aid in obtaining X-ray measurements and Dr. Walter Dean of this department for help in solution of the structures. We also thank the National Science Foundation for a Departmental Instrument Grant in support of the purchase of a Finnigan Model 4000 GC–MS data system.

Registry No.—**1**, 62640-05-5; **5**, 4949-20-6; **6**, 3958-79-0; **8**, 66515-72-8; **9**, 66515-73-9; **10**, 66515-74-0; **11**, 66515-75-1; **12**, 66515-76-2; **15**, 66538-02-1; **16**, 66538-03-2; **17**, 66538-04-3; **18**, 66515-77-3; **19**, 66515-78-4; **20**, 66515-79-5; **21**, 66538-05-4; **23**, 66515-80-8; **24**, 66515-81-9; **29**, 66515-82-0; **30**, 66551-68-6; **31**, 66515-83-1; **32**, 66515-84-2; **33**, 66515-85-3; 2,4-pentadienyl chloride, 40596-30-3; 4a-α-carbomethoxy-5β-chloromethyl-4a,5,8,8a-β-tetrahydronaphthalene-1,4-dione, 66515-86-4; 4a-α-carbomethoxy-5β-chloromethyl-2,3,4a,5,8,8a-β-hexahydronaphthalene-1,4-dione, 66515-87-5.

Supplementary Material Available. Tables listing atom parameters, thermal parameters, bond distances, and bond angles for compounds **10** and **11** (12 pages). Ordering information is given on any current masthead page.

References and Notes

(1) I. Kubo, Y.-W. Lee, V. Balogh-Nair, K. Nakanishi, and A. Chapya, *J. Chem. Soc., Chem. Commun.*, 949 (1976).

(2) K. Nakanishi, T. Goto, S. Ito, S. Natori, and S. Nozoe, Ed., "Natural Products Chemistry", Vol. 1, Academic Press, New York, N.Y., 1974, p 208. For recent examples, see, W. Herz, A.-M. Pilotti, A.-C. Soderholm, I. Shuhama, and W. Vichnewski, *J. Org. Chem.* **42**, 3913 (1977).

(3) (a) K. Munakata in "Control of Insect Behavior by Natural Products", Academic Press, New York, N.Y., 1970, pp 179–187. (b) N. Kato, S. Shibayama, and K. Munakata, *J. Chem. Soc. D* 1632 (1971). (c) S. Hosozawa, N. Kato, K. Munakata, and Y.-L. Chen, *Agric. Biol. Chem.*, **38**, 1045 (1974). (d) S. Hosozawa, N. Kato, and K. Munakata, *Agric. Biol. Chem.*, **38**, 823 (1974). (e) S. Hosozawa, N. Kato, and K. Munakata, **Tetrahedron Lett.**, 3753 (1974).

(4) (a) W. Nudenberg, A. Gaddis, and L. Butz, *J. Org. Chem.*, **8**, 500 (1943). (b) J. Cason, *Org. React.*, **4**, 354.

(5) (a) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967). (b) Z. Stojanac, R. Dickinson, N. Stojanac, R. Waznow, and Z. Valenta, *Can. J. Chem.*, **53**, 616 (1975).

(6) O. Eisenstein, J. Lefour, N. Anh, and R. Hudson, *Tetrahedron*, **33**, 523 (1977), and references therein.

(7) (a) M. F. Ansell, B. W. Nash, and D. A. Wilson, *J. Chem. Soc.*, 3012 (1963). (b) M. F. Ansell and A. H. Clements, *J. Chem. Soc. C*, 270 (1971).

(8) This Diels–Alder combination yields the "ortho" product exclusively and quantitatively. Unpublished results of this laboratory.

(9) In our experience, Diels–Alder reactions with carbomethoxy-*p*-benzoquinone are best carried out at room temperature. Elevated temperatures lead to lower yields of less pure products.

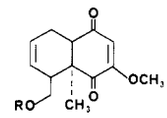
(10) M. F. Ansell, J. W. Lown, D. W. Turner, and D. A. Wilson, *J. Chem. Soc.*, 3036 (1963).

(11) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.

(12) The cis compound **11** is also produced as the major product in the hydrolysis of enol ether ketal **12**, as well as when either **11** or **17** is treated with DABCO.

(13) Our assignment of stereochemistry to the methyl group of **22** is tentative. Since isomerization of the ring junction occurs in the hydrolysis of **20** to **22**, we assume that epimerization also occurs at C-8 to produce the more stable equatorial isomer.

(14) It has been reported recently [J.-L. Gras, *Tetrahedron Lett.*, 4117 (1977)] that 3-methoxy-2,4-toloquinone reacts with **5** to give adduct i (R = H) and that the latter is converted to its tetrahydropyranyl ether ii (R = THP) with dihydropyran at 0 °C. We have also found that the mixture of adducts **8** and **9** also form a THP derivative under these conditions. Unfortunately, this diketo ether has not proven synthetically useful. We would also suggest that Gras' adduct is almost certainly the hemiketal compound equivalent to **8** rather than the free hydroxymethyl material.



i, R = H
ii, R = THP

(15) Structure **12** is formally a Bredt's rule violation. The outer 11-membered ring is sufficiently large, however, to easily accommodate a trans double bond: (a) J. Marshall and H. Faubi, *J. Am. Chem. Soc.*, **92**, 948 (1970); (b) J. R. Weisman and W. A. Pletcher, *J. Am. Chem. Soc.*, **92**, 956 (1970).

(16) H. Uberwasser, K. Heusler, J. Kalvoda, Ch. Meystre, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 344 (1963).

(17) Ketalization could of course occur by protonation of the enol ether double bond and addition of the hydroxymethyl oxygen to the resulting cation.

(18) The NMR spectrum of the crude product from zinc reduction of **30** reveals the presence of a small amount of the alternative enol ether **25**.

(19) S. Oida and E. Ohki, *Chem. Pharm. Bull.*, 1990 (1969).

(20) L. Crombie, S. H. Harper, and D. Thompson, *J. Chem. Soc.*, 2906 (1951).

(21) H. O. House, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **36**, 2361 (1971).

Synthesis of the New Nucleoside Antibiotic 1-(2-Deoxy-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione[1]

Harvey Skulnick

The Upjohn Company, Experimental Chemistry Research, Kalamazoo, Michigan 49001

Received June 28, 1977.

