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APPLICATIONS OF A NOVEL CARBON-NITROGEN BOND CLEAVAGE REACTION (PART-I).A NEW SYNTHESIS / DERIVATISATION OF 5H-INDENO[1,2d] PYRIMIDINES AND PYRIMIDO[6,1-a]ISOINDOLES.

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Abstract: Substituted 6-(4,5-dimethoxy-2-vinylphenyl)-2,4-(1H,3H) pyrimidinediones (**2**) undergo ring closure in the presence of a mixture of formic acid and orthophosphoric acid, to give 5H-indeno[1,2-d]pyrimidines (**3**) and/or pyrimido[6,1-a]isoindoles (**4**). Cyclization to **3** and/or **4** depends on the nature of substitution in the pyrimidine ring in **2**. Electron withdrawing groups at position 4 in **2** favour the formation of the skeleton **3**, however, electron donating groups gave more of **4**. Compound **2a** on acid treatment,gave in addition to **3a**, a dimeric product **5**. Phosphorus oxychloride treatment of compound **3a** generated the 2,4-dichloro compound **7**. Two chloro groups behaved differently in their chemical reactivity. When **7** reacted with amines in benzene, generally 2-positional regioisomers predominated, however, in amyl alcohol 2,4-disubstituted amino compounds were formed.

As an extension of our recently published reaction[1], in which a carbon-nitrogen bond was cleaved in non-basic tri and tetracyclic ring system by NaH in DMF, a variety of novel versatile intermediates were generated. We believe that these intermediates may be useful synthons. In this paper we will demonstrate,the use of these intermediates in the building of new ring systems and the synthesis of known heterocycles.

The synthesis of 5H-indeno[1,2-d]pyrimidines have achieved added significance, as these compounds represent a novel class of potent, orally active aromatase and estrogen inhibitors[2,3].

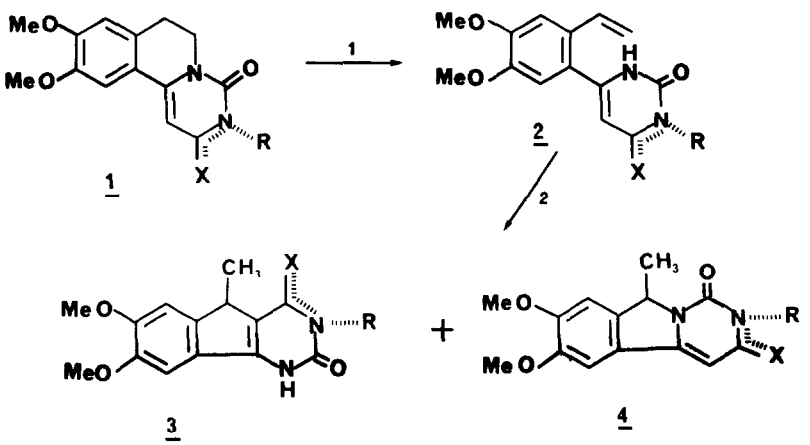
Polonovski et al.[4] reported synthesis of 5H-indeno[1,2-d] pyrimidin-2-thio-4,5(1H,3H)-dione, starting with 2-carbethoxy-1,3-indandione and thiourea. Several other groups[5] have also reported synthesis of these systems starting from 1-indanone or 1,3-indandione, and pyrimidine,

through the use of dicyandiamide, urea or guanidine.

Except for the limited work of Kovutunenko[6] and Eberle[7,8] on the synthesis of uniquely substituted pyrimido[6,1-a]isoindoles, no other literature report on this skeleton is available.

We have developed an unconventional approach into synthesis of both 5H-indeno[1,2-d]pyrimidines and pyrimido[6,1-a]isoindole systems.

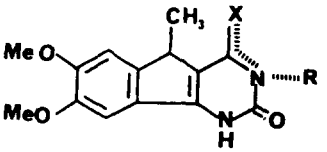
An efficient synthesis of pyrimido[6,1-a]isoquinolines has been previously reported from these laboratories[9]. These compounds were utilized as starting materials for the present study (Scheme I). Compound 1 on treatment with NaH-DMF is known to give compound 2[1]. Intra-molecular cyclization of compound 2 with a mixture of formic acid and orthophosphoric acid[10] (2.2:1) either gave exclusively compound 3 or a mixture of 3 and 4. The ratio of the formation of 3 and 4 is dependent on the nature of group X in the compound 2. When X is an electron withdrawing group compound 3 predominates. However with an electron donor X, mixture of 3 and 4 is formed. Table-I indicates the pattern of the formation of 3 and 4 in some of these reactions.



1. NaH-DMF; 2. $HCOOH/H_3PO_4$

SCHEME I

Table 1



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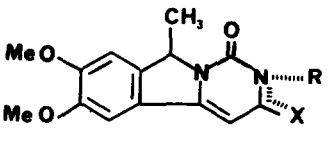
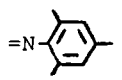
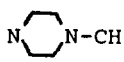


