SYNTHESIS OF NEW POLYFUNCTIONALLY SUBSTITUTED PYRIDAZINES, PHTHALAZINES, CINNOLINES AND THIENO[3,4-*c*]PYRIDAZINES

Salah EL-KOUSY[a], Ibraheim EL-SAKKA[a], Abdel Monem EL-TORGOMAN[a], Hesham ROSHDY[a] and Mohamed Hilmy ELNAGDI[b]

[a] *Department of Chemistry, Faculty of Science, Menofia University, Shibin El-Rom, A. R. Egypt*

[b] *Department of Chemistry, Faculty of Science, Cairo University, Giza, A. R. Egypt*

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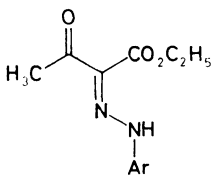
The reaction of ethyl 2-arylhydrazono-3-oxobutyrates (*Ia, Ib*) with active methylene ketones afforded pyridazin-5-carbonitrile derivatives. The methyl function in the ethyl pyridazin-3--carboxylate derivatives *IIa, IIb* reacted with arylidenemalononitrile to yield the phthalazine derivatives *Va—Vf* and with elemental sulphur to yield the thienopyridazines *XIXa, XIXb*. The cinnolines are producted from reaction of *IIa, IIb* with diethyl acetonedicarboxylate.

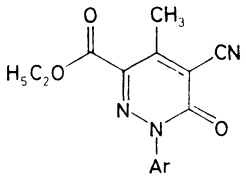
Polyfunctionally substituted heterocycles are interesting as potential biodegradable agrochemicals.[1] Our group has been involved for some time is programme aimed at developping new polyfunctionally substituted heterocycles as potential antischistosomal agents.[2-4] As part of this programme samples of polyfunctionally substituted pyridazines were required. We investigated possible utility of the readily obtainable 4-methylpyridazin-5-carbonitriles as starting for synthesis of the required samples. Recently we have shown that alkylazinylcarbonitriles are excellent starting for preparation of polyfunctionally substituted benzoazines.[1-3] In the present work we report our further results in this area.

Thus, ethyl 2-arylhydrazono-3-oxobutyrates (*Ia, Ib*) condensed with ethyl cyanoacetate in presence of ammonium acetate to yield the pyridazinones *IIa, IIb*. Compounds *IIa, IIb* were also obtained via coupling of *III* with arenediazonium salts and subsequent treatment of the crude products with acetic acid, following a general procedure described earlier by Gewald et al.[5] Compounds *IIa, IIb* so obtained, reacted with arylidenemalononitrile *IVa—IVc* to yield products of condensation via hydrogen cyanide elimination. These can be formulated as the phthalazines *V* or *VI*. Thus, one may assume addition of *IIa, IIb* to *IVa—IVc* to yield a Michael adduct which on cyclization and aromatisation, via hydrogen cyanide elimination, may afford *V*. Alternately one can assume addition of the methyl function to one of the cyano groups in *IV*. This would yield an acyclic diene which may then undergo

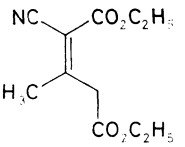
4 + 2 cycloaddition followed by hydrogen cyanide elimination to yield the isomeric phthalazine *VI*. Structure *V* could be established for reaction product based on their identity with products obtained via condensing *IIa*, *IIb* with aldehydes and subsequent treatment of resulting styryl derivatives *VIIa – VIIf* with malononitrile, clearly these products can only be *V*.



