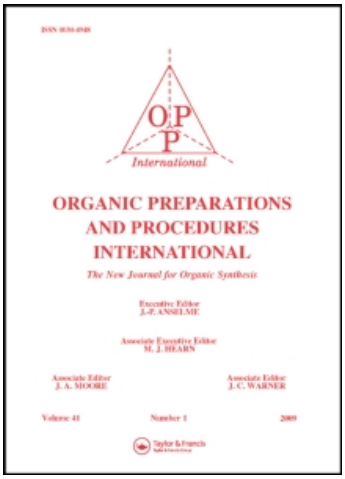

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SYNTHESIS OF NOVEL 9-ARYL-2,8-DIMETHYL-9H-PURIN-6-AMINES BASED ON STERICALLY HINDERED o-BROMOANILINES

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SYNTHESIS OF NOVEL 9-ARYL-2,8-DIMETHYL-9H-PURIN-6-AMINES BASED ON STERICALLY HINDERED *o*-BROMOANILINES

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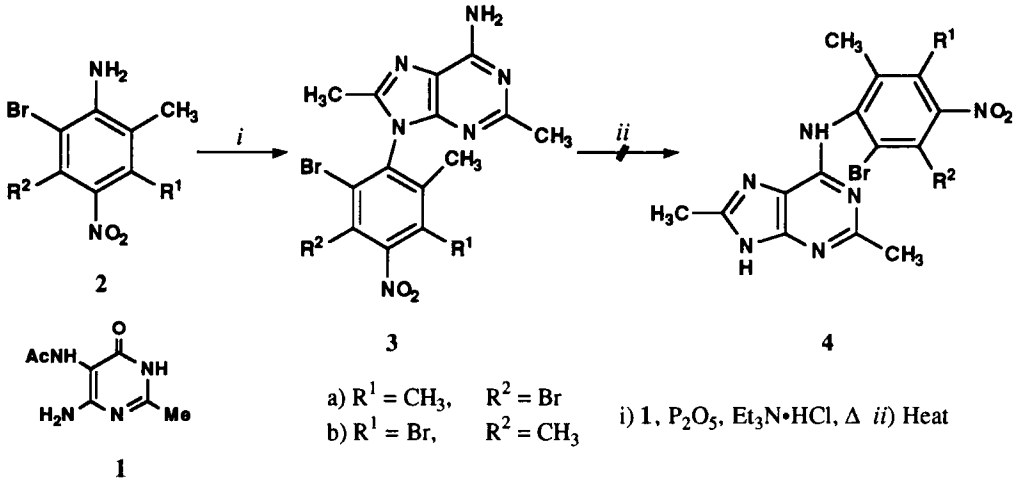
Purines, well known as constituents of genetic material also exhibit other useful biological action, *e.g.* antiviral antitumour and anticonvulsant activity.[1] 9-Arylpurinamines has been prepared by Pedersen *et al.*[2] from the reaction of various *o*-disubstituted anilines (mainly Cl, Me or $CHMe_2$ groups as substituents) with 5-acetamido-4-amino-2-methylpyrimidine-6-(1H)-one (**1**) in the presence of P_2O_5 and $Et_3N{\bullet}HCl$. On the other hand, the use of sterically unhindered anilines in this reaction gave 6-arylaminopurines. Since highly sterically hindered dibromo and dichloroanilines had been synthesised by us,[3] we desired to investigate the above reaction using the o-bromoanilines. In our hands, the reactions of the dibromoanilines **2a** and **2b** proceeded smoothly and led to formation of new 9-arylpurinamines **3a** and **3b**.

However, in contrast to Pedersen *et al.*,[2] our attempts to perform the same reaction with dichloroaniline analogues of **2a** and **2b** were unsuccessful and no purines could be isolated. The ethyl acetamidocyanoacetate[4] required for this synthesis was prepared from commercially available ethyl cyanoacetate by nitrosation[5] followed by reductive acetylation; condensation with acetamidine hydrochloride under basic conditions, yielded pyrimidine **1**.[6] Reaction of **1** with 2,3-dibromo-5,6-dimethyl-4-nitroaniline (**2a**) gave the 9-(2,3-dibromo-5,6-dimethyl-4-nitrophenyl)-2,8-dimethyl-9H-purin-6-amine (**3a**). A similar reaction with 2,5-dibromo-3,6-dimethyl-4-nitroaniline (**2a**) led to the



formation of 9-(2,5-dibromo-3,6-dimethyl-4-nitrophenyl)-2,8-dimethyl-9H-purin-6-amine (**3b**). Prolonged reaction time gave neither purines **3** or **4** nor any rearrangement products. The structures

of the new purines were established by spectral studies and in particular by their mass spectra. Both **3a** and **3b** showed a significant molecular ion peak at m/z 468 with isotopic peaks in the ratio of 1:2:1, characteristic for the presence of two bromine atoms. This was followed by successive loss of bromine atoms and the NO_2 group to give a peak at m/z 264 from which the purine moiety was possibly lost, leading to a peak at m/z 102. Peaks arising out of the loss of CH_3 and NO_2 groups from the molecular ion were also observed.