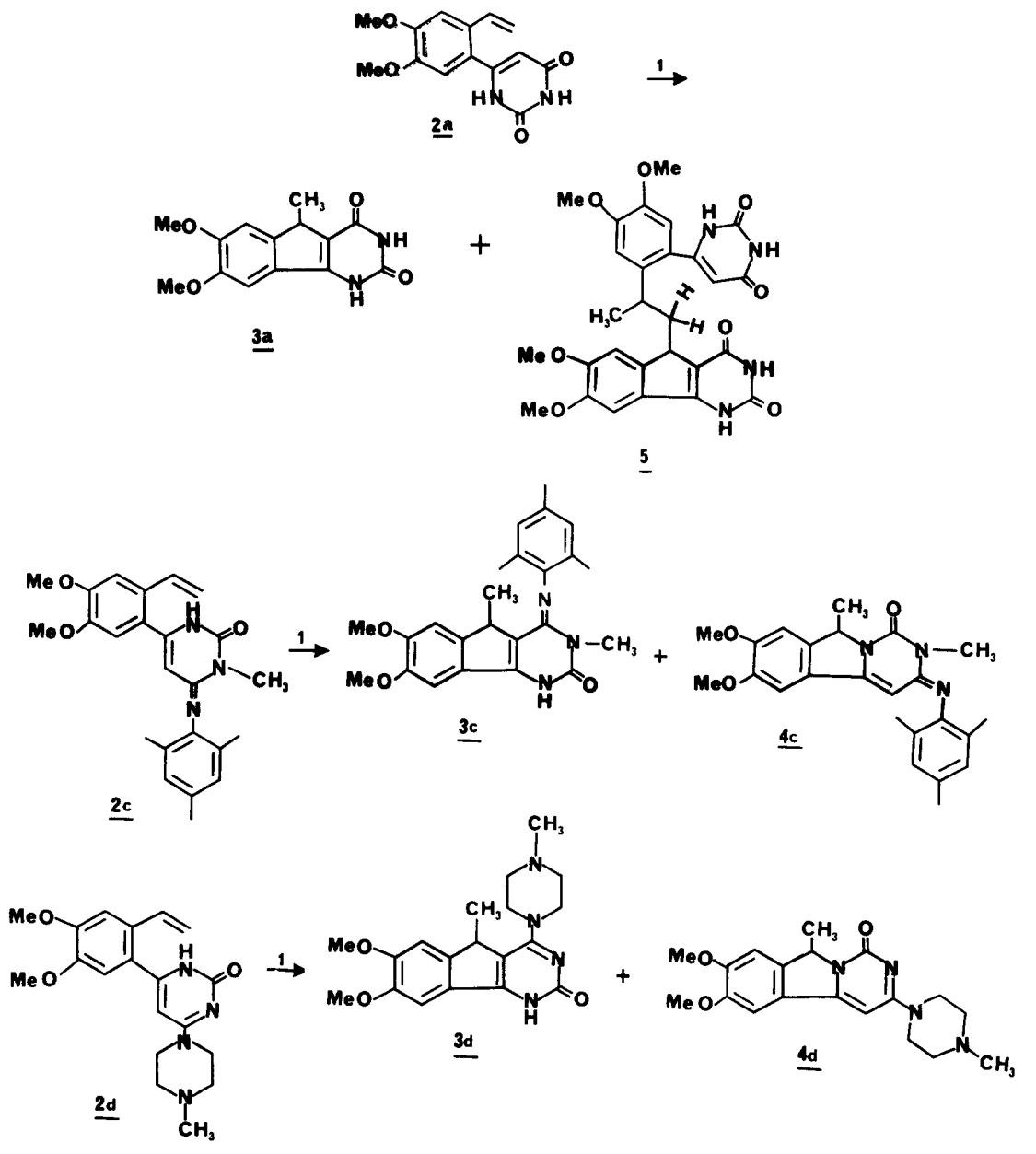
4

Starting Compound	R	X	3	%	4	%
2a	H	O	3a	85	-	-
2b	CH_2Ph	O	3b	78	-	-
2c	CH_3		3c	29	4c	15
2d			3d	8	4d	56

Compound 2a[1] on treatment with a mixture of formic acid and orthophosphoric acid gave the expected 5H-indeno[1,2-d]pyrimidinedione 3a in 78% yield. A side product 5 was also isolated in 9.0% yield (Scheme II).The mass spectrum of compound 5 exhibited M + 1 at 549 and analyzed correctly for $C_{28}H_{28}N_4O_8$. Its ^1H NMR spectrum ($CDCl_3$ + a drop of TFA) exhibited a complex pattern with some of the salient signals at δ 1.44 (d, 3H, $CH\underline{CH}_3$), 1.66-2.07 (m, 1H, H- b), 2.30-2.67 (m, 1H, $\underline{CH}CH_3$), 2.88 - 3.28 (m, 1H, H- a), 4.80 (dd, 1H, H-5),(for the remaining peaks see the Experimental).The IR spectrum exhibited band at 1715, 1695, 1667 and 1639 cm^{-1}. These data are consistent with two molecules of 2a condensing together to form compound 5.

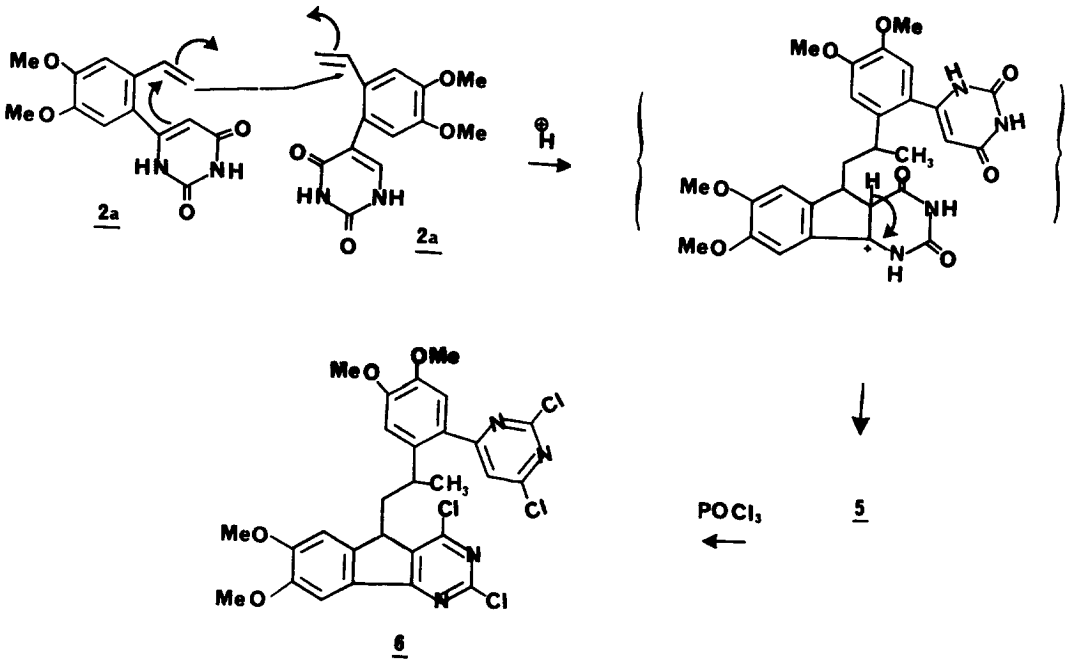
The cyclodimerization of styrene in the presence of sulfuric and or Amberlyst-15 is known[11] to give a mixture of cis- and trans- 1-methyl-3-phenylindane. Such a mechanism is also plausable for the cyclodimerization of compound 2a which is depicted in Scheme III.

Further support for the structure 5 came,when it was treated with



1. $HCOOH/H_3PO_4$

SCHEME II



SCHEME III

$POCl_3$; the corresponding tetrachloro derivative 6 was isolated. The mass spectrum of compound 6[12] showed M^+ at 620. It also exhibited peaks at 622, 624, 626 and 628 indicating the presence of four chlorine atoms. Another important mass peak at 323 was assigned to the fragment shown below (Fig. 1).

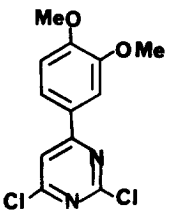


Fig 1

Compound **6** analyzed for $C_{28}H_{24}Cl_4N_4O_4$. ^{1}H-NMR showed complex pattern and double resonance decoupling studies[12] indicated correctness of the assigned structure. Irradiating methyl signal at δ 1.42 simplified the multiplet at δ 2.88-3.00. When multiplet at δ 2.18-2.28 was irradiated, **dd** at δ 5.24 collapsed to a **d** with J = 10 Hz. Similarly, saturating **dd** at δ 5.24 simplified multiplets at δ 3.0-3.10 and at δ 2.18-2.28. When all the above data was combined, it was possible to interpret the ^{1}H NMR of compound **6** (see experimental).

Treatment of compound **2c**[1] with a mixture of formic acid and orthophosphoric acid gave two compounds **3c** and **4c** in 25% and 15% yield respectively (Scheme II). The ^{1}H NMR spectrum of compound **3c** showed characteristic **d** for the methyl signal, a peak for the NH proton and the absence of signal for an olefinic proton was observed. The methyl and methine protons at position 5 are shielded, probably due to the mesitylimino group present at position 4 and appeared at δ 0.78 and 3.18 respectively. The ^{1}H NMR spectrum of compound **4c** exhibited signals at δ 1.75 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$) 5.37 (q, J = 8 Hz, 1H, $\underline{CH}CH_3$), 5.53 (s, 1H, **H-4**). The presence of an olefinic H-4 proton and the absence of a NH signal indicated that the nitrogen atom has participated in the cyclization to give a nitrogen containing five membered ring system. Downfield shift of H-9 methine proton showed its proximity to the nitrogen atom. Its mass spectrum exhibited M^+ at 403 and analyzed correctly for $C_{24}H_{27}N_3O_3$.