1-(2-Deoxy-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione, "DHAdT" (I), a new nucleoside with both antiviral and antibacterial activity, has been synthesized along with its ribosyl analogue via the silyl ether modification of the Hilbert–Johnson reaction. Condensation of the mono- or disilyl-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-diones (V and VI) with 3,5-ditoluoyl-2-deoxy-D-ribofuranosyl chloride (VII) gave the protected nucleosides VIII and IX which, after removal of the protecting groups, afforded "DHAdT" (I) and its α anomer X. Condensation of V with tribenzoylribofuranosyl bromide (XI) or acetate (XII) gave the N_3 riboside. When V was condensed with tetraacetyl ribose (XIII), the N_1 and N_3 isomers were isolated. The ribose analogue was devoid of both antiviral and antibacterial activity.

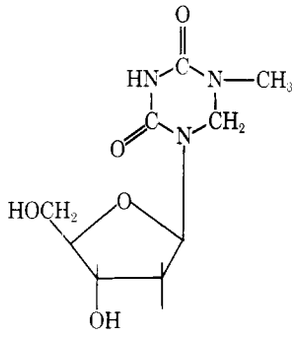
Bannister and DeBoer recently reported the isolation of a nucleoside antibiotic, 1-(2-deoxy-β-D-ribofuranosyl)-5,6-dihydro-*s*-triazine-2,4(1*H*,3*H*)-dione, I (DHAdT), from the culture *Streptomyces platensis* var. *clarensis*.[2] This same culture produces the nucleoside 1-*N*-methylpseudouridine, a compound whose isolation was reported by Argoudelis and Mizsak[3] and whose synthesis was recently reported by Fox et al.[4]

DHAdT exhibited in vitro activity against a variety of DNA viruses, including herpes simplex type 1, herpes simplex type 2, varicella zoster, and vaccinia, and gram-negative bacteria, although modest activity was observed vs. *Streptococcus hemolyticus* bacteria and poor activity vs. *Diplococcus pneumoniae*.[5] Thymidine and deoxyuridine completely reversed the antiviral activity, while deoxycytidine was partially effective.

0022-3263/78/1943-3188$01.00/0

DHAdT was active, in vivo, when administered PO, SQ, and IP; however, to date topical activity has not been demonstrated. Administered SQ, the nucleoside was active both prophylactically and therapeutically in mice innoculated IV with herpes simplex virus.[6]

This paper details the synthesis of the new nucleoside I, DHAdT, and its riboside analogue via the silyl ether modifi-



I

5,6-dihydro-5-azathymidine (DHAdT)

cation of the Hilbert–Johnson condensation. This is the first reported application, to my knowledge, of the silyl ether procedure to the synthesis of a 5,6-dihydro nucleoside.

The initial objective is the synthesis of the silyltriazine V. In 1961 Piskala and Gut reported the synthesis of 5-*N*-methyl-5,6-dihydro-*s*-triazine-2,4(1*H*,3*H*)-dione (IV) via the ring closure of *N*-methylbiuret with ethyl formate to yield III, followed by the reduction of the *N*-methyl-*s*-triazine with Raney Nickel (W2) or 5% Rh/C.[7]

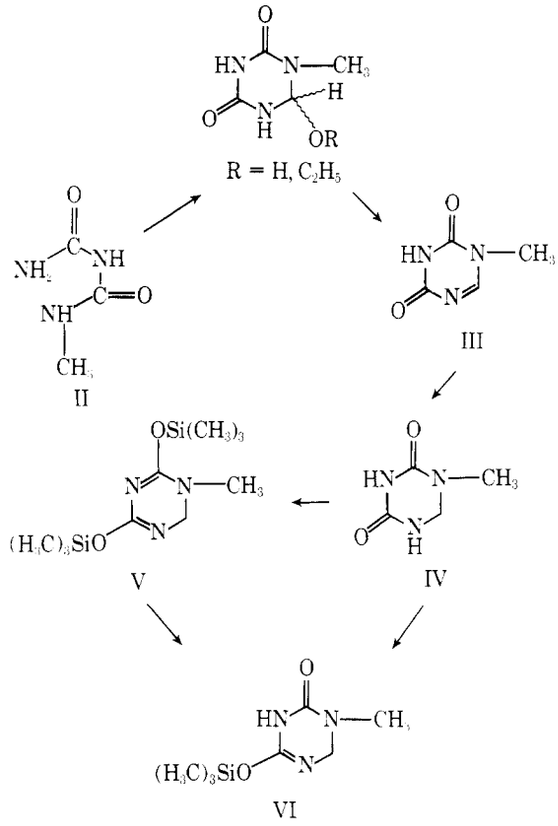
We found that the *N*-methyltriazine III is recovered as an ethanol or water adduct which can be reduced directly to IV. Alternatively, this adduct can be converted to triazine III by azeotroping from benzene with *p*-toluenesulfonic acid added. Silylation of the dihydro-*s*-triazinone IV with refluxing hexamethyldisilazane gave 2,4-bis(trimethylsilyloxy)triazine (V) as an oil. This disilyl base slowly hydrolyzed on standing to a crystalline monosilyltriazine whose ^{1}H NMR is consistent with the assigned structure VI.

The ^{1}H NMR signal observed for the methylene of IV appears at 4.30 ppm (Me_2SO) as a doublet. Irradiation of the N_1–H at 7.60 ppm reduced the methylene to a singlet, consistent with the assigned isomer, IV. The ^{1}H NMR of V has a singlet at 4.30 ppm ($CDCl_3$) for the methylene. When V hydrolyzed to the monosilyl triazine VI with the appearance of an N–H at 7.25 ppm ($CDCl_3$), the methylene remained a singlet, consistent with hydrolysis of the 4-*O*-trimethylsilyl group. The monosilyl triazine VI can also be synthesized directly using bis(trimethylsilyl)trifluoroacetamide in pyridine at 25 °C for 18 h.

The plan to prepare nucleoside I involved the condensation of the silylated triazine with the appropriate sugar. Although there is no reported synthesis of a nucleoside from a monosilylated triazine or pyrimidine, the synthesis of *s*-triazine nucleosides from their disilyl bases has been reported previously. In 1970 Winkley and Robins described the synthesis of 5-azacytidine and related derivatives employing direct glycosidation of a bissilyl-1,3,5-triazine ring.[8] The use of $SnCl_4$ as a Friedel–Crafts catalyst in Hilbert–Johnson type reactions is exemplified in the syntheses of 5-azacytidine[9] and *as*-triazine nucleosides by Vorbrüggen and co-workers.[10] There is, however, no reported synthesis of a dihydro (nonaromatic) triazine ring nucleoside via an acid-catalyzed condensation.

