . The solid product, so formed, was collected by filtration and crystallized from the proper solvent.

Diethyl 4-amino-5-oxodibenzo[*b,d*]pyran-2,3-dicarboxylate (12a): Compound **12a** was obtained as yellow crystals from dioxane/ethanol mixture (80%); m.p. 149°C; **IR:** 3405 and 3295 (NH_2), 1718 (ester CO) and 1695 cm^{-1} (ring CO).[1] **H NMR :** δ 1.19-1.43 (m, 6H, $2CH_3$,), 4.20-4.38 (m, 4H, $2CH_2$), 7.38-7.56 (m, 4H, Ar-H) and 8.20-8.26 ppm (m, 3H, NH_2 and 1-H); **^{13}C NMR:** δ167.77 and 166.34 (ester CO), 161.56 (C-5), 152.37 (C-4), 151.53 (C-6a), 141.75 (C-2), 139.51 (C-10b), 138.9 (C-10a), 132.51 (C-8), 125.32 (C-9), 125.14 (C-10), 117.30 (C-7), 110.25 (C-4a), 107.62 (C-1), 105.03 (C-3), 62.04 and 61.81 (2 OCH_2), 14.27 and 14.05 (2 CH_3); **MS:** m/z (EI) 356 (M+1); Anal. Calcd. for $C_{19}H_{17}NO_6$ (355.34): C,64.22; H,4.82; N,3.94. Found: C,63.98; H,5.16; N,3.87.

Dimethyl 4-amino-5-oxodibenzo[*b,d*]pyran-2,3-dicarboxylate (12b) : Compound **12b** was obtained as light green crystals from dioxane/ethanol mixture (74%); m.p. 250°C; **IR:** 3505 and 3305 (NH_2), 1729 (ester

CO) and 1699 cm^{-1} (ring CO). **^{1}H NMR:** δ 3.382 (s, 3H, CH_3), 3.87 (s, 3H, CH_3), 7.38 - 8.35 ppm (m, 7H, Ar-H and NH_2); **^{13}C NMR:** δ 168.00 and 167.71 (ester CO), 161.06 (C-5), 151.76 (C-4), 151.34 (C-6a), 144.22 (C-2). 140.87 (C-10b), 139.47 (C-10a), 132.07 (C-8), 124.87 (C-9), 124.64 (C-10), 116.92 (C-7), 116.83 (C-4a), 110.37 (C-1), 107.21 (C-3), 52.68 and 52.39 ($2CH_3$); **MS:** m/z (EI) 328 (M+1); Anal. Calcd. for $C_{17}H_{13}NO_6$ (327.29) : C,62.38; H,4.00; N,4.27. Found: C,61.91; H,4.15; N,4.24.

Diethyl 6-amino-2-oxonaphtho[1,2-*b*]benzo[*d*]pyran-4,5-dicarboxylate 13a: Compound **13a** was obtained as light brown crystals from dioxane/ethanol mixture (75%); m.p. 178°C; **IR:** 3420 and 3310 (NH_2), 1710 (ester CO) and 1697 cm^{-1} (ring CO).**^{1}H NMR:** δ 1.32 (t, 6H, $2CH_3$, J = 7 Hz), 4.28 (q, 4H, $2OCH_2$, J = 7 Hz) and 7.61-8.34 ppm (m, 9H, Ar-H and NH_2); **^{13}C NMR:** δ 167.88, 166.35 (ester CO), 161.45(ring CO), 152.55 (C-6), 147.77 (C-1a), 142.00 (C-2a), 140.36(C-3), 134.81 (C-4), 124.96(C-5), 129.04, 128.30, 127.89, 122.84, 121.90, 120.99, 112.84, 108.03 and 104.91 (ring carbons), 62.07 and 61.81 (2 OCH_2) , 14.30 and 14.09 (2 CH_3); **MS:** m/z (EI) 406 (M^+); Anal. Calcd. for $C_{23}H_{19}NO_6$ (405.40) : C,68.14; H,4.72; N,3.45. Found: C,67.72; H,4.55; N,3.41.

