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# KETENE-S,S-ACETALS–V[1]

## THE REACTIONS OF α-KETO AND α-CYANOKETENE-S,S-ACETALS WITH GUANIDINE AND THIOUREA: A NEW GENERAL SYNTHESIS OF ALKOXY-PYRIMIDINES†

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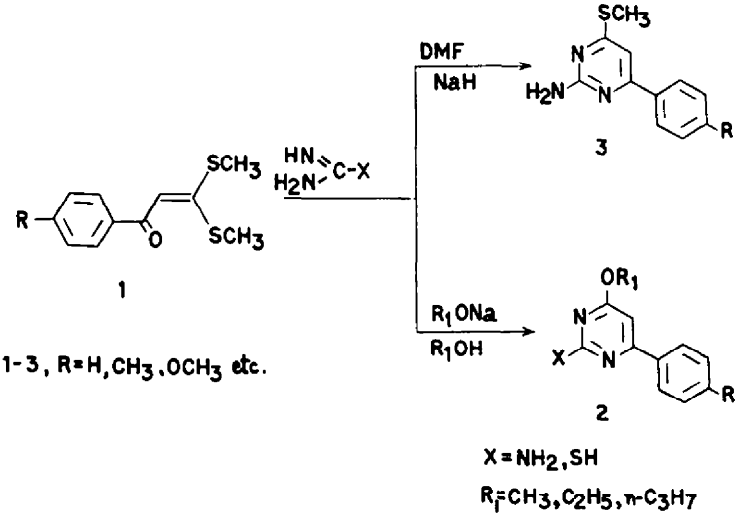
**Abstract**—The ketoketene-S,S-acetals (**5a–c**) react with guanidine and thiourea in the presence of alcoholic sodium alkoxides to give 2-amino- and 2-mercapto-4-alkoxy-5-aryl-6-methyl-pyrimidines (**6a–k**) respectively in good yields. The α-cyanoketene-S,S-acetals (**9a–d**) similarly gave 5-substituted-2,4-diamino-6-alkoxy-pyrimidines (**10a–e**) with guanidine in 50–60% overall yields. The unexchanged 2,4-diamino-5-*p*-chlorophenyl-6-methylthio-pyrimidine (**11**) was prepared from **9c** as a typical example using identical conditions described for **7**. The synthesis of 5,6-fused pyrimidines (**14a–f**), (**19**) and (**23a–e**) was also accomplished using the cyclic ketene-S,S-acetals (**13a–c**) and (**22a–b**). The present method is found to be more convenient and efficient than reported methods for alkoxy and methylthiopyrimidines.

Ketene-S,S-acetals prepared by the reaction of ketones[2] or nitriles[3] with carbon disulphide in the presence of a base, followed by alkylation, have become a subject of current interest.[4] Although several papers have appeared regarding their preparation and structural studies in the recent literature,[5] the synthetic utility of these intermediates has not been extensively explored.[6] The objective of the present investigation has been to examine some of the reactions of α-keto and α-cyanoketene S,S-acetals with different nucleophiles like guanidine and thiourea with a view to synthesising various heterocyclic ring systems.

In our earlier communication, we have reported that,[1a] the α-ketoketene-S,S-acetals (**1**) undergo facile condensation with guanidine and thiourea in the presence of sodium alkoxides to give 2-amino and 2-mercapto-4-alkoxy-6-aryl-pyrimidines (**2**) respectively (Scheme 1) in one step in yields ranging between 50 and 90%. The replacement of 4-methylthio by alkoxy groups in these reactions has been confirmed by the spectral studies as well as by using various alcohols as solvents. Further, we have shown that the reaction of **1** with guanidine in hot dimethylformamide in the presence of sodium hydride gives 2-amino-4-methylthio-6-aryl-pyrimidines **3** in 50–54% overall yields (Scheme 1).

The synthesis of alkoxy-pyrimidines from oxo-pyrimidines in basic medium poses some difficulties, since the alkylation can take place either on oxygen or on the basic nitrogen.[7] This difficulty is overcome by the conversion of oxo-pyrimidines to the corresponding chloro-derivatives, which react smoothly with alkoxides to give the desired alkoxy-pyrimidines. However, the preparation of chloro-pyrimidines[8] from the corresponding oxo-derivatives is not always a smooth reaction. Besides, a practical difficulty can also arise when the $pK_b$




Scheme 1.

†CDRI Communication No. 2139.

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of the chloro-pyrimidines are close to that of dialkylaniline[9] (a medium which is often used in these reactions) and the isolation of the products becomes a serious problem. Further, the conversion of the oxo-pyrimidines to the corresponding chloro-derivatives in the presence of a free-SH group leads to the dimerisation of the pyrimidines,[10] and hence any convenient method for the synthesis of alkoxy-pyrimidines containing free-SH group is highly desirable. The alkoxy-pyrimidines themselves are valuable intermediates for the synthesis of N-alkyl-pyrimidones.[11] The present paper highlights the synthetic utility and advantages of ketene-S,S-acetals as versatile intermediates for the preparation of various 4 or 6-alkoxy and 4 or 6-methylthio-pyrimidines.

## RESULTS AND DISCUSSION

In principle a wide variety of active methylene compounds can be converted to the corresponding S,S-acetals, which were appropriate precursors for the synthesis of alkoxy-pyrimidines.† Thus, the reaction of guandine with α-ketoketene-S,S-acetals **5a–c** (from the corresponding phenylacetones **4a–c**) was studied. Treatment of equimolar quantities of **5a** and guanidine in the presence of two equivalent of sodium methoxide in boiling methanol gave **6a** in 40% yield. The homologous alkoxy-pyrimidines **6a–i** prepared similarly using various alcohols are described in Table 1. The 2-mercapto-4-alkoxy-pyrimidines (**6j–l**) were prepared similarly by reacting thiourea with **5a** to **5c** respectively using identical conditions in 33–34% yields (Scheme 2).

The reactions of α-cyanoketene-S,S-acetals, **9a–d** (from the corresponding malononitrile **8a** and the arylacetonitriles **8b–d**) e.g. **8a**, with guanidine in the presence of sodium ethoxide in boiling ethanol, yielded **10a** in 60% yield. The pyrimidine **10a** has been prepared by Middleton *et al.*[12] in low yield by treating guanidine with dicyanoketene-O,O-diacetal $(CN)_2C{=}C(OEt)_2$, which is prepared in three steps from undesirable intermediates like dibromomalonitrile and tetracyanoethylene,‡ while in the present case, **9a** is prepared from the same starting material in two steps in 40% overall yield. The other cyanoketene-S,S-acetals **9b–d** similarly reacted with guanidine in the presence of various sodium alkoxides to give the corresponding alkoxy-pyrimidines **10b–e** in 53–54% yields, (Scheme 3, Table 3) whereas **9c** with guanidine in the presence of sodium hydride in aprotic solvents gave **11** in 40% yield.

