Synthesis of Heterocycles *via* Enamines. Part 12.[1] Intramolecular Additions of Nucleophiles to 1,4-Dihydropyrimidine-2(3*H*)-thione Derivatives: Single-step Synthesis of Condensed Heterocyclic Compounds

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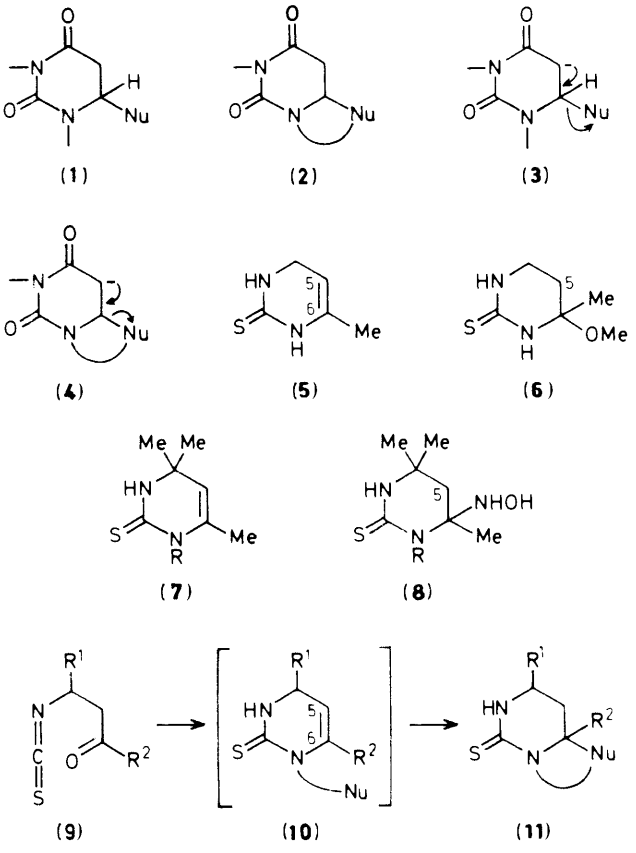
In a single-pot operation, 4-isothiocyanotobutan-2-one (**9**; R^1 = H, R^2 = Me), and functionalised amines, *viz.* 2-aminoethanol, 2-aminoethanethiol, ethane-1,2-diamine, *o*-aminophenol, *o*-aminothiophenol, and propane-1,3-diamine provide the corresponding oxazolo-, thiazolo-, imidazolo-pyrimidines and pyrimido-benzoxazole, -benzothiazole, and -pyrimidines respectively. It is proposed that the intermediate 1-substituted 1,4-dihydropyrimidine-2(3*H*)-thiones (**10**) undergo base-catalysed intramolecular addition of the nucleophile at their enamine α carbon, *i.e.* at C-6. 3-Isothiocyanatobutanal (**9**; R^1 = Me, R^2 = H) reacted similarly with functionalised amines.

Base-catalysed inter-[2-5] and intra-molecular[6a] nucleophilic additions on the C(5)–C(6) enamine double bond[7,8] of uracils are mostly reversible,† the adducts (**1**), (**2**) easily forming the enolate ions (**3**), (**4**), which bring about the elimination responsible for the back reaction. Intermolecular base-catalysed additions of methanol and hydroxylamine to the enamine C(5)–C(6) double bond of 6-methyl-1,4-dihydropyrimidine-2(3*H*)-thione (**5**) and 4,4,6-trimethyl- and 1,4,4,6-tetramethyl-1.4-dihydropyrimidine-2(3*H*)-thione (7; R = H, Me) respectively give 6-methoxy-6-methyl-1,4,5,6-tetrahydropyrimidine-2(3*H*)-thione(6)[10] and 6-hydroxyamino-4,4,6-trimethyl/1,4,4,6-tetramethyl-1,4,5,6-tetrahydropyrimidine-2(3*H*)-thione (**8**; R = H, Me).[1] These adducts are isolated under basic conditions. their anions at C-5 not being stabilised and the chances of reversible elimination of added nucleophile being less. From this we argued that 1,4-dihydropyrimidine-2(3*H*)-thiones which had a nucleophile on the chain attached at N–1(10) could, *via* intramolecular nucleophilic addition, provide synthetic methodology for condensed heterocyclic systems (**11**). In order to achieve this objective, we needed 1-(β or γ-functionalised: OH, NH_2, SH) alkyl-1,4-dihydropyrimidine-2(3*H*)-thiones and for this purpose 4-isothiocyanatobutan-2-one (**9**; R^1 = H. R^2 = Me) and 3-isothiocyanatobutanal (**9**; R^1 = Me. R^2 = H) were condensed with amines bearing the second nucleophile, *viz* OH (2-aminoethanol, 3-aminopropan-1-ol, *o*-aminophenol), SH (2-mercaptoethylamine, *o*-aminothiophenol), or NH_2 (ethane-1,2-diamine. propane-1,3-diamine).[11]

