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Cyclocondensation of sulphaguanidine acetate with chalcones in dimethylsulphoxide at 110° gave 4,6-diphenylsulphapyrimidine acetates.

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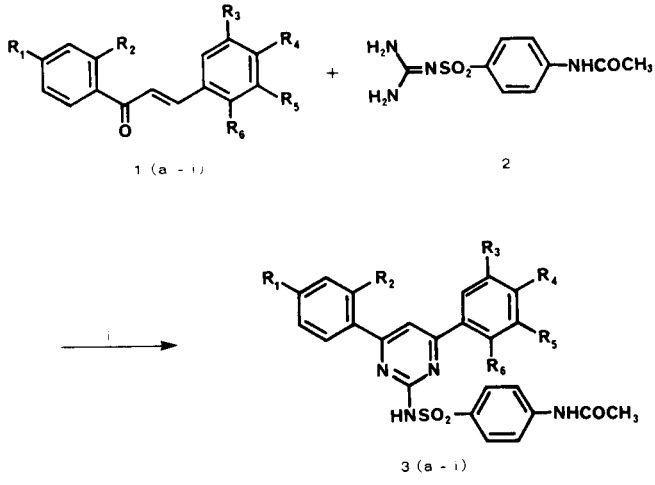
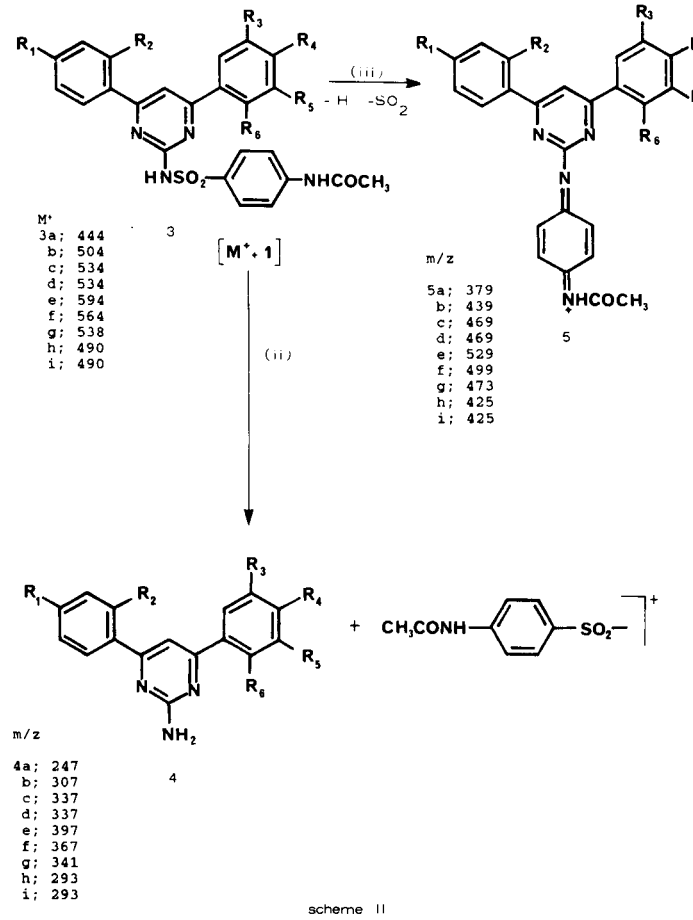
Further to our studies on antiparasitic agents [4,5,6], some 4,6-diphenylsulphapyrimidine acetates **3a-3i** were prepared from chalcones **1a-1i** and sulphaguanidine acetate **2** in hot alkaline dimethylsulphoxide. Sulphaguanidine acetate **2** had been condensed with β-diketones or β-diketocarboxylic esters in the presence of boiling glacial



