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INVESTIGATIONS ON DERIVATIVES OF 5'-O-TOSYLADENOSINE

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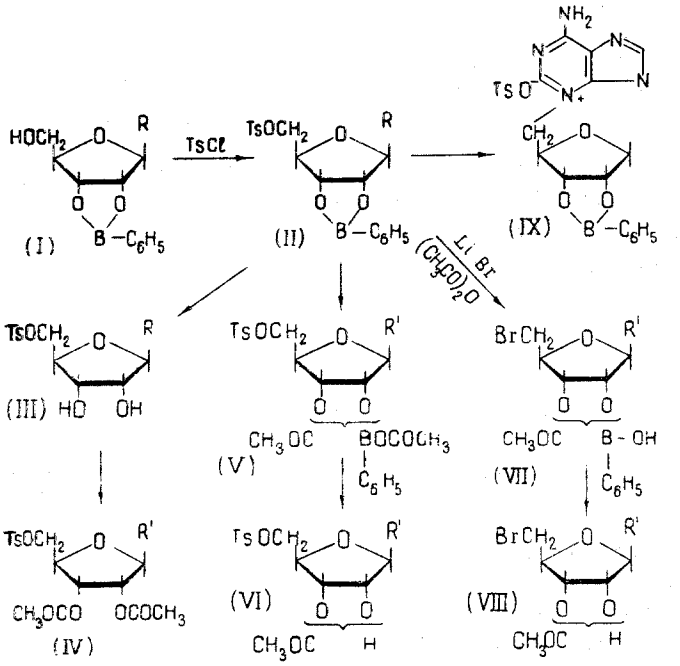
Derivatives of 5'-O-tosyladenosine are used for the synthesis of S-adenosylmethionine [1], 5'-deoxyadenosyldimethylbenzimidazolylcobamide coenzyme [2], and other derivatives of 5'-deoxyadenosine. However, when 2',3'-isopropylidene-5'-O-tosyladenosine is used, the situation is complicated by the cyclization of the tosylate and the formation of cycloadenosine-5' toluenesulfonate [3]. Intramolecular alkylation was excluded by the previous acylation of the amino group of the purine base. In this way halogen derivatives of 5'-deoxyadenosine have been obtained. But, in this case also, the subsequent removal of the protective grouping has been found difficult [4].



A study of the benzeneboronates of the nucleosides has enabled us to use benzeneboronic acid in phosphorylation reactions as a stable and easily removed protective grouping and to obtain nucleoside mono-, di-, and triphosphates [5].

In the present paper we give the results of further investigations of reactions with adenosine-2',3' benzeneborate by preparation from tosyl derivatives and their reactions. The use of such compounds for the synthesis of adenosylcobaloxime has been reported previously [6].

The action of p-toluenesulfonyl chloride on adenosine-2',3' benzeneboronate (I) gave 5'-O-tosyladenosine-2',3' benzeneboronate (II). After its treatment with 1,3-propanediol, 5'-O-tosyladenosine (III) was isolated. The acylation of the tosylate (III) with acetic anhydride on heating gave N^6-acetyl-2'-3'-di-O-acetyl-5'-O-tosyladenosine (IV).

Heating the tosylate (II) with acetic anhydride led to the partial cleavage of the B—O bond and the formation of the mixed anhydride (V). The removal of the benzeneboronate group from the mixed anhydride (V) under mild conditions gave a mixture of the 2'- and 3'-acetates (VI), which may be important in the synthesis of oligonucleotides.

By the reaction of the tosylate (II) with lithium bromide in acetic anhydride at 100° C, we obtained N^6-acetyl-3'(2')-O-acetyl-5'-bromo-5'-deoxyadenosine-2'(3') benzeneboronate (VII). The same bromide (VII) was obtained from the mixed anhydride (V). When the bromide (VII) was treated with 1,3-propanediol, N^6-acetyl-2'(3')-O-acetyl-5'-bromo-5'-deoxyadenosine (VIII) was isolated.

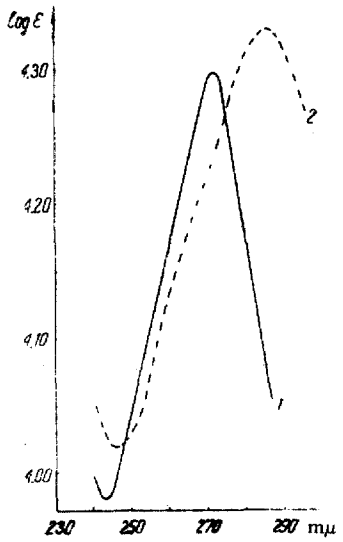
The prolonged heating of the tosylate (II) in acetone yielded a salt of the cyclonucleoside (IX). In dioxane at 20° C, the cyclization of the tosylate (II) is complete only a few minutes after its dissolution. In comparison with the

tosylate (II), the salt of the cyclonucleoside is less mobile on chromatography and has a bathochromic shift of the maximum of the absorption band in the UV spectrum by 13 mμ.