EXPERIMENTAL SECTION

All melting points are uncorrected. UV spectra were recorded on Shimadzu UV-260 spectrophotometer. IR spectra were recorded on Perkin-Elmer 1710 FT-IR and Shimadzu IR-435 spectrophotometers. ^1H NMR spectra were recorded on JEOL JNM-FX 100 and FX 200 FT-NMR spectrometers. Mass spectra were recorded at the Max-Planck-Institute for Biochemistry, Munich. Satisfactory elemental analysis were obtained on Heraus CHN-RAPID instrument.

5-Acetamido-4-amino-2-methylpyrimidin-6(H)-one (1),[6] mp. 340-345°, yield 49%. IR (nujol mull): 3280, 3130, 1680, 1280 cm^{-1} MS: m/z (relative intensity): 182 (M^+, 16.6), 166 (2.7), 140 (65.1), 112 (14.3).

General Procedure for the Synthesis of 9-Arylpurinamines (3).- A mixture of dibromoaniline 2 (3.1 mmoles), $Et_3N{\bullet}HCl$ (5.8 mmoles) and P_2O_5 (5.6 mmoles) were mechanically stirred in an oil bath at about 180° for 10 min. To this melted mixture was added pyrimidine **1** (4.9 mmoles) and stirring was continued at 200° for 2 hrs. The reaction mixture was cooled to 100°, basified with 2N NaOH and stirred at room temperature for 30 min, then acidified with conc. HCl. The brown solid was collected, washed with H_2O, hot acetone and dried to give 0.9 g. of crude product. The product was purified by trituration with minimum amount of DMF and filtered. The filtrate was concentrated in fume hood at room temperature. Addition of MeOH to this concentrated DMF solution resulted in the formation of the brown crystals of **3**.

9-(2,3-Dibromo-5,6-dimethyl-4-nitrophenyl)-2,8-dimethyl-9H-purin-6-amine (3a), mp. >300°, yield 14%, FT-IR (KBr): 3490, 3445, 2990, 1650, 1540, 1355 cm^{-1} ; UV (DMF): 268 (ε 12,076). ^1H NMR (DMSO-d_6) : δ 2.31 (s,3 H, CH_3), 2.52 (s, 3H, CH_3), 2.74 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 7.34 (br. s, 2H, NH_2); MS:m/z (relative intensity): 472 (M+4, 4.0), 470 (M+2, 9.3), 468 (M^+, 5.0), 457 (7.3), 455 (15.4), 453 (8.7), 391 (10.8), 389(11.4), 310 (11.2), 264 (18.2) 164 (100), 102 (33.5).

Anal. Calcd for $C_{15}H_{14}Br_2N_6O_2$: C, 38.32; H, 3.00; N, 17.87. Found: C, 38.80; H, 2.80; N, 17.50

9-[2,5-Dibromo-3,6-dimethyl-4-nitrophenyl)-2,8-dimethyl-9H-purin-6-amine (3b), mp. >300°, yield 32%, FT-IR (KBr): 3450, 3400, 1655, 1540, 1470, 1355 cm^{-1}; UV (DMF): 269 (ε 18,530); ^1H NMR (DMSO-d_6): δ 2.41 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 7.21 (br. s, 2H, NH_2); MS:m/z (relative intensity): 472 (M+4, 53.9), 470 (M+2, 105.2), 468 (M^+, 52.6), 457 (98.0), 455 (196.0), 453 (100.0), 411 (34.2), 409 (61.8), 407 (28.9), 391 (33.2), 389 (33.6), 310 (14.6), 264 (64.7), 102 (22.1).

Anal. Calcd for $C_{15}H_{14}Br_2N_6O_2$: C, 38.32; H, 3.00; N, 17.87. Found: C, 38.50; H, 3.20; N, 17.90

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SYNTHESIS OF 2,3-DIDEOXY-D-*arabino*-HEPTONO-1,4-LACTONE *via* A WITTIG REACTION ON UNPROTECTED D-ARABINOSE

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The Wittig reaction using phosphonium ylides stabilized by electron-withdrawing groups (EWG) has proven to be extremely useful for the construction of chain-extended carbohydrates.[1] Suitably protected monosaccharides (**1**) are conveniently lengthened *via* the reaction with phosphonium ylides of generic structure **2.**

It had been reported by Kochetkov and Dmitriev that completely unprotected monosaccharides also react readily with stabilized phosphoranes, eliminating the normal three-step synthesis of the hydroxyl blocked aldose.[2] This procedure has been used for the synthesis of leukotrienes[3a] and more