yielded benzyl alcohol containing less than 0.5 atom % ^{18}O.

The data presented above clearly establish that the source of oxygen in the microsomal dealkylation reaction is molecular oxygen. This finding provides further support for a reaction pathway involving direct hydroxylation of the carbon atom, a mechanism compatible with other biochemical data.[1,2,10]

The experiments described herein pertain only to the mammalian hepatic microsomal system. Their relationship to other dealkylases of animal or plant origin is at present unknown.

Acknowledgment. The authors are indebted to Mrs. Catherine Cobb for assistance with the enzyme studies.

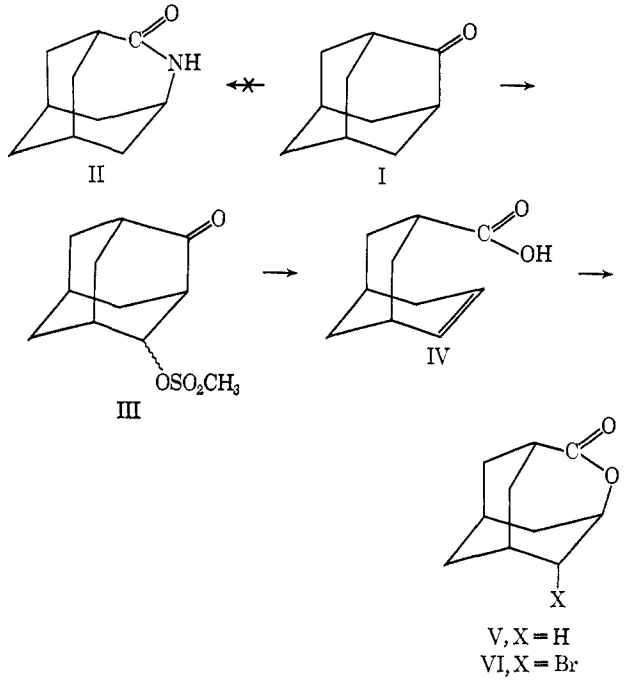
(10) M. H. Bickel, H. J. Weder, and H. Aebi, *Biochem. Biophys. Res. Commun.*, **33**, 1012 (1968).

Robert E. McMahon, Hilman W. Culp, John C. Occolowitz
Lilly Research Laboratories
Indianapolis, Indiana 46206
Received March 27, 1969

Novel Substitution Reaction of Adamantanone. A Simple Synthesis of Bicyclo[3.3.1]non-2-ene-7-carboxylic Acid[1]

Sir:

In spite of the extensive studies on the substitution reactions of adamantane and its derivatives,[2] there seem



to be no reports on direct substitution reactions of adamantanone (I). We wish to report a new and novel substitution reaction of I at its 4 position.

(1) Synthesis of Adamantane Derivatives. VIII. Part VII: T. Sasaki, S. Eguchi and T. Toru, *Tetrahedron*, in press.

(2) (a) For a review, see R. G. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.* 64, 277 (1964); (b) for the bridgehead reactivity, see R. C. Fort, Jr., and P. von R. Schleyer, *Advan. Alicyclic Chem.*, **1**, 283 (1966); (c) for some recent works on 2-substitution reactions, see W. V. Curran and R. B. Angier, *Chem. Commun.*, 563 (1967); M. A. McKervy, *Chem. Ind.* (London), 1791 (1967); W. H. W. Lunn, W. D. Podmore, and S. S. Szinai, *J. Chem. Soc., C*, 1657 (1968); I. Tabushi, J. Hamuro, and R. Oda, *J. Org. Chem.*, **33**, 2108 (1968); A. C. Udding, J. Strating, and H. Wynberg, *Tetrahedron Letters*, 1345 (1968).

In view of the expected conversion of I into the ring-enlarged 2-aza-3-oxotricyclo[4.3.1.1^{4,7}]undecane (II) by the Schmidt reaction, I was treated with sodium azide in methanesulfonic acid under the reaction conditions given by Smith and Berry.[3] The product, obtained as colorless crystals, mp 73–75°, in 90% yield, was characterized unexpectedly as 4-methylsulfonoxyadamantanone (III) on the basis of the analytical data (*Anal.* Calcd for $C_{11}H_{16}O_4S$: C, 54.07; H, 6.60. Found: C, 53.82; H, 6.69) and the following spectral data; the infrared spectrum (KBr) exhibited strong bands at 1720 ($\nu_{C=O}$) and 1340 and 1180 (ν_{SO_2}) cm^{-1} but no NH band. In the nmr spectrum (100 MHz, $CDCl_3$) signals at τ 5.20 (1 H, unsymmetrical triplet, J = 3.5 Hz, C-4 proton),[4] 6.95 (3 H, singlet, OSO_2CH_3), 7.11 (1 H, broad singlet, C-3 proton), 7.44 (1 H, broad singlet, C-1 proton), 7.51–8.40 (10 H, complex multiplet, other adamantane ring protons) appeared and the mass spectrum had peaks at *m/e* 244 (5, M$^+$), 149 (58), 121 (17), and 79 (100); 2,4-dinitrophenylhydrazone mp 227–229°; oxime mp 131–133.°.

