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STUDIES ON ALKYLHETEROAROMATIC COMPOUNDS. THE REACTIVITY OF ALKYL POLYFUNCTIONALLY SUBSTITUTED AZINES TOWARDS ELECTROPHILIC REAGENTS

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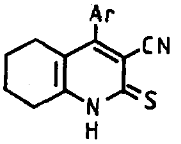
Abstract - Several new alkylpyridine, pyridazine and pyrimidine derivatives are synthesized from acyclic intermediates. The reactivity of these alkylazines towards aromatic aldehydes and arylidenemalononitrile is reported. New synthesis for substituted phthalazines cinnolines and quinazolines could be achieved.

In the past we were involved in programme aiming to develop new synthetic approach for polyfunctionally substituted azanaphthalenes and azaindenes for potential utility as biodegardable agrochemicals.[1-5] Although several high yield syntheses to azanaphthalenes and polyazanaphthalenes are well documented, non of these synthesis offers ready access to polyfunctionally substituted azanaphthalenes.[6] In the present work we report a new general route to polyfunctionally substituted azanaphthalenes utilizing alkylazines as starting materials. Compounds 1a,b were synthesized via reacting the arylidene derivatives of cyanothioacetamide (6a,b) with cyclohexanone in refluxing dioxane in presence of catalytic amounts of piperidine. The structure of the reaction products could be established via inspection of their spectral data. Thus, mass spectrum of 1b revealed a molecular formula of $C_{17}H_{16}N_2OS$ corresponding to condensation of 6b with cyclohexanone via water and hydrogen molecules elimination. ^1H-NMR revealed signals for four CH_2 functions, four aryl protons, OCH_3 and NH. ^{13}C-NMR showed a pattern that can be only intelligibly interpreted for the C=S form 1 and not potential tautomeric thiol form as its showed a C=S signal at 175.51. Thiol signal is expected to appear at much higher field (~160 ppm).[7] The formation of 1a,b from reaction of 6a,b and cyclohexanone is assumed to proceed via addition of cyclohexanone to the double bond in 6 to yield the intermediate Michael adduct 7. This then cyclizes via addition of the nitrogen nucleophile at the carbonyl group yielding the tetrahydropyridine 8 which is readily oxidized into 1 under reaction conditions. Oxidation of tetrahydropyridines into pyridines under similar conditions has been observed earlier.[7] Products of cyclization of the intermediate adduct via attack at the carbonyl function by the sulphur nucleophile could not be traced. Although their intermediacy on the way of formation of 1 cannot be ruled out. We have shown earlier that cinnamonitriles react with cyanothioacetamide to yield thiopyrans that rearrange into pyridines under reaction conditions.[7]

Similar to the behaviour of 6a,b towards cyclohexanone, 6b reacted with ethyl acetoacetate to yield the pyridine thione derivative 2 in 60 % yield.

The alkyl moiety in 1a,b proved to be highly inert towards aromatic aldehydes. Under a variety of conditions 1a,b were recovered unreacted.

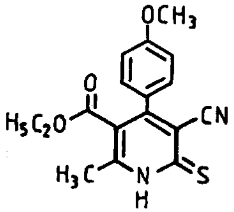
Compound 2 reacted with aromatic aldehydes to yield the styryl derivatives 9a,b. These styryl derivatives were also obtained on treatment of 2 with 10a,b. Compounds 9a,b are assumed to be formed



1

1-a, Ar = C_6H_4Cl-p

b, Ar = $C_6H_4OCH_3$-p



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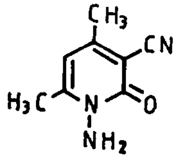

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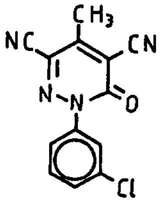

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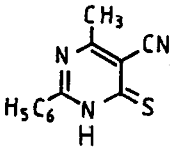

