REACTIONS OF 5-(p-ANISYL)-2-METHYL-7-(p-TOLYL)-4H-PYRIDO-[2, 3-d][1, 3]OXAZIN-4-ONE

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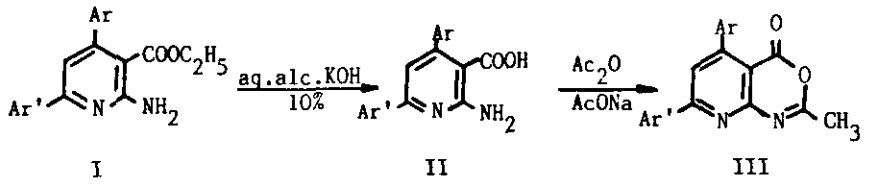
Abstract- 5-(p-Anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2, 3-d][1,3]oxazin-4-one (III) was prepared . The reactivity of III towards nucleophilic reagents was investigated. 5-(p-Anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one(VI)was synthesised from III by the action of ammonium acetate and zinc chloride . The structure of VI was chemically confirmed by reactions with acetic anhydride , benzoyl chloride , chloroacetic acid , methyl iodide , dimethyl sulphate and ethyl bromoacetate . Compound (VI) reacted with secondary and primary amines under Mannich conditions to afford 5-(p-anisyl)-2-methyl-3-methylene substituted amino-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-ones (XIV) and (XV), respectively. Thiation of VI gave the thione 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2, 3-d]pyrimidin-4-thione (XIX) .

Recently , a series of substituted 4H-3,1-benzoxazin-4-ones were assayed as inhibitors of human leukocyte elastase and other serine proteases .[1] In the present work , the authors aim to synthesize the aza-analogues of 4-benzoxazones in the hope of obtaining unreported pyridoxazinones of expected biological value and to achieve ring transformation of the synthesized pyridoxazinones into pyridopyrimidinones which were reported to be highly active against a variety of pathogenic bacteria [2] and have a potential activity as antipyretic, diuretic, bacteriostatic, sedative and coronary dilating.[3] Our precursor 2-amino-4-(p-anisyl)-6-(p-tolyl)pyridine-3-carboxylic acid (II) was prepared by alkaline hydrolysis of

the corresponding ethyl ester .[4,5] Treatment of II with acetic anhydride and fused anhydrous sodium acetate gave the title compound (III) (cf. Scheme 1) .[6,7]



I II III

Ar = C_6H_4-OCH_3-P

Ar' = C_6H_4-CH_3-P

Scheme 1

Reaction of compound (III) with hydrazines such as hydrazine hydrate , phenylhydrazine, and hydroxylamine hydrochloride in boiling alcohol yielded the respective 2-acetylaminonicotinic hydrazides (IVa,b) and the hydroxamic acid (IVc) . Treatment of the pyridoxazinone (III) with primary amines such as benzylamine, p-toluidine, aniline, and ethylamine resulted in the formation of the corresponding 2-acetylaminonicotinamides (IVd-g), respectively.

The compounds (IVa,d and f) underwent acid catalyzed cyclodehydration upon fusion with anhydrous zinc chloride to afford the 3-substituted -2-methyl-4H-pyrido[2,3-d]pyrimidin-4-ones and the corresponding 3-benzyl and 3-phenyl derivatives (Va-c) which were also synthesized by the interaction of compound (III) with hydrazine hydrate, benzylamine, and aniline, respectively ,in the presence of fused zinc chloride .

When the oxazinone (III) was allowed to react with a mixture of ammonium acetate and zinc chloride at elevated temperature, 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one (VI) was obtained .

Hydrolysis of Va was accompanied with ring fission to yield 2-acetylamino-4-(p-anisyl)-6-(p-tolyl)pyridine-3-carboxylic acid (VII) which was also isolated from the parent pyridoxazinone (III)by hydrolysis with aqueous ethanolic KOH .

Compound (III) condensed with benzaldehyde at high temperature in the presence of zinc chloride to give the 2-styryl derivative (VIII) . Bromination of VIII using bromine in acetic anhydride yielded the vicinal dibromide (XI).

The stereodynamic of compound (VIII) requires the bulky groups (phenyl and 4H-3,1-benzoxazin-2-yl) to be at opposite sides of the double bond i.e. E-configuration (J=13.30 Hz). That seems sensible because all chemical and physical methods of isolation give only one compound which is identified as compound (VIII).

Benzoylation and acetylation of 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one (VI) with benzoyl chloride in pyridine and acetic anhydride yielded the desired 3-benzoyl-5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one (X) and the corresponding acetate (XI), respectively. (cf. Scheme 2). The triazole derivative (XII) was derived from X upon treatment with hydrazine hydrate in boiling ethanol . Reaction of compound (VI) with chloroacetic acid under basic conditions gave 5-(p-anisyl)-2,3-dimethyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one (XIII) accompanying with a loss of carbon dioxide.