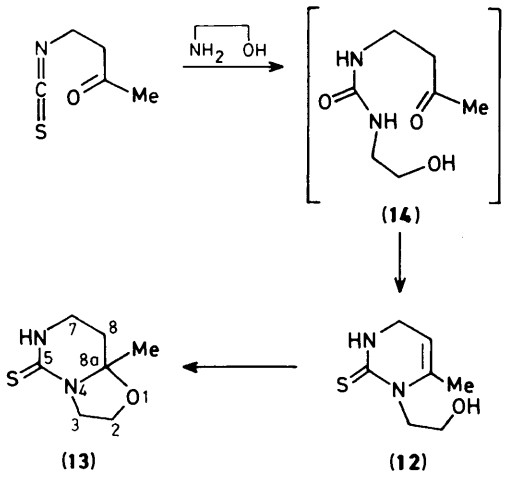


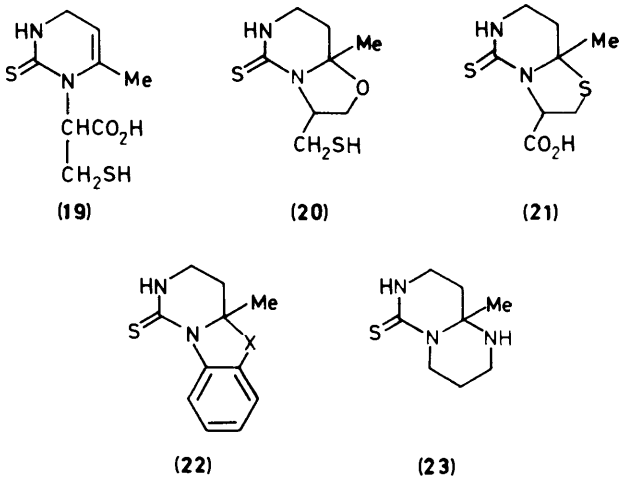
Results and Discussion

4-Isothiocyanatobutan-2-one (**9**; R^1 = H, R^2 = Me) and 2-aminoethanol gave a product (m.p. 140 °C, M^+, *m/z* 172), the structure of which could have been (**12**) or (**13**). Its ^{1}H n.m.r. spectrum exhibited an upfield shift for the Me group (δ 1.37) as compared with the 6-Me (δ 1.77) in compound (**5**); it also showed the absence of an enamine proton [*cf.* 5-H, δ 4.5—4.6 for (**5**)[10]]. The ^{13}C n.m.r. spectrum showed only one sp^2 carbon for (**13**) as against three sp^2 carbons in (**12**) and in the mass spectrum the parent ion (*m/z* 172) lost an acetyl radical (*m/z* 43) to form the fragment ion at *m/z* 129; the latter could arise only in (**13**) where a C(8a)–O bond was formed. The product was therefore assigned structure (**13**).

The progress of the above reaction when monitored by i.r. spectroscopy showed the disappearance of isothiocyanate and carbonyl absorption after 2.5 and 6 h respectively. Clearly. the amine first reacted with the isothiocyanate group to form (**14**) and then with the carbonyl group. U.v. spectroscopic monitoring of the reaction mixture showed that after 15 min absorption appeared at 275 nm and this was followed by the appearance of further absorption at 245 nm (45 min). Subsequently, the intensity of the band at 275 nm decreased and that of the band at 245 nm increased until after 6 h the reaction mixture absorbed only at 245 nm. From these observations, it is clear that compound (**12**), (analogue of which absorbs at 255—275nm[12]) is initially formed and this then undergoes base-catalysed addition of OH at the enamine double bond to form (**13**). T.l.c. also showed after 2 h, the presence of two products, that with the lower R_F value changing to that with the higher. Attempts to isolate the former after 2 h were unsuccessful,

