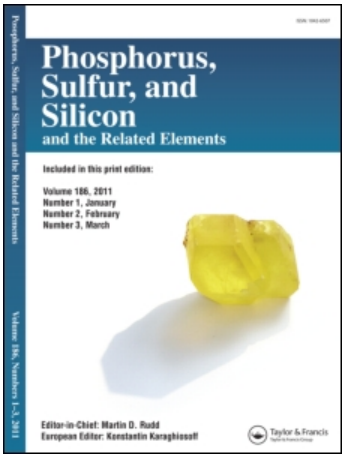

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SYNTHESIS OF A NOVEL HETEROCYCLIC SYSTEM, IMIDAZOL[1',2':1,2]PYRIMIDO[5,4-D] [1,3]THIAZOLE

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SYNTHESIS OF A NOVEL HETEROCYCLIC SYSTEM, IMIDAZOL[1',2':1,2]PYRIMIDO[5,4-D][1,3]THIAZOLE

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7-Substituted amino-6-amino-2,3-dihydro-5-methylimidazo[1,2-a]pyrimidines (**1**) were condensed with carbon disulfide in hot pyridine to afford the novel heterocyclic system 9-methyl-1,2,6,7-tetrahydroimidazo[1',2':1,2]pyrimido[5,4-d][1,3]thiazole-2-thione (**2**). This compound was then converted to several substituted derivatives.

Keywords: Imidazopyrimidothiazole; pyrimidines; carbon disulfide; tricyclic heterocycles; Phrmacological importance

INTROUDCTION

Our interest in the syntheses of novel bicyclic and tricyclic heterocycles of pharmacological importance[1-4] has prompted us to synthesize a novel heterocyclic system, imidazo[1',2':1,2]pyrimido[5,4-d][1,3]thiazole and its derivatives. We recently reported that the intramolecular nucleophilic displacement of tertiary amino groups in certain substituted pyrimidines offer a convenient method for the preparation of bicyclic heterocycles[5]. Further work has now been extended to the synthesis of tricyclic compounds.

In our attempt to synthesize the novel heterocyclic system, (**2**), 7-substituted amino-6-amino-2,3-dihydro-5-methylimidazo[1,2-a]pyrimidines (**1**)

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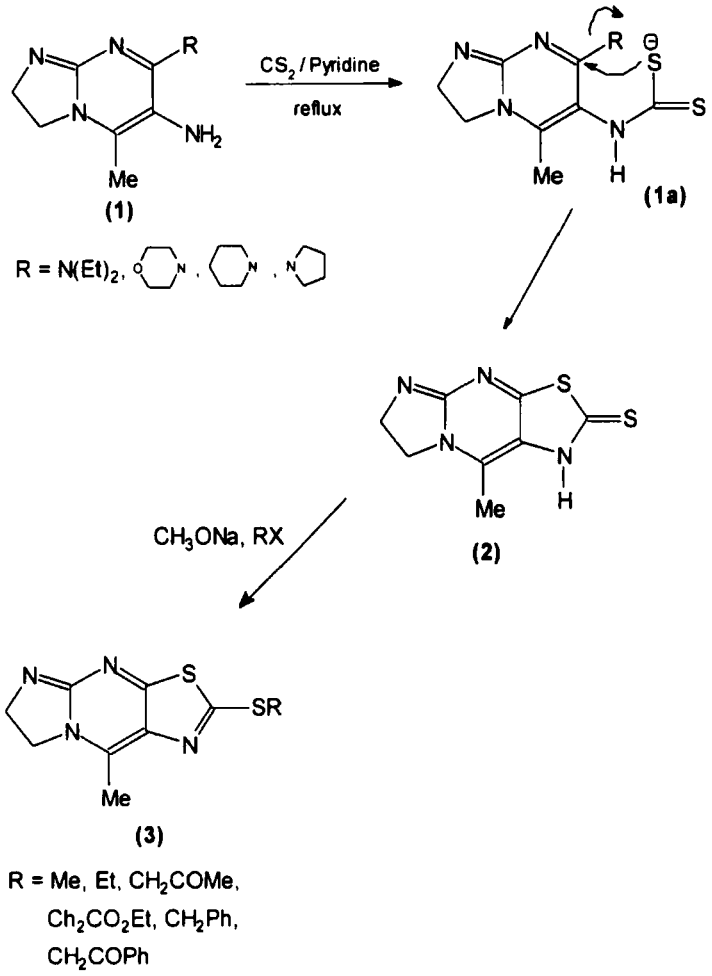

SCHEME 1

were first prepared[6]. These compounds were condensed with carbon disulfide in boiling pyridine. 6,7-Diaminoimidazo[1,2-a]pyrimidines (1; R=NHMe or NHPh) and carbon disulfide normally yield 2-mercaptoimidazo[1,2-a]purines(4)[7], but the present diamines (1; R=diethylamino, piperidino, morpholini, pyrrolidino) and carbon disulfide gave only a single product, imidazopyrimidothiazole-2-thione (2). The structures of the products followed from their ^{1}HNMR spectra each of which showed no signal for

the tertiary amino group but did show a signal at δ8.85 for -NH which indicates the involvement of the primary amino group in the cyclization process.

