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NOTE

Synthesis of 7-Aryl-3H-[1,2,4]triazolo[3,1-i]purines from 1-Amino-9-aryl-6-iminopurines

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The title compounds have been prepared in high yield from 9-aryl-6-iminopurine derivative by reaction with diethoxymethyl acetate.

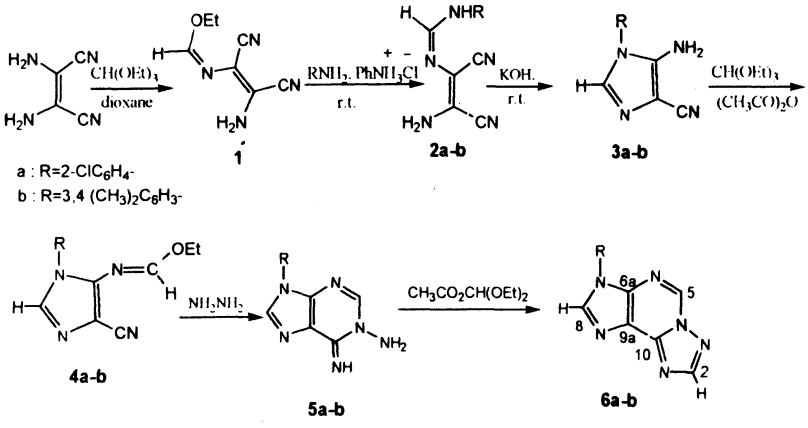
Key Words: Purine, Imino-purine, Triazolo-purine, Diamino-maleodinitrile.

Fused triazoles have been found to exhibit a wide range of biological activities[1–3]. Most of these compounds show significant *in vivo* antitumour and antiviral activity and in addition, possess fluorescent properties, which makes them of interest as biological probes[4–7].

As a class of compounds the s-triazolo[3,1-i]purines have been prepared from the corresponding 6-hydrazinopurines by reaction with diethoxymethyl acetate (DEMA)[8–11]. As part of our ongoing study of the use of diaminomaleodinitrile as a cheap starting material for a range of imidazole, purine, dihydropurine and pyrimidine derivatives, the synthesis of some derivatives of 1-amino-9-aryl-(or benzyl)-6-iminopurines have been reported[12–14]. In the present paper, the reaction of 1-amino-9-aryl-6-iminopurines**15 (5)** with cyclizing agent diethoxymethyl acetate has been investigated in order to see whether this might provide a route to 7-aryl-3H-[1,2,4]triazolo[3,1-i]purines, which may have potential biological activity.

1-Amino-9-aryl-6-iminopurines **(5a–b)** were prepared *via* a multistep synthesis from ethyl (Z)-N-(2-amino-1,2-dicyanovinyl)formimidate[12–17], by treatment with an aryl-amine in a 1 : 1 molar ratio in ethanol in the presence of a catalytic amount of anilinium hydrochloride to give the corresponding formamidines. Cyclization of the formamidines in the presence of a strong base, aqueous KOH solution, provided the corresponding 5-amino-1-aryl-4-cyanoimidazoles[13, 14], which are readily converted to 1-amino-9-aryl-6-iminopurines by treatment with $HC(OEt)_3$ and Ac_2O followed by reaction with hydrazine hydrate[13, 15].

On heating **5a–b** with an excess of diethoxymethyl acetate (DEMA), 7-aryl-3H-[1,2,4]triazolo[3,1-i]purines **(6a–b)** were obtained in good yield. Compounds **6a, b** were refluxed in diethoxymethyl acetate for 4–5 h, after which time TLC showed that all starting materials had been consumed. Removal of the solvent and addition of water to the residue followed by extraction with chloroform gave pure compounds **6a–b** in 84–88% yield as pale yellow crystals and after recrystallization from chloroform-hexane, these were characterized fully.



The mass spectra of the isolated triazolo-purines **6a–b** were satisfactory. The ^{1}H NMR spectra had some interesting features. The H-8 of the imidazoles ring shifted to higher field at 8.52-8.66 with H-2 of the purine ring at 8.50–8.70 ppm and H-5 at 9.30–9.61 ppm. The ^{13}C NMR spectra of the compound **2** had the expected number of bands with the C-8 carbon having a chemical shift at δ 140.4–140.7, C-5 at δ 146.2–146.2 and C-2 at δ 156.7–157.2 ppm. The infrared spectrum confirmed the presence of the ν(C=N) stretching vibration in the region of 1600–1670 cm^{-1}.

All solvents were purified and dried using established procedures. The ^{1}H NMR spectra were recorded on Hitachi-Perkin-Elmer R24B (60 MHz) or Bruker XL 300 (500 MHz) instruments (with J-values given in Hz), ^{13}C NMR spectra either on a Bruker WP 80 or XL300 instrument and IR spectra on a Shimadzu IR-435 spectrophotometer. Mass spectra were recorded on a Kratos Concept instrument. The melting points were measured on an Electrothermal digital melting point apparatus and are uncorrected.

General procedure for the preparation of 1-amino-9-aryl-6-iminopurines (5a–b): To a stirred solution of the 1-aryl-4-cyano-5-[(ethoxymethylene) amino]imidazoles[13–17] **(4a–b)** (0.30 g) in dry methanol (8–10 mL) under an argon atmosphere at room temperature were added hydrazine monohydrate (1 M equivalent). After 15–20 min, the separated precipitate was filtered off, washed with a mixture of dry diethyl ether/hexane (1 : 1) and dried under vacuum to give **5a–b**.

General procedure for the preparation of 7-phenyl-3H-[1,2,4]triazolo [3,1-i]purine (6a–b): To a stirred solution of 1-amino-9-phenyl-6-iminopurines **5a–b** (0.2 g) in diethoxymethyl acetate (15 cm^3) were refluxed for 5 h. After TLC ($CHCl_3$/EtOH 1 : 1) showed that no starting material remained, most of the solvent was removed under vacuum, then a mixture of EtOH and $CHCl_3$ (1 : 1) was added to give a pale yellow precipitate. This was filtered and washed with diethyl ether to give compounds **6a–b.**

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