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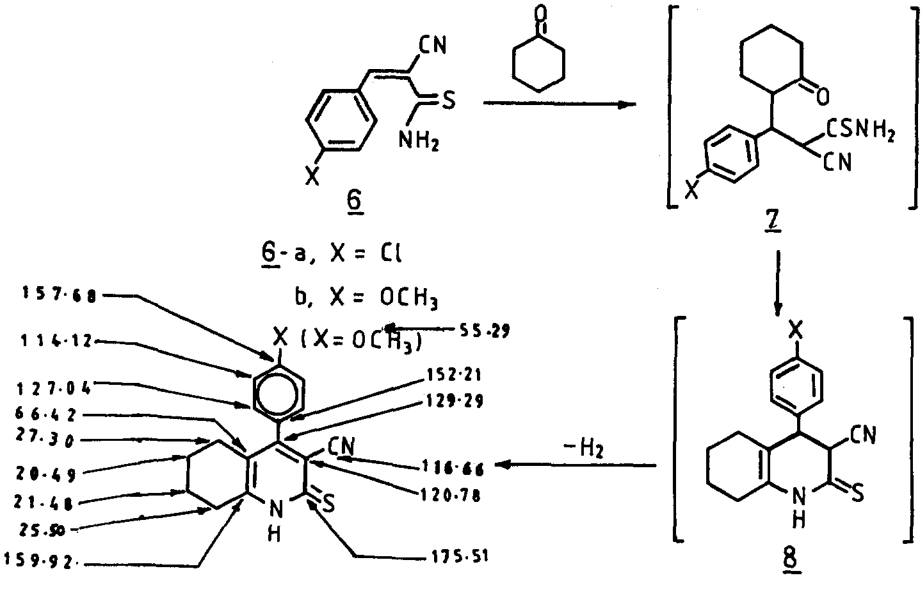
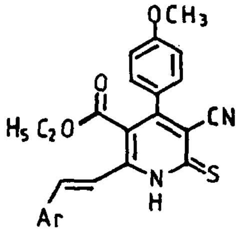
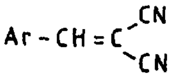


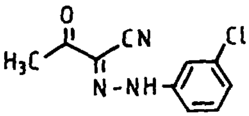
1 a,b



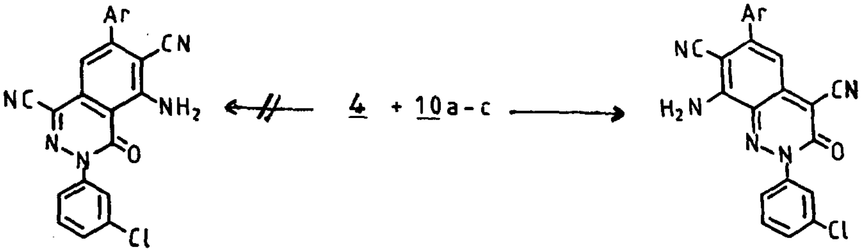
9 a, Ar = C_6H_5
b, Ar = $C_6H_4OCH_3$-p