The method was next extended to prepare 5,6-fused pyrimidines. The cyclic ketene-S,S-acetals **13a–c** (from the corresponding cycloalkanones), e.g. **13a** smoothly reacted with guanidine in boiling methanolic sodium methoxide solution to give **14a** in 32% overall yield. It is interesting to note that Baker *et al.*[13] have prepared **14a** from **12a** through four steps (**12a→15→16→17→14a**) in 9.5% overall yield and of **19** from **12a** in 7% overall yield (**12b→15→16→17→18→19**) while in the present study this compound was obtained in one step by reacting **13a** with guanidine in methanolic sodium hydroxide at room temperature in 40% overall yield. Also, the synthesis of **19** from moisture sensitive enamine **20** has been described[14] in an unspecified yield (Scheme 4). The other componds

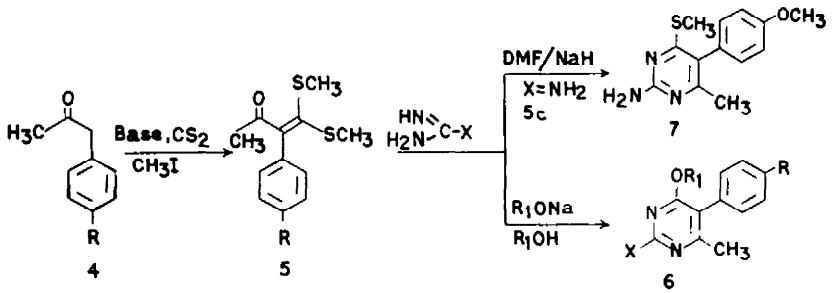
†The pyrimidines described in this paper were primarily intended for screening as antitumor agents, and they are being tested at the National Institute of Health, Bethesda, Maryland, U.S.A., and the results will be published elsewhere.

‡Dibromomalononitrile is irritating to the eyes and nose and tetracyanoethylene is harmful to the skin; See *Org. Synthesis Coll. Vol.* 4, pp. 276, 871. Wiley, New York (1963).

Table 1. Preparation of 2-Amino-4-alkoxy-5-aryl-6-methyl-pyrimidines **5a–l**, 2-Mercapto-4-ethoxy-5-aryl-6-methyl-pyrimidines **5j–l** and 2-Amino-4-methylthio-5-*p*-methoxyphenyl-6-methyl-pyrimidines **7**

| Product | Method | Reflux time (h) | Reaction† solvent | Yield‡ (%) | Cryst.§ solvent | m.p. (°C) | Molecular formula | Analysis (%) Calcd. / Found | C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **6a** | A | 14 | a | 40 | a | 154 | $C_{12}H_{13}N_3O$ | Calcd. | 66.96 | 6.09 | 19.52 |
| | | | | | | | (215.3) | Found | 66.71 | 5.89 | 19.43 |
| **6b** | A | 14 | b | 42 | a | 125 | $C_{13}H_{15}N_3O$ | Calcd. | 68.10 | 6.59 | 18.33 |
| | | | | | | | (229.3) | Found | 68.42 | 6.35 | 17.98 |
| **6c** | A | 14 | c | 40 | a | 108 | $C_{14}H_{17}N_3O$ | Calcd. | 69.11 | 7.04 | 17.28 |
| | | | | | | | (243.3) | Found | 68.82 | 6.84 | 17.00 |
| **6d** | A | 16 | a | 35 | a | 141 | $C_{12}H_{12}N_3ClO$ | Calcd. | 57.71 | 4.81 | 16.84 |
| | | | | | | | (249.8) | Found | 58.01 | 4.68 | 16.67 |
| **6e** | A | 16 | b | 36 | a | 136 | $C_{13}H_{14}N_3ClO$ | Calcd. | 59.17 | 5.31 | 15.93 |
| | | | | | | | (263.8) | Found | 58.89 | 5.54 | 15.88 |
| **6f** | A | 16 | c | 38 | a | 165 | $C_{14}H_{16}N_3ClO$ | Calcd. | 60.54 | 5.79 | 15.13 |
| | | | | | | | (277.8) | Found | 60.22 | 5.54 | 15.46 |
| **6g** | A | 16 | a | 46 | a | 204 | $C_{13}H_{15}N_3O_2$ | Calcd. | 63.66 | 6.16 | 17.13 |
| | | | | | | | (245.3) | Found | 63.50 | 6.45 | 17.36 |
| **6h** | A | 16 | b | 54 | a | 155 | $C_{14}H_{17}N_3O_2$ | Calcd. | 64.86 | 6.61 | 16.20 |
| | | | | | | | (259.3) | Found | 64.92 | 6.76 | 16.23 |
| **6i** | A | 16 | c | 50 | a | 124 | $C_{15}H_{19}N_3O_2$ | Calcd. | 65.91 | 7.01 | 15.37 |
| | | | | | | | (273.3) | Found | 65.75 | 7.05 | 15.53 |
| **6j** | B | 16 | b | 34 | a | 194-6 | $C_{13}H_{14}N_2OS$ | Calcd. | 63.40 | 5.73 | 11.38 |
| | | | | | | | (246.3) | Found | 63.21 | 5.62 | 11.46 |
| **6k** | B | 16 | b | 33 | a | 184 | $C_{13}H_{13}N_2OSCl$ | Calcd. | 55.61 | 4.63 | 9.98 |
| | | | | | | | (280.8) | Found | 55.32 | 4.56 | 10.12 |
| **6l** | B | 16 | b | 33 | a | 169–70 | $C_{14}H_{16}N_2O_2S$ | Calcd. | 60.86 | 5.84 | 10.14 |
| | | | | | | | (276.3) | Found | 60.96 | 6.12 | 9.87 |
| **7** | C | 16 | d | 35 | b | 195–6 | $C_{13}H_{15}N_3OS$ | Calcd. | 59.78 | 5.75 | 16.09 |
| | | | | | | | (261.3) | Found | 59.39 | 5.43 | 15.89 |

†a = methanol; b = ethanol; c = *n*-propanol; d = benzene-dimethylformamide.
‡The yields were not critically optimized.
§a = ethanol; b = benzene–hexane.




4-5 a, R = H
b, R = Cl
c, R = $OCH_3$

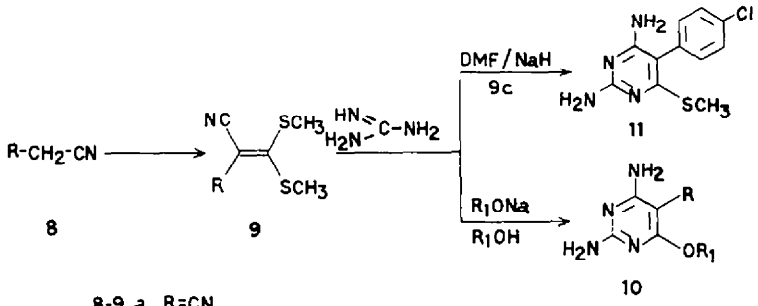
| | R | $R_1$ | X | | R | $R_1$ | X |
|---|---|---|---|---|---|---|---|
| 6 | a, H | $CH_3$ | $NH_2$ | | g, $OCH_3$ | $CH_3$ | $NH_2$ |
| | b, H | $C_2H_5$ | $NH_2$ | | h, $OCH_3$ | $C_2H_5$ | $NH_2$ |
| | c, H | $^nC_3H_7$ | $NH_2$ | | i, $OCH_3$ | $^nC_3H_7$ | $NH_2$ |
| | d, Cl | $CH_3$ | $NH_2$ | | j, H | $C_2H_5$ | SH |
| | e, Cl | $C_2H_5$ | $NH_2$ | | k, Cl | $C_2H_5$ | SH |
| | f, Cl | $^nC_3H_7$ | $NH_2$ | | l, $OCH_3$ | $C_2H_5$ | SH |

Scheme 2.