The role of group **X** in structure **2** to dictate the pattern of cyclization is obvious. Compounds **2a**[1] and **2b**[1] having an electron withdrawing carbonyl group, results in deactivation of the nitrogen atom at position 1, higher electron denisty at position 5 facilitates the olefinic carbon to participate in the cyclization to give exclusively compounds **3a** and **3b** respectively. However, in compound **2c**[1], electron withdrawing properties of the mesitylimino group are relatively less and no clear cut activation or deactivation is possible, therefore a mixture of compounds **3c** and **4c** results. In case of compound **2d**[1] having N-methyl-piperazine with electron donating properties at position 4, there is no deactivation of nitrogen atom at position 1, which helps the nitrogen atom to participate in the cyclization reaction.This results into the formation of compound **3d** in 8% and compound **4d** in 56%.

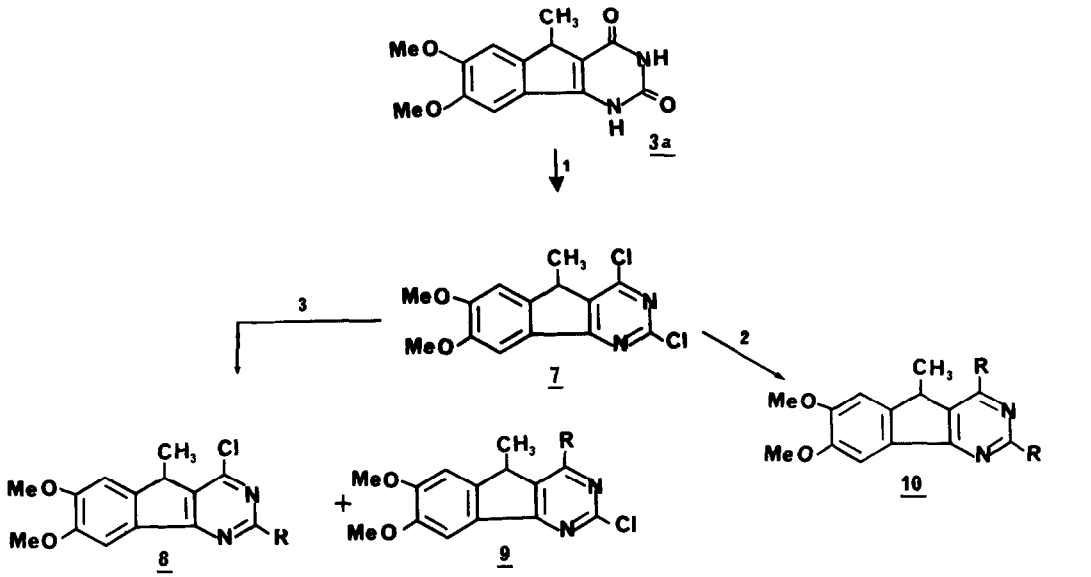
Treatment of compound **3a** with $POCl_3$ gave the dichloro derivative **7** (Scheme IV) which, on reaction with different amines in refluxing benzene,

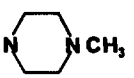
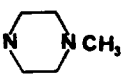
gave predominantly 2-substituted derivatives with minor or n substitution at 4-position. This was amply demonstrated by the isolation of the following 2-substituted amino derivatives (Scheme IV) reactions; N-methylpiperazino **8a** (77%), morpholino **8b** (56%) and piperidino **8c** (77%). Only in the case of piperidine, was the corresponding 4-isomer **9c** isolated in 1.2% yield. However, reaction of compound **7** in benzene with alcoholic methylamine gave a better distribution of regioisomers. 2-Substituted isomer **8d** and 4-substituted isomer **9d** were isolated in 53% and 29% yields respectively. The regioisomers formed in the above reaction were differentiated as follows: The mass spectrum[13] of compound **8d** exhibited M^+ at 305. Its ^1H NMR spectrum showed signals at δ 1.54 (d, J = 7Hz, 3H, $CH\underline{CH}_3$) and δ 3.88 (q, J = 7Hz, 1H, $\underline{CH}CH_3$). These signals compared very well with the chemical shifts of the starting compound **7**, indicating that n environmental change has occurred at position 4. NOE[13] studies also indicated that there is no NOE between NH and $CHCH_3$ groups, hence $NHCH_3$ must be at position 2 and the compound was assigned structure **8d**.

The mass spectrum[13] of compound **9d** showed M^+ at 305. Its ^1H NMR spectrum exhibited signals at δ 1.45 and δ 3.67 for methyl and methine protons (at position 5) respectively indicating a shielding of 0.13 ppm for CH_3 and 0.16 ppm for H-5 proton as compared to the corresponding signals of compound **7**. This environmental change could occur when $NHCH_3$ has entered at position 4, hence the structure **9d** was assigned. Final confirmation for this structure came through NOE[13] studies. Irradiation of the NH signal at δ 4.77 exhibited positive NOE for the doublet at δ 1.44 due to $CH\underline{CH}_3$ and also for the quartet at δ 3.71 due to $\underline{CH}CH_3$, proving that $NHCH_3$ group must be located at C_4 position.

In ^1H- NMR spectrum of pyrimidines[14], C_2-H appears at δ 9.26 and C_4-H at δ 8.78 as singlets. In an attempt to correlate the above analogy, compounds **8d** and **9d** were subjected to reductive dehalogenation in the presence of 5% Pd-C and NaOAc[15] in MeOH-DMF to give the corresponding **11d** and **12d**, respectively. The ^1H NMR C_4-H in **11d** appeared at δ 8.23 and in **12d** C_2-H appeared at δ 8.57. Similarly, compounds **8a** and **8c** gave **11a** and **11c**, respectively, confirming the correctness of the assignement of substitution.

When dichloro compound **7** was treated with N-methylpiperazine or morpholine or piperidine in amyl alcohol at 125-130°C, only 2,4-disubstituted compounds, **10a**, **10b** and **10c** were isolated in 53, 76 and 61% yield respectively, indicating that in amyl alcohol only disubstituted



S.NO.	R	S.NO.	R	S.NO.	R
8a		—	—	10a	
8b		—	—	10b	
8c		9c		10c	
8d	$NHCH_3$	9d	$NHCH_3$	—	—

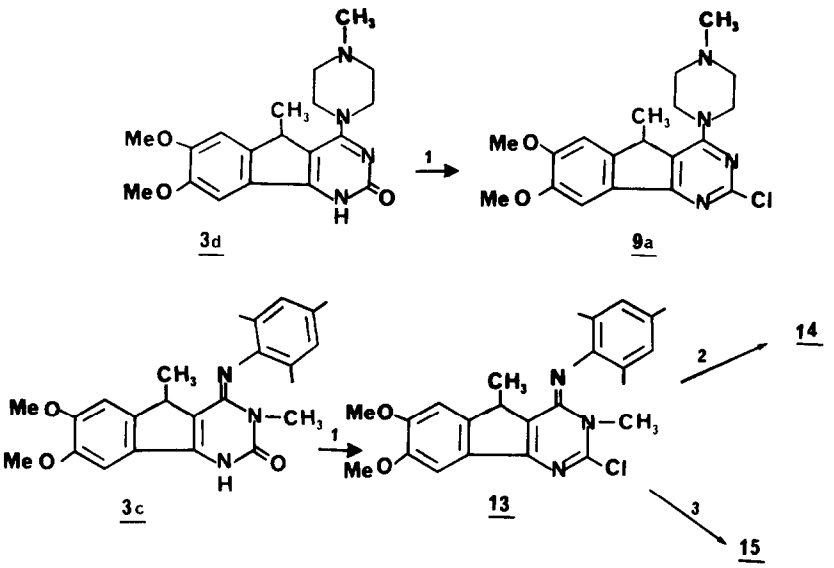
1. $POCl_3$; 2. HNR_1R_2 (=R), Amyl Alcohol Heat; 3. HNR_1R_2 (=R), C_6H_6, Heat

SCHEME IV

compound were formed.