$Ar-CH=C(CN)_2$

10 a, Ar = C_6H_5
b, Ar = C_6H_4Cl-p
c, Ar = $C_6H_4OCH_3$-p

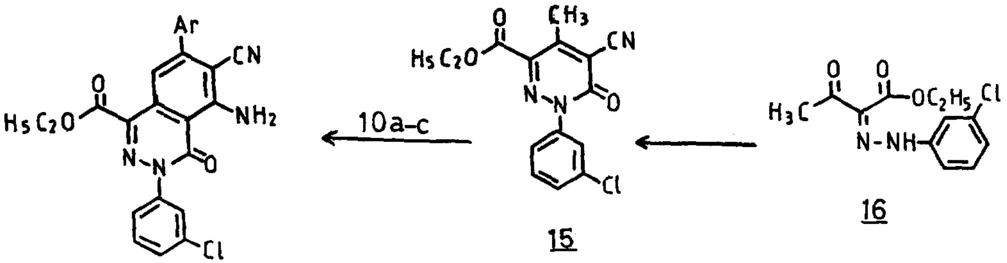


11



12

13 a-c

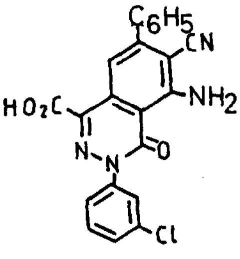


14 a-c

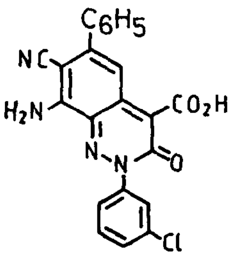
15

16

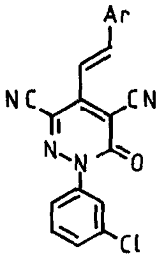
13,14 & 19 a, Ar = C_6H_5
b, Ar = C_6H_4Cl-p
c, Ar = $C_6H_4OCH_3$-p



17



18



19 a-c

from 2 and 10 via intermediacy of a Michael adduct. This then looses malononitrile yielding 9. Similar mechanism has been suggested earlier to account for fomration of arylidene derivatives on treatment of 10 with active methylene reagents.[3]

The alkyl function in 3 proved highly inert towards aromatic aldehydes and cinnamonitriles under a variety of conditions, 3 was recovered unreacted. In contrast alkyl function in 4 and 5 proved highly reactive. Thus, compound 4, prepared via condensing the m-chlorophenylhydrazone derivative 11 with ethyl cyanoacetate in presaence of ammonium acetate, reacted readily with 10a-c to yield products of condensation via hydrogen cyanide elimination. These may be formulated as the phthalazines 12 or isomeric cinnolines 13. The cinnoline structure 13 was established based on spectral and chemical evidence. Thus, UV spectra of the reaction products proved different than UV of the phthalazines 14a-c. The UV of reaction product (13a) showed maximum at λ = 406 nm, ϵ = 2.62 x 10^3. The UV spectrum of the phthalazine 14a revealed maximum at λ = 412 nm, ϵ = 1.065 x 10^4. The difference in ϵ indicates that the reaction products are not phthalazines. Thus, structure 13 was assumed for the reaction products. The phthalazines 14a-c were obtained via condensing the pyridazinones 15 with 10a-c. Compound 15 was prepared via condensing the hydrazone 16 with ethyl cyanoacetate. Synthesis of phthalazines via this reaction sequence has been recently reported by us.[3]

In addition to UV evidence we have also found that both the phthalazine 14 and the product of reaction of 4 with 10a afford carboxylic acid on hydrolysis in alkaline medium. The acid 17, obtained by hydrolysis of 14a, was found different from the acid resulting of hydrolysis of product of reaction of 10a with 4. Thus structure 13a was established for this product and structure 18 was established for the hydrolysis product. Compound 4 also condensed readily with aromatic aldehydes to yield the styryl derivatives 19a-c. These reacted with malononitrile to yield the cinnolines 13a-c.

The pyrimidine thione 5 could be prepared in good yield via reacting 3-aminocrotononitrile (20) with benzoylisothiocyanate in refluxing acetone or dioxane. The thione 5 reacted with 10a-c to yield the quinazolines 21a-c. Compounds 21a-c were also obtained via condensing 5 with aromatic aldehydes to yield the styrylpyrimidines 22a-c and reacting the latter derivatives with malononitrile.

Spectroscopic measurements were performed at the City University London by Dr. S.A. Maltin, thanks to the support of International Organisation of Chemical Sciences in Development (IOCD).

EXPERIMENTAL

All m.ps are uncorrected. IT spectra were recorded on a Pye-Unicam spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were measured on a Varian EM-390 spectrometer. Microanalytical data were performed by the Microanalytical Data Unit at Cairo University. Mass spectra were recorded with a mass spectrometer MS 30 and MS 9 (AEI), 70 eV.