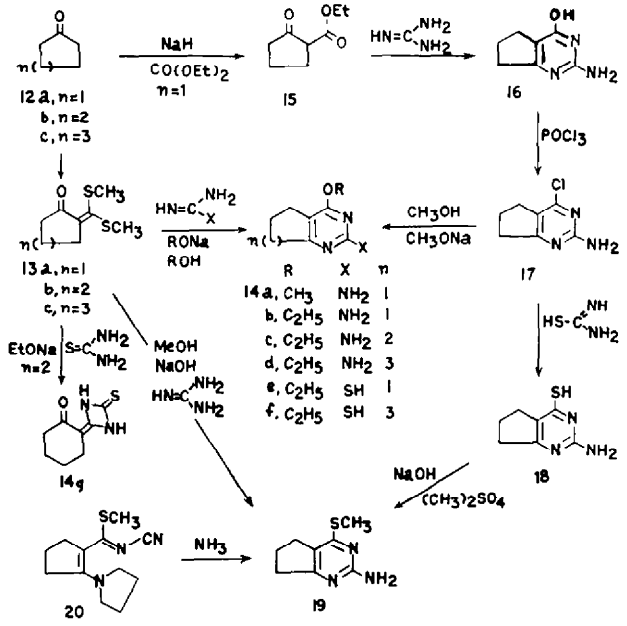
Table 2. Spectral data for **6a–l**

| Product | IR ($cm^{-1}$)† | $^1H$ NMR ($\delta$/ppm)‡ |
|---|---|---|
| **6a** | 3480, 3295, 3189 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] 3535, 3428, 3310, 3180 ($\nu_{NH_2}$); 1605 ($\delta_{NH_2}$)[b] | 2.12 (s, 3H, 6-$CH_3$); 3.82 (s, 3H, 4-$OCH_3$); 5.37 (bm, 2H, $-NH_2$); 7.30 (m, 5H arom).[a] |
| **6b** | 3413, 3286, 3189 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] 3538, 3425, 3320, 3189 ($\nu_{NH_2}$); 1605 ($\delta_{NH_2}$)[b] | 1.20 (t, 3H, $-OCH_2CH_3$); 2.12 (s, 3H, 6-$CH_3$); 4.30 (q, 2H, $-OCH_2CH_3$); 5.30 (bm, 2H, $-NH_2$); 7.27 (m, 5H arom).[a] |
| **6c** | 3435, 3256, 3186 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] | 0.83 (t, 3H, $-OCH_2CH_2CH_3$); 1.62 (sext, 2H, $-OCH_2CH_2CH_3$); 2.13 (s, 3H, 6-$CH_3$); 2.55 (t, 2H, $-OCH_2CH_2CH_3$); 5.15 (bm, 2H, $-NH_2$); 7.30 (m, 5H arom).[a] |
| **6d** | 3425, 3256, 3189 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] | 2.12 (s, 3H, 6-$CH_3$); 3.83 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 5.28 (bm, 2H, $-NH_2$); 7.15–7.42 (dd, 4H arom, $A_2B_2$).[a] |
| **6e** | 3435, 3256, 3195 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] | 1.23 (t, 3H, $-OCH_2CH_3$); 2.13 (s, 3H, 6-$CH_3$); 4.30 (q, 2H, $-OCH_2CH_3$); 5.12 (bm, 2H, $-NH_2$); 7.13–7.38 (dd, 4H arom, $A_2B_2$).[a] |
| **6f** | 3445, 3249, 3189 ($\nu_{NH_2}$); 1645 ($\delta_{NH_2}$)[a] | 0.83 (t, 3H, $-OCH_2CH_2CH_3$); 1.66 (sext, 2H, $-OCH_2CH_2CH_3$); 2.12 (s, 3H, 6-$CH_3$); 4.20 (t, 3H, $-OCH_2CH_2CH_3$); 5.20 (bm, 2H, $-NH_2$); 7.17–7.42 (dd, 4H arom, $A_2B_2$).[a] |
| **6g** | 3445, 3300, 3180 ($\nu_{NH_2}$); 1645 ($\delta_{NH_2}$)[a] | 2.12 (s, 3H, 6-$CH_3$); 3.80 (s, 3H, 4-$OCH_3$); 3.83 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 5.18 (bm, 2H, $-NH_2$); 6.93–7.37 (dd, 4H arom, $A_2B_2$).[a] |
| **6h** | 3446, 3295, 3186 ($\nu_{NH_2}$); 1655 ($\delta_{NH_2}$)[a] | 1.05 (t, 3H, $-OCH_2CH_3$); 2.12 (s, 3H, 6-$CH_3$); 3.82 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 4.30 (q, 2H, $-OCH_2CH_3$); 5.21 (bm, 2H, $-NH_2$); 6.90–7.13 (dd, 4H arom, $A_2B_2$).[a] |
| **6i** | 3440, 3295, 3186 ($\nu_{NH_2}$); 1655 ($\delta_{NH_2}$)[a] | 0.85 (t, 3H, $-OCH_2CH_2CH_3$); 1.60 (sext, 2H, $-OCH_2CH_2CH_3$); 2.12 (s, 3H, 6-$CH_3$); 3.83 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 5.12 (bm, 2H, $-NH_2$); 6.88–7.12 (dd, 4H arom, $A_2B_2$).[a] |
| **6j** | 3145 (>NH); 1165 (C=S)[a] 3375 (>NH); 1165 (C=S)[b] | 0.93 (t, 3H, $-OCH_2CH_3$); 2.33 (s, 3H, 6-$CH_3$); 4.38 (q, 2H, $-OCH_2CH_3$); 7.05 (m, 5H arom).[a] |
| **6k** | 3133 (>NH); 1145 (C=S)[a] | 1.23 (t, 3H, $-OCH_2CH_3$); 2.13 (s, 3H, 6-$CH_3$); 4.30 (q, 2H, $-OCH_2CH_3$); 5.12 (bm, 2H, $-NH_2$); 7.13–7.45 (dd, 4H arom, $A_2B_2$).[a] |
| **6l** | 3125 (>NH); 1165 (C=S)[a] | 1.28 (t, 3H, $-OCH_2CH_3$); 2.27 (s, 3H, 6-$CH_3$); 3.87 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 4.57 (q, 2H, $-OCH_2CH_3$); 6.93–7.18 (dd, 4H arom, $A_2B_2$).[a] |
| **7** | 3445, 3295, 3185 ($\nu_{NH_2}$); 1642 ($\delta_{NH_2}$)[a] | 2.13 (s, 3H, $-SCH_3$); 2.38 (s, 3H, 6-$CH_3$); 3.85 (s, 3H, $p$-$H_3CO$–$C_6H_4$); 5.27 (bm, 2H, $NH_2$); 7.13–7.38 (dd, 4H arom, $A_2B_2$).[a] |

†IR medium: a = KBr; b = $CHCl_3$ solution.
‡NMR solvent: a = $CDCl_3$.




