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REACTIONS OF N^6-ACYL-9-SUBSTITUTED ADENINES
APPLICATIONS TO CHEMICAL MODIFICATIONS AND RING-TRANSFORMATIONS OF ADENINE DERIVATIVES

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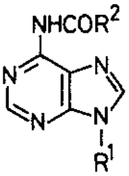
Our previous work has shown that N^6-benzoyl-9-benzyladenine (1: R^1=CH_2Ph, R^2=Ph) is easily reduced with sodium borohydride in acetic acid to give unexpectedly 7,8-dihydro derivative. The nmr spectroscopic study has suggested that contrary to 9-benzyladenine, protonation of (1: R^1=CH_2Ph, R^2=Ph) occurs in preference at N_7-nitrogen rather than N_1-nitrogen. These observations point the remarkable substituent effect of the N^6-acyl group in the 9-substituted adenines and, therefore, were expanded to their C_8-hydrogen exchange and N_7-alkylation. The ring-transformations of 9-substituted adenines via (1) and 7-alkylated adenines (2) to 7-substituted adenines (5) and pteridines (6) was also investigated.

On the basis of a kinetic study, it was found that introduction of the acyl group into the N^6-amino group of 9-substituted adenines results in the significant acceleration of their C_8-hydrogen exchange. Previous works have shown that the C_8-hydrogen exchange of 9-substituted adenines is likely to occur via the N_7-protonated form presumably present to a small extent in equilibrium with the predominant N_1-protonated form. The facile C_8-hydrogen exchange of (1) can be considered to take place efficiently as a result of enhancement of the N_7-protonation by virtue of the N^6-acyl group.

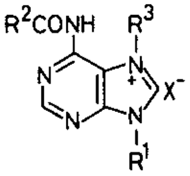
In a sharp contrast to 9-substituted adenine, the N^6-acyl substituted adenines (1) caused almost exclusive alkylation at N_7-nitrogen rather than N_1-nitrogen to afford (2) in moderate and high yields. Deacylation of (2) was achieved by using hydrazine hydrate in acetic acid - pyridine. The 7,9-disubstituted adenines (3) thus obtained are not generally well-known.

Mild alkaline treatment of (2) (0.05N ethanolic NaOH, room temperature, 0.5h) occurred smoothly to give the ring-opening products (4). Acid treatment of (4) (10% HCl, 100°, 2h) resulted in the cyclization to 7-substituted adenines (5). Alkaline treatment of (4: R^3=CH_2COPh) (0.1N ethanolic NaOH, 100°, 2h), however, gave pteridine derivative (6).

Further extension of the present results to the new types of chemical modifications of 9-substituted adenines are now in progress.



(1)



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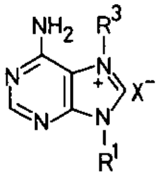

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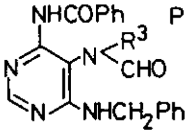

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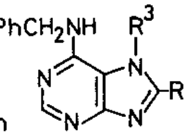
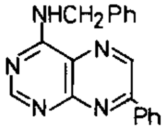


(5)



(6)