4-Aryl-1,2,5,6,7,8-hexahydro-2-thioxoquinolin-3-carbonitriles (1a,b)

To a solution of cyclohexanone (0.9 gm, 0.01 mole) in dioxane (20 ml), either 6a (2.2 gm, 0.01 mole) or 6b (2.1 gm, 0.01 mole), was added with a catalytic amount of piperidine. The reaction mixture was refluxed for 3 h. The precipitate, formed on cooling, was collected by filtration.

Compound 1a formed yellow crystals from dioxane; yield 1.5 g (50 %) m.p. 260 °C. - IR (KBr): 3300 cm^{-1} (NH); 2220 (CN), 1200-1190 (C=S). (Found: C, 63.80; H, 4.20; N, 9.40; S, 10.50. Calc. for $C_{16}H_{13}N_2SCl$: C, 63.89; H, 4.32; N, 9.31; S, 10.64 %).

Compound 1b formed yellow crystals from dioxane; yield 1.4 g (46 %); m.p. 280 °C. - IR (KBr): 3200 cm^{-1} (NH), 2220 (CN), 1200 (C=S). - ^{1}H-NMR: δ = 1.6-2.8 (m, 8H, cyclohexyl protons); 3.6 (s, 1H, NH); 3.8 (s, 3H, OCH_3); 7.0-7.4 (m, 4H, aromatic protons). - MS: m/z = 296.1187. - ^{13}C NMR: See formula. (Found: C, 68.90; H, 5.40; N, 9.40; S, 10.70. Calc. for $C_{17}H_{16}N_2OS$: C, 68.91; H, 5.40; N, 9.45; S, 10.81 %).

Ethyl 3-cyano-1,2-dihydro-4-p-methoxyphenyl-6-methyl-2-thioxopyridin-4-carboxylate (2):

To a solution of ethyl acetoacetate (1.3 gm, 0.01 mole) in 20 ml of dixoane catalyzed with few drops of piperidine, 6b (2.1 gm, 0.01 mole) was added. The reaction mixture was refluxed for 3 h, poured into ice-cold water and acidified with conc. HCl. The solid product, so formed, was collected by filtration and crystallized from ethanol as yellow crystals; yield 2.0 gm (61 %); m.p. 220 °C. - IR (KBr): 3300 cm^{-1} (NH); 2220 (CN), 1720 (CO), 1210 (CS). - ^1H NMR: δ = 1.2 (t, 3H, CH_3); 2.7 (s, 3H, CH_3); 4.0 (s, 3H, OCH_3); 4.2 (q, 2H, CH_2); 7.2-7.7 (m, 4H, aromatic protons). MS: m/z = 328 (M^+). (Found: C, 62.10; H, 4.80; N, 8.50; S, 9.60. Calc. for $C_{17}H_{16}N_2O_3S$: C, 62.19; H, 4.87; N, 8.53; S, 9.75 %).

Ethyl 3-cyano-1,2-dihydro-4-p-methoxyphenyl-6-styryl-2-thioxopyridine 5-carboxylates (9a,b):

Method (a): To a solution of 2 (3.2 gm; 0.01 mole) in 20 ml of dioxane catalyzed with few drops of piperidine, either benzaldehyde (1.06 gm, 0.01 mole) or anisaldehyde (1.3 gm, 0.01 mole) was added. The reaction mixture was refluxed for 3h, then poured into ice-cold water. The solid product, so formed, was collected by filtration.

Method (b): To a solution of 2 (3.2 gm; 0.01 mole) in 20 ml of pyridine, compounds 10a,b (0.01 mole) were added. The reaction mixture was refluxed for 3h, poured into ice-cold water and acidified with conc. HCl. The solid product, so formed, was collected by filtration.

Compound 9a formed yellow crystals from ethanol, yield 1.8 g (44 %); m.p. 135°. - IR (KBr); 3400 cm^{-1} (NH); 2220 (CN), 1725 (CO); 1190 (CS). - ^1H NMR: δ = 1.2 (t, 3H, CH_3); 2.6 (s, 1H, NH); 3.9 (s, 3H, OCH_3); 4.2 (q, 2H, CH_2); 7.0-7.5 (m, 11H, aromatic and styryl protons). (Found C, 68.80; H, 4.90; N, 6.90; S, 7.80. Calc. for $C_{24}H_{20}N_2O_3S$: C, 69.23; H, 4.80; N, 6.73; S, 7.69 %).