The only other previous *s*-triazine nucleoside synthesis was that reported by A. Piskala and F. Sŏrm via the orthoformate cyclization of 1-peracetylglycosyl-4-methylisobiuret to give the corresponding 4-methoxy-5-azauracil nucleosides.[11]

Scheme I



Condensation of the mono- or disilylated dihydro-*s*-triazines (V and VI) with 3,5-di-*o*-toluoyl-D-ribofuranosyl chloride in an acetonitrile/ethylene dichloride mixture using anhydrous $SnCl_4$ as Lewis acid catalyst[12] gave a 1:1 mixture of α and β anomers of the 3′,5′-ditoluate esters of DHAdT (VIII and IX). The assignment of isomers was determined by ^{1}H NMR wherein the β isomer exhibited the characteristic triplet for the anomeric proton and the α isomer the characteristic quartet (see Experimental Section).

The site of glycosidation was determined to be N_1 based on a comparison of the synthesized nucleoside with the known DHAdT isolated from microbial sources. The structure of DHAdT was determined by B. Bannister to be a β-N_1 nucleoside.[13] X-ray analysis of the nucleoside confirmed its structure.[14]

The condensation reaction was carried out under a variety of conditions as shown in Table I. On a 1-mmol scale, the best yields of DHAdT (based on bioassay vs. Kp)[19] were obtained in the more polar solvents such as acetonitrile and nitromethane. However, nitromethane was eliminated as a possible solvent due to a difficulty in controlling reaction rates.

When the reaction scale was increased to 0.1 M using a 1:2 mM ratio of sugar/base, 1.3 mM $SnCl_4$ in CH_3CN at −25 °C for 18 h, the reaction time increased markedly (7–10 days) and yields of the β-nucleoside isomer decreased to 1–2%. In addition, the ratio of α/β anomers increased to 15:1. Making the reaction mixture homogeneous by first dissolving the 3,5-di-*o*-toluoyl-D-ribofuranosyl chloride in ethylene dichloride, adding this solution to the acetonitrile/$SnCl_4$/silyl triazine solution at −25 °C, and then warming to +25 °C brought the α/β ratio back to 1:1 and overall yields of the dihydro nucleosides to 70%. A 25–30% yield of the desired β-nucleoside isomer can be directly crystallized out. Following the reaction progress by TLC indicates that the kinetics involve initial α-anomer formation at −25 °C followed by slow formation of the β-anomer at +25 °C. In addition, the reaction could now be warmed to 40–50 °C without any noticeable decomposition,

Table I

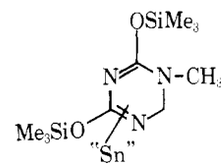
mM sugar/ mM base[a]	catalyst, mM $SnCl_4$	solvent	temp, °C	time	α/β	DHAdT yield,[23] %
1:1	0.7	$C_2H_4Cl_2$	5	18 h		0
1:2	0.7	$C_2H_4Cl_2$	5	18 h	4:1	2.85
2:1	0.7	$C_2H_4Cl_2$	5	18 h		<0.1
1:1	0.7	$C_2H_4Cl_2$	−25	18 h		0
1:2	0.7	$C_2H_4Cl_2$	−25	18 h	4:1	2.14
2:1	0.7	$C_2H_4Cl_2$	−25	18 h		0
1:1	0.7	CH_3CN	5	18 h		0
1:2	0.7	CH_3CN	5	18 h	1:1	9.1
1:1	0.7	CH_3CN	−25	18 h	1:1	8.9
1:2	0.7	CH_3CN	−25	18 h	1:1	19.0
2:1	0.7	CH_3CN	−25	18 h	1:1	12.0
1:1	0.35	CH_3CN	−25	18 h	1:1	12.8
1:2	0.35	CH_3CN	−25	18 h	1:1	8.8
2:1	0.35	CH_3CN	−25	18 h	1:1	12.2
1:1	1.3	CH_3CN	−25	18 h	1:1	14.4
1:2	1.3	CH_3CN	−25	18 h	1:1	24.0
2:1	1.3	CH_3CN	−25	18 h	1:1	14.9
1:2	0.9	CH_3NO_2	−25	5 min	1:1	29.0
1:2	0.9	CH_3NO_2	−25	18 h		<5.0

[a] Reactions based on 1 mM base.

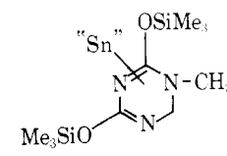
in contrast to the rapid decomposition of the sugar or nucleoside in a $SnCl_4$/acetonitrile mixture at 25 °C.

Niedballa and Vorbrüggen have recently reported on the $SnCl_4$-mediated reaction of protected 1-*O*-acyl sugars with silylated uracils.[15] Their results strongly suggest the formation of intermediate $SnCl_4$–uracil complexes which undergo ribosilylation upon addition of excess catalyst.

Our results with the disilylated triazine and the deoxyribofuranosyl bromide, as seen in Table I, exhibit analogous features which invite similar interpretations. Since there is (1) a higher rate of reaction in more polar solvents and higher catalyst concentrations, and (2) a "stability" upon warming the reaction, an initial $SnCl_4$–triazine complex such as **1** and **2** could exist, similar to that proposed by Niedballa and Vorbrüggen. As evidenced from Table I, the more stable the