In order to investigate the active hydrogen in the pyrimidinone (VI), the authors carried out Mannich reaction. Thus, treatment of an ethanolic solution of VI with different secondary amines such as piperidine and morpholine and aqueous formaldehyde in the presence of few drops of hydrochloric acid yielded the Mannich bases (XIVa,b) , respectively .

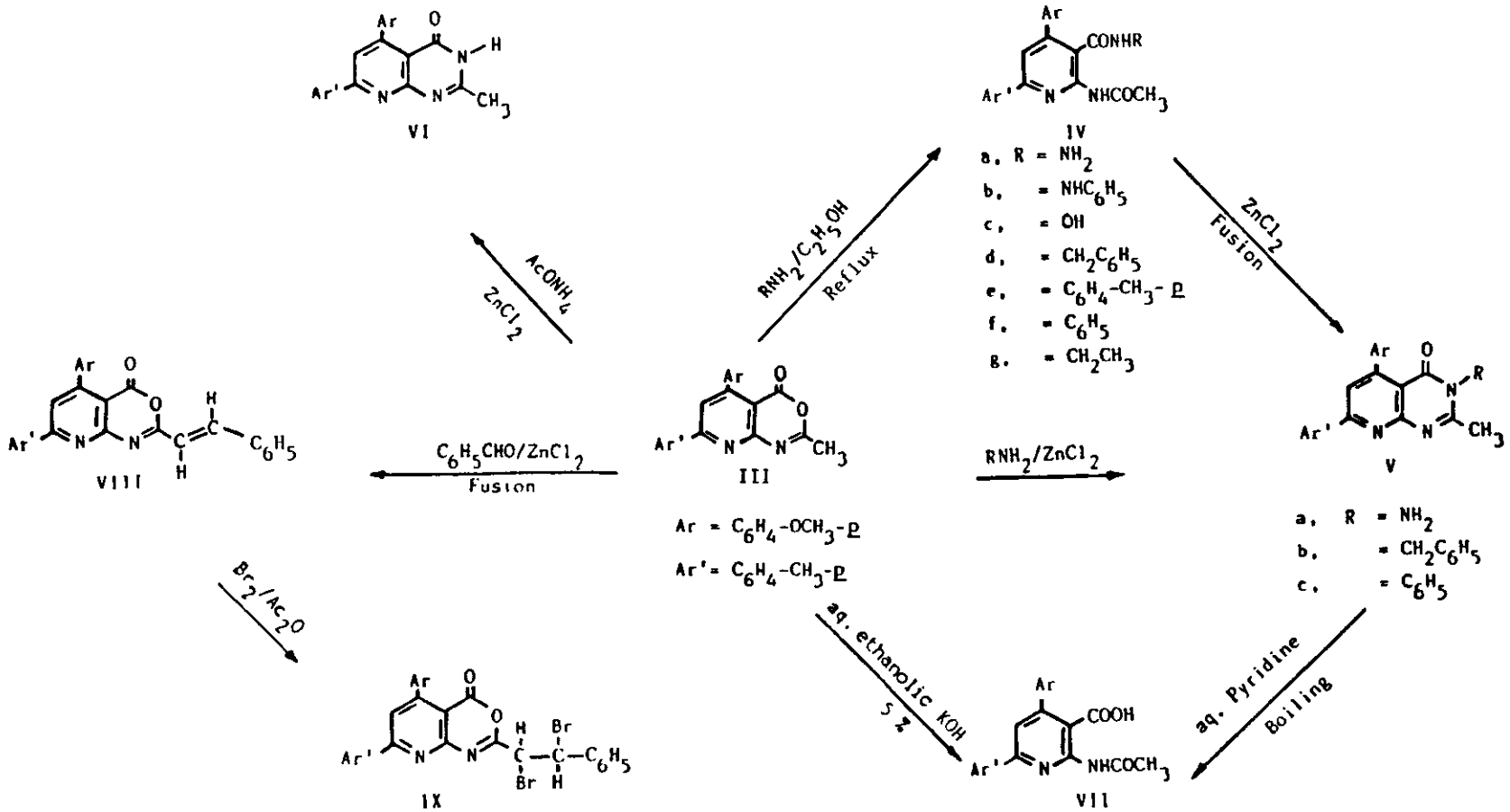
On the other hand , when VI was subjected to Mannich reaction conditions with primary amines such as methylamine and aniline , the isolated products were not the normal Mannich bases , instead the bases underwent further reaction via their addition with formaldehyde to give the products (XVa-c), respectively .

No N-methyle derivative was obtained when compound (VI) was allowed to react with methyl iodide in the presence of anhydrous K_2CO_3 in boiling dry acetone and the product was identified to be 5-(p-anisyl)-4-methoxy-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d] pyrimidin-4-one (XVI) . On the other hand , methylation accompanied with ring fission of the pyrimidinone nucleus took place when compound (VI) was treated with dimethyl sulphate in boiling acetone to afford the product (XVII) .