Dimethyl 6-amino-2-oxonaphtho[1,2-*b*]benzo[*d*]pyran-4,5-dicarboxylate 13b: Compound **13b** was obtained as yellow crystals from dioxane/ethanol mixture (78%); m.p. 279°C; **IR:**3420 and 3310 (NH_2), 1730 (ester CO) and 1698 cm^{-1} (ring CO). **^{1}H NMR:** δ 3.84 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3) and 7.61-8.31 ppm (m, 9H, Ar-H and NH_2); **^{13}C NMR:** δ 167.96, 166.48 (ester CO), 155.31 (ring CO), 141.40 (C-6), 140.17 (C-1a), 134.68 (C-2), 128.03(C-4), 124.75(C-5), 128.03, 127.62, 124.75, 121.75, 120.69, 107.92, 104.91 (ring carbons), 52.85 and 52.54 (2 OCH_3); **MS:** m/z (EI) 378 (M+1); Anal. Calcd. for $C_{21}H_{15}NO_6$ (377.35): C,66.84; H,4.00; N,3.71.Found: C,66.40; H,4.09; N,3.65.

b) In Refluxing Dioxane: A mixture of each of **3b,c** (0.01mol) and ethyl propiolate or dimethyl acetylenedicarboxylate (0.01mol) in dioxane was treated under reflux for four to twenty hours. The reaction mixture was evaporated under vacuo till half of its volume, the solid product ,so formed, was collected by filtration and crystallized from the proper solvent.

Ethyl 4-amino-6-oxo-6H-thiepino[3,4-*c*]benzo[*b*]pyran-3-carboxylate (24a) : Compound **24a** was obtained as light green crystals in refluxing dioxane for 20 h., crystallized from DMF (80%); m.p. 286 °C ; **IR:** 3415 and 3330 (NH_2),1720 (ester CO) and 1662 cm^{-1} (ring CO). **^{1}H NMR:** δ 1.26 (t, 3H, CH_3, J =7 Hz), 4.19 (q, 2H, OCH_2 , J =7 Hz), 5.90 (d, 1H, H-2 , J =14 Hz), 7.21-7.95 (m, 4H, Ar-H), 8.23 (d, 1H, H-1, J = 14 Hz) and 8.34 ppm (br, 2H, NH_2); **^{13}C NMR:** δ 166.23 (ester CO), 166.05 (C-6), 159.04 (C-4), 133.40, 135.33, 132.95, 130.43, 125.50, 124.80, 117.98, 117.70, 114.11 and 111.86 (ring carbons), 110.50 (C-3), 59.85 (OCH_2) and 14.22 (CH_3); **MS:** m/z (EI) 315 (M^+); Anal. Calcd. for $C_{16}H_{13}NO_4$ S (315.27): C,60.95; H,4.16; N,4.44.Found: C,60.73; H,4.20; N,4.48.

Dimethyl 4-amino-6-oxo-6H-thiepino[3,4-*c*]benzo[*b*]pyran-2,3-dicarboxylate (24b): Compound **24b** was obtained as red crystals in refluxing dioxane for 4 h., crystallized from ethanol (80%); m.p. 162°C ; **IR:** 3425 and 3330 (NH_2),1720 (ester CO) and 1695 cm^{-1} (ring CO). **^{1}H NMR :** δ 3.58 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 7.28 (s, 1H, H-1), 7.30-7.46 (m,4H, Ar-H) and 7.96 ppm (br, 2H, NH_2); **MS:** m/z (EI) 359 (M^+); Anal. Calcd. for $C_{17}H_{13}NO_6$ S (359.27): C,56.83; H,3.65; N,3.90.Found: C,56.66; H,3.63; N,3.50.

Ethyl 4-amino-6-oxo-6,7-dihydro-thiepino[3,4-*c*]quinoline-3-carboxylate (24c): Compound **24c** was obtained as brown crystals in refluxing dioxane for 20 h., crystallized from DMF (77%); m.p. 323°C ; **IR:** 3360 and 3290 (NH_2),1690 (ester CO) and 1651 cm^{-1} (ring CO). **^{1}H NMR :** δ 1.26 (t, 3H, CH_3, J = 7 Hz), 4.18 (q, 2H, OCH_2 , J = 7 Hz), 5.75 (d, 1H, H-2 , J = 14 Hz), 7.17-7.94 (m, 4H, Ar-H), 8.22 (d, 1H, H-1 , J = 14 Hz) , 8.34 (br, 2H, NH_2) and 10.73 ppm (br, 1H, NH); **^{13}C NMR:** δ 166.49 (ester CO), 163.65 (C-6), 160.98 (C-4), 138.90, 136.54, 136.20, 129.56, 128.03, 125.58, 123.33, 121.67, 117.59, 110.22 and 107.10 (ring carbons), 59.59 (OCH_2) and 14.30 (CH_3); **MS :** m/z (EI) 314 (M^+); Anal. Calcd. for $C_{16}H_{14}N_2O_3$ S (314.29): C,61.14; H,4.49; N,8.91.Found: C,60.93; H,4.63; N,9.12.