1

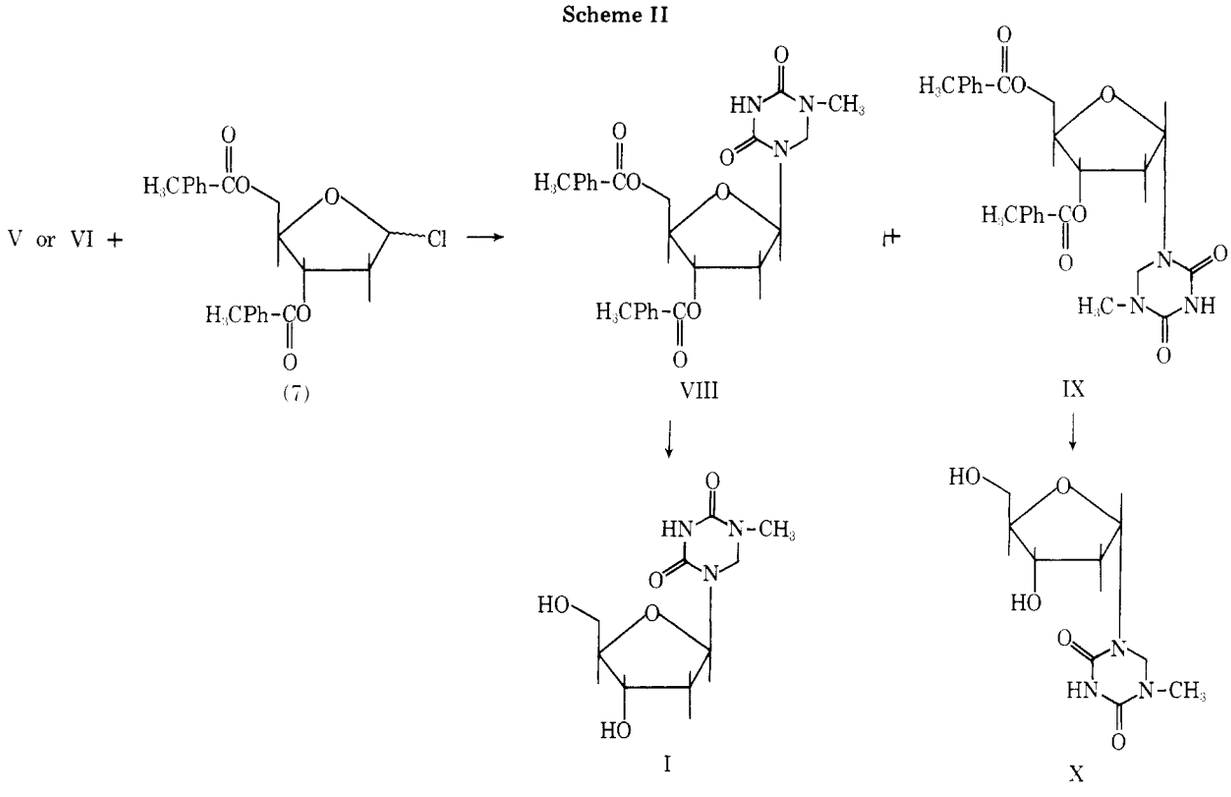


2

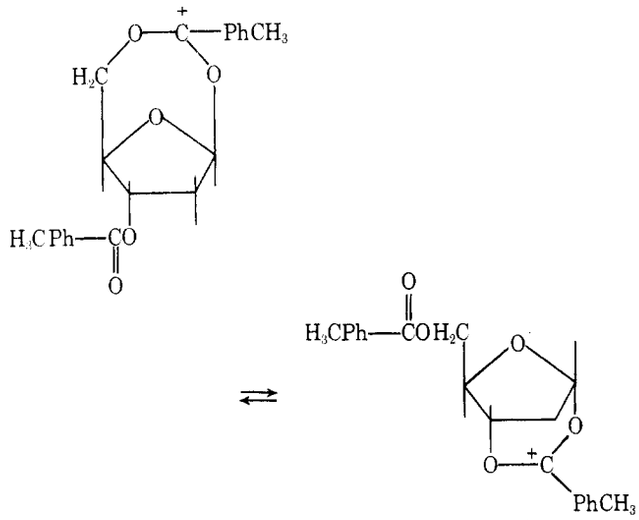
complex (favored by less polar solvents and minimal catalyst), the slower the rate of reaction. Conversely, more polar solvents or simultaneous mixing of catalyst, sugar, and triazine favor a more rapid rate of reaction/decomposition. The same rationalization is applicable to the monosilylated triazine.

The exclusive formation of the N_1-deoxynucleoside under the reaction conditions, in contrast to the ribosylation reaction of Niedballa and Vorbrüggen, suggests that complex **1** is either

Scheme II



Scheme III



the predominant or the more reactive species (assuming equilibria occurs). This coincides with expectation, since (1) the N_1 has only one α-electron withdrawing group whereas N_3 has two, (2) Niedballa and Vorbrüggen find N_1 predominates, and (3) N_1/N_3 reactivities in the ribosilylation of the disilyltriazines are greater than 1.

Sŏrm and co-workers[16] proposed a transannular participation effect of the 5-substituent of the α-chloro sugar, as shown in Scheme III, to rationalize the formation of α-nucleosides from the α-chloro sugar (the α configuration was initially suggested by Fletcher[17] and Zinner[18]).

If one assumes that the tin–dihydro-*s*-triazine complex reacts with the carbonium ion formed via transannular displacement of the ditoluoyl sugar halide, then the α anomer, that formed via the 5,1 carbonium ion, would be the kinetic product, and the β-anomer formed from the 3,1 carbonium ion would the thermodynamic product of the reaction.

There is little evidence to suggest that the α-chloro sugar at −25 °C is reacting directly with the silylated base via S_N2 displacement, since the initial product formed is the α anomer as opposed to the β.

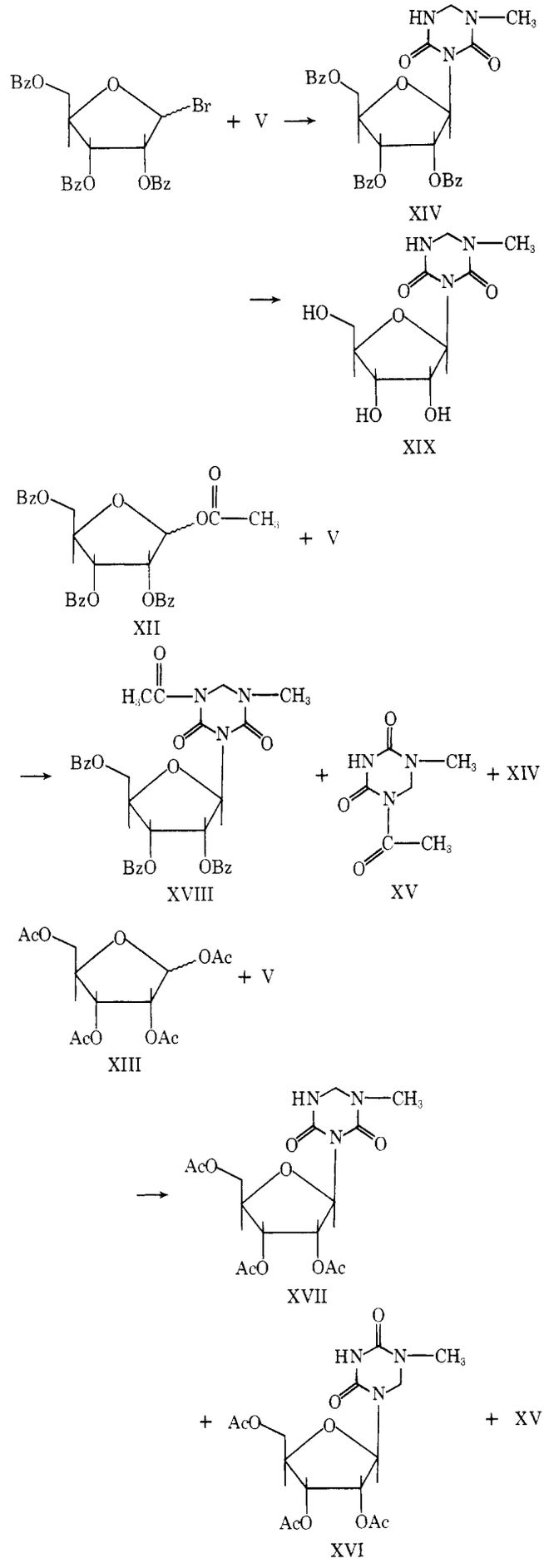
The condensation reaction can also be carried out with mercuric bromide as catalyst in the presence of molecular sieves. Acetonitrile is the solvent of choice. Yields are considerably lower (ca. 5%), although the β isomer predominates over the α. When molecular sieves are omitted, only the α anomer is isolated. These results are similar to those reported by Szabolcs involving the condensation of 5-alkyluracils with protected 2′-deoxyribofuranosyl chlorides in the presence of mercuric bromide and molecular sieves.[19]