Scheme 3.




Scheme 4.

Table 3. Preparation of 2,4-Diamino-5-cyano-6-ethoxy-pyrimidine **10a**; 2,4-diamino-5-aryl-6-alkoxy-pyrimidines **10b–e** and 2,4-diamino-5-(*p*-chlorophenyl)-6-methylthio-pyrimidine **11**

| Product | Method | Reflux time (h) | Reaction† solvent | Yield‡ (%) | Cryst.§ solvent | m.p. (°C) | Molecular formula | Analysis (%) Calc. / Found | C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **10a** | A | 8 | a | 55 | a | 220[12] | — | | — | — | — |
| **10b** | A | 10 | a | 50 | a | 108–9 | $C_{12}H_{14}N_4O$ | | 62.61 | 6.08 | 24.33 |
| | | | | | | | (230.3) | | 62.29 | 6.09 | 24.05 |
| **10c** | A | 10 | a | 53 | a | 136 | $C_{12}H_{13}N_4ClO$ | | 54.44 | 4.95 | 21.14 |
| | | | | | | | (264.8) | | 54.95 | 5.30 | 20.87 |
| **10d** | A | 10 | a | 54 | a | 124 | $C_{13}H_{15}H_4ClO$ | | 55.94 | 5.38 | 20.08 |
| | | | | | | | (278.8) | | 55.86 | 5.43 | 20.19 |
| **10e** | A | 10 | a | 54 | a | 146 | $C_{13}H_{16}N_4O_2$ | | 60.00 | 6.20 | 21.52 |
| | | | | | | | (263.3) | | 59.89 | 6.55 | 21.24 |
| **11** | C | 14 | b | 50 | b | 138 | $C_{11}H_{11}N_4ClS$ | | 49.53 | 4.13 | 20.99 |
| | | | | | | | (266.8) | | 49.46 | 4.36 | 20.79 |

†a = ethanol; b = benzene-dimethylformamide.
‡The yields were not critically optimized.
§a = ethanol; b = benzene–hexane.

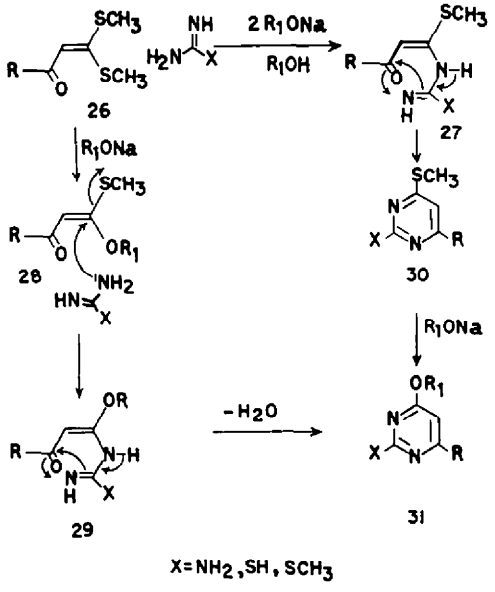
**14b–d** in this series were similarly prepared from **13a–c** and guanidine in the presence of sodium ethoxide in 46–57% yields. While the reaction of **13a** and **13c** with thiourea in the presence of sodium ethoxide gave the expected 2-mercapto-pyrimidines **14e** and **14f** respectively, the acetal **13b** was the only exception which did not give the expected pyrimidine, and yielded a product which was identified as 1-(1,3-uritidino-2-thione)-methylene cyclohexanone **14g** m.p. 296–7° (thioamide absorption at 3090 $cm^{-1}$ and $\alpha,\beta$-unsaturated carbonyl band at 1660 $cm^{-1}$ C=C, 1560 $cm^{-1}$, thioamide I and III 1138 and 1229 cm $^{-1}$; two broad multiplets $\delta$1.83 (4H) and $\delta$2.57 (4H) were due to the eight cyclohexanone protons, proving the exocyclic nature of the double bond). The ketene-S,S-acetals **22a–b** (from the corresponding tetralones **21a–b**) gave 2-amino and 2-mercapto-4-alkoxy-5,6-dihydrobenzo(h)quinazolines **23a–e**. **22a** has been reported[14] to be formed from **21a** in three steps involving the moisture-sensitive enamine intermediates **24** and **25**, in unspecified yields.

*Mechanism*

The general mechanistic pathways for the formation of alkoxy-pyrimidines from the corresponding $\alpha$-ketoketene-S,S-acetals with amidines can be rationalized as shown in Scheme 6. One of the probable routes could be the attack of guanidine on **26** to give **27** which on subsequent intramolecular cyclization followed by elimination of water yields pyrimidine **30**. Since 4-methylthio-pyrimidines are known to undergo nucleophilic displacement with alkoxide ions,[15] **31** could be assumed to be formed from **30**. However, **30** could not be isolated at any stage when the reaction of **26** with guanidine was carried out in the presence of sodium ethoxide, although, in an another experiment, **30** (prepared by sodium hydride method) was completely converted to **31** on refluxing with sodium ethoxide for 8–10 h. In general it is observed that the formation of alkoxy-pyrimidines is more facile and gives improved yields, while the corresponding methylthio-pyrimidines are formed in lower yields (NaH and DMF).[1a] It is also known that the $\alpha$-ketoketene-O,S-acetals are more reactive towards nitrogen nucleophiles than the corresponding S,S-acetals.[16] It is thus probable that the O,S-acetal **28** is formed, prior to the attack of guanidine on **26** which then gives **31** via **29**. The formation of **31** was further confirmed, when one of the intermediates **29**[1a] (R=$C_6H_5$, X=SH, $R_1$=$CH_3$) (Scheme 6) was isolated uncyclized. The structure of this open chain compound was deduced, on the basis of its physical data. The IR spectrum showed a strong band at 1700 $cm^{-1}$ (C=O) which rules out the formation of cyclic pyrimidine. The NMR spectrum showed a singlet, $\delta$4.00 (3H, $OCH_3$), 6.6 (1H, vinylic), (5H, arom). The intermediate **29** could only be formed from the corresponding **28** and hence the O,S-acetal pathway appears to be operative.†

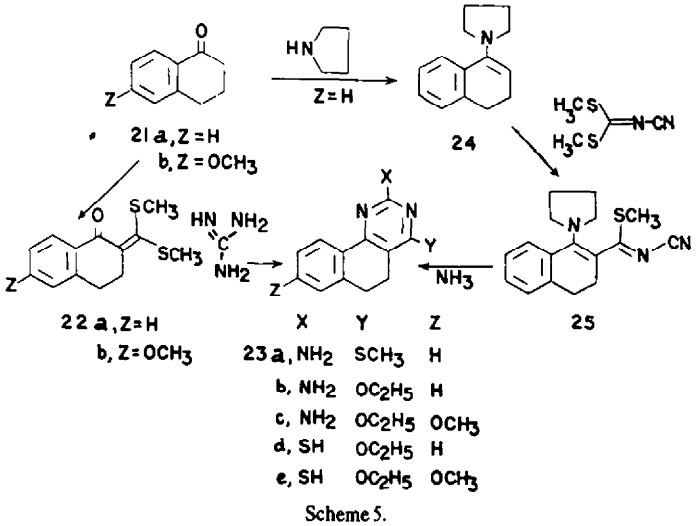
*Spectral studies*

The IR spectra of 2-amino and 2,4-diaminopyrimidines reveal that they exist in their true amino form in both solid and solutions.The 2-amino-4-alkoxy-6-aryl-pyrimidines exhibit absorptions in the stretching vibration region at




Scheme 6.