Frequencies of the Vibrations in the IR Spectra of the Compounds Synthesized, cm^{-1}

Compound	δNH_2	Vibrations of the purine ring	$\nu_s(SO_2)$	$\nu_{as}(SO_2)$	B–O	B–C_6H_5	ν(C–O)	Amide (I)	Amide (II)
Adensoine-2′, 3′ benzeneboronate (I)	1645	1605 1580	—	—	1370	1440	—	—	—
5′-O-Tosyladenosine-2′,3′ benzeneboronate (II)	1645	1600 1580	1180	1360	1370	1440	—	—	—
5′-O-Tosyladenosine (III)	1645	1600 1580	1175	1360	—	—	—	—	—
N^6-Acetyl-2′,3′-di-O-acetyl-5′-O-tosyladenosine (IV)	—	1600 1575	1180	1365	—	—	1735	1715	1625
N^6-acetyl-3′(2′)-O-acetyl-5′-O-tosyladenosine-2′-(3′)-acetylbenzeneboronate	—	1610 1585	1180	1375	—	1440	1755	1715	1630

The structure of compounds (I)–(V) was confirmed by their IR spectra (table). The figure gives the UV spectra of the derivatives of 5′-O-tosyladenosine synthesized. The introduction of an acetyl group into the molecule of (II) led to a bathochromic shift of the maximum of the absorption band in the UV spectrum by 11, 26, and 10 mμ, respectively, for compounds (IV), (V), and (VII) [7].



UV spectra (in ethanol) of N^6-acetyl-2′,3′-di-O-acetyl-5′-O-tosyladenosine (1) and N^6-acetyl-3′(2′)-O-acetyl-5′-O-tosyladenosine-2′(3′) O-acetylbenzeneboronate (2).

Experimental

The substances were identified by chromatography on FN-1 paper. The following systems of solvents were used: 1) n-butanol—acetic acid—water (4 : 1 : 5); 2) isopropanol—ammonia—water (7 : 1 : 2). The IR spectra were recorded on a UR-10 instrument (tablets with KBr and chloroform solutions) and the UV spectra on an SF-4 instrument.

5′-O-Tosyladenosine-2′,3′-benzeneboronate (II). With stirring, 0.96 g of p-toluenesulfonyl chloride was added to a solution of 1.76 g of adenosine-2′,3′ benzeneboronate (I) in 40 ml of pyridine, and the mixture was left at 0° C for 24 hr. Then it was neutralized at 3–5° C. The solvent was distilled off to small volume. An amorphous precipitate was formed using ether. Yield 1.26 g (49.5%), R_{Ad} 2.0 (1); 1.22 (2). UV spectrum: λ_{max} (in methanol) 260 mμ (log ε 4.16).

Found, %: C 54.22; H 4.64. Calculated for $C_{23}H_{22}BN_5O_6S$, %: C 54.46; H 4.37.

5′-O-Tosyladenosine (III). In drops, 0.08 ml of 1,3-propanediol was added to a solution of 0.3 g of the amorphous ester (II) in 10 ml of chloroform. The chloroform was driven off. The residue was washed with ether. Yield 0.22 g (96.5%), mp 152–154° C; R_f 0.74 (1); 0.72 (2); UV spectrum: λ_{max} (in methanol) 260 mμ (log ε 4.11).

Found, %: C 48.5; H 5.19. Calculated for $C_{17}H_{19}N_5O_6S$, %: C 48.45; H 5.02.

N^6-Acetyl-2′,3′-di-O-acetyl-5′-O-tosyladenosine (IV). A mixture of 0.28 g of 5′-O-tosyladenosine (III) and 18 ml of acetic anhydride was heated at 100° C for 1 hr. The solvent was driven off, and the residue was dissolved in benzene and precipitated with n-hexane. Yield 0.36 g (94.5%); R_f 0.92 (1): UV spectrum: λ_{max} (in ethanol) 271 mμ (log ε 4.3).

Found, %: C 50.00; H 4.93. Calculated for $C_{23}H_{25}N_5O_9S$, %: C 50.46; H 4.60.

N^6-Acetyl-3′(2′)-O-acetyl-5′-O-tosyladenosine-2′(3′) O-acetylbenzeneboronate (V). A solution of 0.12 g of the tosylate (II) in 8 ml of acetic anhydride was heated at 100° C for 1 hr and the solution was evaporated. The residue was an amorphous substance. Compound (V) was isolated by precipitation from chloroform with n-hexane. Yield 0.165 g (94.5%); R_f 0.9 (1), 0.8 (2); UV spectrum: λ_{max} (in ethanol) 286 mμ (log ε 4.34).

N^6-Acetyl-3′(2′)-O-acetyl-5′-bromo-5′-deoxyadenosine-2′(3′) benzeneboronate (VII). A solution of 0.5 g of the tosylate (II) in 40 ml of acetic anhydride was heated with 44 g of lithium bromide at 100° C for 1 hr. The cooled solution was mixed with 20 ml of chloroform, washed with 15 ml of saturated sodium sulfite solution and 10 ml of water,

and was then evaporated in vacuum. The residue was dissolved in benzene and precipitated with n-hexane. Yield 0.36 g (86%), mp 90–92° C; R_f 0.95 (1); UV spectrum: λ_{max} (in ethanol) 270 mμ (log ε 4.03).

Found, %: C 46.63, H 4.25, 13.57. Calculated for $C_{19}H_{22}BN_5O_6Br$, %: C 46.60; H 4.10, 13.63.

Conclusions

Acylation and nucleophilic substitution reactions in a number of derivatives of 5'-O-tosyladenosine have been described.

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