The structure of compound **8a** was also confirmed by an unambiguous synthesis of its regioisomeric 2-chloro derivative **9a**. When compound **3d** was treated with $POCl_3$, it gave **9a** (Scheme V). The spectral features of this compound were different, compared with those of compound **8a**.

In order to have two different substituted amino groups at 2- and 4-positions, compound **3c** having a mesitylimino group at position 4 was chosen as the starting material. Attempts to functionalize compound **3c** at position 2 through the use of $POCl_3$, P_2S_5, P_2S_5-Et_3N or Lawesson's



1. $POCl_3$; 2. Piperidine, Heat; 3. H_2/10% Pd-C/DMF/MeOH/NaOAC

SCHEME V

reagent[16] met with a failure. However, the reaction was successful, when a combination of $POCl_3$ and 4-dimethylaminopyridine was used to give the corresponding 2-chloro dervative **13** (Scheme V). This was treated with piperidine at 70 C^0 to give the 2-piperidino-4-mesitylimino derivative **14**. Compound **13** was subjected to reductive dehalogenation, as described earlier,to give the compound **15**. The spectral data of **14** and **15** were

consistent with their assigned required structures.

Conclusion : Through the use of new styrene synthons, a synthesis of 5H-indeno[1,2-d]pyrimidines and pyrimido[6,1-a]isoindoles was developed. An interesting indenopyrimidine dimeric product was isolated. The method reported herein offers a route to 2-and 4- functionalized 5H-indeno[1,2-d]pyrimidines.

Experimental Section :

All melting points are uncorrected and were obtained with a kofler hot stage apparatus. IR spectra were recorded on a Perkin-Elmer Model 157 and Perkin-Elmer 782 spectrometer using KBr disks and are reported in reciprocal centimeters. ^{1}H-NMR spectra were recorded on a Varian T-60 and a Jeol Fx-90 Q spectrometer. ^{13}C-NMR spectra were recorded on Jeol Fx-90 Q spectrometer. UV spectra were taken using a Carl Zeiss Specord and Konitron Uvikon 10 spectrophotometer. Mass spectra were obtained on a Kratos MS 80RFA instrument. TLC was performed on aluminum plates coated with a 0.2 mm layer of silica gel F_{254} (Merck).

3-Benzyl-7,8-dimethoxy-5-methyl-5H-indeno[1,2-d]pyrimidine-2,4(1H,3H) dione(3b): To a solution of compound **2b** (0.20 g, 0.55 mmol) in chloroform (5 mL), was added formic acid (0.2 mL) and orthophosphoric acid (0.48 mL) and the reaction mixture was refluxed for 18 h. The reaction mixture was cooled and washed with water until free from acid. The organic layer was dried (Na_2SO_4) and the solvent was evaporated to give the compound **3b** (0.17 g, 85%). **3b** was crystallized from CH_2Cl_2-C_2H_5OH, m.p.> 306°C. IR 2985, 1742, 1672, 868, 794, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 1.47 (d, J = 8 Hz, 3H, CH<u>CH</u>$_3$), 3.85 (s, 3H, <u>OCH</u>$_3$), 3.87 (q,J= 8Hz, 1H, <u>CH</u>CH$_3$), 3.90 (s, 3H, <u>OCH</u>$_3$), 5.07 (s, 2H, <u>CH</u>$_2$C$_6$H$_5$), 6.97 (s, 1H, Ar<u>H</u>), 7.06-7.53 (m, 5H, Ar<u>H</u>), 7.57 (s, 1H, Ar<u>H</u>), 11.77 (s, 1H, N<u>H</u>, exchanges with D_2O). Anal. Calcd. for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found : C, 68.86; H, 5.44, N, 7.49.

Reaction of compound 2a with a mixture of formic acid and orthophosphoric acid: To compound **2a** (53.0 g, 193.2 mmol), formic acid (775 mL) and orthophosphoric acid (350 mL) was added. The reaction mixture was maintained at 55-60°C for 18 h, and then poured into crushed ice,to give a precipitate, which was filtered, washed with water until free from acid and dried (Na_2SO_4) to furnish compound **3a** (41.2 g, 78%). The compound was crystallized from chloroform-methanol-pet.ether, m.p.> 310°C. IR 3030,

2899, 2841, 1680, 1626, 1470 cm^{-1}; ^1H NMR ($CDCl_3$ + TFA) δ 1.55 (d, J = 8Hz, 3H,CH<u>CH</u>$_3$), 4.05 (q, J = 8 Hz, 1H, <u>CH</u>CH_3), 4.08 (s, 6H, 2 X <u>OCH</u>$_3$), 7.23 (s, 1H, Ar<u>H</u>), 7.33 (s, 1H, Ar<u>H</u>). Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.30; H, 5.14; N, 10.22; Found : C, 61.45; H, 5.11; N, 9.82.

From the mother liquor, a second compound separated out, which was filtered, washed with water and dried to furnish **5** (5.0 g, 9%), after cyrstallization from $CHCl_3$-CH_3OH, m.p. > 312°C. IR 3175, 1715, 1695, 1667, 1639, 1563, 893 cm^{-1}; ^1H NMR ($CDCl_3$ + TFA) δ 1.44 (d, J = 7.2 Hz, 3H, CH<u>CH</u>$_3$), 1.66-2.07 (m, 1H, <u>H-b</u>), 2.30-2.67 (m, 1H, <u>CH</u>CH_3) 2.88-3.28 (m, 1H, <u>H-a</u>), 3.57 (s, 3H, <u>OCH</u>$_3$), 3.88 (s, 3H, <u>OCH</u>$_3$), 4.02 (s, 3H, <u>OCH</u>$_3$), 4.06 (s, 3H, <u>OCH</u>$_3$), 4.80 (dd, J = 10.8, 7.2 Hz, 1H, <u>CH</u>CH_2), 6.04 (s, 1H, Ar<u>H</u>), 6.25 (s, 1H, Ar<u>H</u>), 6.74 (s, 1H, Ar<u>H</u>), 6.98 (s, 1H, Ar<u>H</u>), 7.18 (s, 1H, Ar<u>H</u>), 11.23 (s, 4H, N<u>H</u>); MS, m/e (%) : 549 (M^+ + 1, 81), 301 (41), 287 (80), 275 (41), 164 (18), 154 (100), 129 (20), 122 (46), 106 (22), 93 (20), 85 (34). Anal. Calcd. for $C_{28}H_{28}N_4O_8$: C, 61.31; H, 5.14; N, 10.21. Found : C, 60.91; H, 5.20; N, 10.18.