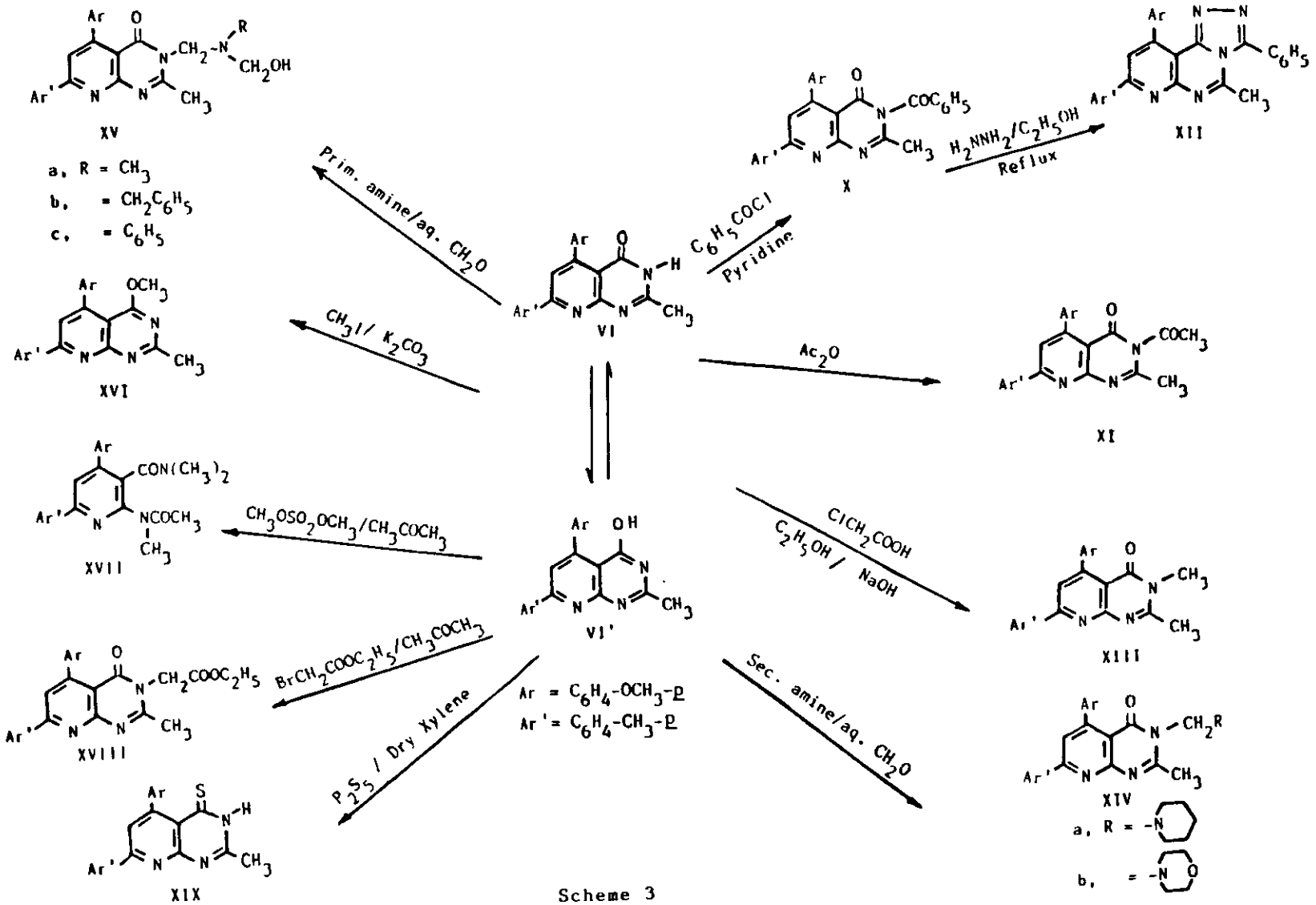
The reaction of pyridopyrimidinone (VI) with ethyl bromoacetate in boiling acetone yielded the respective ethyl [5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one-3-yl]acetate (XVIII) . Thiation of VI was achieved by the action of phosphorous pentasulphide in boiling dry xylene to afford 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]-pyrimidin-4-thione (XIX) (cf. Scheme 3).

EXPERIMENTAL

Melting points are not corrected . Ir spectra were recorded on a Beckmann ir-20 spectrophotometer and Pye Unicam SP 3-300 spectrophotometer.[8] The ^{1}H-nmr spectra were determined on a Varian T-60 and on a JEOL FX 90 spectrometer . In all nmr experiments the internal standard was TMS.[9] All chemical shifts were written in ppm downfield from TMS. Ethyl 2-amino-4-(p-anisyl)-6-(p-tolyl)nicotinate (I) was synthesized from the reaction of p-methoxybenzal-4-methylacetophenone with ethyl cyanoacetate under Michael's reaction conditions.[4]


