hydrazoic acid may take any role since no trace of III was produced without sodium azide, only recovered I.

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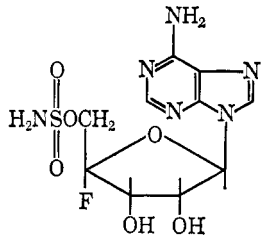
The Synthesis of Adenine 5′-*O*-Sulfamoyl Nucleosides Related to Nucleocidin[1]

Sir:

Continued interest in the potent antitrypanosomal[2] antibiotic nucleocidin[3] has been prompted by the demonstration of its activity as an inhibitor of protein biosynthesis.[4] A recent communication[5] has redefined the structure of nucleocidin as 5′-*O*-sulfamoyl-4′-*C*-fluoroadenosine (**1**) (or a stereoisomer) based on ^1H and ^{19}F nmr data and mass spectroscopy. Nucleocidin is the only known antibiotic containing the sulfamate ester group and is one of the very few naturally occurring fluoro compounds.[6] Indeed, sulfamate esters with an unsubstituted nitrogen are rare; only a few simple aliphatic examples have been described.[7]



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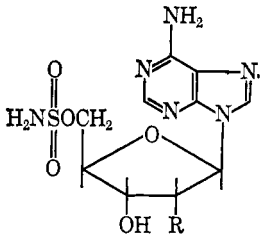

2, R = OH
3, R = H

We wish to report the preparation of 5′-*O*-sulfamoyladenosine (**2**) and 5′-*O*-sulfamoyl-2′-deoxyadenosine (**3**), which are the first synthetic sulfamate esters of nucleosides and are direct structural models of nucleocidin. A solution of 2′,3′-*O*-ethoxymethylideneadenosine[8] in 1,2-dimethoxyethane (glyme) was treated with 1 equiv of sodium hydride. After reaction ceased, a solution of 1 equiv of sulfamoyl chloride in glyme was added to the stirred suspension. Purification of 5′-*O*-sulfamoyl-2′,3′-*O*-ethoxymethylideneadenosine by chromatography on silca gel followed by deblocking with 5% formic acid and then aqueous ammonia gave 5′-*O*-sulfamoyladenosine (**2**) monohydrate[9] in 33% over-all yield. The product **2** softens at 153–155°, decomposes at 165°; $[\alpha]^{33}D$ −33.6° (*c* 1.0, DMF); $[\alpha]^{27}D$ −33° (*c* 1.0, EtOH–0.1 *N* HCl, 1:1); uv max (pH 1) 257 mμ (ε 14,800), (pH 11) 259 mμ (ε 15,400); ir (KBr) 1180 cm^{-1} (5′-OSO_2NH_2); nmr (DMSO-d_6) δ 4.31 (broad s, 3, 5′-H (2) plus 4′-H (1)), 3.50 (s, 2, H_2O), 7.33 (s, 2, 6-NH_2), 7.63 (s, 2, 5′-OSO_2NH_2); addition of D_2O caused the peaks at δ 3.50, 7.33, and 7.63 to disappear with a corresponding increase at δ 3.70 (HDO).

Two equivalents of sulfamoyl chloride was added slowly to a solution of 3′-*O*-acetyl-2′-deoxyadenosine[10] in pyridine–glyme at 0°. The residue obtained after addition of sodium carbonate and evaporation of the solvent was partitioned between ethyl acetate and water and the solid remaining after evaporation of the organic phase was recrystallized from ethanol to give a 39% yield of 5′-*O*-sulfamoyl-3′-*O*-acetyl-2′-deoxyadenosine,[9] mp 157–159°; uv max (pH 1) 257 mμ (ε 14,000), (pH 11) 259 mμ (ε 16,300); ir (KBr) 1180 cm^{-1} (5′-OSO_2NH_2), 1740 cm^{-1} (3′-OAc); nmr (DMSO-d_6–$CDCl_3$, 30:70) δ 4.43 (broad s, 3, 5′-H (2) plus 4′-H (1)), 2.15 (s, 3, 3′-OAc), 6.92 (s, 2, 6-NH_2), 7.50 (s, 2, 5′-OSO_2NH_2).