†The intermediacy of **28** has been further confirmed through the following sequence of reactions: when **26** was refluxed with sodium ethoxide followed by gradual addition of hydrazine hydrate, the 5-ethoxypyrazole was formed in 68% yield, while the 5-methylthio-analogue prepared from **26** and $N_2H_4$ failed to undergo exchange reaction even after prolonged heating.




Scheme 5.

3333 and 3190 $cm^{-1}$ and 3226–3205 $cm^{-1}$[1,1a] which are due to associated asymmetric and symmetric vibrational modes respectively. In solution ($CHCl_3$) both these bands shift to a higher wave number in the range 3520–3535 and 3415–3435 $cm^{-1}$ respectively and are due to unassociated $NH_2$ group of the same vibrational modes.[17]

The 2-amino-4-alkoxy-5-aryl-6-methyl-pyrimidines **6a–i** (Table 2) 2,4-diamino-5-aryl-6-alkoxy-pyrimidines **10a–e** (Table 4); and 2-amino-5,6-fused pyrimidines **14a–d** (Table 6) and **21a–c** (Table 8) exhibit characteristic vibrational modes in this region. Apart from the band observed in the range 3300–3225 and 3200–3125 $cm^{-1}$ which can be ascribed to the same (associated) vibrational modes as described above, a strong third band is uniformly observed in all these compounds in the range of 3535–3340 $cm^{-1}$ which is probably due to one amino hydrogen atom remaining unassociated. In $CHCl_3$, however, this band disappears and only two bands in the region 3540–3500 and 3445–3410 $cm^{-1}$ are present. This observation is in conformity with the reported values, for similar assignment made by Thomson[18] for some 2-aminopyrimidines and Daves and Hallam[19] in acetamide.

All the 2-amino and 2,4-diamino-pyrimidines exhibit (KBr) strong band in the region 1660–1625 $cm^{-1}$ which is also the region of $NH_2$ deformations. Short and Thomson[18] and Brown *et al.*[17a] have assigned this band to H–N–H internal deformation on the basis of their deuteration experiments. However, the fate of this band in solution ($CHCl_3$) has not been reported except in one case, where it is known to shift in DMSO towards lower frequency.[20] We have observed that this band I (1650 $cm^{-1}$ in KBr) moves significantly to a lower value of 1600 $cm^{-1}$ in $CHCl_3$. Its assignment† to the $NH_2$ deformation arises from the fact that in solid (KBr) the 1600 $cm^{-1}$ band (shoulder) which is weak and could be due to the aryl ring vibration, is found greatly intensified (see Fig. 1) in solution ($CHCl_3$) while the strong absorption bands at 1580 and 1560 $cm^{-1}$ (KBr) remain little affected in $CHCl_3$. In addition, Spinner[21] has observed that this band is absent in the Raman spectrum which could have appeared had it been due to either ring or C=N stretching vibrations which are Raman active. We thus conclude that the 1650 $cm^{-1}$ band could only be due to $NH_2$ deformation and that it moves to a value of 1600 $cm^{-1}$ in $CHCl_3$.

†We gratefully thank Prof. D. J. Brown of The Australian National University, Canberra, Australia for conveying Dr. E. Spinner's opinion regarding the behavior of 1650 $cm^{-1}$ band. This band was erroneously reported[1a] by us having disappeared in $CHCl_3$, and should be corrected, as described in this paper.

Table 4. Spectral data for **10a–e** and **11**

| Product | IR (cm $^{-1}$)† | $^1$H NMR ($\delta$/ppm)‡ |
|---|---|---|
| **10a** | 3398, 3285, 3195 ($\nu_{NH_2}$); 1655 ($\delta_{NH_2}$) | 1.02 (t, 3H, $-OCH_2CH_3$); 4.25 (q, 2H, $-OCH_2CH_3$); 6.80 (bm, 2H, $-NH_2$).[b] |
| **10b** | 3401, 3289, 3195 ($\nu_{NH_2}$); 1659 ($\delta_{NH_2}$) | 1.23 (t, 3H, $-OCH_2CH_3$); 4.32 (q, 2H, $-OCH_2CH_3$); 4.78 (bm, 2H, 4-$NH_2$); 5.00 (bm, 2H, 2-$NH_2$); 7.37 (m, 5H arom).[a] |
| **10c** | 3405, 3289, 3189 ($\nu_{NH_2}$); 1656 ($\delta_{NH_2}$) | 1.25 (t, 3H, $-OCH_2CH_3$); 4.32 (q, 2H, $-OCH_2CH_3$); 4.72 (bm, 2H, 4-$NH_2$); 4.95 (bm, 2H, 2-$NH_2$); 7.19–7.45 (dd, 4H arom, $A_2B_2$).[a] |
| **10d** | 3484, 3289, 3186 ($\nu_{NH_2}$); 1635 ($\delta_{NH_2}$) | 0.87 (t, 3H, $-OCH_2CH_2CH_3$); 1.62 (sext, 2H, $-OCH_2CH_2CH_3$); 4.17 (t, 2H, $-OCH_2CH_2CH_3$); 4.82 (bm, 2H, 4-$NH_2$); 5.07 (bm, 2H, 2-$NH_2$); 7.17–7.42 (dd, 4H arom, $A_2B_2$).[a] |
| **10e** | 3401, 3286, 3189 ($\nu_{NH_2}$); 1635 ($\delta_{NH_2}$) | 1.20 (t, 3H, $-OCH_2CH_3$); 3.85 (s, 3H, *p*-$H_3CO-C_6H_4$); 4.28 (q, 2H, $-OCH_2CH_3$); 4.72 (bm, 2H, 4-$NH_2$); 5.17 (bm, 2H, 2-$NH_2$); 6.90–7.23 (dd, 4H arom, $A_2B_2$).[a] |
| **11** | 3389, 3289, 3195 ($\nu_{NH_2}$); 1639 ($\delta_{NH_2}$) | 2.37 (s, 3H, $-SCH_3$); 4.70 (bm, 2H, 4-$NH_2$); 5.03 (bm, 2H, 2-$NH_2$); 7.19–7.47 (dd, 4H arom, $A_2B_2$).[a] |

†All the IR spectra were recorded with KBr film.
‡NMR solvents: a = $CDCl_3$; b = trifluoro acetic acid.