Deprotection of VIII and IX with 25% sodium methoxide in methanol gave the unprotected nucleosides I and X. The synthetic antibiotic by physical and biological methods was identical to material obtained from the microbial source.

A greater than 70% yield of thymidine (α/β = 1:4.5) was obtained when the bis(silyl ether) of thymine was reacted with 3,5-di-*o*-toluoylribofuranosyl chloride in a manner identical to that which gave best yields of I.

The yields and α/β ratios compare favorably with those reported previously for the synthesis of thymidine via the Hilbert–Johnson reaction.[1,2] M. Prystas and F. Sorm reported yields of 39–74% of nucleoside with a 3.6–5.7:1 α/β ratio, while M. Kotick et al. had ratios of 1:3.2 but total nucleoside yields of only 34–36%. In the preparation of 5-ethyl-2-deoxyuridine via the silyl ether modification of the Hilbert–Johnson reaction (using $SnCl_4$ as catalyst), Niedballa and Vorbruggen always found a nearly constant ratio of anomers (α/β = 1) which could not be influenced by variation of the reaction conditions.[3]

Scheme IV



The condensation with 2,3,5-tribenzoyl-D-ribofuranosyl acetate or bromide to give the riboside analogue of DHAdT was markedly different from the deoxy series. A variety of products was obtained, depending upon solvent, sugar leaving group, and the sugar protecting group.

Only the N_3 isomers XIV and XVIII were isolated when the tribenzoyl sugars XI or XII were used in the condensation. When the protecting groups on the sugar were changed to acetyl (XIII), both the N_3 (XVII) and N_1 (XVI) isomers were obtained.

Isomeric and anomeric assignments were made on the basis of proton NMR spectra. Only one anomer was obtained in the condensation reaction between the tribenzoyl ribose and the silylated triazine. The coupling constant of 1.5 Hz for the anomeric proton at XIV was consistent with the coupling constants of β-ribofuranosyl nucleosides.[20] The coupling constant of 5 Hz obtained from the triacetyl nucleoside (XVI) was too large to make a definite assignment of β configuration. However, it was close to the coupling of the unprotected β-N_3 isomer (XIX) (4 Hz), and coupled with the knowledge that, in the presence of a Lewis acid acylated ribofuranosyl sugars in condensation with silylated pyrimidines yield mainly β-nucleosides,[21] the β configuration was assigned.

The assignment of N_1 vs. N_3 was made on the basis of coupling between the NH and methylene in the nucleoside *s*-triazine. In the acetyl sugar condensations a pair of isomers were obtained. In the benzoyl case only one isomer was found. In each case the assigned N_3 isomer exhibited a doublet for the methylene coupled to the triazine NH, and the assigned N_1 isomer showed a singlet for the methylene. Irradiation of the NH in the coupled spectra collapsed the methylene doublet to a singlet. The assignments were consistent with ^1H NMR data obtained from both the N_1 acetyl nucleoside (XVIII) and the N_1 acetyl base (XV), where no coupling was possible and whose methylene, as expected, appeared as singlets.

Why a change in protecting groups for benzoate to acetate should give some N_1 isomer rather than all N_3 is unclear. This is further contrasted with the fact that no N_3 isomer was ever isolated in the deoxyriboside condensations.

The acetyltriazine XV was a minor product in these reactions. However, when acetonitrile was used as solvent in the $SnCl_4$-catalyzed condensation of XII with V, only XV (identical to an authentic sample prepared via the acylation of 5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione[22]) was isolated.

Neither the N_3 nor the N_1 ribofuranosyl nucleosides exhibited activity in any of the assays in which DHAdT was active.

Experimental Section

General. All solvents employed were reagent grade. ^1H NMR spectra were recorded on Varian A-60A and XL-100 instruments. Infrared spectra were recorded on a Digilab Model 140 spectrophotometer. Melting points were determined on a Thomas-Hoover melting-point apparatus and are uncorrected. Silica gel 60 (0.063–0.200 mm) and plates precoated with silica gel 60F-254 (both from E. Merck) were used for column and thin-layer chromatography, respectively.

1-(2-Deoxy-3,5-di-*o*-toluoyl-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (VIII) and 1-(2-Deoxy-3,5-di-*o*-toluoyl-α-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (IX). A reaction mixture consisting of 1.9 g (0.015 M) of 5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione, 50 mL of hexamethyldisilazane and 2 mg of ammonium sulfate is heated at reflux under N_2 atmosphere for 48 h. The solution is then cooled to 25 °C and the excess hexamethyldisilazane is removed by evaporation under reduced pressure; the resulting bis(trimethylsilyl)-*s*-triazine (V) is used immediately. Under N_2, a solution consisting of 13.6 g (0.05 M) of 2,4-bis(trimethylsilyloxy)-5,6-dihydro-5-methyl-*s*-triazine (V) and 625 mL of acetonitrile (Burdick and Jackson Laboratories, Inc.) is chilled to −24 °C and 3.75 mL of fuming anhydrous stannic chloride is added. This solution is stirred for 5 min (at this point all $SnCl_4$ is in solution) before a 25 °C solution consisting of 9.7 g (0.025 M) of 2-deoxy-3,5-ditoluoyl-D-ribofuranosyl chloride in 100 mL of reagent grade ethylene dichloride is added. This reaction mixture is stirred at −20 °C for 5 min before being warmed to 25 °C. Stirring is continued as the solution gradually becomes a dark green. TLC (1:1 acetone–cyclohexane) shows the initial appearance of the α anomer followed by the slow appearance of the β anomer. After 3–5 h, the ratio of α/β becomes 1:1 with very little unreacted sugar left. The reaction mixture is decomposed by the addition of 100 mL of saturated aqueous $NaHCO_3$ and stirred for 1 h and chloroform is added until the aqueous phase separates. The organic phase is recovered, washed with aqueous $NaHCO_3$ and water, and dried over anhydrous $MgSO_4$. The organic solution is filtered and evaporated to dryness to give a foamy residue. This residue is dissolved in 50 mL of ethyl acetate and, after seeding, is cooled to 5 °C for 48 h (occasionally agitated). The solids are collected to give 3.46 g (28.8%) of VIII. An analytical sample is prepared by recrystallizing from ethyl acetate to give pure 1-(2-deoxy-3,5-di-*o*-toluoyl-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (VIII): mp 184–185 °C; $[\alpha]^{25}_D$ −46° (*c* 1.087, $CHCl_3$); UV (ethanol) λ end absorption, 241 (ϵ 31 800), 269 (2250), 281 (1300) nm; IR 3200, 3080, 1730, 1710, 1610, 1575, 1520, 1275, 1265, 1250, 1180, 1110, 1100, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H, arom CH_3), 2.68 (s, 3 H, N–CH_3), 4.90–4.25 (m, 5 H, 5′-CH_2, 4′-H, ring CH_2), 5.8–5.5 (m, 1 H, 5.8–5.5 (m, 1 H, 3′-H), 6.60–6.28 (t, $J_{1,2}$ = 8 Hz, 1 H, 1′-H), 7.5–7.2 (m, 2 H, arom), 8.1–7.8 (m, 2 H, arom).