I

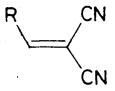


II

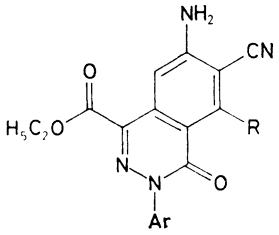


III

In formulae *I* and *II*: *a*, Ar = 2-$CH_3OC_6H_4$
b, Ar = 2-$CH_3C_6H_4$



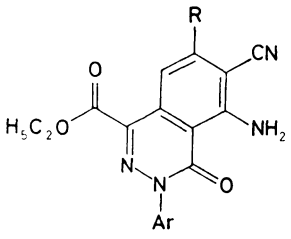
IVa, R = C_6H_5
IVb, R = 4-$OCH_3C_6H_4$
IVc, R = 2-thienyl



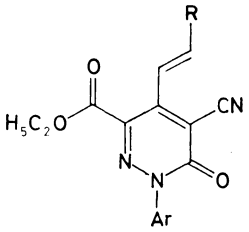
VI

Compounds *Va – Vf* were assigned the amino structure and not possible tautomeric imino structure based on ^{1}H NMR which revealed absence of any protons linked to sp^3 carbons, other than those of the ester function as required for the imine structure. The ^{1}H NMR revealed amino function at δ 7·7 ppm and phthalazine ring H-4 at δ 7·5 ppm. These protons appeared at a lower field as they are deshielded by ring C=O and ester C=O anisotropy.

In order to synthesize other substituted phthalazines a variety of new methylpyridazinecarbonitriles were syntesised via condensing *Ia* and *Ib* with active methylene reagents. Thus, *Ia*, *Ib*, condensed with malononitrile to yield products that may be formulated as the imine *VIII* or amino carboxylate derivative *IX*. ^{1}H NMR revealed existance of NH_2 signal at δ 7·57 ppm indicating that the aromatic form *IX* is the one predominating in CD_3SOCD_3 solutions.



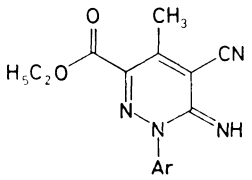
V



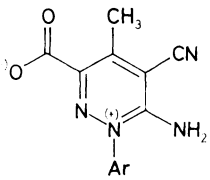
VII

In formulae *V* and *VII*: *a*, Ar = 2-$CH_3OC_6H_4$; R = C_6H_5
b, Ar = 2-$CH_3C_6H_4$; R = C_6H_5 *c*, Ar = 2-$CH_3OC_6H_4$; R = 4-$CH_3OC_6H_4$
d, Ar = 2-$CH_3C_6H_4$; R = 4-$CH_3OC_6H_4$ *e*, Ar = 2-$CH_3OC_6H_4$; R = 2-thienyl
f, Ar = 2-$CH_3C_6H_4$; R = 2-thienyl

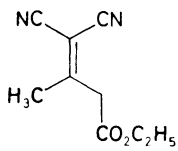
The formation of *IX* from *I* and malononitrile is assumed to proceed via condensation of the nitrile with the CO group in *I*. This condensation product then cyclises into ethyl iminopyridazine carboxylate derivative which then hydrolyses by water, eliminated in condensation step, to yield the final isolable *IX*. Intermediates for formation of *IX* could not be isolated. Compounds *IXa*, *IXb* could be also prepared via coupling *X* with aryldiazonium salts and subsequent reflux of crude coupling product in aqueous acetic acid.



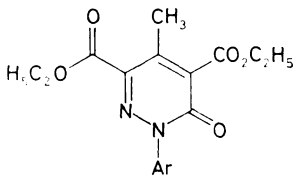
VIII



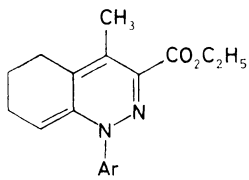
IX



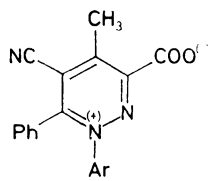
X



XI



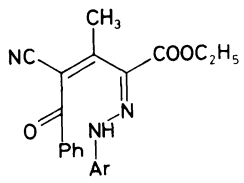
XII



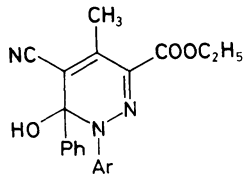
XIII

In formulae *IX*, *XI*–*XIII*: *a*, Ar = 2-$CH_3OC_6H_4$ *b*, Ar = 2-$CH_3C_6H_4$

Compounds *Ia* and *Ib* also condensed with diethyl malonate and with cyclohexanone to yield the pyridazin-6-ones *XI* and *XII*. Formation of these products is assumed to proceed via sequence similar to that suggested previously to account for formation of *II*. The reaction of *I* with benzoylacetonitrile gave a product that is formulated as *XIII*. Formation of *XIII* is assumed to proceed via intermediacy of *XIV* which on cyclization would yield *XV*. The latter on hydrolysis, by water eliminated in the condensation step, would yield *XIII*. The methyl function in *XI*, *XII* and *XIII* proved inactive toward *IV* under a variety of conditions.