VI
IV
a. R = NH2
b. = NHC6H5
c. = OH
d. = CH2C6H5
e. = C6H4-CH3-p
f. = C6H5
g. = CH2CH3
AcONH4
ZnCl2
RNH2/C2H5OH
Reflux
ZnCl2
Fusion
VIII
C6H5CHO/ZnCl2
Fusion
III
RNH2/ZnCl2
V
a. R = NH2
b. = CH2C6H5
c. = C6H5
Ar = C6H4-OCH3-p
Ar' = C6H4-CH3-p
Br2/Ac2O
aq. ethanolic KOH
5 %
aq. Pyridine
Boiling
IX
VII

Scheme 2


XV
a, R = CH3
b, = CH2C6H5
c, = C6H5
Prim. amine/aq. CH2O
C6H5COCl
Pyridine
H2NNH2/C2H5OH
Reflux
X
XII
XVI
CH3I / K2CO3
VI
Ac2O
XI
XVII
CH3OSO2OCH3/CH3COCH3
ClCH2COOH
C2H5OH / NaOH
VI'
XIII
XVIII
BrCH2COOC2H5/CH3COCH3
Ar = C6H4-OCH3-p
Ar' = C6H4-CH3-p
P2S5 / Dry Xylene
Sec. amine/aq. CH2O
XIV
a, R =
b, =
XIX

Scheme 3

Reaction of 2-amino-4-(p-anisyl)-6-(p-tolyl)pyridine-3-carboxylic acid (II) with acetic anhydride; Formation of 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d] [1,3] oxazin-4-one (III) :

A mixture of II (3.34 g, 0.01 mol), fused anhydrous AcONa (3 g, 0.365 mol)and freshly distilled Ac_2O (50 ml, 0.530 mol) was refluxed for 6 h. The mixture was left to cool and then poured into ice-water. The solid obtained was filtered off, washed with water, dried and then crystallized from pet. ether to give compound (III) (cf. Table 1).

Reaction of III with hydrazine and primary amines; Formation of 2-acetylaminonicotinic acid hydrazides (IVa-c) *and 2-acetylaminonicotinamides (IVd-g)*:

A mixture of pyridoxazinone (III) (3.58 g, 0.01 mol) and appropriate hydrazine or primary amine (0.02 mol) was heated under reflux in ethanol (50 ml) for 4 h. Most of ethanol was removed and the solid separated out on cooling was filtered off and recrystallized from appropriate solvent to give the products (IVa-g).

Fusion of III with hydrazine hydrate and primary amines; Synthesis of 3-amino-2-methyl-4H-pyrido[2,3-d]-pyrimidin-4-ones and the corresponding 3-benzyl and 3-phenyl derivatives (Va-c) :

A mixture of III (0.01 mol), suitable hydrazine or primary amine (0.02 mol) and fused anhydrous $Zncl_2$ (2 g, 0.015 mol) was fused at 150-160°C for 8 h. The reaction mixture was left to cool then triturated with 1N HCl. The solid deposited was filtered off, washed with water, dried and recrystallized from the proper solvent to give compounds(Va-c), respectively.

Conversion of 2-acetylaminonicotinamides (IVa,d,f) into 3-amino-2-methyl-4H-pyrido[2,3-d] pyrimidin-4-ones and the corresponding 3-benzyl and 3-phenyl derivatives (Va-c) :

A mixture of (IVa,d,f) (0.01 mol) and anhydrous $ZnCl_2$ (3 g, 0.02 mol)was heated at 150-160°C for 6 h. The reaction mixture was allowed to cool, poured into water and the solid separated out was collected, dried and recrystallized to afford the products (Va-c).

Action of ammonium acetate on III ; Formation of 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d] pyrimidin-4-one (VI) :

Pyridoxazinone III (3.58 g, 0.01 mol), ammonium acetate (10 g, 0.13 mol) and anhydrous $ZnCl_2$ (2 g, 0.0146 mol) was thoroughly mixed and heated at 150- 160°C for 4 h. The reaction mixture was cooled down at room temperature and poured into ice-water. The solid that deposited was separated out as a white solid, washed several times with water, dried and recrystallized to give the pyridopyrimidinone (VI).

Hydrolysis of Va ; Formation of 2-acetylamino-4-(p-anisyl)-6-(p-tolyl)pyridine-3-carboxylic acid (VII) :

A solution of Va (0.5 g, 0.00134 mol) in aqueous pyridine was refluxed for 4 h, left to cool and then acidified with conc.

HCl (5 ml). The solid product that precipitated was collected and washed thoroughly with water then recrystallized to yield VII.

Another method for synthesis of VII ; Hydrolysis of III:

Compound (III) (0 5 g, 0.0014 mol) was refluxed in 5% aqueous ethanolic KOH solution (5 ml) for 1 h. The solid salt was filtered off, dissolved in water and acidified with conc. HCl (2 ml) to give the acid (VII) which was found to be identical with that obtained from hydrolysis of Va via mp, mixed mp, and ir comparisons.

Condensation of III with benzaldehyde ; Formation of 5-(p-anisyl)-2-styryl-7-(p-tolyl)-4H-pyrido[2,3-d] [1,3]-oxzin-4-one (VIII) :

To a mixture of III (3.58 g , 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) , anhydrous $ZnCl_2$ (2 g, 0.0146 mol) was added and the mixture was swirled then fused at 170-180°C for 4 h. The reaction mixture after cooling, was poured into water and the solid product which separated as a deep brown solid was filtered off , dried and recrystallized to give VIII .