This product was deblocked with methanolic ammonia and recrystallized from aqueous ethanol, dissolved in water, and then lyophilized to give a 76% yield of amorphous 5′-*O*-sulfamoyl-2′-deoxyadenosine monohydrate[9] (**3**), softens at 114°, decomposes at 170°; $[\alpha]^{30}D$ −23.5° (*c* 1, H_2O); uv max (pH 1) 258 mμ (ε 15,600), (pH 11) 259 mμ (ε 16,800); ir (KBr) 1180 cm^{-1} (5′-OSO_2NH_2); nmr (DMSO-d_6) δ 4.16 (broad s, 3, 5′-H (2) plus 4′-H (1)), 7.25 (s, 2, 6-NH_2), 7.57 (s, 2, 5′-OSO_2NH_2), 5.53 (broad s, 1, 3′-*OH*), 3.35 (s, 2, H_2O); addition of D_2O caused the peaks at δ 7.25, 7.57, 5.53, and 3.35 to disappear with a corresponding increase at δ 3.55 (HDO).

The ir spectra of **2** and **3** are similar to that of nucleocidin[3a] and show the same band at 1180 cm^{-1} (covalent $ROSO_2NH_2$). The nmr peak assigned to the 5′ protons in **2** or **3** is shifted downfield approximately 0.6 δ in DMSO-d_6 (relative to that of adenosine or 2′-deoxyadenosine), which corresponds to the position assigned[5] to the 5′ protons of nucleocidin. The uv spectra of nucleocidin[3a] are identical with those of **2** and **3**. Optical rotations of nucleocidin[3a] (**1**) and **2** are essentially identical.

A solution of 5′-*O*-sulfamoyl-2′,3′-*O*-isopropylideneadenosine[9] in 0.5% MeOH in MeCN was heated at reflux for 28 hr. The starting material was absent and one new chromatographically homogeneous product (tlc) was present which exhibited identical mobility with 2′,3′-*O*-isopropylideneadenosine-$N^3 \rightarrow C^{5'}$-cyclonucleoside[11] in 5% aqueous ammonium chloride on SilicAR-7GF[12] and had uv max (H_2O) 272.5 mμ.[13] Compound *2* was heated in absolute DMF for 24 hr at

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100° with exclusion of moisture. The reaction mixture was chromatographed on SilicAR-7GF and the salt-like product, uv max (MeOH) 269 mμ, was eluted with methanol. Identical treatment of nucleocidin[14] gave similar material, uv max (MeOH) 272 mμ, and 5′-*O*-tosyladenosine[15] (**4**) gave the $N^3 \rightarrow 5'$-cyclonucleoside, uv max (MeOH) 271 mμ. This parallel behavior of **1**, **2**, and **4** defines the stereochemistry of the 1′-adenine and 4′-sulfamoyloxymethyl substituents of nucleocidin as *cis*.[11]

The circular dichroism curves of nucleocidin[14] and **2** in water are identical within experimental error throughout the range 230–290 mμ and are similar to that of adenosine.[16] This indicates that the adenine ring is above the sugar plane.[16,17] Thus, structure **1** for nucleocidin[5] is consistent with the present data.

It is of interest that 5′-*O*-sulfamoyladenosine (**2**) produces 50% inhibition of *S. faecalis* at 4×10^{-6} *M* compared to a similar inhibition by nucleocidin at 5×10^{-7} *M*.[18] Compound **2** also has been found to exhibit pronounced *in vitro* inhibition of *Trypanosoma rhodesiense* at 10^{-9} *M*.[19] 5′-*O*-Sulfamoyladenosine (**2**) may be viewed[20] as an analog of adenosine 5′-phosphate (AMP) which, however, should readily cross cellular membranes due to the nonionic character of the sulfamoyl ester group.