Reaction of compound 5 with $POCl_3$: To compound **5** (1.8 g, 3.28 mmol) , $POCl_3$ (25 mL) was added and the reaction mixture was maintained at 90°C for 19 h. Excess of $POCl_3$ was distilled under reduced pressure. The residue was basified with 10% NaOH under ice cold conditions and extracted with $CHCl_3$. The chloroform layer was washed with water, dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3/C_6H_6$, 10:90) to give compound **6** (0.484 g, 24%) after crystallization from acetone - pet. ether, m.p. 157-159°C. IR 2941, 1600, 1504 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (d, J = 8 Hz, 3H, CH<u>CH</u>$_3$), 2.18-2.28 (m, CH<u>CH</u>$_2$), 2.88-3.00 (m, 1H, <u>CH</u>CH_3), 3.00-3.10 (m, 1H, CH<u>CH</u>$_2$), 3.54 (s, 3H, <u>OCH</u>$_3$), 3.82 (s, 3H, <u>OCH</u>$_3$), 3.94 (s, 3H, <u>OCH</u>$_3$), 3.98 (s, 3H, <u>OCH</u>$_3$), 5.24 (dd, J = 10, 6.5 Hz, 1H, <u>CH</u>CH_2), 6.26 (s, 1H, Ar<u>H</u>), 6.66 (s, 1H, Ar<u>H</u>), 6.85 (s, 1H, Ar<u>H</u>), 7.30 (s, 1H, Ar<u>H</u>), 7.43 (s, 1H, Ar<u>H</u>); ^{13}C NMR ($CDCl_3$) 19.68, 33.68, 39.83, 48.28, 56.14, 107.44, 112.10, 112.70, 113.62, 118.9, 127.81, 132.46, 135.34, 139.78, 147.86, 150.13, 152.14, 157.12, 160.04, 163.08, 163.46, 168.5, 171.10; MS m/e (%) : 626 (M^+ + 6, 12), 622 (M^+ + 4, 47), 622 (M^+ + 2, 98), 620 (M^+, 74), 605 (26), 591 (38), 578 (32), 549 (12), 473 (6), 437 (15), 337 (9), 323 (88), 310 (91), 297 (35). Anal. Calcd. for $C_{28}H_{24}Cl_4N_4O_4$: C, 54.03; H, 3.88; N, 9.00; Cl, 22.79. Found : C, 54.22; H, 3.78; N, 8.84; Cl, 23.08.

7,8-Dimethoxy-3,5-dimethyl-4-mesitylimino-3,4-dihydro-5H-indeno[1,2-<u>d</u>] pyrimidin-2(1H)-one (3c) and 6,7-dimethoxy-2,9-dimethyl-3- mesitylimino-

2,3-dihydro-9H-pyrimido[6,1-a]isoindol-1-one (4c) : Compound **2c** (25.0 g, 61.65 mmol) was dissolved in a mixture of formic acid (375 mL) and orthophosphoric acid (175 mL) and the reaction mixture was heated at 110°C for 26 h. The reaction mixture was cooled in an ice bath and neutralised with 30% sodium hydroxide solution. The precipitated solid was extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4) and solvent was evaporated under reduced pressure. The residue was crystallised from CH_2Cl_2 - CH_3OH to furnish compound **3c** (6.28 g, 25%), m.p. 318°C. IR 2899, 1667, 1612, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (d, J = 6 Hz, 3H, $CH\underline{CH}_3$), 1.90 (s, 3H, $Ar\underline{CH}_3$), 2.20 (s, 3H, $Ar\underline{CH}_3$),2.30 (s, 3H, $Ar\underline{CH}_3$, 3.18 (q, J = 6Hz, 1H, $\underline{CH}CH_3$), 3.60 (s, 3H, $\underline{NCH}_3$), 3.87 (s, 3H, $\underline{OCH}_3$), 4.00 (s, 3H, $\underline{OCH}_3$), 6.80 (s, 3H, Ar$\underline{H}$), 7.58 (s, 1H, Ar$\underline{H}$), 12.08 (s, 1H, $\underline{NH}$, exchanges with D_2O). Anal. Calcd. for $C_{24}H_{27}N_3O_3$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.86; H, 6.77; N, 10.07.

The filtrate obtained after crystallisation of compound **3c** was concentrated and flash chromatographed on silica gel ($CHCl_3/CH_3OH$, 98:2) to furnish compound **4c** (3.71 g, 15%), which crystallised from acetone-pet. ether, m.p. 165°C. IR 2899, 1672, 1645, 1567, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 2.12 (s, 6H, 2 X $Ar\underline{CH}_3$), 2.37 (s, 3H, $Ar\underline{CH}_3$), 3.65 (s, 3H, $\underline{NCH}_3$), 3.97 (s, 3H, $\underline{OCH}_3$), 4.02 (s, 3H, $\underline{OCH}_3$), 5.37 (q, J = 8 Hz, 1H, $\underline{CH}CH_3$), 5.53 (s, 1H, $\underline{C_4}$-H), 6.90 (s, 1H, Ar$\underline{H}$), 6.97 (s, 1H, Ar$\underline{H}$); ^{13}C NMR ($CDCl_3$) 18.09, 19.61, 20.69 (C-13, C-14, C-15 and C-16), 28.71 (C-10), 56.23, 56.45 (C-11 and C-12), 60.35 (C-9), 84.19 (C-4), 104.13, 104.56 (C-5 and C-8), 122.66 (C-4b), 128.51 (C-3' and C-5') 131.11 (C-8a), 138.37 (C-2' and C-6'), 144.55, 147.37 (C-4a and C-4'), 150.18, 150.40, 150.62 (C-3, C-6, C-7 and C-1'). 152.89 (C-1); MS m/e (%) 405 (M^+, 61), 390 (85), 374 (16), 274 (35), 202 (39),132 (65), 117 (15), 84 (100). Anal. Calcd. for $C_{24}H_{27}N_3O_3$: C, 71.09; H, 6.71; N, 10.36. Found : C, 71.25; H, 6.82; N, 10.48.

7,8-Dimethoxy-5-methyl-4-N-methylpiperazino-5H-indeno[1,2-d]pyrimidin-2(1H)-one (3d) and 6,7-dimethoxy-9-methyl-3-N-methylpiperazino-9H-pyrimido [6,1-a]isoindol-1-one (4d): Compound **2d** (0.50 g, 1.4 mmol) was subjected to the same procedure as is described for **3c** and **4c**. The reaction mixture was chromatographed on a neutral alumina column ($CHCl_3/CH_3OH$, 99:1) to furnish compound **4d** (0.28 g, 56%), which crystallised from acetone - pet. ether, m.p. 175-177°C (d). IR 2915, 1637, 1282, 1266, 1012, 990, 775 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 1.75 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 2.37 (s, 3H, $\underline{NCH}_3$), 2.52 (t, J = 4 Hz, 4H, piperazine protons), 3.85 (t, J = 4 Hz, 4H, piperazine protons), 4.00 (s, 6H, 2 X $\underline{OCH}_3$), 5.30 (q, J = 7 Hz, 1H,

CHCH$_3$), 6.28 (s, 1H, C$_4$-H), 6.95 (s, 1H, ArH), 7.22 (s, 1H, ArH); Ms, m/e (%) : 356 (M$^+$, 13), 299 (22), 286 (100), 274 (74) 257 (24), 215 (22), 199 (13), 178 (15), 83 (87), 70 (50). Anal. Calcd. for $C_{19}H_{24}N_4O_3$: C, 64.02; H,6.79; N,15.72. Found : C,63.75; H,6.92; N,15.43.