Table 5. Preparation of 2-amino-4-alkoxy-5,6-polymethylene pyrimidines **14a–d**; 2-mercapto-4-alkoxy-5,6-polymethylene pyrimidines **14e–f** and 2-amino-4-methylthio-5-,6-trimethylene pyrimidine **19**

| Product | Method | Reflux time (h) | Reaction† solvent | Yield‡ (%) | Cryst.§ solvent | m.p. (°C) | Molecular formula | Analysis (%) Calc. / Found | C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **14a** | A | 10 | a | 56 | a | 120[13] | — | | — | — | — |
| **14b** | A | 10 | b | 57 | a | 125 | $C_9H_{13}N_3O$ (179.2) | | 60.32 60.15 | 7.31 7.22 | 23.45 23.16 |
| **14c** | A | 10 | b | 54 | a | 86 | $C_{10}H_{15}N_3O$ (193.3) | | 62.15 61.82 | 7.82 7.78 | 21.75 21.96 |
| **14d** | A | 10 | b | 46 | a | 90 | $C_{11}H_{17}N_3O$ (207.3) | | 63.74 64.00 | 8.27 8.21 | 20 27 19.87 |
| **14e** | B | 12 | b | 50 | a | 169–70 | $C_9H_{12}N_2SO$ (196.2) | | 55.09 54.76 | 6.16 6.02 | 14.28 13.86 |
| **14f** | B | 12 | b | 44 | a | 179–80 | $C_{11}H_{16}N_2SO$ (224.2) | | 58.91 58.59 | 7.19 6.86 | 12.50 12.19 |
| **19** | C¶ | 14 | c | 47 | a | 139–40[13,14] | — | | — | — | — |

†a = methanol; b = ethanol; c = benzene-dimethylformamide.
‡The yields were not fully optimized.
§a = ethanol; b = benzene-hexane.
¶This compound was obtained in improved yields in methanolic sodium hydroxide.

Table 6. Spectral data for **14a–f** and **19**

| Product | IR (cm $^{-1}$)† | $^1$H NMR($\delta$/ppm)‡ |
|---|---|---|
| **14a** | 3415, 3289, 3195 ($\nu_{NH_2}$); 1650 ($\delta_{NH_2}$) | 2.02 (m, 2H, H-6); 2.60 (m, 4H, H-5 and H-7); 3.83 (s, 3H, $-OCH_3$); 5.15 (bm, 2H, $-NH_2$).[a] |
| **14b** | 3420, 3289, 3186 ($\nu_{NH_2}$); 1656 ($\delta_{NH_2}$) | 1.33 (t, 3H, $-OCH_2CH_3$); 2.07 (m, 2H, H-6); 2.60 (m, 4H, H-5 and H-7); 4.33 (q, 2H, $-OCH_2CH_3$); 5.12 (bm, 2H, $-NH_2$).[a] |
| **14c** | 3410, 3287, 3155 ($\nu_{NH_2}$); 1635 ($\delta_{NH_2}$) | 1.33 (t, 3H, $-OCH_2CH_3$); 1.80 (m, 4H, H-6 and H-7); 2.50 (m, 4H, H-5 and H-8); 4.33 (q, 2H, $-OCH_2CH_3$); 5.12 (m, 2H, $-NH_2$).[a] |
| **14d** | 3410, 3289, 3189 ($\nu_{NH_2}$); 1634 ($\delta_{NH_2}$) | 1.33 (t, 3H, $-OCH_2CH_3$) 1.75 (m, 6H, H-6, H-7 and H-8); 2.66 (m, 4H, H-5 and H-9); 4.30 (q, 2H, $-OCH_2CH_3$); 4.85 (bm, 2H, $-NH_2$).[a] |
| **14e** | 3175 (>NH); 1125 (C=S) | 1.38 (t, 3H, $-OCH_2CH_3$); 2.17 (m, 2H, H-6); 2.80 (m, 4H, H-5 and H-7); 4.55 (q, 2H, $-OCH_2CH_3$).[a] |
| **14f** | 3145 (>NH); 1131 (C=S) | 1.38 (t, 3H, $-OCH_2CH_3$); 1.77 (m, 6H, H-6, H-7 and H-8); 2.80 (m, 4H, H-5 and H-9).[a] |
| **19** | 3415, 3289, 3189 ($\nu_{NH_2}$); 1656 ($\delta_{NH_2}$) | 2.02 (m, 2H, H-6); 2.45 (s, 3H, $-SCH_3$); 2.60 (m, 4H, H-5 and H-7); 5.15 (bm, 2H, $-NH_2$).[a] |

†All the IR spectra were recorded with KBr film.
‡NMR solvents: a = $CDCl_3$.

Table 7. Preparation of 2-amino-4-methylthio-5,6-dihydrobenzo-[h]-quinazoline **23a**; 2-amino-4-alkoxy-5,6-dihydrobenzo-[h]-quinazolines **23b–c** and 2-mercapto-4-alkoxy-5,6-dihydrobenzo-[h]-quinazolines **23d–e**

| Product | Method | Reflux time (h) | Reaction† solvent | Yield‡ (%) | Cryst.§ solvent | m.p. (°C) | Molecular formula | Analysis (%) Calc. / Found | C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **23a** | C | 14 | b | 54 | a | 198[a] | $C_{13}H_{13}N_3S$ | | 64.19 | 5.39 | 17.27 |
| | | | | | | | (234.3) | | 63.89 | 5.18 | 17.04 |
| **23b** | A | 12 | a | 60 | a | 207 | $C_{14}H_{15}N_3O$ | | 69.69 | 6.27 | 17.41 |
| | | | | | | | (241.3) | | 69.51 | 6.44 | 17.17 |
| **23c** | A | 12 | a | 63 | a | 96 | $C_{15}H_{17}N_3O_2$ | | 66.40 | 6.32 | 15.49 |
| | | | | | | | (271.3) | | 66.60 | 5.88 | 15.31 |
| **23d** | B | 12 | a | 74 | a | 170 | $C_{14}H_{14}N_2OS$ | | 65.11 | 5.46 | 10.85 |
| | | | | | | | (258.3) | | 65.02 | 5.23 | 10.42 |
| **23e** | B | 12 | a | 54 | a | 195 | $C_{14}H_{16}N_2O_2S$ | | 62.49 | 5.59 | 9.73 |
| | | | | | | | (288.3) | | 62.26 | 5.72 | 9.41 |

†a = ethanol; b = benzene-dimethylformamide.
‡The yields were not critically optimized.
§a = ethanol.