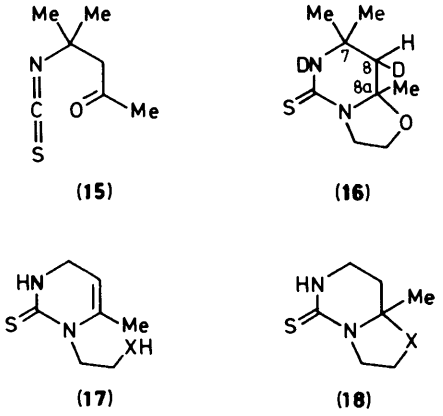
† Uracil derivatives substituted at C-5 with electron-withdrawing groups form stable adducts.[9]





chromatography inducing the transformation of (**12**) to (**13**). Further evidence for this mode of reaction was provided by the reaction of (**15**) and 2-aminoethanol in D_2O to give (**16**).[13]

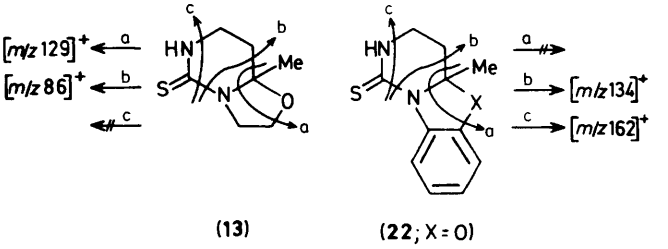
Similarly, (**9**; R^1 = H, R^2 = Me) with ethane-1,2-diamine and 2-mercaptoethylamine *via* (**17**; X = NH, or S) as an intermediate gave (**18**; X = NH) and (**18**; X = S) respectively. Again mass spectrometry showed formation of the corresponding acetylimine (*m/z* 42) and thioacetyl (*m/z* 59) cations respectively.



For a comparison of the reactivity of hard (OH) and soft (SH) nucleophiles[14] on enamine double bonds, the reaction of cysteine hydrochloride with the butanone (**9**; R^1 = H, R^2 = Me) was investigated. In its u.v. spectrum the product,[15] absorbed at $\lambda_{max.}$ 245 nm and was evidently a cycloadduct of the initially formed thione (**19**). Of the two possible structures, (**20**) or (**21**) for this product, a clear distinction came from its mass spectrum, in which the presence of peaks at *m/z* 173 (232—MeC=S) and *m/z* 59 ($MeC\overset{+}{=}S$) supported (**21**), a peak at *m/z* 189 (232—$CH_3\dot{C}$=O) for structure (**20**) being absent. This structure assignment was corroborated by the presence of absorption at 1 730 cm^{-1} for CO_2H and the solubility of the compound in aqueous sodium hydrogen carbonate.

Similar reactions of (**9**; R^1 = H, R^2 = Me) with *o*-aminophenol and *o*-aminothiophenol gave the tricyclic heterocyclic systems (**22**; X = O) and (**22**; X = S) (see Experimental section).

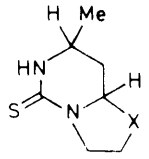
In the mass spectra of these compounds, the fragmentation patterns of oxazolo-(**13**), thiazolo- (**18**; X = S), and imidazolo-(**18**; X = O)-pyrimidines were significantly different from those of pyrimidobenzoxazoles (**22**; X = O) and pyrimidobenzothiazoles (**22**; X = S). In representative cases, *i.e.* (**13**) and (**22**) (X = O) of each category, the parent ion loses the angular methyl group to give peaks of medium intensity at *m/z* 157 and 205 respectively. The loss of acetyl radical from the parent ion was prominent in (**13**) as compared with (**22**; X = O) (path a). The cleavage of the pyrimidine ring of the parent ions took place in both (**13**) and (**22**) (X = O) (path b). In the former, the oxazole entity was lost and part of the pyrimidine moiety formed a cation at *m/z* 86 but in (**22**; X = O), the pyrimidine moiety was cleaved forming a stable benzoxazolium cation (*m/z* 134). Also from the parent ion of (**22**; X = O), thiocyanic acid was preferentially eliminated to form a benzoxazolium cation (*m/z* 162) but such cleavage was not observed in (**22**; X = O) (path c).



