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ACETALS OF 4-AMINO-2-BUTYNAL : APPLICATION TO THE SYNTHESIS OF N^6-SUBSTITUTED ADENINES WITH AN ACETYLENIC SIDE CHAIN, POTENTIAL CYTOKININS

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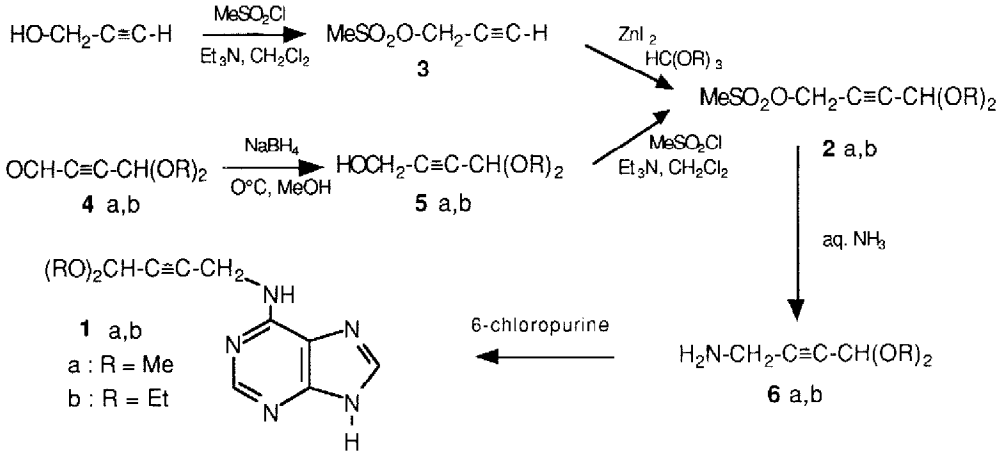
Summary : Acetylenedicarbaldehyde monoacetals **4** are good precursors for the synthesis of the 4-amino-1,1-dialkoxy-2-butynes **6**, through simple reactions. Coupling of these amines **6** with 6-chloropurine leads to the N^6-substituted adenines **1**, potential cytokinins.

In N^6-substituted adenines, the main family of the plant hormones cytokinins, short side chain (about 5 C atoms) and unsaturation at the 2-C of this chain are common features for increasing activity (1). The synthesis of the compounds **1** bearing an aliphatic chain with a masked α-ynal function has been undertaken in order to test their activity (2) and to study their influence on enzymatic degradation of cytokinins (3).



The key compounds are the mesylates **2** which were obtained through two different routes. **2b** had been previously prepared (4) from the propargyl alcohol mesylate **3** (caution : allergenic) by using the Howk and Sauer method. This reaction gave us low yields (30%) of **2a** and **2b**, and decompositions were often observed at the end of their distillation.

We explored a new route to **2** from the acetylenedicarbaldehyde monoacetals **4** (5) that we found preferable for the synthesis of **2**b [the aldehyde-acetal **4**a is less accessible than **4**b (6)]. The aldehydes **4** were quantitatively transformed into the alcohols **5** (6,7), then into the mesylates **2** (8) further used without any purification.

The mesylates **2** were converted into the amines **6** by simple stirring (1.5 h at 20°C) with an aqueous NH_3 solution (11 mol.l^{-1} - 5 ml per mmol of **1**)(50 - 60% yield - distilled under vacuum in N_2 stream after usual workup but with continuous Et_2O extraction). Refluxing of these amines **6** with 6-chloropurine (9) for 4 h in methanol (**6**a) or for 12 h in ethanol (**6**b) gave the expected N^6-substituted adenines **1** which were isolated by filtration of the cooled reaction mixture (90 and 64% yield of pure **1**a and **1**b respectively).

Note that direct conversion **4**→**6** by treatment with $LiBH_3CN$ in the presence of ammonium acetate (10) gave us poor results.

Acetals of 4-Amino-2-butynal ***2*** :

2a : colorless liq. ; bp_2 – 69-73°C ; ^{1}H nmr (∂/TMS in 10^{-6}, CCl_4) : 1.30 (s, D_2O exch., NH_2), 3.27 (s, 2 Me), 3.40 (d, ^5J = 2 Hz, CH_2), 4.58 (t, ^5J = 2 Hz, CH) ; ir (neat) in cm^{-1} : 3360 and 3300 (NH_2), 2240 (C≡C).

2b : colorless liq. ; $bp_{0.1}$ = 71-76°C ; ^{1}H nmr (CCl_4) : 1.18 (t, ^3J = 6.2 Hz, 2 CH_3), 1.18 (s, D_2O exch., NH_2), 3.40 (d, ^5J = 1.8 Hz, CH_2N), 3.3 to 3.8 (m, 2 CH_2O), 5.10 (t, ^5J = 1.8 Hz, CH) ; ir (neat) : 3360 and 3300 (NH_2), 2240 (C≡C).

N^6-substituted adenines ***1*** :

1a : white powder, mp(MeOH) = 244°C (inst.); ^{1}H nmr (DMSO-d_6) : 3.25 (s, 2 Me), 5.20 (t, ^5J = 1.2 Hz, CHO_2), 4.42 (dd, ^3J = 6 Hz, ^5J = 1.2 Hz, CH_2), 8.04 (t, ^3J = 6 Hz, D_2O exch., HN^6), 8.20 and 8.32 (2 s, H-2 and H-8).

1b : white powder, mp(EtOH) = 228°C (inst.) ; ^{1}H nmr : same characteristics as **1**a except $CH(O\underline{R})_2$ signals.

1a and **1**b exhibited weak cytokinin activity in cell division experiments. Enzymatic studies are in progress.

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