Acylation of 2′,3′,5′-Tri-*O*-acetylguanosine

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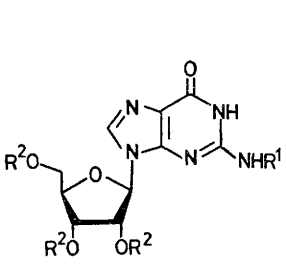
Summary 2′,3′,5′-Tri-*O*-acetylguanosine (**1b**) reacts with 2,6-dichlorobenzoyl and mesitylenesulphonyl chlorides to give the corresponding crystalline *O*(6)- acyl derivatives [(**2**) and (**3a**), respectively].

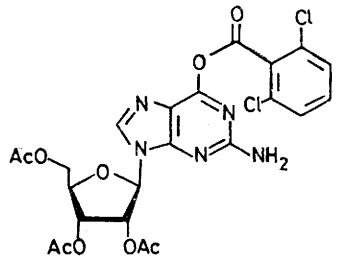
GUANOSINE (**1a**) reacts with acetic anhydride in pyridine solution to give 2′,3′,5′-tri-*O*-acetylguanosine[1] (**1b**) which then undergoes further acylation on N(2) to give the tetra-acetyl derivative[2] (**1c**). Treatment of guanosine with benzoyl chloride in pyridine solution gives *N*(2),*O*(2′),*O*(3′),*O*(5′)-tetrabenzoylguanosine[2] (**1d**), and (**1b**) similarly undergoes acylation on N(2) when it is treated with *p*-anisoyl chloride under the same conditions. We now report that when (**1b**) is allowed to react with 2,6-dichlorobenzoyl chloride or with arenesulphonyl chlorides in pyridine solution, acylation takes place on O(6) of the guanine residue.

Treatment of (**1b**) with an excess of 2,6-dichlorobenzoyl chloride in pyridine solution gives the *O*(6)-aroyl derivative (**2**) as virtually the sole product. The latter compound (**2**) has been isolated pure in 61% yield and obtained as colourless crystals, m.p. 185 °C; its structure has been assigned on the basis of microanalytical and spectroscopic data.† 2′,3′,5′-Tri-*O*-acetylguanosine[1] (**1b**) reacts similarly with mesitylene-, *p*-bromobenzene-, and toluene-*p*-sulphonyl chlorides to give the corresponding *O*(6)-arenesulphonyl derivatives (**3a**, **3b** and **3c**, respectively). Of these compounds only the first (**3a**) has been obtained crystalline (68% yield, m.p. 141–142 °C). However, the spectroscopic properties of all three compounds closely resemble those of 2-amino-6-chloro-9-β-D-(2′,3′,5′-tri-*O*-acetylribofuranosyl) purine[3] (**4a**) and also those of (**2**). The structure of (**3a**) follows conclusively from its conversion, in nearly quantitative yield, to (**4b**)[3] by treatment first with a 3-fold excess of dimethylamine in dioxan–methanol (10 : 1 v/v) for 1 h at 20 °C followed by deacetylation with methanolic ammonia. Reaction between (**1b**) and methanesulphonyl chloride in pyridine solution also appears, on the basis of spectroscopic evidence, to give the *O*(6)-mesyl derivative (**3d**) but the latter compound has so far been isolated only in modest yield.‡

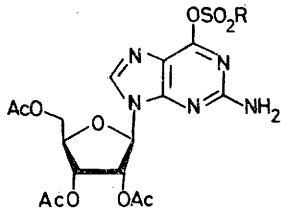


(1)

a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Ac$
c; $R^1 = R^2 = Ac$
d; $R^1 = R^2 = PhCO$

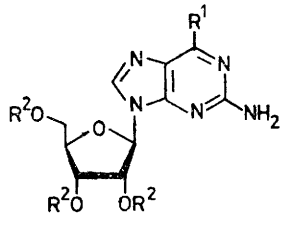


(2)



(3)

a; R = 2,4,6-$Me_3C_6H_2$
b; R = 4-BrC_6H_4
c; R = 4-MeC_6H_4
d; R = Me



(4)

a; $R^1 = Cl$, $R^2 = Ac$
b; $R^1 = NMe_2$, $R^2 = H$
c; R^1 = morpholino, $R^2 = Ac$

† Satisfactory microanalyses have been obtained for all new crystalline compounds described. The most notable feature of the n.m.r. spectrum ($CDCl_3$) of (**2**) is a broad singlet at δ 5·30 (2H), assignable to the resonance of the NH_2 protons, which disappears on shaking with D_2O. The i.r. spectrum of (**2**) (KBr disc), which has no absorption bands between 1630 and *ca.* 1740 cm^{-1}, suggests the absence of an *N*-aroyl group; the u.v. spectrum (95% EtOH) of (**2**) exhibits a maximum at 305 nm and is uncharacteristic of an *N*(2)-acyl derivative of guanosine (see ref. 2).

‡ We previously reported (P. K. Bridson, W. Markiewicz, and C. B. Reese, *J.C.S. Chem. Comm.*, 1977, 447) that (**1d**) reacts with methanesulphonyl chloride and triethylamine in dichloromethane solution to give its *O*(6)-mesyl derivative which may be isolated as a pure crystalline solid in 75% yield.

It is as yet unclear why the guanine residue of (**1b**) is attacked by some acylating agents on N(2) and by others on O(6). However, the crystalline *O*(6)-acyl guanosine derivatives [(**2**) and (**3a**)] are potentially useful synthetic intermediates. The mesitylenesulphonyl derivative (**3a**) is, as indicated above, particularly susceptible to nucleophilic substitution at C(6); indeed, it reacts with morpholine in dioxan solution to give (**4c**) at *ca.* twice the rate of (**4a**). Both derivatives [(**2**) and (**3a**)] are readily unblocked at O(6) ($t_{\frac{1}{2}}$ = 75 and 70 min, respectively) by treatment with 0·5 M potassium carbonate in water–ethanol (1 : 1 v/v) at 20 °C; it is therefore possible that they may be used as intermediates in the synthesis of otherwise inaccessible guanosine derivatives.

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