In all these reactions the nucleophile was attached to the β-carbon of the 1-substituent of the 1,4-dihydropyrimidine-2(3*H*)-thiones and thus five-membered rings (oxazole, thiazole, imidazole) were formed. If, instead, the nucleophile was at the γ-carbon six-membered heterocycles were formed. Thus (**9**; R^1 = H, R^2 = Me) and propane-1,3-diamine gave the thione (**23**).

In these intramolecular additions the enamine α-carbon, *i.e.* C-6, possessed an electron-donating methyl group. We envisaged that this group both by electron donation and steric hindrance might be obstructing the reaction of the nucleophile at C-6 and we therefore investigated similar reactions with 1,4-dihydropyrimidine-2(3*H*)-thiones unsubstituted at C-6. Thus, the reactions of 3-isothiocyanatobutanal (**9**; R^1 = Me, R^2 = H) with the functionalised amines 2-aminoethanol, 2-mercaptoethylamine, *o*-aminothiophenol, 3-aminopropan-1-ol, and propane-1,3-diamine gave the thiones (**24**; X = O), (**24**; X = S), (**25**), (**26**; X = O), and (**26**; X = NH) respectively. Structural assignments were on the basis of spectral evidence. In ^{13}C n.m.r. spectra, the appearance of double signals for almost every carbon, indicated the presence of two inseparable isomers.

In all these reactions, 1,4-dihydropyrimidine-2(3*H*)-thiones which undergo *in situ* intramolecular nucleophilic addition differed from uracil derivatives both in lacking a 4-carbonyl group and also in possessing a 2-thioxo rather than a 2-oxo



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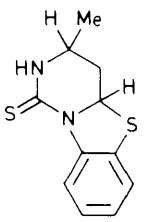

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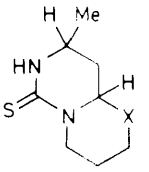

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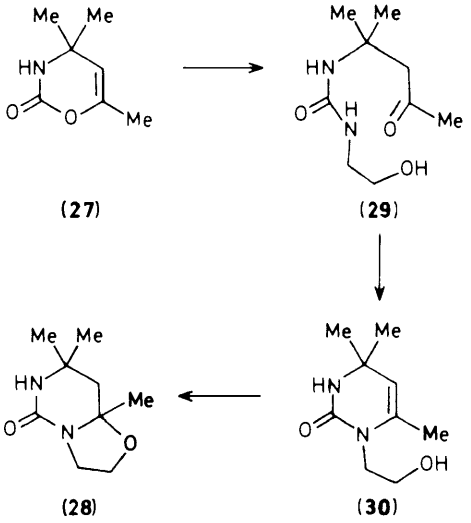
group. In order to investigate the effect of the later difference the reactions of 1,4-dihydropyrimidin-2(3*H*)-ones were studied. Since 1,3-oxazines and alkylamines[15-17] give the corresponding 1-alkylpyrimidines the oxazinone (**27**)[18] was treated with 2-aminoethanol to give a product which from spectral evidence was assigned structure (**28**). Its formation was thought to proceed *via* (**29**), formed by amine attack on the 2-oxo group of (**27**), followed by cyclodehydration to give (**30**) and subsequent intramolecular nucleophilic addition of OH at C-6.



(27) (29) (28) (30)

In thymidylate synthetase-catalysed reductive methylation of 2′-deoxyuridylate (DUMP) to 2′-deoxythymidylate with N^5,N^{10}-methylenetetrahydrofolate (THF), the proposed mechanism involves nucleophilic attack[6b] (enzyme) at C-6 (the enamine α-carbon) and electrophilic attack at C-5 (enamine β-carbon) of (DUMP), to form an adduct which subsequently loses a nucleophile *via* anion formation at C-5. The observation that similar adducts obtained in the present investigation are stable in the absence of a 4-carbonyl group, indirectly supports the proposed mechanism.