Compound 9b formed yellow crystals from ethanol yield 2.1 g (48 %); m.p. 191 °C. - IR (KBr): 3350 cm^{-1} (NH); 2225 (CN); 1725 (CO); 1190 (C=S). - ^1H NMR: δ = 1.0 (t, 3H, CH_3); 3.3 (s, 1H, NH); 3.8 [s, 6H, two (OCH_3)]; 4.0 (q, 2H, CH_2); 6.8-7.5 (m, 10H, aromatic and styryl protons). (Found C, 67.20; H, 5.00; N, 6.40. Calc. for $C_{25}H_{22}N_2O_4S$: C, 67.26; H, 4.93; N, 6.27 %).

2-(m-Chlorophenylhydrazono)-3-oxobutyronitrile (11)

To a solution of 3-aminocrotononitrile (20) (0.8 g, 0.01 mole) in ethanol (20 ml) containing sodium acetate (3 g), an ice cold solution of m-chlorophenyldiazonium chloride (0.01 mole) was added with stirring. After 30 mn., the solid product was collected by filtration and crystallized from acetic acid. The resulted aminophenylhydrazone derivative was converted into the ketone (11) by refluxing in 20 ml acetic acid-hydrochloric acid (2 ml) for ½ h. The reaction mixture was poured into ice-water. The solid product, so formed, was collected by filtration and crystallized from ethanol as yellow crystals; yield 1.8 g (85 %); m.p. 182°C. - IR (KBr): 3400, 3300 cm^{-1} (NH); 2200 (CN), 1700 (CO). (Found: C, 54.20; H, 3.60; N, 18.80; Cl, 16.10. Calc. for $C_{10}H_8N_3OCl$: C, 54.17; H, 3.61; N, 18.96; Cl, 16.02 %).

1,6-Dihydro-1-(m-chlorophenyl)-4-methyl-6-oxopyridazin-3,5-dicarbonitrile (4)

To a suspension of 11 (22 g; 0.1 mole) in benzene (200 ml), ethylcyanoacetate (11.3 g, 0.1 mole), 12 ml of glacial acetic and 8 gm of ammonium acetate were added. The reaction mixture was refluxed in a flask fitted with a device for continual water separation till no more water was separated (24 h). The solvent was then removed in vacuo and the remaining product was crystallized from ethanol as colourless crystals; yield 17 g (63 %); m.p. 210 °C .-IR (KBr): 2225 cm^{-1} (CN); 1690 (CO). - ^1H NMR: δ = 2.5 (s, 3H, CH_3); 7.5-7.8 (m, 4H, aromatic protons). (Found: C, 57.60; H, 2.40; N, 20.80. Calc. for $C_{13}H_7N_4OCl$: C, 57.67; H, 2.58; N, 20.70 %).

8-Amino-6-aryl-2,3-dihydro-2-(m-chlorophenyl)-3-oxocinnoline-4,7-dicarbonitriles (13a-c).

To a solution of 4 (2.7 g, 0.01 mole) in ethanol (20 ml), the appropriate amount of arylidenemalononitriles 10a-c (0.01 mole) and a catalytic amount of piperidine were added. The reaction mixture was refluxed for 1h. The precipitate, formed on cooling, was collected by filtration and crystallized from the proper solvent.

Compound 13a yellowish-green crystals from dioxane; yield 1.5 g (38 %); m.p. 262°C. - IR (KBr): 3480, 3360 cm^{-1} (NH_2); 2220, 2200 (CN); 1710 (CO). - ^1H NMR: δ = 6.9 (s, 2H, NH_2); 7.5-7.8 (m, 10H, aromatic protons). (Found: C, 66.40; H, 3.10; N, 17.70. Calc. for $C_{22}H_{12}N_5OCl$: C, 66.41; H, 3.01; N, 17.61 %).