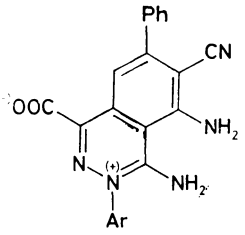


XIV

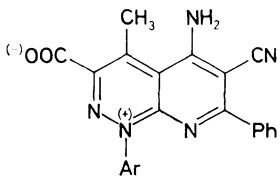


XV

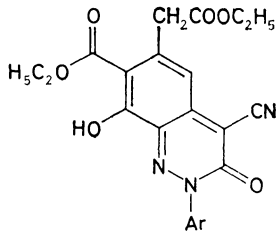
In formulae *XIV* and *XV*: *a*, Ar = 2-$CH_3OC_6H_4$
b, Ar = 2-$CH_3C_6H_4$



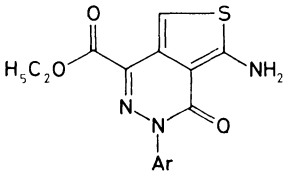
XVI



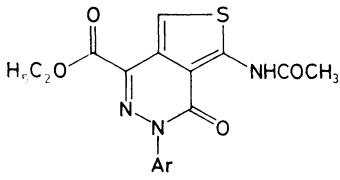
XVII



XVIII



XIX



XX

In formulae *XVI*–*XX*: *a*, Ar = 2-$CH_3OC_6H_4$ *b*, Ar = 2-$CH_3C_6H_4$

Compounds *IXa* and *IXb* reacted with *IVa* to yield products that were formulated as the phthalazines *XVIa* and *XVIb* rather than the triazanaphthalenes *XVIIa* and

XVIIb based on ^{1}H NMR which revealed absence of signal for methyl function and two NH_2 signals.

The observation that *IIa*, *IIb* react with *IVa–IVc* to yield phthalazines leads us to inspect the behaviour toward other polydentate reagents. Compounds *IIa*, *IIb* reacted with diethyl 1,3-acetonedicarboxylate to yield products of addition and ethanol elimination. These were formulated as the cinnolines *XVIIIa* and *XVIIIb*. Compounds *IIa* and *IIb* reacted with benzoylisothiocyanate to yield adducts. These were very unstable and decomposed into *IIa*, *IIb* on attempted crystallization.

It has been found that *IIa* and *IIb* react with elemental sulphur when refluxed in ethanol in presence of triethylamine to yield the thienopyridazines *XIXa* and *XIXb*. These compounds could be converted into the acetyl derivatives *XXa* and *XXb* on reflux in acetic anhydride. These acylaminothiophenes did not afford 4 + 2 cycloadducts on treatment with α,β-unsaturated double bonds to yield phthalazines in a way similar to that recently reported[6] by us for aminothieno[3,4-*c*]pyridazinones. It seems that strong electron donating substituent should be present on the thiophene moiety to lower HOMO–LUMO energy of the diene system in thienopyridazine to match with that in electron poor dienophiles.

EXPERIMENTAL

All melting points are uncorrected. Infrared spectra were recorded on a Perkin–Elmer SP 177 spectrometer in KBr disc (wavenumbers in cm^{-1}). Proton NMR spectra were taken on a Varian A-90 (90 MHz) instrument at 25°C in CD_3SOCD_3 with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale) coupling constants (*J*) in Hz.