Bromination of VIII; Formation of vicinal dibromide IX :

To a warmed solution of VIII (4.46 g, 0.01 mol) in distilled acetic anhydride (30 ml , 0.318 mol) , bromine (3.20 g, 0.02 mol) dissolved in acetic anhydride (10 ml) was added dropwise with continuous stirring within 2 h. The reaction mixture was heated on a water bath for further 1 h, left overnight at room temperature , then poured into ice-water The product that deposited was collected , washed with water , dried then recrystallized.

Reaction of VI with benzoyl chloride and acetic anhydride ; Formation of 5-(p-anisyl)-3-benzoyl-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d] pyrimidin-4-one (X) and the corresponding acetate (XI) :

A mixture of VI (3.57 g , 0.01 mol) and benzoyl chloride (2 8 g, 0.02 mol) in pyridine (15 ml) and freshly distilled acetic anhydride (20 ml) was refluxed for 6-8 h. After cooling , the reaction mixture was poured into 20% HCl solution in water in presence of crushed ice and the solid obtained was filtered off, washed thoroughly with water, dried and recrystallized from proper solvent to afford X and XI, respectively.

Action of hydrazine hydrate on X; Synthesis of triazole derivative XII :

A mixture of benzoyl derivative X (4.61 g, 0.01 mol) and hydrazine hydrate (2.0 g, 0.04 mol) in methanol (50 ml) was refluxed for 10 h . Most of the solvent was distilled off and the solid product was collected and recrystallized .

Effect of chloroacetic acid on VI; Synthesis of 5-(p-anisyl)-2,3-dimethyl-7-(p-tolyl)-4H-pyrido [2,3-d] pyrimidin-4-one (XIII) :

A mixture of chloroacetic acid (2.8 g, 0.03 mol) , pyridopyrimidinone (VI) (3.57 g, 0.01 mol) and 5% ethanolic NaOH solution (20 ml) was refluxed for 6 h, cooled, acidified with 20% HCl solution. The precipitate that separated out was

filtered off, washed with water dried and recrystallized from suitable solvent.

Reaction of VI with primary and secondary amines in presence of formaldehyde; Synthesis of Mannich bases (XIVa,b) and compounds (XVa-c) :

A mixture of VI (3.57 g, 0.01 mol), 37% formaline (5 ml) and appropriate secondary and primary amine (0.03 mol), was refluxed for 4 h in methanol (30 ml) in presence of few drops of 37% HCl solution. The solution was cooled then poured into 1N HCl solution (25 ml). The precipitate was filtered off, washed with water, dried and recrystallized from proper solvent to obtain Mannich bases (XIVa,b) and the products (XVa-c), respectively.

Effect of methyl iodide, dimethyl sulphate and ethyl bromoacetate on pyridopyrimidinone (VI); Formation of 5-(p-anisyl)-4-methoxy-2-methyl-7-(p-tolyl)-4H-pyrido[2,3-d]pyrimidin-4-one(XVI) , compound (XVII) and ethyl [5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido [2,3-d] pyrimidin-4-one-3-yl] acetate (XVIII) :

A mixture of VI (0.01 mol), anhydrous K_2CO_3 (5 g, 0.036 mol), methyl iodide (2.8 g, 0 02 mol), dimethyl sulphate (2 5 g, 0.02 mol) and ethyl bromoacetate (3.4 g, 0.02 mol) in dry acetone (100 ml) was refluxed on a water bath for 36-48 h. Most of the solvent was distilled off and the reaction mixture was poured into cold water The product was collected and crystallized from proper solvent to afford XVI-XVIII respectively.

Neither K_2CO_3 addition nor drying for acetone is carried out in case of XVII .

Reaction of VI with phosphorous pentasulphide; Synthesis of 5-(p-anisyl)-2-methyl-7-(p-tolyl)-4H-pyrido [2,3-d]-pyrimidin-4-thione (XIX) :

A mixture of VI (0 01 mol) and phosphorous pentasulphide (4.4 g, 0.01 mol)in dry xylene (20 ml) was refluxed for 3 h. The reaction mixture was filtered off while hot and the filtrate was allowed to cool down at room temperature to yield compound (XIX) as red needle crystals.