H, 2.50; N, 16.10. Calc. for $C_{22}H_{11}N_5OCl_2$: C, 61.11; H, 2.54; N, 16.20 %).

Compound 13c, yellow crystals from dioxane, yield 1.7 g (42 %); m.p. 225 °C. (Found: C, 64.50; H, 3.30; N, 16.50. Calc. For $C_{23}H_{14}N_5O_2Cl$: C, 64.56; H, 3.27; N, 16.37 %).

Ethyl 8-amino-6-aryl-1,2-dihydro-2-(m-chlorophenyl)-7-cyano-1-oxophthalazine-4-carboxylate(14a-c).

An equimolar amount of compound 15 (3.1 g; 0.01 mole) and the appropriate amount of arylidenemalononitriles 10a-c (0.01 mole) were refluxed in ethanol (20 ml) catalyzed with piperidine for 1 h. The solid product was collected by filtration and crystallized from the proper solvent.

Compound 14a; yellowish green crystals from DMF; yield 2g (51 %); m.p. 206 °C. - IR (KBr): 3480, 3330 cm^{-1} (NH_2); 2220 (CN); 1730, 1720 (CO). - ^{1}H NMR: δ = 1.3 (t, 3H, CH_3); 3.3 (s, 2H, NH_2); 4.3 (q, 2H, CH_2); 7.5-7.8 (m, 10H, aromatic protons). (Found: C, 64.80; H, 3.90; N, 12.70. Calc. for $C_{24}H_{17}N_4O_3Cl$: C, 64.79; H, 3.82; N, 12.59 %).

Compound 14b; yellow crystals from DMF, yield 2.6 g (55 %), m.p. 261 °C. (Found: C, 60.20; H, 3.40; N, 11.70. Calc. for $C_{24}H_{16}N_4O_3Cl_2$: C, 60.12; H, 3.34; N, 11.69 %).

Compound 14c; yellow crystals from DMF; yield 2.3 g (49 %), m.p. 215 °C. (Found: C, 63.40; H, 4.10; N, 11.80. Calc. for $C_{25}H_{19}N_4O_4Cl$: C, 63.22; H, 4.00; N, 11.80 %).

Ethyl 1,6-dihydro-1-(m-chlorophenyl)-5-cyano-4-methyl-6-oxopyridazine-3-carboxylate (15)

To a suspension of 16 (26.8 g; 0.1 mole) in benzene (200 ml), ethyl cyanoacetate (11.3 g; 0.1 mole), 12 ml glacial acetic acid and 8 g of ammonium acetate were added. The reaction mixture was refluxed, with continual water separation, for 15 h. The solvent was then removed in vaccuo and the remaining solid product was crystallized from ethanol as yellow crystals; yield 17 g (54 %); m.p. 125 °C. - IR (KBr): 2220 cm^{-1} (CN); 1725, 1700 (CO). (Found: C, 56.70; H, 3.80; N, 13.40. Calc. for $C_{15}H_{12}N_3O_3Cl$: C, 56.69; H, 3.77; N, 13.22 %).

8-Amino-7-cyano-2,3-dihydro-2-(m-chlorophenyl)-3-oxo-6-phenylcinnoline-4-carboxylic acid (18)

Compound 13a (3.9 g; 0.01 mole) was refluxed in an ethanolic sodium hydroxide solution for 5 h. The reaction mixture was poured into water and neutralized with conc. HCl. The precipitate, so formed, was collected by filtration and crystallized from dioxane as yellow crystals; yield 3.9 g (94 %); m.p. >300 °C. - IR (KBr): 3450, 3280 cm^{-1} (NH_2); 2220 (CN); 1690 (CO). (Found: C, 63.40; H, 3.10; N, 13.60. Calc. for $C_{22}H_{13}N_4O_3Cl$: C, 63.38; H, 3.12; N, 13.44 %).