Experimental

M.p.s were determined in capillaries and are uncorrected. I.r. and u.v. spectra were recorded with Hungarian Spectromom-2000 and Cz VSU-2P spectrophotometers. ^{1}H N.m.r. and ^{13}C n.m.r. spectra were recorded on a Tesla BS 487C 80 MHz instrument and JNM FX-900 FT n.m.r. spectrometers respectively. Mass spectra were recorded on Hitachi-Perkin-Elmer RMU-60, Varian MAT CH-7, and GC-MS Jeol B-300 instruments. For t.l.c., plates coated with silica gel G were used and spots were developed with iodine. Elemental analysis were performed at the microanalytical laboratory of Calcutta University, Calcutta, India.

General Procedures.—A solution of 4-isothiocyanatobutan-2-one (**9**; R^1 = H, R^2 = Me) (10 mmol) or 3-isothiocyanatobutanal (**9**: R^1 = Me, R^2 = H) (10 mmol) and the functionalized amine (12 mmol) in ethanol or methanol was refluxed on a water-bath. The reaction was complete (t.l.c.) in 6—8 h. The solvent was distilled off and the residue was purified by column chromatography on silica gel by using benzene and benzene ethyl acetate mixtures as eluants.

For diamine reactions a solution of the β-isothiocyanatocarbonyl compound was slowly added to an ethanolic solution of the diamine and the mixture then heated under reflux. Where an amine hydrochloride was used, an equivalent amount of triethylamine was added. The reaction of 4,4,6-trimethyl-1,3-oxazine-2(3*H*)-one (**26**) with 2-aminoethanol was performed in acetonitrile.

*Hexahydro-8a-methyl-*6H*-oxazolo*[3,2-*c*]*pyrimidine-5-thione* (**13**): eluant benzene–ethyl acetate (90:10), yield 60%, m.p. 140 °C (Found: C, 49.3; H, 6.8; N, 16.25. $C_7H_{12}N_2OS$ requires C, 48.84; H, 6.98; N, 16.28%): δ_H($CDCl_3$) 1.37 (3 H, s, Me), 1.65—2.37 (2 H, m, CH_2), 3.12—3.40 (2 H, m, CH_2), 3.82—4.38 (4 H, m, 2 × CH_2), and 7.02—7.45 (1 H, br, NH, exchangeable with D_2O); δ_C($CDCl_3$)* 23.4 (q, Me), 31.2 (t, CH_2), 38.4 (t, CH_2), 48.0 (t, CH_2), 62.4 (t, CH_2), 90.0 (s, C), 175.2 (s, C=S); *m*/*z* 172 (M^+), 157 (172 − CH_3), 129 (172 − CH_3CO), 86 ($\underline{S\text{–}\dot{C}\text{=}N\text{–}CH_2\text{–}CH_2}$), 55($CH_3\dot{C}\text{–}\underline{CH_2CH_2}$); λ_{max}(EtOH) 235 nm (ε 5.42 × 10^3).

Hexahydro-7,7,8a-trimethyl-6*H*-[8-$^2H_1$]oxazolo[3,2-*c*]-pyrimidine-5-thione (**16**). A suspension of 4-isothiocyanato-4-methylpentan-2-one (**15**) (1.58 g, 10 mmol) in D_2O (5 ml) containing 2-aminoethanol (610 mg, 10 mmol) was refluxed in an oil-bath at 110 °C. After 6 h, the oily drops vanished and a solid separated. This was filtered off and crystallised from ethyl acetate to give (**16**) (1.75 g, 80%), m.p. 182 °C: δ_H($CDCl_3$) 1.43 (s, 6 H, 2 × Me), 1.53 (s, 3 H, Me), 1.90—2.30 (m, 1 H, CHD), and 3.73—4.60 (m, 4 H, NCH_2CH_2O); *m*/*z* 203 (M^+ + 1), 202 (M^+), 187 (202 − CH_3), 159 (202 − CH_3–C=O), and 127 (187 − DNCS).