Scheme I: i: DMSO, K_2CO_3, 110°

acetic acid to give sulphapyrimidine acetate [7]. Guanidine under basic conditions condense with hydroxymethylene ketones to give 2-aminopyrimidines which were converted to sulphapyrimidine acetate by use of *N*-acetylbenzenesulphonyl chloride [8]. Conversion of sulphaguanidine or its acetate in the presence of sodium methoxide or sodium ethoxide was not successful. The products obtained were mainly benzoic acid derivatives which probably occur through retro-aldol condensation reactions [9]. The structures of the sulphapyrimidine acetates were determined by physico-chemical methods, *viz*, ir, ^{1}H-nmr, mass spectroscopic methods as well as elemental analysis.



scheme II

The ir spectra of the sulphapyrimidine acetate showed absorptions at 3430 and 3340 cm^{-1} due to the presence of bonded NH of both the amide (-NHCO-) and sulphonamido (-$NHSO_2$-) groups; that at 1700-1680 cm^{-1} and also at 1610 cm^{-1} due to amide carbonyl functional group (Band I and II). The strong absorptions at 1370 and 1160

cm^{-1} were due to the presence of sulphonyl group ($-SO_2-$).

The ^1H nmr data showed the *N*-acetyl group at δ 2.0, *O*-methyl protons at δ 3.80-3.95. The phenyl ring and the pyrimidine H-5 protons overlap as multiplets at about δ 6.50-8.20 while two protons were exchangeable in all cases due to the presence of NH protons. The phenolic derivatives **3h-3i** had a third exchangeable proton.

The mass spectra showed two obvious and facile fragmentation pathways [10,11]. The pathway (ii) is due to the heterolytic fission of the products resulting in the extrusion of 2-amino-4,6-diphenylpyrimidines **4a-i** and the pathway (iii) results from the loss of H and SO_2 from the molecule giving compounds **5a-i** which results as the base peak (m/z = 100%).

EXPERIMENTAL

The melting points were determined with electrothermal melting point apparatus and are uncorrected. The infrared spectra were run as potassium bromide disc on Pye Unicam SP3-200. The ^1H nmr spectra were recorded on Varian FT-80A spectrometer operating at 80 MHz. Deuteriodimethyl sulphoxide (DMSO-d_6) was used as solvent in all cases and tetramethylsilane (TMS) as the internal standard. The mass spectra were recorded on Finnigan Model MAT-EDV 44S at 70 eV. The purity of the compounds were monitored using thin layer chromatography (tlc) on silica gel with toluene/ethyl acetate (4:1) as solvent. The chalcones used were prepared by standard method [12].

Preparations of Sulphaguanidine Acetate (**2**).

Sulphaguanidine (100 g, 0.45 mole) was dissolved in distilled and dry pyridine (125 ml) by warming. Acetic anhydride 75 ml (0.8 mole) was added and then boiled for 1 hour. The mixture was left overnight and poured into acidified crushed ice. A precipitate of the acetate was collected and recrystallised from the boiling water-ethanol mixture to give a tlc pure sulphaguanidine acetate 72.4 g (61%), mp 260-262° [Lit value [13], 261-262°].

Preparation of 4,6-Diphenylsulphapyrimidine Acetates **3a-i**.

General Procedure.

To chalcone (0.02 mole) and sulphaguadine acetate (0.02 mole) was added dry and distilled dimethyl sulphoxide (50 ml). The mixture was warmed to complete dissolution and potassium carbonate (20 g, anhydrous) was added in portions until solution became alkaline to litmus. The reaction mixture was boiled at 110° for 6 hours, cooled and poured into 150 g of ice-chips, stirred for 1 hour and left overnight. The mixture was filtered, and the filterate acidified with dilute acetic acid (50%). A yellow solid was usually collected which upon chromatography on silica gel with toluene/ethyl acetate (4:1) gave the sulphapyrimidine acetate. The solid residue was recrystallised from a hot mixture of water and ethanol.

4,6-Diphenylpyrimidine-2-sulphonamido-N^4-acetamide (**3a**).