Ethyl 1-Aryl-5-cyano-1,6-dihydro-4-methyl-6-oxopyridazin-3-carboxylate (*IIa* and *IIb*)

A) A mixture of each of *Ia*, *Ib* (0·1 mol), ethyl cyanoacetate (10·6 ml, 0·1 mol) and of ammonium acetate (15 g) was fused at 130°C for 10 min. The solid product, so formed, was collected by filtration and crystallised from ethanol.

B) A solution of *III* (0·01 mol) in ethanol (50 ml) was treated with sodium acetate (3·0 g) then with a solution of appropriate diazonium salt (prepared from appropriate quantities of amine and sodium nitrite). The solid product, so formed, was collected by filtration then boiled in acetic acid for 5 min and poured into water. The solid product, so formed was identified as *IIa*, *IIb* (m.p. and mixed m.p.). Yield 75% and 70%, respectively.

Pyridazine IIa: m.p. 132°C, yield 89%; IR spectrum: 2 220 (CN); 1 720 (ester C=O); 1 680 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·3 s, 3 H (CH_3); 1·8 s, 3 H (CH_3); 4·3 q, 2 H (CH_2, J = 7); 7·5–7·7 m, 4 H (aromatic protons). For $C_{16}H_{15}N_3O_4$ (313·3) calculated: 61·34% C, 4·74% H, 13·41% N; found: 61·25% C, 4·69% H, 13·50% N.

Pyridazine IIb: m.p. 96°C, yield 88%; IR spectrum: 2 220 (CN); 1 720 (ester C=O); 1 680 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·0 s, 3 H (CH_3); 2·8 s, 3 H (CH_3); 4·2 q, 2 H (CH_2, J = 7); 7·5–7·7 m, 4 H (aromatic protons). For $C_{16}H_{15}N_3O_3$ (297·3) calculated: 64·64% C, 5·05% H, 14·14% N; found: 64·69% C, 5·00% H, 14·00% N.

Ethyl 5-Amino-3-aryl-6-cyano-7-substituted-3,4-dihydro-4-oxophthalazin-1-carboxylate (*Va*—*Vf*)

A) A solution of each of *IIa*, *IIb* (0·01 mol) in ethanol (90 ml) was treated with each of *IVa* to *IVc* (0·01 mol) and piperidine (1 ml). The reaction mixture was refluxed for 4 h then evaporated in vacuo. The solid product so formed was triturated with ethanol, collected by filtration and crystallized from the proper solvent.

B) A suspension of each of *VIIa*—*VIIf* (10 mmol) in ethanol (75 ml) was treated with malononitrile (0·70 g, 10·5 mmol), then with piperidine (two drops). The reaction mixture was refluxed for 5 h then evaporated in vacuo. The remaining product was triturated with ethanol and the so formed solid product was collected by filtration and identified (m.p. and mixed m.p.) as *Va*—*Vf*, yields 55, 56, 57, 56, 55, and 65%, respectively.

Phthalazine Va: crystallized from aqueous DMF, m.p. 268°C, yield 87%; IR spectrum: 3 440, 3 300 (NH_2); 2 220 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum; 1·3 t, 3 H (CH_3, J = 7·1); 2·8 s, 3 H (CH_3); 4·5 q, 2 H (CH_2, J = 7·1); 7·3—7·6 m, 10 H (aromatic protons); 7·7 s, 2 H (NH_2). For $C_{25}H_{20}N_4O_4$ (440·5) calculated: 68·18% C, 4·54% H, 12·72% N; found: 68·25% C, 4·52% H, 12·63% N.

Phthalazine Vb: crystallized from aqueous DMF, m.p. 193°C, yield 81%; IR spectrum: 3 440, 3 300 (NH_2); 2 220 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·1 s, 3 H (CH_3); 4·5 q, 2 H (CH_2, J = 7); 7·3—7·6 m, 10 H (aromatic protons); 7·7 s, 2 H (NH_2). For $C_{25}H_{20}N_4O_3$ (424·5) calculated: 70·75% C, 4·72% H, 13·21% N; found: 70·90% C, 4·80% H, 13·00% N.