Later fractions from the column gave on evaporation compound **3d** (40 mg, 8%), crystallised from CH_2Cl_2-EtOAc, m.p. 260-261°C (d). IR 2857, 1618, 1269, 995, 781 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (d, J = 7 Hz, 3H, CHCH$_3$), 2.40 (s, 3H, NCH$_3$), 2.58 (m, 4H, piperazine protons), 3.98 (m, 4H, piperazine protons) 4.11 (s, 7H, 2 x OCH$_3$ and CHCH$_3$), 6.95 (s, 1H, ArH), 7.95 (s, 1H, ArH). Anal. Calcd. for $C_{19}H_{24}N_4O_3$: C, 64.02; H, 6.79; N, 15.72. Found : C, 63.90; H, 6.41; N, 15.32.

2,4-Dichloro-7,8-dimethoxy-5-methyl-5H-indeno[1,2-d]pyrimidine(7): Phosphorus oxychloride (300 mL) was added to compound **3a** (21.5 g, 78.39 mmol) and the reaction mixture was maintained at 105-110°C for 22 h. The excess of $POCl_3$ was distilled under reduced pressure and the residue was added to ice, basified with 10% NaOH and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$) to furnish compound **7** (17.0 g, 70%), crystallised from EtOAc-pet. ether, m.p. 169-171°C. IR 1550, 1504, 787, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57 (d, J = 7 Hz, 3H, CHCH$_3$), 3.93 (m, 1H, CHCH$_3$), 3.97 (s, 3H, OCH$_3$), 4.00 (s, 3H, OCH$_3$), 7.00 (s, 1H, ArH), 7.45 (s, 1H, ArH). Anal. Calcd. for $C_{14}H_{12}Cl_2N_2O_2$: C, 54.03; H, 3.88; N, 9.00, Cl, 22.78. Found : C, 54.16; H, 3.75; N, 9.11; Cl, 22.71.

4-Chloro-7,8-dimethoxy-5-methyl-2N-methylamino-5H-indeno[1,2-d]pyrimidine (8d) and 2-chloro-7,8-dimethoxy-5-methyl-4-N-methyl amino-5H-indeno[1,2-d]pyrimidine (9d) : To a solution of compound 7 (2.86 g,9.19 mmol) in dry benzene (80 mL) was added methylamine in absolute ethanol (35%, 10 mL). The reaction mixture was maintained at 80-85°C for 45 h. The solvent was evaporated under reduced pressure and the residue was dissolved in chloroform. The solution was successively washed with 10% NaOH and water. Subsequent drying (Na_2SO_4) and evaporation in vacuo afforded a syrup which was chromatographed on silica gel (EtOAc/C_6H_6, 2:98) to give compound **8d** (1.48 g, 53%), which was crystallised from acetone, m.p. 214-215°C. IR 3300, 2941, 1587, 1515, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53 (d, J = 7 Hz, 3H, CHCH$_3$), 3.07 (d, J = 5Hz, 3H, NCH$_3$), 3.90 (q, J = 7 Hz, 1H, CHCH$_3$), 3.97 (s, 6H, 2 X OCH$_3$), 5.30 (bs, 1H, NH), 7.00 (s, 1H, C$_6$-H), 7.44 (s, 1H, C$_7$-H); MS, m/e (%) : 307 (M$^+$ + 2, 33), 305 (M$^+$, 100), 290

(65), 274 (81), 246 (8), 232 (7), 152 (14), 76 (7). Anal. Calcd. for $C_{15}H_{16}ClN_3O_2$: C, 58.92; H, 5.28; N, 13.74; Cl, 11.59. Found: C, 58.72; H, 5.40; N, 13.43; Cl, 11.56.

Further elution of the column with EtOAc-C_6H_6 (5;95) gave compound **9d** (0.809 g, 29%), which was crystallised from acetone-pet. ether, m.p. 224-225°C. IR, 3425, 2941, 1582, 1538, 952, 926 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 3.15 (d, J = 5 Hz, 3H, $NH\underline{CH}_3$), 3.71 (q, J = 7 hz, 1H, $\underline{CH}CH_3$), 3.94 (s, 3H, $\underline{OCH}_3$), 3.95 (s, 3H, $\underline{OCH}_3$), 4.77 (bs, 1H, $\underline{NH}$), 7.00 (s, 1H, $\underline{C_6\text{-}H}$), 7.53 (s, 1H, C_7-H); Ms, m/e (%) : 307 (M^+ + 2, 33), 305 (M^+, 100), 290 (26), 274 (41), 254 (13), 238 (8), 152 (7). Anal. Calcd. for $C_{15}H_{16}ClN_3O_2$: C, 58.92; H, 5.28; N, 13.74; Cl, 11.59. Found : C, 59.14; H, 5.19; N, 13.78; Cl, 11.32.

In a similar way, compounds **8a, 8b, 8c** and **9c** were prepared by reacting compound **7** with the corresponding amine.

4-Chloro-7,8-dimethoxy-5-methyl-2-N-methylpiperazino-5H-indeno[1,2-d] pyrimidine (8a): m.p. 154-156°C, yield 77%. IR 1538, 1527, 794, 763 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.49 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 2.27 (s, 3H, $\underline{NCH}_3$), 2.33-2.63 (m, 4H, $(\underline{CH}_2)_2NCH_3$), 3.8-4.10 (m, 5H, $\underline{CH}CH_3$ and $(\underline{CH}_2)_2$ N), 3.97 (s, 6H, 2 X $\underline{OCH}_3$), 7.40 (s, 1H, Ar$\underline{H}$), 7.50 (s, 1H, Ar$\underline{H}$). Anal. Calcd. for $C_{19}H_{23}ClN_4O_2$: C, 60.88; H, 6.18; N, 14.95; Cl, 9.46. Found : C, 60.65; H, 5.95; N, 14.68; Cl, 9.18.

4-Chloro-7,8-dimethoxy-5-methyl-2-morpholino-5H-indeno[1,2-d]pyrimidine (8b) : m.p. 234°C, yield 56%, IR 2840, 1587, 1515, 1099, 851 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 1.53 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 3.80 (bs, 8H, morpholine protons), 3.90 (s, 7H, $\underline{CH}CH_3$ and 2 X $\underline{OCH}_3$), 6.96 (s, 1H, Ar$\underline{H}$) 7.30 (s, 1H, Ar$\underline{H}$). Anal. Calcd. for $C_{18}H_{20}ClN_3O_3$: C, 59.75; H, 5.57; N, 11.61; Cl, 9.80. Found: C, 59.75; H, 5.30; N, 11.24; Cl, 10.13.

4-Chloro-7,8-dimethoxy-5-methyl-2-piperidino-5H-indeno[1,2-d]pyrimidine (8c) : m.p. 174-175°C; yield 77%. IR 2857, 1587, 1120, 855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 1.58-1,68 (m, 6H, piperidine protons) 3.76-4.05 (m, 11 H, 2 x $\underline{OCH}_3$, $\underline{CH}CH_3$ and $(\underline{CH}_2)_2N$), 6.97 (s, 1H, Ar$\underline{H}$), 7.40 (s, 1H, Ar$\underline{H}$), Anal. Calcd. for $C_{19}H_{22}ClN_3O_2$: C, 63.41, H, 6.16; N, 11.68; Cl, 9.85. Found: C, 62.96; H, 6.38; N, 11.89; Cl, 10.08.