Chalcone **1a** (4.16 g, 0.02 mole) and sulphaguanidine acetate (**2**), 5.12 g (0.02 mole), treated as described under the general procedure gave a colourless precipitate which when crystallised from water-ethanol mixture gave colourless crystals of 4,6-diphenylpyrimidine-2-sulphonamido-N^4-acetate (**3a**), 3.2 g (68%), mp 242-244°; ir (potassium bromide): 3380 (NH), 1700, 1605 (C=O, amide), 1580 (C=C), 1380, 1160 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.0 (s, CH_3CO, 3H), 7.4-8.2 (m, phenyl + H-5 pyrimidine, 15H), 10.15 (s, NH, deuterium oxide exchangeable, 1H), 11.20 (broad, NH, deuterium oxide exchangeable, 1H); ms: 444 (M^+, 0.2), 445 (M+1, 0.5), 379 (M-H-64, 100), 337, 300, 247, 129, 116, 92, 77, 65.

Anal. Calcd. for $C_{24}H_{20}N_4O_3S$: C, 64.85; H, 4.35; N, 12.60. Found: C, 65.02; H, 4.44; N, 12.93.

4,6-Bis(4,4'-dimethoxyphenyl)pyrimidine-2-sulphonamido-N^4-acetamide (**3b**).

4,4'-Dimethoxychalcone **1b**, (5.36 g, 0.02 mole) and sulphaguanidine acetate (**2**), (5.12 g, 0.02 mole) in hot alkaline dimethyl sulphoxide and crystallisation from water-ethanol mixture gave 4,6-bis(4,4'-dimethoxyphenyl)pyrimidine-2-sulphonamido-N^4-acetamide (**3b**), 2.3 g (43%) as colourless solid, mp 295-297°; ir (potassium bromide): 3340 (NH), 1680, 1620 (C=O, amide), 1600 (C=C), 1380, 1160 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.04 (s, CH_3CO, 3H), 3.80 (s, CH_3O, 6H), 7.00-8.15 (m, phenyl + H-5 pyrimidine, 13H), 10.20 (s, NH, deuterium oxide exchangeable, 1H), 11.50 (broad, NH, deuterium oxide exchangeable, 1H); ms: 504 (M^+, 0.3), 439 (M-H-64, 100), 397, 307, 179, 134, 64.

Anal. Calcd. for $C_{26}H_{24}N_4O_5S$: C, 61.89; H, 4.79; N, 11.10. Found: C, 62.10; H, 4.83; N, 10.90.

[4(2,4-Dimethoxyphenyl)-6-(4-methoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3c**).

3',4',4-Trimethoxychalcone, **1c** (5.96 g, 0.02 mole) and sulphaguanidine acetate, (**2**) (5.12 g, 0.02 mole) in hot alkaline dimethyl sulphoxide and crystallisation from a water-ethanol mixture gave [4-(2,4-dimethoxyphenyl)-6-(4-methoxyphenyl)]pyrimidine-2-sul-phonamido-N^4-acetamide (**3c**), 1.20 g (22%) as a colourless solid, mp 182-184°; ir (potassium bromide): 3430 (NH), 1700, 1605 (C=O, amide), 1580 (C=C), 1330, 1180 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.05 (s, CH_3CO, 3H), 3.80, 3.85, 3.90 (s, CH_3O, 9H), 6.60-8.10 (m, phenyl + H-5 pyrimidine, 12H), 10.22 (s, NH, deuterium oxide exchangeable, 1H), 11.0 (broad, NH, deuterium oxide exchangeable, 1H); ms: 534 (M^+, 0.3), 533 (M-H, 1), 469 (M-H-64, 100), 439, 397, 337, 307, 203, 92, 77, 65.

Anal. Calcd. for $C_{27}H_{26}N_4O_6S$: C, 60.66; H, 4.90; N, 10.48. Found: C, 60.45; H, 4.76; N, 10.51.

[4-(2,4-Dimethoxyphenyl)-6-(2-methoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3d**).