Phthalazine Vc: crystallized from aqueous DMF, m.p. 284°C, yield 81%; IR spectrum: 3 450, 3 310 (NH_2); 2 220 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·8 s, 6 H (2 × CH_3); 4·4 q, 2 H (CH_2, J = 7); 7·3—7·6 m, 9 H (aromatic protons); 7·7 s, 2 H (NH_2). For $C_{26}H_{22}N_4O_5$ (470·5) calculated: 66·38% C, 4·68% H, 11·91% N; found: 66·11% C, 4·45% H, 12·10% N.

Phthalazine Vd: crystallized from aqueous DMF, m.p. 258°C, yield 78%; IR spectrum: 3 430 to 3 320 (NH_2); 2 225 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·0 s, 3 H (CH_3); 2·8 s, 3 H (CH_3); 4·5 q, 2 H (CH_2, J = 7); 7·3—7·6 m, 9 H (aromatic protons); 7·7 s, 2 H (NH_2). For $C_{26}H_{22}N_4O_4$ (454·5) calculated: 68·72% C, 4·85% H, 12·33% N; found: 48·55% C, 5·00% H, 12·45% N.

Phthalazine Ve: crystallized from chloroform–ether, m.p. 250°C, yield 71%; IR spectrum: 3 420, 3 300 (NH_2); 2 230 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3); 2·7 s, 3 H (CH_3); 4·5 q, 2 H (CH_2); 7·3—7·8 m, 10 H (aromatic protons, NH_2 and thienyl protons). For $C_{23}H_{18}N_4O_4S$ (446·5) calculated: 61·88% C, 4·04% H, 12·56% N, 7·17% S; found: 61·78% C, 3·80% H, 12·65% N, 7·17% S.

Phthalazine Vf: crystallized from chloroform–ether, m.p. 239°C, yield 72%; IR spectrum: 3 420, 3 330 (NH_2); 2 290 (CN); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3); 2·0 s, 3 H (CH_3); 4·5 q, 2 H (CH_2); 7·3—7·8 m, 10 H (aromatic protons, NH_2 and thienyl protons). For $C_{23}H_{18}N_4O_3S$ (430·5) calculated: 64·19% C, 4·19% H, 13·02% N, 7·44% S; found: 64·21% C, 4·00% H, 13·2% N, 7·59% S.

Reaction of Pyridazines *IIa*, *IIb* with Aldehydes. Preparation of *VIIa*—*VIIf*

A solution of each of *IIa*, *IIb* (0·01 mol) in ethanol (50 ml) was treated with the appropriate

aldehyde (0·01 mol) then with few drops of piperidine. The reaction mixture was refluxed for 4 h then poured onto water. The solid product, so formed, was collected by filtration and crystallized from the proper solvent.

Pyridazine VIIa: crystallized from ethanol, m.p. 172°C, yield 68%; IR spectrum: 2 230 (CN); 1 700 (C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·3 t, 3 H (CH_3, J = 7); 2·7 s, 3 H (CH_3); 4·4 q, 2 H (CH_2, J = 7); 6·6 d, 1 H (CH, J = 11, styryl proton); 6·8 d, 1 H (CH, J = 11, styryl proton); 7·6—7·7 m, 5 H (aromatic protons); 7·8—7·9 m, 4 H (aromatic protons). For $C_{23}H_{19}N_3O_4$ (401·4) calculated: 68·83% C, 4·74% H, 10·47% N; found: 68·62% C, 4·61% H, 10·10% N.

Pyridazine VIIb: crystallized from ethanol, m.p. 138°C, yield 71%. For $C_{23}H_{19}N_3O_3$ (385·5) calculated: 71·68% C, 4·94% H, 10·91% N; found: 71·77% C, 5·00% H, 11·40% N.

Pyridazine VIIc: crystallized from DMF, m.p. 179°C, yield 78%. ^{1}H NMR spectrum: 1·4 t, 3 H (CH_3, J = 7); 2·7 s, 6 H (2 × CH_3); 4·4 q, 2 H (CH_2, J = 7); 6·6 d, 1 H (CH, J = 11·2); 6·8 d, 1 H (CH, J = 11·2); 7·6—7·7 m, 4 H (aromatic protons); 7·8—7·9 m, 4 H (aromatic protons). For $C_{24}H_{21}N_3O_5$ (431·5) calculated: 66·82% C, 4·87% H, 9·74% N; found: 66·73% C, 4·83% H, 9·62% N.