Hexahydro-8a-methylimidazolo[1,2-*c*]pyrimidine-5(1*H*)-thione (**18**; X = NH): eluant chloroform–ethyl acetate (90:10), yield 20%, m.p. 184 °C, δ_H[$(CD_3)_2SO$] 1.2 (3 H, s, Me), 2.66—3.48 (8 H, m, 4 × CH_2), and 7.65—7.92 (2 H, br, 2 NH, exchangeable with D_2O); δ_C[$(CD_3)_2SO$] 22.2 (q, Me), 30.4 (t, CH_2), 37.6 (t, CH_2), 41.7 (t, CH_2), 50.2 (t, CH_2), 75.4 (s, C), and 173.3 (s, C=S); *m*/*z* 171 (M^+), 156 (171 − CH_3), 129 (171 − $CH_3\dot{C}$=NH), 86 ($\underline{S\text{–}\dot{C}\text{=}N\text{–}CH_2\text{–}CH_2}$), and 55 ($CH_3\underline{\dot{C}CH_2CH_2}$); λ_{max}(EtOH) 235 nm (ε 4.94 × 10^3).

Hexahydro-8a-methyl-6*H*-thiazolo[3,2-*c*]pyrimidine-5-thione (**18**; X = S): eluant benzene–ethyl acetate (90:10), yield 25%, m.p. 166—67 °C; δ_H($CDCl_3$) 1.65 (3 H, s, Me), 2.05—2.30 (2 H, m, CH_2), 2.97—3.52 (4 H, m, NCH_2CH_2S), 3.87—4.30 (1 H, m, NCH_2), and 7.20—7.47 (1 H, br, NH, exchangeable with D_2O); δ_C($CDCl_3$) 26.8 (t, CH_2), 28.0 (q, CH_3), 32.6 (t, CH_2), 37.4 (t, CH_2), 54.1 (t, CH_2), 67.1 (s, C), 174.1 (s, C=S); *m*/*z* 188 (M^+), 173 (188 − CH_3), 129 (188 − CH_3C=S), 86 ($\underline{S\text{–}\dot{C}\text{=}N\text{–}CH_2\text{–}CH_2}$), and 55 ($CH_2\underline{\dot{C}CH_2CH_2}$); λ_{max}(EtOH) 235 nm (ε 5.1 × 10^3).

*Hexahydro-8a-methyl-5-thioxo-*6H*-thiazolo*[3,2-c]*pyrimidine-3-carboxylic acid* (**21**), eluant benzene–ethyl acetate (80:20), yield 50%, m.p. 168 °C† (Found: C, 41.45; H, 5.2; N, 11.95. $C_8H_{12}N_2O_2S$ requires C, 41.37; H, 5.17; N, 12.07%): δ_H[$(CD_3)_2SO$] 1.85 (3 H, s, Me), 2.27—2.57 (2 H, m, 8-CH_2),

* Multiplicities of ^{13}C n.m.r. signals refer to the off resonance proton-decoupled spectra.

† Another product with lower R_F value could not be isolated in amount sufficient for structure elucidation.

3.57—3.97 (4 H, m, including a doublet, J 7 Hz, 7-CH_2 and 2-CH_2), 5.45 (t, 1 H, J 7 Hz, CH), and 8.50—8.70 (br, 1 H, NH, exchangeable with D_2O); δ_C[$(CD_3)_2SO$] 31.12 (q, CH_3), 34.09 (t, CH_2), 36.95 (t, CH_2), 41.86 (t, CH_2), 71.97 (d, CH), 73.66 (s, C), and 175.72 and 178.73 (s, C=S, C=O); m/z 232 (M^+), 217 (232 − CH_3), 188 (232 − CO_2), 173 (232 − CH_3C=S), and 59 (CH_3–$\overset{+}{C}$=S); $\nu_{max.}$(KBr) 1 730 cm^{-1} (C=O); $\lambda_{max.}$(EtOH) 245 nm.

2,3,4,4a-*Tetrahydro*-4a-*methyl*-1H-*pyrimido*[6,1-b]*benzoxazole*-1-*thione* (**22**; X = O): eluant chloroform–ethyl acetate (90:10), yield (25%, m.p. 162—163 °C (Found: C, 60.25; H, 5.45; N, 12.6. $C_{11}H_{12}N_2OS$ requires C, 60.00; H, 5.45; N, 12.72%); δ_H($CDCl_3$) 1.67 (3 H, s, CH_3), 2.17—2.60 (2 H, m, CH_2), 3.33—3.73 (2 H, m, NCH_2), 6.84—7.33 (4 H, m, ArH), and 7.33—7.40 (1 H, br, NH, exchangeable with D_2O); m/z 220 (M^+), 205 (220 − CH_3), 102 (220 − HNCS), and 134 (220 − $\underline{CH_2CH_2N=\overset{+}{C}}$–S); $\lambda_{max.}$(EtOH) 245 and 320 nm.