8-Amino-2-(m-chlorophenyl)-7-cyano-1,2-dihydro-1-oxo-6-phenylphthalazine 4-carboxylic acid (17)

Compound 14a (4.4 g; 0.01 mole) was refluxed for 0.5 h in ethanol (20 ml) containing 0.01 mole of sodium hydroxide. The reaction mixture was then diluted with water and neutralized with conc. HCl till pH 7. The solid product was collected by filtration and crystallized from ethanol as brown crystals; yield 2.7 g (65 %); m.p. 235 °C. - IR (KBr): 3470, 3400, 3300 cm^{-1} (NH_2); 2200 (CN); 1725 (CO). - ^{1}H NMR: δ = 3.4 (s, 2H, NH_2); 7.4-7.7 (m, 10H, aromatic protons); 8.2 (br.,1H, OH). (Found: C, 63.30; H, 3.00; N, 13.60. Calc. for $C_{22}H_{13}N_4O_3Cl$: C, 63.38; H, 3.12; N, 13.44 %).

1-(m-Chlorophenyl)-1,6-dihydro-6-oxo-4-styrylpyridazin-3,5-dicarbonitrile (19a,b)

To a solution of compound 4 (2.7 g; 0.01 mole) in 20 ml of ethanol, either benzaldehyde (1.06 g, 0.01 mole) or p-chlorobenzaldehyde (1.4 g; 0.01 mole) was added. The solution was refluxed for 0.5 h. The solid product, formed on cooling, was collected by filtartion and crystallized from ethanol.

Compound 19a, brown crystals; yield 2 g (61 %); m.p. 210 °C. - IR (KBr): 2220, 2200 cm^{-1} (CN); 1710 (CO). - ^{1}H NMR: δ = 7.3-7.9 (m, aromatic and styryl protons). (Found: C, 67.00; H, 3.10; N, 15.70. Calc. for $C_{20}H_{11}N_4OCl$: C, 66.94; H, 3.06; N, 15.62 %).

Compound 19b, brown crytals; yield 2.3 g (60 %); m.p. 235 °C. (Found: C, 61.00; H, 2.40; N, 14.40. Calc. for $C_{20}H_{10}N_4OCl_2$: C, 61.06; H, 2.54; N, 14.24 %).

Reaction of 19 with malononitrile

0.01 mole of either 19a or 19b was refluxed with 0.01 mole of malononitrile in ethanol (20 ml), catalyzed with 1 ml of piperidine for 3 h. The solid product was collected by filtration, crystallized from dioxane, and indentified as either compound 13a (m.p. and mixed m.p. 262 °C) or compound 13b (m.p. and mixed m.p. 240 °C) respectively.

1,6-Dihydro-4-methyl-2-phenyl-6-thioxopyrimidine-5-carbonitrile (5)

To a suspension of ammonium thiocyanate (7.6 g; 0.1 mole) in drydioxane (100 ml); benzoyl chloride (14 g, 0.1 mole) was added. The reaction mixture was refluxed for 5 mn., then treated with compound 20 (8.2 g; 0.1 mole). The reaction mixture was refluxed for 2 h and poured into ice water. The solid product was collected by filtration and crystallized from ethanol as yellow needles; yield 17 g (74 %); m.p. 210 °C. - IR (KBr): 2225 cm^{-1} (CN); 1200 (C=S). - ^1H NMR: δ = 2.5 (s, 3H, CH_3); 2.9 (s, 1H, NH); 7.3-8.3 (two m, 3H and 2H, aromatic protons). (Found: C, 63.40; H, 4.00; N, 18.60. Calc. for $C_{12}H_9N_3S$: C, 63.43; H, 3.96; N, 18.50 %).

5-Amino-7-aryl-3,4-dihydro-2-phenyl-4-thioxoquinazoline-6-carbonitrile (21a-c):

Method (A): An equimolar amount of compound 5 (2.2 g; 0.01 mole) and the appropriate amount (0.01 mole) of arylidenemalononitrile (10a-c) in pyridine (10 ml) was refluxed for 4 h. The reaction mixture was poured into water. The solid product was collected by filtration and crystallized from dioxane/ethanol (1:1).