Anal. Calcd for $C_{25}H_{27}N_3O_7$: C, 62.36; H, 5.65; N, 8.73. Found: C, 62.22; H, 5.50; N, 8.74.

Chromatographing the mother liquors over 500 g of silica gel using 1:3 acetone–cyclohexane as eluent gave IX as an amorphous foam which could be crystallized from acetone–SSB to give pure IX: mp 145.5–146.5 °C; $[\alpha]^{25}_D$ +4° (*c* 0.7440, $CHCl_3$); UV (ethanol) λ end absorption, 241 (ϵ 31 250), 269 (2250), 281 (1300) nm; IR 3200, 3060, 1725, 1690, 1610, 1580, 1520, 1275, 1180, 1095, 1020, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H, arom CH_3) 2.88 (s, 3 H, N-CH_3), 4.80–4.40 (m, 5 H, 5′-CH_2, 4′-H, ring CH_2), 5.64–5.46 (m, 1 H, 3′-H), 6.5–6.32 (q, $J_{1'-2'\beta}$ = 3.5 Hz, $J_{1'-2'\alpha}$ = 8 Hz, 1 H, 1′-H).

Anal. Calcd for $C_{25}H_{27}N_3O_7$: C, 62.36; H, 5.65; N, 8.73. Found: C, 62.22; H, 5.50; N, 8.74.

1-(2-Deoxy-3,5-di-*o*-toluoyl-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (VIII) and 1-(2-Deoxy-3,5-di-*o*-toluoyl-α-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (IX) from the Monosilyltriazine (VI). To 1.28 g (0.010 M) of 5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione was added 40.0 mL of reagent-grade pyridine and 4.0 mL of BSTFA (Regis Chemical Co.). The reaction was allowed to stir at ambient temperature for 18 h and then evaporated to dryness under reduced pressure. The crude monosilyl triazine (VI) was azeotroped under reduced pressure twice with dry acetonitrile. The monosilyltriazine, isolated as a white powder, was used immediately in the condensation reaction.

To 0.1 M VI, under a N_2 atmosphere, was added 1250 mL of acetonitrile. The reaction mixture was cooled to −24 °C and 7.50 mL of fuming $SnCl_4$ was added. After stirring at −24 °C for 5 min to complete solution, 19.4 g (0.050 M) of 3,5-ditoluoyl-2-deoxy-D-ribofuranosyl chloride in 200 mL of ethylene chloride was added. The reaction is run exactly as described for the synthesis of VIII and IX from the disilyltriazine V above. Yield of VIII, identical to that obtained above, was 5.6 g (23.3%), mp 183–185 °C.

1-(2-Deoxy-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione, DHAdT (I). To 7.85 g (0.016 M) of 1-(2-deoxy-3,5-di-*o*-toluoyl-β-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (VIII) is added 160 mL of methanol and 0.8 mL of a 25% solution of $NaOCH_3/CH_3OH$. The reaction is stirred at 25 °C for 18 h, a few chips of CO_2 are added, and stirring is continued for 10 min. Silica gel (40 g) is added and the methanol is removed by evaporation under reduced pressure. The residual powder thus obtained is transferred to a column of 150 g of silica gel, and the column is developed with 5% methanol in chloroform. Fractions containing the desired material were combined to give 4.05 g (97.2%) of crude I. An analytical sample is prepared by dissolving 1.0 g in 4 mL of hot methanol and adding 25 mL of ethyl acetate. There is thus obtained 0.79 g of pure I: mp 142–143 °C; $[\alpha]^{25}_D$ −6° (*c* 0.9792, H_2O); IR 3440, 3340, 1695, 1683, 1510, 1483, 1440, 1396, 1243, 1060, 1011, 985, 943, 792, 755 cm^{-1}; ^1H NMR (D_2O) δ 2.43–2.13 (m, 2 H, 2′α 2′β-H), 3.0 (s, 3 H, NCH_3), 4.08–3.66 (m, 3 H, 4′-H, 5′-CH_2), 4.53–4.3 (m, 1 H, 3′-H), 4.66 (s, 2 H, ring CH_2), 6.36–6.05 (t, *J* = 7 Hz, 1 H, 1′-H); ^1H NMR (Me_2SO) δ 2.25–1.71 (m, 2 H, 2′α–2′β-H), 2.83 (s, 3 H, NCH_3), 3.70–3.36 (m, 4 H, 5′-CH_2, 4′-H, NH), 4.33–3.96 (m, 1 H, 3′-H),

4.46 (s, 2 H, ring CH_2), 4.88–4.71 (t, 1 H, 5′-OH), 5.13–5.06 (d, 1-H, 3′-OH), 6.15–5.91 (t, J = 7 Hz, 1 H, 1′-H).

Anal. Calcd for $C_9H_{15}N_3O_5$: C, 44.07; H, 6.16; N, 17.13. Found: C, 44.25; H, 6.28; N, 17.20.