Dimethyl 4-amino-6-oxo-thiepino[3,4-*c*]dihydroquinoline-2,3-dicarboxylate (24d): Compound **24d** was obtained as red crystals in refluxing dioxane for 4 h., crystallized from ethanol (74%); m.p. 248°C ; **IR:** 3425 and 3330 (NH_2),1720 (ester CO) and 1695 cm^{-1} (ring CO). **^{1}H NMR :** δ 3.58 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 7.04 (s, 1H, H-1), 7.20-7.38 (m,4H, Ar-H), 7.69 (br, 2H, NH_2) and 10.61 (br, 1H, NH); **^{13}C NMR:** δ166.27 and 164.96 (ester CO), 162.66 (C-6), 161.60 (C-4), 138.17, 137.52, 135.40, 131.17, 128.90, 125.58, 124.75, 121.98 and 117.99 (ring carbons), 116.48 (C-3), 115.62 (C-2), 53.54 and 52.26 ($2OCH_3$); **MS:** m/z (EI) 358 (M^+); Anal. Calcd. for $C_{17}H_{14}N_2O_5$ S (358.27): C,56.98; H,3.94; N,7.82, S,8.93. Found: C,56.60; H,4.06; N,7.56; S,9.15.

Dimethyl 4-amino-2-oxo-thiepino[3,4-*c*]naphtho[1,2-*b*]pyran-5,6-dicarboxylate (25) :Compound **25** was obtained as red crystals in refluxing dioxane for 4 h., crystallized from ethanol (84%); m.p.233°C ; **IR:** 3420 and 3315 (NH_2),1730 (ester CO) and 1712 cm^{-1} (ring CO). **^{1}H NMR :** δ 3.55 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 7.56 (s, 1H, H-7), 7.45-7.87 (m, 6H, Ar-H) and 8.32 ppm (br, 2H, NH_2); **^{13}C NMR:** δ166.67 and 165.23 (ester CO), 164.71 (C-2), 161.58 (C-4), 158.68, 148.20, 142.31, 136.38, 133.46, 133.06, 132.94, 127.96, 127.82, 127.62, 124.16, 123.57, 122.00, 121.25 and 113.53 (ring carbons), 53.71 and 52.41 (2 OCH_3); **MS:** m/z (EI) 409 (M^+); Anal. Calcd. for $C_{21}H_{15}NO_6S$ (409): C,61.61; H,3.69; N,3.42, S,7.81. Found: C,61.83; H,3.76; N,3.21; S,7.40.

Reaction of (3b,c) and (11) with N-phenylmaleimide: A mixture of each of **3b,c** and **11** was fused with N-phenylmaleimide at 250°C for 5 min., then left to cool at room temperature and triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from dimethyl formamide.

Compound **26a** was obtained as yellow powder (86%); m.p.>350°C; **IR:** 3430 and 3353 (NH_2), 1752 (ring CO) and 1699 cm^{-1} (amide CO); **MS:** m/z (EI) 357 (M+1); Anal. Calcd. for $C_{21}H_{12}N_2O_4$ (356.32) : C,70.78; H,3.39; N,7.86. Found: C,70.20; H,3.39; N,7.76.

Compound **26b** was obtained as orange powder (85%); m.p.>350°C; **IR:** 3430 and 3280 (NH_2), 1739 (amide CO) and 1694 cm^{-1} (ring CO);^{1}**H NMR :** δ 4.86 (br, 2H, NH_2), 7.27-7.68 (m, 8H, Ar-H), 7.99 (s, 1H, H-1), 8.45 (d, 1H, H-1, J =7.6 Hz) and 10.45 ppm (br, 1H, NH); **MS:** m/z (EI) 356 (M+1); Anal. Calcd. for $C_{21}H_{13}N_3O_3$ (355.09): C,70.98; H,3.69; N,11.82. Found: C,70.98; H,3.76; N,11.83.