Pyridazine VIId: crystallized from acetic acid, m.p. 125°C, yield 75%. For $C_{24}H_{21}N_3O_4$ (415·5) calculated: 69·40% C, 5·06% H, 10·12% N; found: 69·41% C, 5·12% H, 10·00% N.

Pyridazine VIIe: crystallized from ethanol, m.p. 184°C, yield 67%. ^{1}H NMR spectrum: 1·4 t, 3 H (CH_3, J = 7); 2·7 s, 3 H (CH_3); 4·4 q, 2 H (CH_2, J = 7); 6·6 d, 1 H (CH, J = 11); 6·8 d, 1 H (CH, J = 11); 7·6—7·7 m, 4 H (aromatic protons); 7·8—7·9 m, 3 H (thienyl protons). For $C_{21}H_{17}N_3O_4S$ (407·5) calculated: 61·92% C, 4·18% H, 10·32% N, 7·86% S; found: 61·81% C, 4·11% H, 10·21% N, 7·55% S.

Pyridazine VIIf: crystallized from acetic acid, m.p. 154°C, yield 71%. For $C_{21}H_{17}N_3O_3S$ (391·5) calculated: 64·45% C, 4·35% H, 10·74% N, 8·18% S; found: 64·61% C, 4·45% H, 11·10% N, 8·15% S.

6-Amino-5-cyano-1-aryl-4-methylpyridazinium-3-carboxylate (*IXa* and *IXb*)

A) A mixture of each of *Ia*, *Ib* (10 mmol) nad malononitrile (660 mg, 10 mmol) was treated with ammonium acetate (3·0 g) then heated at 120°C for 10 min. The reaction mixture was then left to cool and triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from DMF.

B) A solution of *X* (0·01 mol) in ethanol (30 ml) was treated with sodium acetate (3·0 g) then with a solution of the aryldiazonium salt (prepared from appropriate amounts of amine and sodium nitrite as has been previously described). The solid product, so formed, was collected by filtration, boiled in acetic acid for 10 min and then poured onto water. The solid product, so formed, was collected by filtration and identified (m.p. and mixed m.p. as *IXa*, *IXb*), yield 75% and 70%, respectively.

Pyridazine IXa: m.p. 220°C, yield 91%; IR spectrum 3 420—3 330 (NH_2); 2 200 (CN); 1 740 (C=O). ^{1}H NMR spectrum: 2·1 s, 3 H (CH_3); 2·9 s, 3 H (CH_3); 6·5 s, 2 H (NH_2); 7·5—7·7 m, 4 H (aromatic protons). For $C_{14}H_{12}N_4O_3$ (284·3) calculated: 59·15% C, 4·22% H, 19·71% N; found: 59·10% C, 4·00% H, 19·62% N.

Pyridazine IXb: m.p. 178°C, yield 88%; IR spectrum: 3 420, 3 340 (NH_2); 2 220 (CN); 1 740 (C=O). For $C_{14}H_{12}N_4O_2$ (268·3) calculated: 62·68% C, 4·47% H, 20·89% N; found: 62·58% C, 4·51% H, 20·66% N.

Preparation of Pyridazines *XI—XIII*

A mixture of each of *Ia*, *Ib* (0·01 mol) and the appropriate active methylene reagent; diethyl malonate, cyclohexanone or benzoylacetonitrile (0·01 mol) was treated with ammonium acetate (3 g) and acetic acid (4 ml), then suspended in benzene (150 ml). The reaction mixture was refluxed in a flask fitted with a device for continual water elimination and reflux was continued 6, 10, 17 h, respectively, till no more water was eliminated. The benzene layer was then decanted and evaporated in vacuo, the formed solid product was triturated with petroleum ether, collected by filtration and crystallized from the proper solvents.