2-Chloro-7,8-dimethoxy-5-methyl-4-piperidino-5H-indeno[1,2-d]pyrimidine (9c) : m.p. 137-138°C, yield 1.2%. IR 2941, 1543, 1099, 847 cm^{-1}; ^1H NMR

($CDCl_3$) δ 1.40 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 1.73 (bs, 6H, piperidine protons), 3.50-3.96 (m, 5H, $\underline{CH}CH_3$ and $(\underline{CH}_2)_2N$), 3.97 (s, 6H, 2 X $\underline{OCH}_3$), 6.97 (s, 1H, Ar$\underline{H}$), 7.46 (s, 1H, Ar$\underline{H}$). Anal. Calcd. for $C_{19}H_{22}ClN_3O_2$: C, 63.41; H, 6.16; N, 11.68; Cl, 9.85. Found: C, 63.51; H, 6.39; N,11.80; Cl, 10.00.

7,8-Dimethoxy-5-methyl-2-N-methylamino-5H-indeno[1,2-d]pyrimidine (11d) : Pd/C (5%, 0.47 g) and anhydrous CH_3COONa (0.281 g, 3.43 mmol) was added to compound **8d** (1.05 g, 3.43 mmol), which was dissolved in warm DMF (30 mL) and methanol (100 mL) and it was hydrogenated at 25 psi for 1 h using a Parr hydrogenator. The catalyst was removed and the solvent was evaporated under reduced pressure. The residue was dissolved in chloroform and the solution was washed with water. Subsequent drying (Na_2SO_4) and evaporation in vacuo, afforded a residue which was crystallised from ethanol to yield compound **11d** (0.84 g, 90%), m.p. 199-201°C. IR 3246, 2941, 1587, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 3.10 (d, J = 8 Hz, 3H, $NH\underline{CH}_3$), 3.83 (q, J = 8 Hz, 1H, $\underline{CH}CH_3$), 3.96 (s, 6H, 2 x $\underline{OCH}_3$), 5.30 (bs, 1H, $\underline{NH}$, exchanges with D_2O), 6.97 (s, 1H, Ar$\underline{H}$), 7.40 (s, 1H, Ar$\underline{H}$), 8.23 (s, 1H, $\underline{H}$-4). Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.72; H, 6.05; N, 15.26.

Similarly, compound **8a**, **8c** and **9d** were subjected to hydrogenolysis to furnish compounds **11a, 11c** and **12d** respectively.

7,8-Dimethoxy-5-methyl-4-N-methylamino-5H-indeno[1,2-d]pyrimidine(12d): m.p. 193-194°C. Yield 58%. IR 3455, 1605, 870, 850, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (d, J = 7.7 Hz, 3H, $CH\underline{CH}_3$), 3.17 (d, J = 5.1 Hz, 3H, $\underline{NCH}_3$), 3.76 (q, J = 7.7 Hz, 1H, $\underline{CH}CH_3$), 3.98 (s, 6H, 2 X $\underline{OCH}_3$), 6.96 (s, 1H, Ar$\underline{H}$), 7.52 (s, 1H, Ar$\underline{H}$), 8.57 (s, 1H, $\underline{H}$-2). Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.80; H, 6.49; N, 15.39.

7,8-Dimethoxy-5-methyl-2-N-methylpiperazino-5H-indeno[1,2-d]pyrimidine (11a): m.p. 150-151°C, yield 61%. IR 2899, 2793, 1582, 855, 794 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 2.35 (s, 3H, $\underline{NCH}_3$), 2.52 (t, J = 6 Hz, 4H, $(\underline{CH}_2)_2NCH_3$), 3.77-4.13 (m, 5H, $\underline{CH}CH_3$ and $(\underline{CH}_2)_2N$), 3.97 (s, 6H, 2 X $\underline{OCH}_3$), 6.97 (s, 1H, Ar$\underline{H}$), 7.40 (s, 1H, Ar$\underline{H}$), 8.25 (s, 1H, $\underline{H}$-4). Anal. Calcd. for $C_{19}H_{24}N_4O_2$: C, 67.03; H, 7.10; N, 16.46. Found: C, 66.63; H, 7.31; N, 16.43.

7,8-Dimethoxy-5-methyl-2-piperidino-5H-indeno[1,2-d]pyrimidine(11c): m.p.

145°C, yield 94%. IR 2941, 1582, 1538, 855 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.44 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 1.68 (bs, 6H, piperidine protons), 3.73-4.0 (m, 5H, $\underline{CH}CH_3$ and $(CH_2)_2N$), 3.97 (s, 3H, $\underline{OCH}_3$), 4.0 (s, 3H, $\underline{OCH}_3$), 6.97 (s, 1H, Ar$\underline{H}$), 7.40 (s, 1H, Ar$\underline{H}$), 8.22 (s, 1H, $\underline{H}$-4). Anal. Calcd. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 70.36; H, 7.10; N, 13.10.

2-Chloro-7,8-dimethoxy-5-methyl-4-N-methylpiperazino-5H-indeno[1,2d] pyrimidine (9a): Phosphorus oxychloride (12 mL) was added to compound **3d** (0.25 g, 0.7 mmol) and the reaction mixture was maintained at 100-110°C for 5.5 h. The excess of $POCl_3$ was evaporated under reduced pressure. The residue was added to ice, basified with aqueous NaOH and extracted with chloroform. The chloroform layer was washed with H_2O, dried (Na_2SO_4) and the solvent was evaporated. The residue was chromatographed on silica gel ($CHCl_3/CH_3OH$, 99:1) to furnish compound **9a** which was crystallised from chloroform - pet. ether.(0.101 g, 38%), m.p. 192°C. IR 2941, 2841, 2778, 1538, 1486 cm^{-1}; UV (MeOH) max ( ) : 219 (20,800), 261 (19,200), 304 (10,600), 329 (19,200) nm; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 1.42 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 2.40 (s, 3H, $\underline{NCH}_3$), 2.62 (m, 4H, piperazine protons), 3.88 (m, 4H, piperazine protons), 3.90 (q, J = 7Hz, 1H, $\underline{CH}CH_3$), 3.97 (s, 6H, 2 X $\underline{OCH}_3$), 7.02 (s, 1H, Ar$\underline{H}$), 7.42 (s, 1H, Ar$\underline{H}$). Anal. Calcd. for $C_{19}H_{23}ClN_4O_2$: C, 60.88; H, 6.18; N, 14.95; Cl, 9.46. Found: C, 61.02; H, 6.15; N, 14.83; Cl, 9.82.

7,8-Dimethoxy-2,4-dimorpholino-5-methyl-5H-indeno[1,2-d]pyrimidine (10b): To a solution of compound **7** (0.50 g, 1.6 mmol) in dry amyl alcohol (15 mL), morpholine (0.90 g, 10.3 mmol) was added and the reaction mixture was maintained at 125-130°C for 18 h. The solvent was evaporated under reduced pressure and the residue was dissolved in ethyl acetate. The solution was successively washed with NaOH solution and water. The organic layer was dried (Na_2SO_4) and the solvent was evaporated and the residue was triturated with ether to furnish compound **12b** (0.506 g, 76%). It was crystallised from C_2H_5OH-CH_2Cl_2, m.p. 200-202°C. IR 2941, 2849, 1563, 1538 cm^{-1};^{1}H NMR ($CDCl_3$) δ 1.35 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 3.8 (bs, 17 H, $\underline{CH}CH_3$ and all morpholine protons), 3.93 (s, 3H, $\underline{OCH}_3$), 3.97 (s, 3H, $\underline{OCH}_3$), 6.93 (s, 1H, Ar$\underline{H}$), 7.37 (s, 1H, Ar$\underline{H}$). Anal. Calcd. for $C_{22}H_{28}N_4O_4$: C, 64.06; H, 6.84; N, 13.58. Found: C, 64.23; H, 7.10, N, 13.70.