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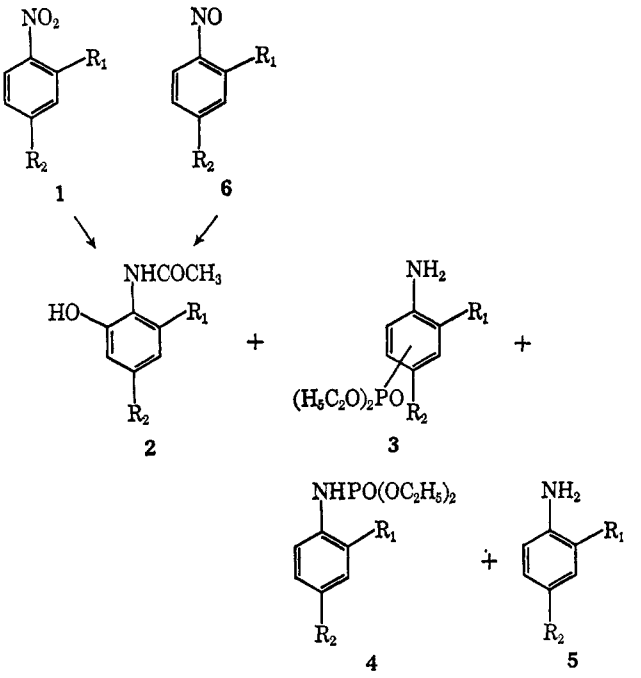
Generation of Aryl Nitrenes in the Presence of Acetic Acid by Deoxygenation of Aromatic Nitro and Nitroso Compounds[1]

Sir:

We wish to report that the presence of acetic acid (5% by volume) in triethyl phosphite solutions employed for photochemical deoxygenation of aromatic nitro compounds[2] or deoxygenation of aromatic nitroso compounds[3] profoundly affects the nature of the reaction products. Our results suggest that a substantial fraction of the aryl nitrenes generated under these conditions are converted to aryl nitrenium ions. This result implies that aryl nitrenes are relatively basic, a conclusion which is of significance to the interpretation of the chemistry of aryl nitrenes in general.

The product mixtures from photochemical deoxygenation of aromatic nitro compounds in the presence of acetic acid include significant amounts of *o*-hydroxyacetanilides (**2**) and diethyl aminophenylphosphonates



(**3**). Diethyl N-arylphosphoramidates (**4**) are also formed but in yields generally lower than those observed in the absence of acetic acid. Anilines are also found. The formation of N-aryl 2-acetimidylpyridines from *o*-methylnitrobenzenes, which is an important process in the absence of acetic acid,[2] is completely suppressed. Diethyl aminophenylphosphonates are not formed in the absence of acetic acid. Nonphotochemical deoxygenation of aromatic nitroso compounds is also believed[4] to generate aryl nitrenes, and the product composition from deoxygenation of nitroso compounds is affected in a similar way when acetic acid is present. Table I summarizes the data. Structural assignments for the new compounds *o*-**3a**, *o*-**3b**, *p*-**3b**, *o*-**3c**, *o*-**3d**, and *m*-**3d** rest on correct elemental analyses and definitive infrared and nmr spectral data. The known compounds **2a–d**, *p*-**3a**, **4b–d**, and **5a–d** show spectral data in accord with expectation and physical constants in agreement with literature data.

Table I. Product Distribution from Deoxygenations

	% yields[a]					
		3[b]				
Reactant	2	*o*	*m*	*p*	4	5
1a	6	8	*c*	8	*c*	4
6a	11	3	*c*	6	3	*c*
1b	*c*	2	*c*	10	7	2
6b	*c*	2	*c*	9	12	2
1c	27	11	*c*		2	10
6c	23	9	*c*		3	2
1d	14	6	6		9	4

[a] Yields are isolated yields, normally after column chromatography. [b] The designations *o*, *m*, and *p* denote the relationship between the amino and phosphoryl substituents. [c] Not definitively characterized; yield is less than 3%.

Aryl nitrenium ions are expected to undergo nucleophilic attack principally at the *ortho* and *para* carbon atoms[5] and can be invoked as intermediates in the

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