2,3',4'-Trimethoxychalcone **1d**, (5.96 g, 0.02 mole) with sulphaguanidine acetate (**2**), (5.12 g, 0.02 mole) in hot alkaline dimethyl sulphoxide gave [4-(2,4-dimethoxyphenyl)-6-(2-methoxyphenyl)]-pyrimidine-2-sulphonamido-N^4-acetamide (**3d**), 2.78 g (50%) as a colourless solid from water-ethanol, mp 224-226°; ir (potassium bromide): 3360 (NH), 1680, 1610 (C=O, amide) 1590 (C=C), 1380, 1160 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.05 (s, CH_3CO, 3H), 3.75, 3.80, 3.85 (s, CH_3O, 9H), 6.6-8.0 (m, phenyl + H-5 pyrimidine, 12H), 10.24 (s, NH, deuterium oxide exchangeable, 1H), 12.00 (broad, NH, deuterium oxide exchangeable, 1H); ms: 534 (M^+, 0.4), 533 (M-H, 1), 469 (M-H-64, 100), 427, 397, 337, 306, 203, 134, 92, 77, 65.

Anal. Calcd. for $C_{27}H_{26}N_4O_6S$: C, 60.66; H, 4.90; N, 10.48. Found: 60.42; H, 4.82; N, 10.60.

[4-(2,4-Dimethoxyphenyl)-6-(3,4,5-trimethoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3e**).

2',4',3,4,5-Pentamethoxychalcone (**1e**), (7.16 g, 0.02 mole) with sulphaguanidine acetate (**2**), (5.12 g, 0.02 mole) in hot alkaline dimethyl sulphoxide gave [4-(2,4-dimethoxyphenyl-6-(3,4,5-trimethoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3e**), 1.93 g (32%) as a colourless solid from water-ethanol, mp 205-207°; ir (potassium bromide): 3340 (NH), 1700, 1610 (C=O, amide), 1590 (C=C), 1360, 1140 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.00 (s, CH_3CO, 3H), 3.65, 3.72, 3.80, 3.95 (s, CH_3O, 15H), 6.50, 8.0 (m, phenyl + H-5 pyrimidine, 10H), 10.25 (s, NH, deuterium oxide exchangeable, 1H), 13.20 (broad, NH, deuterium oxide exchangeable, 1H); ms: 594 (M^+, 2), 529 (M-H-64, 100), 487, 397, 366, 244, 203, 150, 108, 92, 65.

Anal. Calcd. for $C_{29}H_{30}N_4O_8S$: C, 58.58; H, 5.08; N, 9.42. Found: C, 58.44; H, 5.11; N, 9.42.

[4,6-Bis(2',4',3,4 tetramethoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3f**).

2',4',3,4-Tetramethoxychalcone **1f** (6.56 g, 0.02 mole) in hot alkaline dimethyl sulphoxide with sulphaguanidine acetate (**2**) (5.12 g, 0.02 mole) gave from water-ethanol mixture [4,6-bis(2',4',-3,4-tetramethoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3f**) as a colourless solid, 2.07 g (37%), mp 214-216°; ir (potassium bromide): 3460 (NH), 1700, 1610 (C=O, amide), 1580 (C=C), 1330, 1148 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.00 (s, CH_3CO, 3H), 3.80, 3.85 (s, CH_3O, 12H), 6.50-8.0 (m, phenyl + H-5 pyrimidine, 11H), 10.25 (s, NH, deuterium oxide exchangeable, 1H), 11.50 (broad, NH, deuterium oxide exchangeable, 1H); ms: 564 (M^+, 0.5); 563 (M-H, 1); 499 (M-H-64, 100), 367, 308, 296, 164, 108, 92, 77, 65.

Anal. Calcd. for $C_{28}H_{28}N_4O_7S$: C, 59.56; H, 5.00; N, 9.92. Found: C, 59.90; H, 4.98; N, 9.74.

[4-(2,4-Dimethoxy)-6-(4-chlorophenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3g**).