Table 1 : Physical Characteristics of New Compounds

Compd.	mp °C (yield)	Crystallization solvent (colour)	Molecular formula	Analysis% Found	Calcd	ir(νcm^{-1})	^{1}H-nmr (δ ppm)
III	205-207 (90)	L. P.(90-100)+B (Buff)	$C_{22}H_{18}N_2O_3$	C 73.63 H 5.11 N 7.94	73.74 5.03 7.82	C=O(1740), C=N (1650) and -O-(1110)	2.40(s, 3H, Ar-CH_3) 2 60(s, 3H, N=$COCH_3$) 3 90(s, 3H, Ar -OCH_3) 7.00-7.60 and 8.10-8.20 (m, 8H, Ar-H) 7.70(s, 1H, CH of pyridine ring)
IVa	225-227 (60)	B+E (Deep yellow)	$C_{22}H_{22}N_4O_3$	C 67 59 H 5.49 N 14.22	67.69 5.64 14.36	$CONH_2$(1670-1680), NH(3340-3370)	2.35(s, 3H, Ar-CH_3) 2.90(s, 3H, NHCOCH_3) 3.90(s, 3H,Ar-OCH_3) 7.40-7.90(m, 9H, Ar-H) 8.20-8.40(br s, 2H, 2xNH) 8.60(br s, 2H, NH_2)
IVb	221-223 (65)	B+E (Orange)	$C_{28}H_{26}N_4O_3$	C 72.25 H 5.64 N 12.11	72.10 5.58 12.02	C=N(1640-1660), C=C(1600-1610)	2.30(s, 3H, Ar-CH_3) 2.90(s, 3H, NHCOCH_3) 3.90(s, 3H, Ar-OCH_3) 7.30-8.00(m, 14H, Ar-H) 8.20-8 40(br s, 2H, 2xNH) 8.55(br s, 1H, PhNH)
IVc	233-235 (71)	B+E (Yellow)	$C_{22}H_{21}N_3O_4$	C 67.33 H 5.50 N 10.92	67.52 5.37 10.74	C=O(1652-1640) NH, OH(br 3120-3450)	2.35(s, 3H, Ar-CH_3) 2.90(s, 3H, NHCOCH_3) 3.90(s, 3H, Ar-OCH_3) 7.30-7.90(m, 9H, Ar-H) 8.30(br s, 2H, 2xNH), 9 30(s, 1H, OH)
IVd	190-192 (63)	B+E (Pale yellow)	$C_{28}H_{25}N_3O_3$	C 74.71 H 5.69 N 9.44	74.50 5.54 9.31	C=O(1648-1639) NH(3220-3225)	2.30(s, 3H , Ar-CH_3) 2.90(s, 3H , NHCOCH_3) 4.10(s, 3H , Ar-OCH_3) 4.90-5.20(dxd, J=5.00, J=7.00 Hz, 2H, CH_2-Ph), 7.20-8.00(m, 14H , Ar-H) 8.20-8.40(br s, 2H , 2xNH)
IVe	195-196 (50)	B+E (White)	$C_{29}H_{27}N_3O_3$	C 75.10 H 5.91 N 9.17	74.84 5.81 9.03	C=O(1655-1641) NH(3280-3218)	2.10(s, 3H, Ar-CH_3) 2.30(s, 3H, Ar-CH_3) 2.90(s, 3H, NHCOCH_3) 3 80(s, 3H, Ar-OCH_3) 7.30-780(m, 13H, Ar-H) 8.30(br s, 2H, 2xNH)
IVf	215-217 (67)	B+E (White)	$C_{29}H_{27}N_3O_3$	C 75.05 H 5.94 N 9.22	74.84 5.81 9.03	C=O(1649-1632) NH(3260-3221)	2.30(s, 3H, Ar-CH_3) 2.85(s, 3H, NHCOCH_3) 3.90(s, 3H, Ar-OCH_3)