Compound 21a, brown crystals; yield 1.4 g (42 %); m.p. 245 °C. - IR (KBr): 3400, 3220 cm^{-1} (NH_2 and NH); 2200 (CN); 1190 (CS). - ^1H NMR: δ = 2.5 (s, 2H, NH_2); 7.3-7.7 (m, 11H, aromatic protons); 8.4 (s, 1H, NH). (Found: C, 71.20; H, 4.00; N, 15.90. Calc. for $C_{21}H_{14}N_4S$: C, 71.18; H, 3.95; N, 15.81 %).

Compound 21b; brown crystals; yield 1.9 g (51 %); m.p. 202 °C. (Found: C, 64.90; H, 3.40; N, 14.30. Calc. for $C_{21}H_{13}N_4SCl$: C. 64.86; H, 3.34; N, 14.41 %).

Compound 21c, yellow crystals; yield 1.8 g (48 %); m.p. 252 °C. (Found: C, 68.70; H, 4.20; N, 14.60. Calc. for $C_{22}H_{16}N_4SO$: C, 68.75; H, 4.16; N, 14.58 %).

Method (B):

i. 1,6-Dihydro-2-phenyl-4-styryl-6-(thioxopyrimidine-5-carbonitrile (22a-c).

To a solution of 5 (2.2 g; 0.01 mole) in 20 ml of dioxane, 0.01 mole of the appropriate aldehyde and a catalytic amount of piperidine were added. The reaction mixture was refluxed for 5 h. The solid product, formed on cooling, was collected by filtration and crystallized from dioxane/ethanol (1:1).

Compound 22a; yellow crystals; yield 3 g (96 %); m.p. 250 °C. - IR (KBr): 3400, 3170 cm^{-1} (NH); 2220 (CN); 1200 (CS). - ^1H NMR: δ = 2.5 (s, 1H, NH); 7.2 (d, 1H, styryl proton); 7.5-7.9 (m, 9H, aromatic and the other styryl proton); 8.3 (d,d, 2H, two ortho H of phenyl at C-2 of pyrimidine). (Found: C, 72.40; H, 4.10; N, 13.50. Calc. for $C_{19}H_{13}N_3S$: C, 72.38; H, 4.12; N, 13.33 %).

Compound 22b, orange crystals; yield 2.9 g (85 %); m.p. 259 °C. (Found: C, 65.20; H, 3.50; N, 12.20. Calc. for $C_{19}H_{12}N_3SCl$: C, 65.23; H. 3.43; N, 12.01 %).

Compound 22c, yellow crystals, yield 3 g (88 %); m.p. 266 °C. (Found: C, 69.50; H, 4.40; N, 12.20. Calc. for $C_{20}H_{15}N_3SO$: C, 69.56; H, 4.34; N, 12.17 %).

ii. Reaction of 22 with malononitrile.

0.01 mole of either 22a, 22b or 22c was refluxed with 0.01 mole of malononitrile in pyridine (10 ml) for 5 h. The reaction mixture was poured into water. The solid product, so formed, was collected by filtration, crystallized from dioxane/ethanol (1:1) and identified as compound 21a (m.p. and mixed m.p. 245 °C), compound 21b (m.p. and mixed m.p. 202 °C) or compound 21c (m.p. and mixed m.p. 252 °C) respectively.

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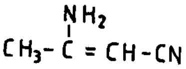
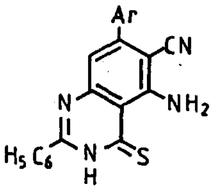
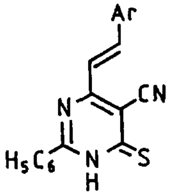


$CH_3-\overset{NH_2}{C}=CH-CN$

20



21 a - c



22 a - c

21& 22- a, Ar = C_6H_5

b, Ar = C_6H_4Cl-p

c, Ar = $C_6H_4OCH_3$-p