2,3,4,4a-*Tetrahydro*-4a-*methyl*-1H-*pyrimido*[6,1-b]*benzothiazole*-1-*thione* (**22**; X = S): eluant chloroform–ethyl acetate (90:10), yield 10%, m.p. 282 °C (Found: C, 56.4; H, 5.05; N, 11.75. $C_{11}H_{12}N_2S_2$ requires C, 56.7; H, 5.17; N, 11.86%); δ_H[$(CD_3)_2SO$] 1.87 (3 H, s, CH_3), 2.52—2.80 (2 H, m, CH_2), 3.65—4.27 (2 H, m, N-CH_2), 7.25—7.72 (4 H, m, ArH); δ_C[$(CD_3)_2SO$] 27.26 (q, CH_3), 31.63 (t, CH_2), 37.86 (t, CH_2), 75.08 (s, C), 122.49 (s, ArC), 123.22 (s, ArC), 123.66 (d, ArCH), 124.91 (d, ArCH), 129.89 (d, ArCH), 138.98 (d, ArCH), and 174.98 (s, C=S); m/z 236 (M^+), 221 (236 − CH_3), 177 (236 − $CH_3\dot{C}$=S), and 150 (236 − $\underline{CH_2CH_2N=\overset{+}{C}}$S); $\lambda_{max.}$(EtOH) 235 and 310 nm.

Octahydro-9a-methyl-6*H*-pyrimido[1,6-*a*]pyrimidine-6-thione (**23**): eluant benzene–acetone (95:5), yield 20%, m.p. 162—163 °C; δ_H[$(CD_3)_2SO$] 2.10 (3 H, s, CH_3), 2.20—2.80 (2 H, m, CH_2), 2.60—2.80 (2 H, m, CH_2), 3.65—4.35 (6 H, m, 3 × CH_2); δ_C[$(CD_3)_2SO$] 19.60 (q, CH_3), 21.15 (t, CH_2), 33.04 (t, CH_2), 35.38 (t, CH_2), 37.87 (t, CH_2), 41.23 (t, CH_2), 70.03 (s, C, 178.59 (s, C=S); m/z 185 (M^+), 170 (M^+ − CH_3), 143 (185 − $CH_3\dot{C}$=NH), 86 ($\underline{S–\overset{+}{C}=N–CH_2–CH_2}$), and 55 ($\underline{CH_3–C–CH_2–CH_2}$); $\lambda_{max.}$(EtOH) 245 nm.

Hexahydro-7-methyl-6*H*-oxazolo[3,2-*c*]pyrimidine-5-thione (**25**; X = O): eluant benzene–ethyl acetate (90:10), yield 50%, m.p. 128—129 °C; δ_H($CDCl_3$) 1.12—1.37 (3 H, m, CH_3), 1.47—2.25 (2 H, m, CH_2), 3.55—4.20 (4 H, m, 2 × CH_2), 4.45—5.00 (2 H, m, 2 × CH), and 6.95—7.32 (1 H, br, NH, exchangeable with D_2O); δ_C($CDCl_3$) 20.04, 20.70 (q, CH_3), 30.81, 33.67 (t, CH_2), 44.0, 44.52 (d, CH), 47.58, 48.03 (t, CH_2), 64.37, 64.73 (t, CH_2), 82.17, 84.88 (d, CH), 173.47, and 174.27 (s, C=S); m/z 172 (M^+); $\lambda_{max.}$(EtOH), 240 nm.

Hexahydro-7-methyl-6*H*-thiazolo[3,2-*c*]pyrimidine-5-thione (**25**; X = S): eluant benzene–ethyl acetate (90:10) yield 20%, m.p. 112—113 °C; δ_H($CDCl_3$) 1.32 (3 H, m, CH_3), 2.90—3.15 (2 H, t, CH_2), 3.57—3.75 (2 H, m, CH_2), and 4.40—4.87 (2 H, m, CH_2); $\lambda_{max.}$(EtOH) 240 nm.