							7.00-7.90(m, 4H, Ar-H) 8.00-8.20(br s, 2H, 2xNH)
IVg	199-200 (79)	B+E (Pale yellow)	$C_{24}H_{25}N_3O_3$	C 71.62 H 6.34 N 10.56	71.46 6.20 10.42	C=O(1634-1630) C-H(2910) NH(3280--3210)	1.10(t, J=6.30 Hz, 3H, CH_2CH_3) 2.10(s, 3H, Ar-CH_3) 2.70(m, 2H , CH_2CH_3) 3.10(s, 3H , $NHCOCH_3$) 3.80(s, 3H , Ar-OCH_3) 7.40-7.70(m, 9H , Ar-H) 8.10-8.20(br s, 2H , 2xNH)
Va	244-246 (83)	B+E (Yellow)	$C_{22}H_{20}N_4O_2$	C 71.10 H 5.42 N 15.18	70.97 5.38 15.05	C=O(1710-1730),C=N (1640-1660), NH_2(3340)	2.30(s, 3H, Ar-CH_3) 2.70(s, 3H, N=CH_3) 3 70(s, 3H, Ar-OCH_3) 7.00-7.80(m, 9H, Ar-H) 8.10-8.30(br s, 2H, 2xNH)
Vb	261-262 (80)	B+E (Orange)	$C_{29}H_{25}N_3O_2$	C 77.69 H 5.62 N 9.44	77.85 5.59 9.39	C=O (1692) C=N (1652)	2 30(s, 3H, Ar-CH_3) 2.70(s, 3H, N=CH_3) 3.70(s, 3H, Ar-OCH_3), 4.90-5.30(dxd, J=5 20 Hz, J=6.80 Hz, 2H, CH_2Ph) 7.00-7.90(m, 14H, Ar-H)
Vc	254-256 (69)	B+E (Yellow)	$C_{28}H_{23}N_3O_2$	C 77.52 H 5 47 N 9.75	77 60 5.31 9.70	C=O(1697) C=N(1632)	2 30(s, 3H, Ar-CH_3) 2.60(s, 3H, N=CH_3) 3.50(s, 3H, Ar-OCH_3) 7.20-8 00(m, 14H, Ar-H)
VI	280-281 (85)	B+E (White)	$C_{22}H_{19}N_3O_2$	C 74.01 H 5.23 N 11.82	73 95 5.32 11.76	OH(3450-3500), NH 3180, C=O (1660) C=N(1620)	2 38(s, 3H, Ar-CH_3), 2.40(s, 3H, N=C-CH_3), 3.88(s, 3H, Ar-OCH_3), 6.95(s, 1H,NHCO), 6.99-7.38 and 8.12-8.15(m, 8H, Ar-H) 7.64(s, 1H, CH of pyridine)
VII	215-217 (73)	L. P.(90-100)+B (Buff)	$C_{22}H_{20}N_2O_3$	C 70.05 H 5.40 N 7.35	70.21 5.32 7.45	C=O(1705), C=N(1610) C=O(1660), OH (br , centered at 3300)	2.10(s, 3H, Ar-CH_3) 2.40(s, 3H, $NHCOCH_3$) 3.10(s, 3H, Ar-OCH_3) 7.40-7.70(m, 9H, Ar-H) 8.10(s, 1H, NH), 10.60(s, 1H, COOH)
VIII	230-233 (88)	B+E (Brown)	$C_{29}H_{22}N_2O_3$	C 77 91 H 4.78 N 6.18	78.03 4.93 6.28	C=O(1740), C=N (1660), C=C(1605)	6.65-6.70(d, J=13.30 Hz, 1H, -CH=CH-Ar), 6.90-6.95(d, J=13.30 Hz, 1H, -CH=CHPh) 8.20-8.30(m, 13H, Ar-H), 7.75 (s, 1H, CH of pyridine)
IX	105-107 (80)	L. P.(90-100)+B (Yellow)	$C_{29}H_{23}N_2O_3$	C 57.48 H 3.87 N 4.74	57.33 3.79 4 61	C=O(1752) C=N(1615)	2.40(s, 3H, Ar-CH_3) 3.60(s, 3H, Ar-OCH_3) 4.20-4.60(dxd, 2H, J=3.00 Hz, J=5.00Hz, -CH-CH-) 7.40-8.00(m, 14H, Ar-H)
X	135-137 (71)	L. P.(90-100)+B (Brown)	$C_{29}H_{23}N_3O_3$	C 75.30 H 5.06	75.49 4.99	C=O(1600), C=N(1620) C=O(1660), C=C(1600)	2.30(s, 3H, Ar-CH_3) 2.60(s, 3H, N=CH_3)