The presence of a C-methyl group at δ 2.28 together with the molecular peak at m/z 224 and micro-analytical data are all consistent with the structure **2**. A suggested mechanism is given (scheme 1) and this is supported by the fact that certain substituted diaminopyrimidines react with carbon disulfide forming an anion similar to (1) which can undergo further reactions[8].

EXPERIMENTAL

M.p's are uncorrected. ^{1}HNMR spectra were measured in [$^2H_6$] dimethyl sulfoxide solution on a Perkin-Elmer R32 instrument. Microanalyses were performed by Butterworth Laboratories Ltd., Teddington, Middleesex. Mass spectra were recorded on a Kratos MS 30 spectrometer using a direct-insertion probe.

9-Methyl-1,2,6,7-tetrahydroimidazo[1',2':1,2]pyrimido[5,4-d][1,3] thiazole-2-thione (2)

The appropriate 7-substituted amino-6-amino-2,3-dihydro-5-methylimidazo[1,2-a] pyrimidine **(1)** (0.001 mole)[7] was heated under reflux for 6 hrs in a mixture of pyridine (4 mL) and carbon disulfide (2 mL). Pyridine was removed under reduced pressure. Recrystallization of the residue from water gave the title compound as green needles (60–75%) which gradually dicomposed above 250°C. Found: C, 42.5; H, 3.4; N, 25.2; calcd for $C_8H_8N_4S_2$, C, 42.8; H, 3.6; N, 25.0%, ^{1}H NMR, δ 2.28 (s, 3H, Me), 3.62 (m, 2H), 4.16 (m, 2H, CH_2-CH_2) and 8.85 (s, 1H, NH), m/z 224 (M).

2-(alkyl or arylalkylsulfanyl)-9-methyl-6,7-tetrahydroimidazo [1',2':1,2]pyrimido [5,4-d][1,3]thiazole (3). General method

Compound **(2)** (0.001 mole) was dissolved in a stirred solution of sodium methoxide in methanol which was prepared by adding sodium metal (0.03 g) to methanol (10 mL). The solution was stirred during the dropwise addition of the appropriate alkyl or arylalkyl halides (0.001 mole) in methanol (5 mL) for a further 16 hrs at room temperature. Then it was acidified to pH 6 with glacial acetic acid; the precipitated solid filtered off, washed with water, dried and crystallized from a suitable solvent (data in Table I).

TABLE I Imidazo [1',2':1,2]pyrimido[5,4-d][1,3]thiazole] (3)

R	*Crystallisation Solvent*	*Yield%*	*M.P. (°C)ý*	*(° Found (%)*			*Required(%)*			δ *(ppm)*
				C	*H*	*N*	*C*	*H*	*N*	
Me	MeOH	67	135–7	45.1	4.2	23.7	45.4	4.2	23.5	2.27 (s, 3H, Me), 2.3 (s, 3H, SMe), 3.54 4.1 (m, 4H, CH_2Cl_2)
Et	MeOH	73	148–150	47.4	4.5	22.1	47.60	4.8	22.2	1.44 (t, 3H, $MeCH_2$), 2.3 (s, 3H, Me), 3,54 4.1 (m, 4H, CH_2CH_2)
CH_2COMe	Propan-1-Ol	69	187–188	46.8	4.1	19.8	47.1	4.4	20.0	2.11 (s, 3H, MeCO), 2.32 (s, 3H, Me), 3.54 4.1 (m, 4H, CH_2CH_2), 4.17 (s, 2H, $COCH_2S$)
CH_2CO_2Et	EtOH	71	170–1	46.0	4.2	18.1	46.4	4.5	18.0	1.01 (t, 3H, Me), 4.22 (q, 2H, CH_2), 2.36 (s, 3H, Me), 3.54 4.1 (m, 4H, CH_2CH_2)
CH_3Ph	Toluene	79	162–4	56.9	4.1	17.7	57.3	4.5	17.8	2.3 (m, 3H, Me), 3.54 4.1 (m, 4H, CH_2CH_2), 4.39 (m, 2H, SCH_2), 7.4–7.74 (m, 5H, Ph)
CH_2COPh	EtOH	72	193–5	56.0	3.9	16.1	56.1	4.1	16.4	2.3 (s, 3H, Me), 3.54 4.1 (m, 4H, CH_2CH_2), 4.39 (m, 2H, SCH_2), 7.4–7.74 (m, 5H, Ph)

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