1-(2-Deoxy-α-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (X). To 1.13 g of 1-(3,5-ditoluoyl-2-deoxy-α-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (IX) (2.3 mM) is added 10.0 mL of methanol and three drops of 25% CH_3ONa/CH_3OH. The reaction mixture is stirred at 25 °C for 18 h, whereupon a few chips of CO_2 are added. The mixture is evaporated to dryness and the residue separated between 50 mL of $CHCl_3$ and 50 mL of H_2O. The aqueous layer is washed with 4 × 20 mL of $CHCl_3$ and evaporated to dryness. The residue is dissolved in 5 mL of methanol, 5 g of silica gel is added, and the mixture is evaporated to a white powder under vacuum. This powder is chromatographed on 50 g of silica gel eluting with 20% $CH_3OH/CHCl_3$ to give 389 mg of crude X (69%). X is recrystallized from CH_3OH/Et_2O to give 279 mg of analytically pure 1-(2-deoxy-α-D-ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (X): mp 174–176 °C; $[\alpha]^{25}_D$ +54° (*c* 0.4320, H_2O); IR 3460, 3360, 3320, 3180, 3060, 1705, 1680, 1520, 1270, 1080, 1020 cm^{-1}.

Anal. Calcd for $C_9H_{15}N_3O_5$: C, 44.07; H, 6.16; N, 17.13. Found: C, 44.33; H, 6.20; N, 16.98.

3-(2,3,5-Tribenzoyl-β-D-ribofuranosyl)-5-methyl-5,6-dihydro-*s*-triazine-2,4(1*H*,3*H*)-dione (XIV) from the Acetyl Sugar (XII). To 5.0 g (10 mM) of tribenzoyl-D-ribofuranosyl acetate in 100 mL of analytical grade benzene is added a solution of 10 mM 2,4-bis(trimethylsilyloxy)-5-methyl-5,6-dihydro-*s*-triazine (V) in 25 mL of AR benzene. Anhydrous $SnCl_4$ (≃3.55 g ≃ 1.6 mL ≃ 13.5 mm) is injected into the reaction, and the mixture is allowed to stir at 25 °C for 18 h.

Saturated aqueous $NaHCO_3$ (5 mL) is added and the reaction is allowed to stir for 30 min. An additional 15 mL of saturated aqueous $NaHCO_3$ is added and stirred for an additional 30 min. Benzene is added, the layers are separated, and the organic phase is washed with 2 × 50 mL of saturated aqueous $NaHCO_3$ and saturated NaCl (aq), and then dried over anhydrous Na_2SO_4. The benzene solution is evaporated to dryness to give crude title compound as an amber gum (R_f 0.25 in 8:12:1 ethyl acetate–hexane–CH_3OH). The crude XIV is chromatographed on 400 g of silica gel and eluted with 8:12:1 ethyl acetate–hexane–CH_3OH, taking 25.0-mL fractions. Fractions 110–128 are combined to give 740 mg of XIV (a crude solid), recrystallization of which from acetone–hexane (1:3) gave 510 mg of pure 3-(2,3,5-tribenzoyl-β-D-ribofuranosyl)-5-methyl-5,6-dihydro-*s*-triazine-2,4(1*H*,3*H*)-dione (XIV): mp 203–203.5 °C; IR 3260, 1745, 1725, 1710, 1670, 1600, 1585, 1485, 1410, 1315, 1290, 1275, 1250, 1135, 1115, 1060, 1025, 985, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.5–4.4 (d, 2 H, NCH_2N), 4.8–4.55 (m, 3 H, 5′-CH_2/β; 4′-H), 6.25–6.15 (m, 2 H, 2′-H, 3′-H), 6.33–6.32 (d, 1 H, J = 1.5 Hz, 1′-H), 7.2 (br, 1 H, NH), irradiation at δ 7.2 causes the methylene to collapse to a singlet.

Anal. Calcd for $C_{30}H_{27}N_3O_9$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.88; H, 4.95; N, 7.18.

3-(2,3,5-Tribenzoyl-β-D-ribofuranosyl)-5-methyl-5,6-dihydro-*s*-triazine-2,4-dione (XIV) from the Bromo Sugar (XI). To 2.5 g (5 mM) of 2,3,5-tribenzoyl-D-ribofuranosyl acetate is added 50 mL of ethylene dichloride. After cooling to 0 °C, HBr is added over a period of 20 min. The solution is allowed to stand at 0 °C for 60 min, followed by warming to +25 °C over a period of 30 min. The solution is evaporated under vacuum to dryness (temp bath = 35 °C max), and the resulting gum is azeotroped with toluene and then held under vacuum (0.5 μm) for 30 min.

The resulting 2,3,5-tribenzoyl-D-ribofuranosyl bromide in 30 mL of ethylene dichloride is added to 1.75 g (6.4 mM) of 2,4-bis(trimethylsilyloxy)-5,6-dihydro-5-methyl-*s*-triazine (V). To the stirred solution is injected 2.2 g (1.0 mL ≃ 8.4 mM) of anhydrous $SnCl_4$. The reaction is allowed to stir at ambient temperature for 48 h following which 20 mL of saturated $NaHCO_3$ (aq) is added and is stirred for an additional 30 min. The layers are separated and the organic layer is washed with 2 × 20 mL of $NaHCO_3$ (aq) and H_2O saturated NaCl (aq) and dried over Na_2SO_4 (anhydrous). The organic phase is concentrated to dryness to yield 2.4 g of crude title compound. Chromatography on 150 g of silica gel, using ethyl acetate –hexane–CH_3OH (8:12:1) as eluent [R_f 0.25 in ethyl acetate–hexane–CH_3OH (8:12:1)], yielded the pure title compound [600 mg (21%), mp 200–202 °C]. This material is identical to that obtained previously.

3-(2,3,5-Tribenzoyl-β-D-ribofuranosyl)-1-acetyl-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (XVIII) from the Acetyl Sugar (XII). To 6.25 g of tribenzoyl-D-ribofuranosyl acetate in 300 mL of CH_3CN is added 25 mM 2,4-bis(trimethylsilyloxy)-5-methyl-5,6-dihydro-*s*-triazine in 100 mL of CH_3CN. Next, $SnCl_4$ (2.0 mL ≃ 4.4 g ≃ 17 mM) is added and the solution is allowed to stir at ambient temperature for 94 h. While stirring, 50 mL of a saturated $NaHCO_3$ (aq) solution is added and the stirring is continued for 30 min, whereupon enough $CHCl_3$ is added to bring the aqueous layer to the top. The layers are separated, and the organic layer is washed successively with saturated $NaHCO_3$ and H_2O and dried over Na_2SO_4. The $CHCl_3$ solution is filtered and evaporated to dryness to yield 7.6 g of a mixture of XVIII and XIV as an amber gum.