2',4'-Dimethoxy-4-chlorochalcone **1g** (6.08 g, 0.02 mole) reacted with sulphaguanidine acetate (**2**) (5.14 g, 0.02 mole) in hot alkaline dimethyl sulphoxide to give [4-(2,4-dimethoxy)-6-(4-chlorophenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3g**), 0.96 g (17%) as a colourless solid from water-ethanol mixture, mp 265-266° dec; ir (potassium bromide): 3380 (NH), 1680, 1610 (C=O, amide), 1600 (C=C), 1370, 1150 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.05 (s, CH_3CO, 3H), 3.82, 3.88 (s, CH_3O, 9H), 6.80-8.10 (m, phenyl + H-5 pyrimidine, 12H), 10.22 (s, NH, deuterium oxide exchangeable, 1H), 11.60 (broad, NH, deuterium oxide exchangeable, 1H); ms: 538 (M^+, 0.6), 537 (M-H, 0.6), 473 (M-H-64, 100), 341, 270, 203, 189, 108, 92, 77, 65.

Anal. Calcd. for $C_{26}H_{23}ClNO_5$: C, 57.94; H, 4.30; N, 10.39; Cl, 6.58. Found: C, 57.56; H, 4.22; N, 10.25; Cl, 6.90.

[4-(2-Hydroxyphenyl)-6-(4-methoxyphenyl)]pyrimidine-2-sulphonamido-N^4-acetamide (**3h**).

2'-Hydroxy-4-methoxychalcone **1h** (5.08 g, 0.02 mole) with sulphaguanidine acetate (**2**) (5.14 g, 0.02 mole) in hot alkaline dimethyl sulphoxide gave [4-(2-hydroxyphenyl)-6-(4-methoxyphenyl)]pyrimidine-2-sulphonamido-N⁴-acetamide (**3h**) 1.78 g (34%) as a colourless solid from water-ethanol mixture, mp 269-271°; ir (potassium bromide): 3360 (NH), 1710, 1605 (C=O, amide), 1580 (C=C), 1380, 1190 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.05 (s, CH_3CO, 3H), 3.87 (s, CH_3O, 3H), 6.80-8.10 (m, phenyl + H-5 pyrimidine, 13H), 10.22 (s, NH, deuterium oxide exchangeable, 1H), 12.5 (broad, NH, OH, deuterium oxide, 2H); ms: 490 (M^+, 26), 491 (M+1, 10), 425 (M-H-64, 100), 383, 293, 134, 107, 92, 77, 65.

Anal. Calcd. for $C_{25}H_{22}N_4O_5S$: C, 61.21; H, 4.52; N, 11.42. Found: C, 60.90; H, 4.48; N, 11.54.

[4-(2-Hydroxyphenyl)-6-(2-methoxyphenyl)]pyrimidine-2-sulphamido-N^4-acetamide (**3i**).

2'-Hydroxy-2-methoxychalcone **1i** (6.56 g, 0.02 mole) in hot alkaline dimethyl sulphoxide with sulphaguanidine acetate (**2**) (5.12 g, 0.02 mole) gave from water-ethanol mixture [4-(2-Hydroxyphenyl)-6-(2-methoxyphenyl)]pyrimidine-2-sulphamido-N^4-acetamide (**3i**) 1.0 g (19%) as a colourless solid, mp 273-275°; ir (potassium bromide): 3380 (NH), 1680, 1605 (C=O, amide), 1580 (C=C), 1380, 1160 (SO_2) cm^{-1}; ^1H nmr (deuteriodimethyl sulphoxide): δ 2.00 (s, CH_3CO, 3H), 3.80 (s, CH_3O, 3H), 6.80-8.20 (m, phenyl + H-5 pyrimidine, 13H), 10.20 (s, NH, deuterium oxide exchangeable, 1H), 11.90, 12.3 (broad, NH, OH, deuterium oxide exchangeable, 2H); ms: 490 (M^+, 30), 491 (M+1, 8), 425 (M-H-64, 100), 384, 340, 293, 252, 159, 108, 91, 77, 65.

Anal. Calcd. for $C_{25}H_{22}N_4O_5S$: C, 61.21; H, 4.52; N, 11.42. Found: C, 61.60; H, 4.52; N, 11.41.

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