Table 8. Spectral data for **23a–e**

| Product | IR (cm $^{-1}$)† | $^1$H NMR ($\delta$/ppm)‡ |
|---|---|---|
| **23a** | 3415, 3289, 3185 ($\nu_{NH_2}$) 1647 ($\delta_{NH_2}$) | 2.52 (s, 3H, $-SCH_3$); 2.83 (m, 4H, H-5 and H-6); 5.00 (bm, 2H, $-NH_2$); 7.35 (m, 3H arom, H-7, H-8 and H-9); 8.23 (m, 1H arom, H-10).[a] |
| **23b** | 3425, 3289, 3189 ($\nu_{NH_2}$); 1657 ($\delta_{NH_2}$) | 1.38 (t, 3H, $-OCH_2CH_3$); 2.80 (m, 4H, H-5 and H-6); 4.40 (q, 2H, $-OCH_2CH_3$); 4.87 (bm, 2H, $-NH_2$); 7.24 (m, 3H arom, H-7, H-8 and H-9); 8.18 (m, 1H arom, H-10).[a] |
| **23c** | 3415, 3295, 3189 ($\nu_{NH_2}$); 1647 ($\delta_{NH_2}$) | 1.37 (t, 3H, $-OCH_2CH_3$); 2.77 (m, 4H, H-5 and H-6); 3.82 (s, 3H, $-OCH_3$); 4.87 (bm, 2H, $-NH_2$); 6.12 (s, 1H arom, H-7); 6.78 (m, 1H arom, H-9); 8.07 (m, 1H arom, H-10).[a] |
| **23e** | 3165 (>NH); 1125 (C=S) | 1.40 (t, 3H, $-OCH_2CH_3$); 2.83 (m, 4H, H-5 and H-6); 4.60 (q, 2H, $-OCH_2CH_3$); 7.23 (m, 3H arom, H-7, H-8 and H-9); 8.19 (m, 1H arom, H-10).[b] |
| **23e** | 3115 (>NH); 1131 (C=S) | 1.22 (t, 3H, $-OCH_2CH_3$); 2.53 (m, 4H, H-5 and H-6); 3.53 (s, 3H, $-OCH_3$); 6.50 (s, 1H arom, H-7); 6.60 (m, 1H arom, H-9); 7.38 (m, 1H arom, H-10).[a] |

†All the IR spectra were recorded with KBr film.
‡NMR solvents: a = chloroform-d; b = trifluoro acetic acid.

The IR spectra of mercaptopyrimidines **6j–l** (Table 2), **14e–f** (Table 6), **23d–e** (Table 8) reveal that they exist in both solid (KBr)[22] and solution ($CHCl_3$) in their thione form.

The NMR spectra of 2-amino and 2,4-diamino-pyrimidines unequivocally establish their amino form in neutral solution ($CDCl_3$) while the 2-mercapto-pyrimidines exist in their thione form under similar conditions (Tables 2, 4, 6 and 8).

## EXPERIMENTAL

M.ps (capillary method) are uncorrected. The IR spectra were

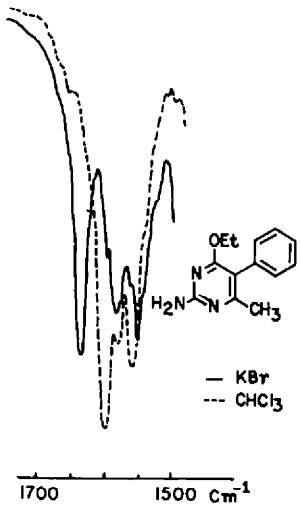



Fig. 1.

recorded on Perkin–Elmer 137, 177 and 337 spectrophotometers. The NMR spectra were recorded on a Varian A–60D spectrometer using TMS as an internal standard and the values are expressed in δ(ppm).

*Starting materials*

The commercial samples, malononitrile, phenylacetonitrile, cyclopentanone, cyclohexanone, cycloheptanone, tetralone and 6-methoxytetralone, were purified before use.

Phenylacetone, b.p. 109–112° (12 mm)[23]; *p*-chlorophenylacetone, b.p. 100° (1 mm)[24]; *p*-methoxyphenylacetone, b.p. 120–125° (5.6 mm)[25]; *p*-chlorophenylacetonitrile, (1 mm)[26]; *p*-methoxyphenylacetonitrile, b.p. 94–97° (3 mm)[27] were prepared by reported procedures.

The following previously reported ketene-S,S-acetals: dicyanoketenedimethyl-S,S-acetal **9a**, m.p. 81°[53a–b]; 1,1-bis(methylthio)-2-cyano-2-phenylethylene **9b**, m.p. 49–51°[53a]; 2-bis(methylthio)-methylene-cyclopentanone **13a**, b.p. 118° (2 mm)[2a]; 2-bis(methylthio)-methylene-cyclohexanone **13b**, m.p. 32°[2a]; 2-bis(methylthio)-methylene-cycloheptanone **13c**, b.p. 112° (2 mm)[2a]; 2-bis(methylthio)-methylene-6-methoxytetralone **22b**, m.p. 78°[2b]; 1,1-bis(methylthio)-2-acetyl-2-phenylethylene **9b**, m.p. 45–46°[51b,5a] and previously unreported componds were prepared by the general methods described below.

*General method for the synthesis of ketene-S,S-acetals using sodium t-butoxide.* A mixture of arylacetones (0.3 moles) and $CS_2$ (22.8 g, 0.3 moles), was added to a well stirred and cooled suspension of t-BuONa (57.2 g, 0.6 moles) in dry benzene (150 ml) and DMF (100 ml) and the reaction mixture was allowed to stand at room temperature for 4 h. Methyl iodide (85.2 g, 0.6 moles) was gradually added with stirring and external cooling (exothermic reaction) and the reaction mixture was allowed to stand for 4 h at room temp. with occasional shaking and then refluxed on a water bath for 3 h. The mixture was poured on crushed ice and the benzene layer was separated. The aqueous portion was extracted with benzene and the combined extracts was washed ($H_2O$), dried ($Na_2SO_4$) and the solvent was removed by distillation. The products thus obtained were purified before use.

Compounds **5b–c**, **22a**, **13a–c**, and **22b** were prepared by this method. The physical data of the new acetals are as follows: 1,1-*Bis(methylthio)*-2-*acetyl*-2-p-*chlorophenylethylene* **5b** b.p. 184–6° (8 mm), yield 37 g, 46%; IR (neat) 1689 (C=O); NMR ($CDCl_3$) 2.18 (s, 3H, $-SCH_3$); 2.23 (s, 3H, $-COCH_3$); 2.38 (s, 3H, $-SCH_3$); 7.17 (d, 2H arom); 7.42 (d, 2H arom). (Found: C, 53.00; H, 4.68. Calc. for $C_{12}H_{13}ClOS_2$ (272.68): C, 52.97; H, 5.01%).

1,1-*Bis(methylthio)*-2-*acetyl*-2-p-*methoxyphenylethylene* **5c** b.p. 202.4° (8 mm), yield 54 g (75%); IR (neat) 1689 (C=O). NMR ($CDCl_3$) 2.17 (s, 3H, $-SCH_3$); 2.23 (s, 3H, $-COCH_3$); 2.38 (s, 3H, $-SCH_3$); 3.82 (s, 3H, $-C_6H_4$–4–$OCH_3$); 6.87 (d, 2H arom, J = 8.50 Hz); 7.23 (d, 2H arom, J = 8.50 Hz). (Found: C, 67.63; H, 6.17. Calc. for $C_{13}H_{16}O_2S_2$ (268.3): C, 68.20; H, 6.01%).

2-*Bis(methylthio)*-*methylene*-1-*tetralone* **21a** from benzene–hexane (1:3), light yellow needles, m.p. 56–58°, yield 46 g (62.5%). IR (KBr) 1642 (C=O); NMR ($CDCl_3$) 2.35 (s, 3H, $-SCH_3$); 2.42 (s, 3H, $-SCH_3$); 3.10 (m, 4H, $(CH_2)_2$); 7.30 (m, 3H arom, H-5, H-6 and H-7); 8.10 (m, 1H arom, H-8). (Found: C, 62.80; H, 5.80. Calc. for $C_{13}H_{14}OS_2$ (250.3): C, 62.39; H, 5.64%).