Pyridazine XIa: crystallized from ethanol, m.p. 123—124°C, yield 60%; ^{1}H NMR spectrum: 1·4 m, 6 H (2 × CH_3); 1·8 s, 3 H (CH_3); 2·7 s, 3 H (CH_3); 4·4 m, 4 H (2 × CH_2); 7·6 m, 4 H (aromatic protons). For $C_{18}H_{20}N_2O_6$ (360·4) calculated: 60·00% C, 5·55% H, 7·77% N; found: 60·21% C, 5·32% H, 7·95% N.

Pyridazine XIb: crystallized from ethanol, m.p. 115°C, yield 62%. For $C_{18}H_{20}N_2O_5$ (344·4) calculated: 62·79% C, 5·81% H, 8·14% N; found: 62·81% C, 5·71% H, 8·21% N.

Diazine XIIa: crystallized from ethanol, m.p. 106°C, yield 64%; IR spectrum: 1 715 (ester C=O); 1 670 (ring C=O). For $C_{19}H_{22}N_2O_3$ (326·4) calculated: 69·90% C, 6·74% H, 8·58% N; found: 69·81% C, 6·61% H, 8·71% N.

Diazine XIIb: crystallized from ethanol, m.p. 108—110°C, yield 55%; IR spectrum: 1 725 (ester C=O). For $C_{19}H_{22}N_2O_2$ (310·2) calculated: 73·55% C, 7·09% H, 9·03% N; found: 73·35% C, 6·88% H, 9·12% N.

Pyridazine XIIIa: crystallized from glacial acetic acid, m.p. 282°C, yield 54%; IR spectrum: 2 220 (CN); 1 715 (C=O). ^{1}H NMR spectrum: 2·0 s, 3 H (CH_3); 2·7 s, 3 H (CH_3); 7·5 m, 9 H (aromatic protons). For $C_{20}H_{15}N_3O_3$ (345·4) calculated: 69·55% C, 4·38% H, 12·17% N; found: 69·90% C, 4·00% H, 12·53% N.

Pyridazine XIIIb: crystallized from dioxane, m.p. 122—123°C, yield 57%; IR spectrum: 2 220 (CN); 1 715 (C=O). For $C_{20}H_{15}N_3O_2$ (329·4) calculated: 72·93% C, 4·54% H, 12·76% N; found: 73·22% C, 4·00% H, 13·01% N.

Preparation of Phthalazines *XVIa* and *XVIb*

A solution of each of *IXa*, *IXb* (0·01 mol) in pyridine (50 ml) was treated with benzylidenemalononitrile (1·54 g, 0·01 mol) and the mixture was refluxed for 4 h. The solvent was evaporated in vacuo, then the residue was triturated with cold water and the solid product was collected by filtration and crystallized from dioxane.

Phthalazine XVIa: m.p. 208—210°C, yield 82%; IR spectrum: 3 420, 3 330 (NH_2); 2 230 (CN); 1 720 (C=O). ^{1}H NMR spectrum: 2·4 s, 3 H (CH_3); 5·5 s, 2 H (NH_2); 5·7 s, 1 H (CH); 6·7 s, 2 H (NH_2); 7·5—7·7 m, 9 H (aromatic protons). For $C_{23}H_{17}N_5O_3$ (411·2) calculated: 67·15% C, 4·13% H, 17·03% N; found: 6·95% C, 3·88% H, 17·00% N.

Phthalazine XVIb: m.p. 210—212°C, yield 68%; IR spectrum: 3 420, 3 330 (NH_2); 2 230 (CN); 1 720 (C=O). ^{1}H NMR spectrum: 1·2 s, 3 H (CH_3); 5·5 s, 2 H (NH_2); 5·7 s, 1 H (CH); 7·5 to 7·7 m, 9 H (aromatic protons). For $C_{23}H_{17}N_5O_2$ (395·4) calculated: 69·87% C, 4·30% H, 17·72% N; found: 69·90% C, 4·35% H, 18·10% N.