By using the similar procedure, compounds **10a** and **10c** were prepared from compound **7** and the appropriate amine.

7,8-Dimethoxy-2,4-di-N-methylpiperazino-5-methyl-5H-indeno[1,2-d] pyrimidine (10a): m.p. 156-158°C, yield 53%. IR 2898, 2816, 2762, 1562, 1526, 1190, 1123, 992 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 2.40 (s, 6H, 2 X $\underline{CH}_3$), 2.53 (bs, 8H, piperazine protons), 3.73 (bs, 9H, $\underline{CH}CH_3$and piperazine protons) 3.97 (s, 3H, $\underline{OCH}_3$), 4.0 (s, 3H, OCH_3), 7.0 (s, 1H, ArH), 7.45 (s, 1H, ArH). Anal. Calcd. for $C_{24}H_{34}N_6O_2.3HCl.4H_2O$: C, 46.49; H, 7.31; N, 13.55; Cl, 17.15. Found: C, 46.11; H, 7.39; N, 13.85; Cl, 17.08.

7,8-Dimethoxy-2,4-dipiperidino-5-methyl-5H-indeno[1,2-d]pyrimidine (10c): m.p. 137-139°C, yield 61%. IR 2924, 2817, 1563, 1526, 998, 862 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (d, J = 8 Hz, 3H, $CH\underline{CH}_3$), 1.66 (bs, 12H, piperidine protons) 3.60 (bs, 9H, $\underline{CH}CH_3$ and piperidine protons), 3.96 (s, 3H, $\underline{OCH}_3$). 4.0 (s, 3H, $\underline{OCH}_3$), 6.93 (s, 1H, Ar$\underline{H}$),7.36(s,1H, Ar$\underline{H}$). Anal. Calcd. for $C_{24}H_{32}N_4O_2.CH_3SO_3H.0.5H_2O$: C, 58.45; H, 7.26; N, 10.90; S, 6.24. Found: C, 58.72; H, 7.02; N, 11.12; S, 5.91.

2-Chloro-7,8-dimethoxy-3,5-dimethyl-4-mesitylimino-3,4-dihydro-5H-indeno [1,2-d]pyrimidine (13): To compound **3c** (4.0 g, 9.86 mmol), phosphorus oxychloride (60 mL) and 4-dimethylaminopyridine (0.225 g, 1.84 mmol) was added and the reaction mixture was refluxed for 3.5 h. Excess of $POCl_3$ was distilled under reduced pressure. The residue was added to ice, basified with aqueous NaOH and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4) and solvent evaporated. The residue was flash chromatographed on silica gel ($CHCl_3/CH_3OH$, 98:2) to furnish compound **13** (1.62 g, 39%), which was crystallised from diethyl ether, m.p. 187-188°C. IR 2960-2900, 1625, 1520, 850 cm^{-1}, ^1H NMR ($CDCl_3$) δ 0.79 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 1.92 (s, 3H, Ar$\underline{CH}_3$), 2.25 (s, 3H, Ar$\underline{CH}_3$), 2.35 (s, 3H, Ar$\underline{CH}_3$), 3.05-3.38 (m, 1H, $\underline{CH}CH_3$), 3.93 (s, 3H, $\underline{NCH}_3$), 4.00 (s, 6H, 2 X $\underline{OCH}_3$), 6.85 (s, 3H, Ar$\underline{H}$), 7.35 (s, 1H, Ar$\underline{H}$) ; MS, m/e (%) : 425 (M^+ + 2, 26) 423 (M^+, 81), 408 (76), 388 (62), 372 (38), 355 (20), 341 (24), 327 (17), 281 (87), 249 (14), 239 (24), 223 (43), 207 (100), 147 (20), 107 (28), 77 (47), 44 (51). Anal. Calcd. for $C_{24}H_{26}ClN_3O_2$: C, 67.99; H, 6.18; N, 9.91; Cl, 8.36. Found: C, 67.69; H, 6.22; N, 9.98; Cl, 8.45.

7,8-Dimethoxy-3,5-dimethyl-4-mesitylimino-3,4-dihydro-5H-indeno[1,2-d] pyrimidine (15): The compound **13** (0.775 g, 1.83 mmol) was subjected to hydrogenation as described for compound **11d**. The residue from the reaction mixture was flash chromatographed on silica gel ($CHCl_3/CH_3OH$, 98:2) to give **15** (0.462 g, 65%), m.p. 226-227°C. IR 2920, 1620, 850, 780

cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 1.90 (s, 3H, $Ar\underline{CH}_3$), 2.23 (s, 3H, $Ar\underline{CH}_3$), 2.32 (s, 3H, $Ar\underline{CH}_3$), 3.05 (q, J = 7 Hz, 1H, $\underline{CH}CH_3$), 3.68 (s, 3H, $\underline{NCH}_3$), 3.93 (s, 3H, $\underline{OCH}_3$), 3.98 (s, 3H, $\underline{OCH}_3$), 6.83 (s, 3H, Ar$\underline{H}$), 7.30 (s, 1H, Ar$\underline{H}$), 8.07 (s, 1H, $\underline{H\text{-}2}$); MS, m/e (%) : 389 (M^+, 52), 374 (69), 356 (16), 333 (15), 281 (47), 207 (100), 147 (20), 107 (20), 77 (25), 44 (100). Anal. Calcd. for $C_{24}H_{27}N_3O_2$: C, 74.00; H, 6.99; N, 10.79. Found: C, 73.85; H, 7.30; N, 10.57.

7,8-Dimethoxy-3,5-dimethyl-4-mesitylimino-2-piperidino-3,4-dihydro-5H-indeno[1,2-$\underline{d}$]pyrimidine (14) : To compound **13** (0.16 g, 0.37 mmol) was added piperidine (3.0 g, 35.2 mmol) and the reaction mixture was maintained at 70°C for 8 h. It was diluted with water and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4) and the solvent was evaporated. The residue was triturated with petroleum ether (40-60) to furnish compound **14** (0.132 g, 74%), which was crystallised from diethyl ether, mp 200-201°C. IR 2950-2920, 1630, 1600, 900, 850, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74 (d, J = 7 Hz, 3H, $CH\underline{CH}_3$), 1.73 (bs, 6H, piperidine protons), 1.88 (s, 3H, $Ar\underline{CH}_3$), 2.23 (s, 3H, $Ar\underline{CH}_3$), 2.30 (s, 3H, $Ar\underline{CH}_3$), 3.13 (m, 1H, $\underline{CH}CH_3$), 3.18-3.37 (m, 4H, $[\underline{CH}_2]_2N$), 3.68 (s, 3H, $\underline{NCH}_3$), 3.87 (s, 3H, $\underline{OCH}_3$), 3.93 (s, 3H, $\underline{OCH}_3$), 6.80 (s, 3H, Ar$\underline{H}$) 7.25 (s, 1H, Ar$\underline{H}$); MS, m/e (%) : 472 (M^+, 92), 457 (100), 339 (80), 255 (14), 236 (27), 133 (40), 125 (24), 91 (20), 84 (68), 69 (33), 56 (29). Anal. Calcd. for $C_{29}H_{36}N_4O_2$: C, 73.70; H, 7.68; N, 11.85. Found: C, 73.64; H, 7.78; N, 11.88.

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