2,3,4,4*a*-*Tetrahydro*-3-*methyl*-1H-*pyrimido*[6,1-b]*benzothiazole*-1-*thione* (**26**): eluant chloroform–ethyl acetate (80:20), yield 40%, m.p. 172 °C (Found: C, 56.9; H, 5.15; N, 11.72. $C_{11}H_{12}N_2S_2$ requires C, 56.77; H, 5.17; N, 11.86%); δ_H(TFA) 1.52 (3 H, m, CH_3), 2.52—2.82 (2 H, m, CH_2), 3.75—4.35 (1 H, m), 5.67—6.00 (1 H, m), and 7.20 —7.72 (4 H, m, ArH); δ_C[$(CD_3)_2SO$] 19.55, 20.47 (q, CH_3), 31.78, 34.21 (t, CH_2), 45.03, 46.64 (d, CH), 62.72, 65.69 (d, C-4a), 121.00, 121.44 (s, ArC), 121.98, 123.58 (d, ArCH) 124.51, 129.67 (d, ArCH), 130.21 (d, ArCH), 140.44, 140.30 (s, ArC), and 174.75 (s, C=S); m/z 236 (M^+); $\lambda_{max.}$(EtOH) 240 and 320 nm.

Hexahydro-8-*methyl*-2H,6H-*pyrimido*[6,1-b][1,3]*oxazine*-6-*thione* (**26**; X = O); crystallised from ethanol, yield 60%, m.p. 153—154 °C (Found: C, 51.8; H, 7.7; N, 15.05. $C_8H_{14}N_2OS$ requires C, 51.61; H, 7.52; N, 15.04%); δ_H($CDCl_3$) 1.07—1.40 (3 H, m, CH_3), 1.40—2.45 (4 H, m, 2 × CH_2), 2.95—4.12 (4 H, m, 2 × CH_2), 4.60—5.02 (1 H, m, CH), 5.20—5.57 (1 H, m, CH), and 7.18—7.55 (1 H, b, NH, exchangeable with D_2O); δ_C($CDCl_3$) 19.30, 19.69 (q, CH_3), 24.67, 25.49 (t. CH_2), 34.21, 35.43 (t, CH_2), 42.40, 43.37 (d, CH), 46.69, 48.69 (t, CH_2), 66.47, 67.45 (t, CH_2), 82.16, 83.04 (d, CH), 176.89, and 177.23 (s, C=S); m/z 186 (M^+); $\lambda_{max.}$(EtOH) 240 nm.

Octahydro-8-methyl-6*H*-pyrimido[1,6-*a*]pyrimidine-6-thione (**26**; X = NH); eluant chloroform–ethyl acetate (90:10), yield 25%, m.p. 203—205 °C; δ_H[$(CD_3)_2SO$] 1.5 (3 H, m, CH_3), 2.10—2.20 (4 H, m, 2 × CH_2), 3.50—4.20 (4 H, m, 2 × CH_2), 4.20—4.65 (m, 1 H, CH), and 5.02—5.38 (1 H, m, CH); δ_C[$(CD_3)_2SO$] 19.62, 19.76 (q, CH_3), 21.52, 22.11 (t, CH_2), 31.49, 34.42 (t, CH_2), 42.18, 42.48 (d, CH), 43.50, 43.80 (t, CH_2), 46.36, 47.50 (t, CH_2), 65.78, 66.29 (d, CH), 177.66, and 179.49 (s, C=S); m/z 185 (M^+); $\lambda_{max.}$(EtOH) 240 nm.

Hexahydro-7,7,8a-trimethyl-6*H*-oxazolo[3,2-*c*]pyrimidine-5-thione (**29**); eluant benzene, yield 80%, m.p. 66—67 °C; δ_H($CDCl_3$) 1.21 (3 H, s, CH_3), 1.32 (3 H, s, CH_3), 1.46 (3 H, s, CH_3), 3.34—3.87 (2 H, m, CH_2), 4.00—4.69 (4 H, m, 2 × CH_2), 7.28 (1 H, br, NH, exchangeable with D_2O); m/z 184 (M^+), 169 (184 − CH_3), and 129 (169 − CH_3–$\dot{C}$=O); $\lambda_{max.}$($CDCl_3$) 1 660 cm^{-1} (C=O).

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