Preparation of Cinnolines *XVIIIa* and *XVIIIb*

A solution of each of *IIa*, *IIb* (0·01 mol) in dioxane (30 ml) and glacial acetic acid (3 ml) was treated with diethyl 1,3-acetonedicarboxylate (2·02 g, 0·01 mol). The reaction mixture was refluxed for 8 h. The solvent was evaporated in vacuo and the solid product was collected by filtration and crystallized from methanol.

Cinnoline XVIIIa: m.p. 162°C, yield 79%. ^{1}H NMR spectrum: 1·1 t, 3 H (CH_3, $J = 7$); 1·4 m, 6 H (2 × CH_3); 4·5 m, 4 H (2 × CH_2); 7·1 s, 1 H (CH); 7·4—7·6 m, 4 H (aromatic protons); 7·6—7·8 m, 1 H (aromatic proton). For $C_{23}H_{21}N_3O_7$ (451·4) calculated: 61·19% C, 4·69% H, 9·31% N; found: 61·64% C, 4·52% H, 9·84% N.

Cinnoline XVIIIb: m.p. 146°C, yield 42%; IR spectrum: 2 200 (CN); 1 720 (ester C=O); 1 680 (ring C=O). For $C_{23}H_{21}N_3O_6$ (435·4) calculated: 63·44% C, 4·86% H, 9·65% N; found: 63·10% C, 4·73% H, 9·50% N.

Ethyl 1-Amino-6-aryl-6,7-dihydro-7-oxothieno[3,4-*d*]pyridazin-4-carboxylate (*XIXa* and *XIXb*)

A solution of each of *IIa*, *IIb* (0·01 mol) in absolute ethanol (75 ml) was treated with sulphur (0·32 g, 0·01 mol) then triethylamine (1 ml) was added. The reaction mixture was refluxed for 3 h, the solvent was evaporated in vacuo and the solid product was collected by filtration and crystallized from ethanol.

Thienopyridazinone XIXa: m.p. 196°C, yield 90%; IR spectrum: 3 450, 3 300 (NH_2); 1 720 (ester C=O); 1 660 (ring C=O). For $C_{16}H_{15}N_3O_4S$ (345·4) calculated: 55·65% C, 4·38% H, 12·17% N, 9·26% S; found: 55·92% C, 4·21% H, 12·25% N, 9·44% S.

Thienopyridazinone XIXb: m.p. 193°C, yield 85%; IR spectrum: 3 450, 3 300 (NH_2); 1 720 (ester C=O); 1 680 (ring C=O). For $C_{16}H_{15}N_3O_3S$ (329·4) calculated: 58·35% C, 4·59% H, 12·76% N, 9·70% S; found: 58·62% C, 4·00% H, 12·88% N, 9·61% S.

Ethyl 1-Acetylamino-6-aryl-6,7-dihydro-7-oxothieno[3,4-*d*]pyridazine-4-carboxylate (*XXa* and *XXb*)

A solution of *XIXa*, *XIXb* (3·0 g) in acetic anhydride (30 ml) was refluxed for three hours. The reaction mixture was then poured into water and the solid product formed on standing was collected by filtration and crystallized from ethanol.

Thienopyridazinone XXa: m.p. 176°C, yield 85%. For $C_{18}H_{17}N_3O_5S$ (287·4) calculated: 55·81% C, 4·42% H, 10·85% N, 8·03% S; found: 55·91% C, 4·22% H, 10·91% N, 9·40% S.

Thienopyridazinone XXb: m.p. 210°C, yield 82%; IR spectrum: 3 300 (NH); 1 720 (ester C=O); 1 670 (ring C=O). ^{1}H NMR spectrum: 1·4 t, 3 H (CH_3, $J = 7$); 2·7 s, 3 H (CH_3); 2·1 s, 3 H (CH_3); 4·5 q, 2 H (CH_2, $J = 7$); 5·2 s, 1 H (NH); 7·4—7·6 m, 4 H (aromatic protons); 7·7 s, 1 H (proton on thienyl ring). For $C_{18}H_{17}N_3O_4S$ (371·4) calculated: 58·22% C, 4·61% H, 11·32% N, 8·60% S; found: 56·85% C, 4·88% H, 11·41% N, 8·25% S.

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