III was cleaved to the known bicyclo[3.3.1]non-2-ene-7-carboxylic acid (IV)[5] on alkaline hydrolysis (aqueous potassium hydroxide and/or sodium carbonate) in 85% yield; this provided chemical proof of structure III, for if a methylsulfonoxy group is present at C-1 and/or C-5, the hydrolysis product should be noradamantane-1-carboxylic acid[6] and/or 1,7-dehydrobicyclo[3.3.1]nonane-3-carboxylic acid, respectively. The structure of IV was confirmed on the basis of its physical (mp 195–196°, lit.[5] mp 195–198°) and spectral data; the infrared spectrum was superimposable with that of an authentic sample[7] and the nmr spectrum (60 MHz, $CDCl_3$), having signals at τ −1.3 (1 H, singlet, COOH), 4.38 (2 H, unsymmetrical singlet with a weak satellite at τ 4.26 and 4.52, –CH=CH–), and 7.3–8.7 (11 H, complex multiplet, other bicyclononene ring protons), was compatible with the assigned structure IV. For further confirmation of the structure, IV was converted to the known lactone V, mp 296–297° (lit.[5] mp 288–290°), in 90% yield, and to a new bromolactone, VI,[8] mp 139°, in 96% yield.

The fact that a facile quasi-Favorskii reaction of III[9] had occurred to give IV in good yield provides evidence of the presence of the 4-methylsulfonoxy group in an adamantanone ring.

Treatment of adamantane with sodium azide under similar reaction conditions gave only recovered adamantane, indicating a carbonyl function is necessary for the new substitution reaction. Formation of III from I under Schmidt reaction conditions might involve 1,3-hydride transfer,[10] followed by oxidation or disproportionation; furthermore, it should be mentioned that

(3) P. A. S. Smith and W. L. Berry, *J. Org. Chem.*, 26, 27 (1961).

(4) For some detailed discussion of the nmr data of 4-substituted adamantanones, see G. Snatzke and G. Eckhardt, *Chem. Ber.*, **101**, 2010 (1968).

(5) A. C. Udding, H. Wynberg, and J. Strating, *Tetrahedron Letters*, 5719 (1968).

(6) B. R. Vogt and J. R. E. Hoover, *ibid.*, 2841 (1967).

(7) The infrared spectrum was kindly sent by Professor H. Wynberg.

(8) The analytical and spectral data were all compatible with VI.

(9) Some cleavage reactions of bicyclic ketones involving a β-tosyloxy group have been reported recently: (a) W. Kraus and W. Rothenwöhrer, *Tetrahedron Letters*, 1007 (1968); (b) *ibid.*, 1013 (1968).

(10) For 1,2-hydride shifts of adamantyl cations in sulfuric acid, see (a) H. W. Geluk and J. L. M. A. Schlatmann, *Tetrahedron*, **24**, 5361 (1968); (b) M. A. McKervy, J. R. Alford, J. F. McGarity, and E. J. F. Rea, *Tetrahedron Letters*, 5165 (1968).

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

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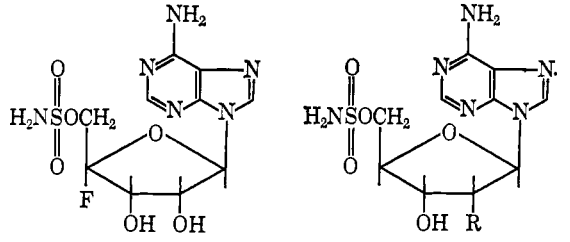
Tadashi Sasaki, Shoji Eguchi, Takeshi Toru
Institute of Applied Organic Chemistry, Faculty of Engineering
Nagoya University, Chikusa-ku, Nagoya, Japan
Received March 5, 1969

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]



1 **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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