				N 9.02 9.11		3.50(s, 3H, Ar-OCH_3) 7.20-8.00(m, 14H, Ar-H)
XI	160-162 (58)	L. P.(90-100)+B (Yellow)	$C_{24}H_{21}N_3O_3$	C 72.38 72 18 H 5 43 5 26 N 10.70 10 53	C=C(1610), C=N(1660), CO(1690), C=O(pyrimidinone, 1730)	2.30(s, 3H, Ar-CH_3) 2.60(s, 3H, N=CH_3) 2.90(s, 3H, $NCOCH_3$) 7.30-8.00(m, 9H, Ar-H)
XII	171-174 (70)	L P.(90-100)+B (Orange)	$C_{29}H_{23}N_5O$	C 75.95 76.15 H 5.23 5.03 N 15 21 15.32	C=N(1652)	2.20(s, 3H, Ar-CH_3) 2 60(s, 3H, N=CH_3) 3 70(s, 3H, Ar-OCH_3) 7 20-8 00(m, 14H, Ar-H)
XIII	220-222 (77)	L. P.(90-100) (Yellow)	$C_{23}H_{21}N_3O_2$	C 74.46 74.39 H 5.49 5.66 N 11.16 11.32	C=O(pyrimidinone, 1660), C=N(1625)	2.10(s, 3H, NCH_3) 2.40(s, 3H, Ar-CH_3) 2.70(s, 3H, N=CH_3) 7.20-8 00(m, 9H, Ar-H)
XIVa	182-184 (81)	L. P.(90-100) (Orange)	$C_{28}H_{30}N_4O_2$	C 73.89 74.00 H 6.80 6.61 N 12.38 12.33	C=O(1650-1660), C=N, (1620-1625),	1.60(br s, 10H, N⟨ ⟩) 2.30(s, 3H, Ar-CH_3) 2.70(s, 3H, N=CH_3) 2.90-3.40(br s, 2H, NCH_2N) 3 70(s, 3H, Ar-OCH_3) 7.10-8.00(m, 9H, Ar-H)
XIVb	160-162 (87)	L P.(90-100)+B (Buff)	$C_{27}H_{28}N_4O_3$	C 70.96 71.05 H 5 96 6.14 N 12.09 12 28	C=O(1682) C=N(1635)	2.30(s, 3H, Ar-CH_3) 2.50(s, 3H, N=CH_3) 3.10(br s, 2H, NCH_2N) 3 60(s, 3H, Ar-OCH_3) 3.90-4.10(m, 8H, N⟨ ⟩O) 7.20-7.90(m, 9H, Ar-H)
XVa	168-170 (90)	L P (90-100)+B (Pale yellow)	$C_{25}H_{26}N_4O_3$	C 69.61 69.77 H 6 16 6.05 N 12 91 13 02	C=C(1580), C=N(1610) C=O(pyridopyrimidinone, 1680), OH(3450)	2.15(s, 3H, N-CH_3), 2 35 (s, 6H, Ar-CH_3 and CH_3 of 2-methylpyrimidinone) 2.70-3.50(br m, 3H, NCH_2N,OH) 3.90-4.30 (br m, 2H, NCH_2OH) 3.80(s, 3H, Ar-OCH_3) 6.85-7.25 and 8.00-8.15(m, 8H, Ar-H) and 7.60(s, 1H, CH of pyridine)
XVb	152-154 (92)	L P (100-120) (Orange)	$C_{31}H_{30}N_4O_3$	C 73.41 73.52 H 6.02 5.93 N 11.50 11.36	C=O(1682) C=N(1632) OH(3420)	2.10(s, 3H, Ar-CH_3) 2.60(s, 3H, N=CH_3) 2 70-3.50(br m, 3H, NCH_2N, OH) 3.80(s, 3H, Ar-OCH_3) 3.90-4 30(br s, 2H, NCH_2OH) 4.90-5.40(dxd, J=5.00 Hz, J=7.00 Hz, 2H, CH_2Ph), 7.40-8.00(m, 14H, Ar-H)
XVc	125-127 (89)	L. P.(100-120)+B (Yellow)	$C_{30}H_{29}N_4O_3$	C 72.90 73.02 H 6.01 5.88 N 11.50 11.36	C=O(1680) C=N(1641) OH(3380-3410)	2.10(s, 3H, Ar-CH_3) 2.60(s, 3H, N=CH_3) 2.70-3.50(br m, 3H, NCH_2N, OH) 3.80(s, 3H, Ar-OCH_3)

							3.90-4.30(br s, 2H, NCH_2OH) 7.10-8.00(m, 14H, Ar-H)
XVI	141-143 (83)	L. P.(90-100)+B (Yellow)	$C_{23}H_{21}N_3O_2$	C 74.49 H 5.69 N 11.37	74.39 5.66 11.32	C=N(1650) C=C(1610)	2.40(s, 3H, Ar-CH_3), 2.70 (s, 3H, N=C(CH_3)N), 3.45 (s, 3H, Ar-OCH_3), 3.80(s, 3H, OCH_3 of Ph-OCH_3), 6.90-7.40 and 8.20-8.40(m, 8H, Ar-H) and 7.65(s, 1H, CH of pyridine ring)
XVII	208-210 (91)	L. P.(90-100) (Brown)	$C_{25}H_{27}N_3O_3$	C 72 05 H 6.50 N 10.10	71.94 6.47 10.07	C=O(1650), C=N(1610) C=C(1580)	2.35(s, 6H, $N(CH_3)_2$), 2.62(s, 3H, $COCH_3$), 2.75(s, 3H, Ar-CH_3),3.20(s, 3H, $CONCH_3$) 3.80(s, 3H, Ar-OCH_3), 6.90-7.55 and 7.85-8.00 (m, 8H, Ar-H) 7.70(s, 1H, CH of pyridine ring)
XVIII	136-138 (95)	L. P.(90-100)+B (Buff)	$C_{26}H_{25}N_3O_4$	C 70.93 H 5.54 N 9.69	71.07 5.69 9.57	C=C(1580), C=N(1610) C=O(pyridopyrimidinone, 1680), C=O(1730)	1.20(t, J=6.80 Hz, CH_7CH_3) 2.20(s, 3H, Ar-CH_3) 2.40(s, 3H, N=CH_3) 2.70(q, J=7.30 Hz, 2H , CH_2CH_3) 3.30(s, 3H , OCH_3) 4.90(dxd, J=5.10 Hz, J=7.00 Hz, 2H, $CH_2COOC_2H_5$) 7.10-7.90(m, 9H , Ar-H)
XIX	211-213 (50)	X* (Red)	$C_{22}H_{19}N_3OS$	C 70.55 H 4.91 N 11.34	70.78 5.09 11.26	C=N(1610), C=S(1160), SH(2640)	2.30(s, 3H, Ar-CH_3) 2 60(s, 3H, N=CH_3) 3.40(s, 3H, Ar-OCH_3) 7.20-8.00(m, 9H, Ar-H) 8.10-8.20(br s, 1H, NH)

* L.P. = light petrol ; B = benzene ; E = ethanol and X = xylene .

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