Reactions of Methylhydrazine and Hydrazine with 8-Bromo-2′-*O*-toluene-*p*-sulphonyladenosine

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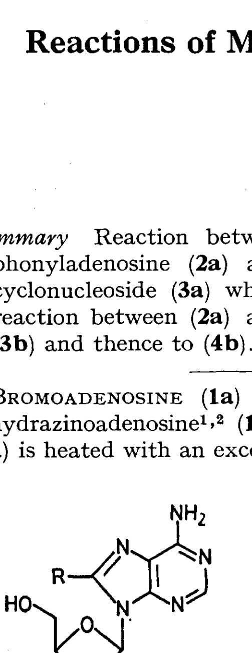
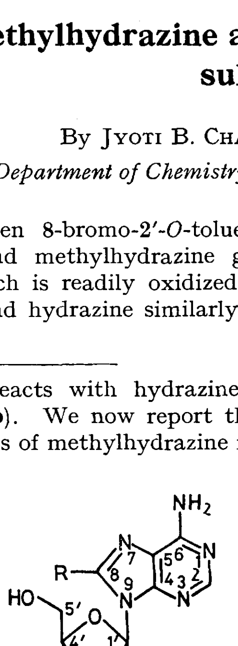
Summary Reaction between 8-bromo-2′-*O*-toluene-*p*-sulphonyladenosine (**2a**) and methylhydrazine gives the cyclonucleoside (**3a**) which is readily oxidized to (**4a**); reaction between (**2a**) and hydrazine similarly leads to (**3b**) and thence to (**4b**).

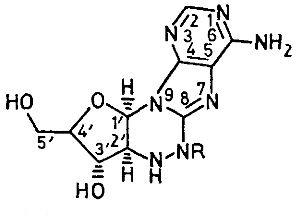
8-Bromoadenosine (**1a**) reacts with hydrazine to give 8-hydrazinoadenosine[1,2] (**1b**). We now report that when (**1a**) is heated with an excess of methylhydrazine in boiling ethanol solution for 14 h, the 8-methylhydrazino-derivative (**1c**) is obtained as a crystalline compound in 79% isolated yield.† The structure of the latter compound (**1c**) follows from its conversion, on treatment with pentyl nitrite and dilute hydrochloric acid, into 8-methylaminoadenosine[2] (**1d**) in high yield. When 8-bromo-2′-*O*-toluene-*p*-sulphonyladenosine[3] (**2a**) is heated with an excess of methylhydrazine in boiling ethanol solution for 165 min, it is quantitatively converted into the 8,2′-cyclonucleoside derivative (**3a**) which may be isolated as a colourless crystalline solid, m.p. 221—222 °C, in 93% yield.



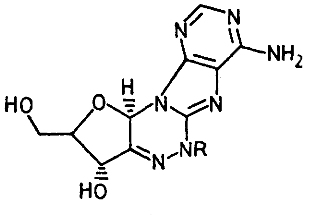
(1) a; R = Br
b; R = -NHNH$_2$
c; R = -NMeNH$_2$
d; R = -NHMe



(2) a; R = Br
b; R = -NHNH$_2$



(3) a; R = Me
b; R = H



(4) a; R = Me
b; R = H

When (**3a**) is heated, under reflux, in methanol solution for 10 min with a stoicheiometric quantity of mercury(II) acetate, it is oxidized to the corresponding 8,2′-cyclonucleoside hydrazone (**4a**) which may be isolated from the products as a crystalline solid in 82% yield. The oxidative transformation of (**3a**) into (**4a**), which may be monitored by u.v. spectroscopy, was established firmly by n.m.r. spectroscopy.‡

When (**2a**) is heated, under reflux, with an excess of hydrazine hydrate in methanol solution for 17 h, the corresponding 8-hydrazino-derivative (**2b**) is obtained and may be isolated as a colourless crystalline compound in 85% yield. When the latter compound (**2b**) is heated, under reflux, in *ethanol* solution for 17 h, it is converted in > 70% yield into the 8,2′-cyclonucleoside derivative (**3b**) contaminated with its oxidation product (**4b**; *ca.* 15%). A mixture of (**3b**) and (**4b**) in similar proportions is more easily obtained and in *ca.* 76% yield when (**2a**) is heated, under reflux, with an excess of hydrazine hydrate in ethanol solution for 18 h. Treatment of this mixture with mercury(II) acetate under the above conditions gives pure (**4b**) which may be isolated as a crystalline solid in 95% yield. It is noteworthy that none of the *N*(1),*N*(1)-substituted hydrazine derivative (**5**) was detected in the products of any of the above reactions.

We are unaware of any previous report of a cyclonucleoside synthesis in which the cyclization leads to the forma-

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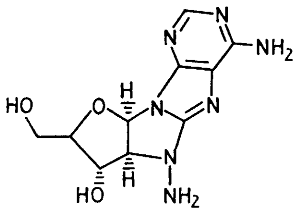
† Satisfactory microanalytical and spectroscopic (u.v., mass, ^1H and ^{13}C n.m.r.) data have been obtained for all new compounds described.

‡ The conversion of (**3a**) [^1H n.m.r., $(CD_3)_2SO$, δ 8·13 (1H, s), 5·84 (1H, d, *J* 4·9 Hz), 4·00 (1H, dd, *J* 3 and 5 Hz), 3·79 (1H, m), 3·52 (3H, m), and 3·20 (3H, s); ^{13}C n.m.r., $(CD_3)_2SO$, includes: δ 60·5, 62·2, 71·9, 79·0, and 85·1 p.p.m.] into (**4a**) [^1H n.m.r., $(CD_3)_2SO$, includes: 8·05 (1H, s), 6·25 (1H, s), 4·52 (1H, d, *J ca.* 2 Hz), 4·09 (1H, m), and 3·61 (3H, s); ^{13}C n.m.r., $(CD_3)_2SO$, includes: δ 60·8, 69·4, 74·8, and 84·8 p.p.m.] is accompanied by the downfield shifts of the H(1′) [from 5·84(d) to 6·25(s)] and C(2′) (from 62·3 to >140 p.p.m.) and by the upfield shifts of the C(1)′ (from 79·0 to 74·8 p.p.m.) and C(3′) (from 71·9 to 69·4 p.p.m.) resonance signals.



(5)

tion of a two-atom bridge between the sugar unit and the purine or pyrimidine base. We are also unaware of examples of reactions other than those described in this Communication in which a change in the oxidation level of a nucleoside sugar carbon atom has been facilitated by cyclonucleoside formation.

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