Compound **27** was obtained as green powder (76%); m.p.>350°C; **IR:** 3445 and 3335 (NH_2), 1754 (ring CO) and 1694 cm^{-1} (amide CO); ^{1}**H NMR :** δ 7.30-8.60 ppm (m, 14H, Ar-H); **MS:** m/z (EI) 407 (M+1); Anal. Calcd. for $C_{25}H_{14}N_2O_4$ (406.40) : C,73.89; H,3.47; N,6.89. Found: C,73.99; H,3.46; N,6.86.

Reactions of 1a,b:

a) With ethyl acrylate: A mixture of **1b** (3.45g, 0.01mol) and ethyl acrylate (1.0g; 0.01mol) was refluxed in dioxane acetic acid 1:1 (10 mL) for 24h then the solvent was evaporated under vacuo, the solid product, so formed, was collected by filtration and crystallized from acetic acid. Compound **31b** was obtained as red crystals (76%); m.p.206°C; **IR:** 3500 and 3400 (NH_2), 1715 (thiolaceton) and 1675 (ester CO) and 1620 cm^{-1} (ring CO); ^{1}**H NMR :** δ 1.22 (t, 3H, CH_3, J=7.0 Hz), 1.80 (s, 3H, CH_3), 3.32 (s, 2H, CH_2), 3.80 (s, 3H, OCH_3), 4.20 (q, 2H, CH_2, J=7.0 Hz), 7.0-7.50 (AA`BB`, 4H, Ar-H) and 8.0 ppm (br, 2H, NH_2); Anal. Calcd. for $C_{20}H_{19}N_3O_5S$ (413.44) : C,58.10; H,4.63; N,10.16; S,7.75. Found: C,57.94; H,4.90; N,10.08; S,8.03.

b) With diethyl fumarate: A mixture of **1a** (3.15g, 0.01mol) and diethyl fumarate (1.72g, 0.01mol) was heated at 250°C for 5 min., left to cool, then triturated with ethanol and crystallized from ethanol. Compound **31c** was obtained as red crystals (75%); m.p.206°C; **IR:** 3505 and 3295 (NH_2), 1714 (ester CO) and 1673 cm^{-1} (ring CO). ^{1}**H NMR :** δ 1.01-1.30 (m, 6H, $2CH_3$), 1.96 (s, 3H, CH_3), 3.95-4.00 (m, 4H, 2 OCH_2), 4.24 (s,1H, H-5), 7.33-7.58 (m, 5H, Ar-H), 8.40 ppm (br, 2H, NH_2); **MS:** m/z (EI) 455 (M^+); Anal. Calcd. for $C_{22}H_{21}N_3O_6S$ (455.11) : C,58.01; H,4.65; N,9.23; S,7.04. Found: C,57.83; H,4.65; N,9.17; S,7.08.

c) With N-phenylmaleimide: A mixture of **1a** (3.15g, 0.01mol) and N-phenylmaleimide (1.73g, 0.01mol) was heated at 250°C for 5 min., left to cool, then triturated with ethanol and crystallized from dioxane. Compound **32** was obtained as yellow crystals (72%); m.p.287°C; **IR:** 3450 and 3350 (NH_2), 1738 (ester CO), 1695 (amide CO) and 1642 cm^{-1} (ring CO). ^{1}**H NMR :** δ 2.55 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 7.47-7.53 (m, 10H, Ar-H) and 8.69 ppm (br, 2H, NH_2); ^{13}**C NMR:** δ 166.34 (C-6) and (C-8), 164.90 (ester CO), 159.89 (C-4), 146.51 (C-1), 140.45 (C-5), 131.75 (C-9), 135.4, 128.65, 127.82 and 127.02 (ring carbons), 125.87 (C-

9a), 125.77 (C-4a), 119.07 (C-8a), 117.31 (C-5a), 53.22 (C-OCH_3),12.09 and 11.15 (CH_3); **MS:** m/z (EI) 455 (M^+); Anal. Calcd. for $C_{25}H_{18}N_4O_5$ (454.43): C,66.07; H,3.99; N,12.33. Found: C,66.24; H,3.99; N,12.69

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