*General method for the synthesis of ketene-S,S-acetals using sodium hydride.* To a solution of sodium hydride (0.45 moles) in benzene (150 ml), a solution of arylacetonitriles (0.2 moles), $CS_2$ (15.2 g, 0.2 moles) in dry DMF (100 ml) was added in portions during 45 min. The reaction micture was kept under stirring for 2 h followed by addition of methyliodide (56.8 g, 0.4 mole) in portions with cooling. The reaction mixture was allowed to stand at room temp. for 2 h and then refluxed for additional 4 h. After usual work up **9a–d** were obtained and the unknown ones are described below.

1,1-*Bis(methylthio)*-2-*cyano*-2-p-*chlorophenylethylene* **9c** was crystallized from ethylacetate-hexane (1:5) mixture as colourless needles, m.p. 81°, yield 25.5 g (50%). IR (KBr) 2212 $cm^{-1}$ (C≡N). NMR ($CDCl_3$) 2.12 (s, 3H, $SCH_3$); 2.60 (s, 3H, $-SCH_3$); 7.19 (d, 2H arom); 7.42 (d, 2H arom). (Found: C, 51.52; H, 4.00; N, 5.30. Calc. for $C_{11}H_{10}ClNS_2$ (255.8): C, 51.33; H, 4.00; N, 5.47%).

1,1-*Bis(methylthio)*-2-*cyano*-2-p-*methoxyphenylethylene* **9d** was crystallised from ethylacetate–hexane (1:3) mixture as a colourless needles, m.p. 50°, yield 28 g (56%). IR (KBr) 2203 $cm^{-1}$ (C≡N). NMR ($CDCl_3$) 2.23 (s, 3H, $-SCH_3$); 2.57 (s, 3H, $-SCH_3$); 3.80 (s, 3H, $C_6H_4$-*p*-$OCH_3$); 6.90 (d, 2H arom); 7.45 (d, 2H arom). (Found: C, 57.58; H, 5.47; N, 5.34. Calc. for $C_{12}H_{13}NOS_2$ (251.20): C, 57.38; H, 5.22; N, 5.58%).

*General method for the synthesis of 2-amino 4- or 6-alkoxy-pyrimidines. Method* A. To a solution of sodium alkoxides (prepared by dissolving sodium 0.04 mole in 75 ml of respective alcohol), guanidine nitrate (2.44 g, 0.02 mole) was added and the reaction mixture was stirred for 10–15 min. The appropriate ketene-S,S-acetal (0.02 mole) was then added and the reaction mixture was refluxed for 8–10 h. The solvent was distilled under reduced pressure and the residue was quenched in crushed ice. It was extracted with chloroform washed ($H_2O$), dried ($Na_2SO_4$) and distilled off to give the crude pyrimidines which were purified either by crystallization or chromatography. The pyrimidines **6a–i** (Table 1), **10a–d** (Table 3), **14a–d** (Table 5), **23b–c** (Table 7) were prepared by this method.

*General method for the preparation of 2-mercapto-4-alkoxy-pyrimidines. Method* B. To a mixture of thiourea (1.52 g, 0.20 mole) and sodium alkoxide soln (prepared by dissolving 0.02 mole of sodium in 75 ml of respective alcohol) was added appropriate ketene-S,S-acetal (0.02 mole) and the reaction mixture was refluxed for 10–14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (7–10 ml) (just enough to dissolve sodium salt of the pyrimidine) and refluxed for 15 min. The reaction mixture was poured on crushed ice and the ppt obtained was purified by crystallization. The pyrimidines **6j–l** (Table 1), **14e–f** (Table 5), and **23d–e** (Table 7) were prepared by this method.

*General method for the preparation of 2-amino 4- or 6-methylthio-pyrimidines. Method* C. A mixture of ketene-S,S-acetal (0.02 mole) and guanidine nitrate (2.44 g, 0.02 mole) was added to (0.05 mole) a suspension of NaH in benzene–DMF (100 + 5 ml) mixture and the reaction mixture was stirred and refluxed for 12–14 h. The excess of solvent was distilled off and the residue was slowly quenched in cold water. The organic layer was separated, and the aqueous portion was extracted with chloroform. The combined extracts washed ($H_2O$), dried ($Na_2SO_4$) and distilled off to give the crude methylthio-pyrimidines which were purified by column chromatography. Compounds **7** (Table 1), **11**(Table 3), **19**(Table 5), and **23a** (Table 7) were prepared by this method.

*Preparation of* **19** *from* **13a** *and guanidine using methanolic sodium hydroxide.* The compound **19** prepared by this method gave improved yields with greater purity than by the General Method C. Guanidine nitrate (2.44 g, 0.02 mole) and **13a** were dissolved in a mixture of methanol (50 ml) and NaOH soln. (1.6 g

NaOH in 10 ml $H_2O$), and contents were allowed to stand at room temp. with stirring for 5 h. The solvent was removed by distillation and the residue was treated with ice cold water when crude **19** obtained, was further purified by crystallization from MeOH as a colourless needles.

*Reaction of* **13b** *with thiourea in the presence of sodium ethoxide: formation of* 1-[1,3-*uritidino*-2-*thione*)-*methylene*]-*cyclohexanone* **14g**. A mixture of **13b** (4.38 g, 0.02 mole) and thiourea (1.5 g, 0.02 mole) was refluxed in ethanolic NaOEt (0.02 mole of sodium dissolved in 50 ml EtOH) for 10 h. The solvent was distilled off and the residue was treated with HOAc (10 ml) and refluxed for 15 min. It was then poured on crushed ice and the ppt obtained was purified by redissolving it in 10% NaOH followed by extraction with benzene to remove impurities. The aqueous solution was acidified (HOAc), filtered and washed ($H_2O$), when an analytically pure **14g** was obtained 2.2 g (60%), m.p. 296–97°. (Found: C, 53.20; H, 5.75; N, 15.29. Calc. for $C_8H_{10}N_2OS$ (182.20): C, 52.75; H, 5.55; N, 15.38%).

*Preparation of* 3-*methoxy*, 3-*thioureido*-1-*phenyl*-2-*propene*-1-*one* **29**. 3,3-Bis(methylthio)-2-propene-1-phenyl-1-one (2.24 g, 0.01 mole) and thiourea (0.76 g, 0.01 mole) were refluxed in the suspension of sodium methoxide (0.01 mole) in methanol for 16 h. The reaction mixture was cooled and poured into water (20 ml) and extracted with benzene to remove the organic impurities. The water layer was washed with benzene twice, acidified with acetic acid when the light yellow crystalline compound obtained, was washed ($H_2O$) and dried, which gave correct analysis (1.2 g, 56%); m.p. 196°. (Found: C, 55.95; H, 5.04; N, 12.31. Calc. for $C_{11}H_{12}N_2O_2S$ (236.2): C, 55.93; H, 5.12; N, 11.86%).

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