Chromatography of 1 kg of silica gel, with 1:2 acetone–cyclohexane, gives 0.71 g of XIV (R_f 0.55, 1:1 acetone–cyclohexane) identical by H^1 NMR to that obtained previously. Fractions with R_f 0.80 were combined to give 2.32 g (41%) of XVIII as an amorphous foam: IR 3060, 1720, 1605, 1585, 1495, 1315, 1270, 1200, 1180, 1120, 1095, 1070, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.45 (s, 3 H, NC(=O)CH_3), 3.05 (s, 3 H, NCH_3), 4.90–4.45 (m, 3-H, 4′-H, 5′-α/βCH_2), 5.0 (s, 2-H, ring CH_2), 6.35–6.10 (m, 3-H, 1′-, 2′-, 3′-H).

Anal. Calcd for $C_{32}H_{29}N_3O_{10}$: C, 62.33; H, 4.90; N, 6.81. Found: C, 62.44; H, 4.69; N, 6.51.

3-(β-D-Ribofuranosyl)-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (XIX). To 200 mg of XIV (0.35 mM) is added 15 mL of a 0 °C saturated solution of NH_3/CH_3OH. The solution is stoppered and stored in a sealed tube at 5°C for 120 h. The reaction mixture is evaporated to dryness. The residue is tritiated with $CHCl_2$ and separated between $CHCl_3$ and H_2O. The aqueous layer is washed four times with $CHCl_3$ and lyophilized to give XIX as an amorphous foam: wt 73 mg (80%); ^1H NMR (D_2O) δ 2.95 (s, 3 H, NCH_3), 4.05–3.6 (s, 3 H, 5′-CH_2, 4′-H), 4.5 (s, 2 H, NCH_2N), 5.85–5.7 (d, 1 H, $J_{1',2'}$ = 4 Hz 1′-H); $(Me_4Si)_4$ *m/e* 549, calcd for $C_{21}H_{47}Si_4N_3O_6$, 549.2542; found 549.2562.

1-(2,3,5-Triacetyl-β-D-ribofuranosyl)-5-methyl-5,6-dihydro-*s*-triazine-2,4-dione (XVI) and 1-Acetyl-5,6-dihydro-5-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione (XV). To 2.4 g (7.5 mM) of 1,2,3,5-tetraacetylribofuranose is added 10 mM 2,4-bis(trimethylsilyl)-5-methyl-5,6-dihydro-*s*-triazine (V) in 50 mL of ethylene dichloride and 1.0 mL (2.2 g ≃ 8.4 mM) of $SnCl_4$ is injected. The mixture is stirred at 25 °C for 72 h, 20 mL of saturated aqueous $NaHCO_3$ is added, and the mixture is stirred at ambient temperature for 30 min. An additional 50 mL of $C_2H_4Cl_2$ is added and the layers are separated. The organic layer is washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and saturated NaCl (20 mL), dried over Na_2SO_4 (anhydrous), and evaporated to dryness to yield 1.2 g of crude XVI as an amorphous foam.

All of XVI is chromatographed on 125 g of base-washed (washed with dilute NH_4OH followed by drying at 60 °C for 18 h) silica gel. The column is eluted with ethyl acetate and, taking 10.0-mL fractions, fractions 32–44 are combined (R_f 0.55 in ethyl acetate) to yield 105 mg of XV (3.6%): ^1H NMR ($CDCl_3$) δ 2.55 (s, 3 H, $COCH_3$), 3.0 (s, 3 H, NCH_3), 5.0 (s, 2 H, NCH_2N), 8.8 (m, 1 H, NH). Fractions 62–82 are combined to yield 120 mg (4.1%) of XVI as a white foam (R_f 0.45 in ethyl acetate): IR 3480, 3230, 3080, 1745, 1705, 1510, 1225, 1100, 1045, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.25–2.0 (m, 9 H, CCH_3), 3.0 (s, 3 H, NCH_3), 4.35–4.2 (m, 3 H, 5′-CH_2, 4′-H), 4.5 (s, 2 H, ring CH_2), 5.96–5.90 (d, J = 6 Hz, 1 H, 1′-H), 8.15 (s, 1 H, NH). There is no change in the ^1H NMR when δ 8.15 is irradiated. Fractions 110–122 were combined to yield a gum whose structure has been assigned the N_3 isomer: ^1H NMR ($CDCl_3$) δ 2.1 (m, 9 H, $COCH_3$), 3.0 (s, 3 H, NCH_3), 4.5–4.2 (m, 3 H, 4′-H, 5′-CH_2), 4.6 (m, 2 H, NCH_2N), 5.65 (m, 1 H, 3′-H), 5.85 (m, 1 H, 2′-H), 6.1 (d, J = 5 Hz, 1 H, 1′-H), 7.0 (br, 1 H, NH). When NH at δ 7.0 is irradiated, δ 4.6 collapses to a singlet.

Anal. Calcd for $C_{15}H_{21}N_3O_9$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.23; H, 5.62; N, 8.00.

Acknowledgments. The author thanks Mr. S. A. Mizsak and Mr. T. A. Scahill for their aid in the interpretation of the ^1H NMR spectra, and Drs. T. Brodasky, B. Bannister, and L. Dolak and Mr. R. Birkenmeyer of our Infectious Diseases section for their helpful consultations.

Registry No.—I, 57350-36-4; IV, 64332-47-4; V, 66515-67-1; VI, 66515-68-2; VII, 3601-89-6; VIII, 66515-69-3; IX, 66515-70-6; X, 66515-71-7; XI, 22860-91-9; XII, 14215-97-5; XIII, 28708-32-9; XIV, 66515-62-6; XV, 66515-63-7; XVI, 66515-64-8; XVII, 66515-65-9; XVIII, 66515-66-0; XIX, 64332-50-9.

References and Notes

(1) Presented in part at the 172nd National Meeting of the American Chemical Society, San Francisco, Calif., 1976, Abstr CARB 43.
(2) C. DeBoer, B. Bannister, A. Dietz, J. E. Gray, and C. Lewis, American Society for Microbiology, Atlantic City, N.J., 1976.
(3) A. D. Argoudelis and S. Mizsak, *J. Antibiot.*, **29**, 818 (1976).

(4) V. Reichman, K. Hirota, C. K. Chu, K. A. Watanabe, J. J. Fox, *J. Antibiot.*, **30**, 129 (1977).
(5) C. DeBoer and B. Bannister, U.S. Patent 3 907 643 and 3 907 779.
(6) H. Renis, B. Court, and E. Edison, American Society of Microbiology, Atlantic City, N.J., 1976.
(7) A. Piskala and J. Gut, *Collect. Czech. Chem. Commun.*, **26**, 2519 (1961).
(8) M. W. Winkley and R. K. Robins, *J. Org. Chem.*, **35**, 491 (1970).
(9) H. Vorbrüggen and U. Niedballa, *Tetrahedron Lett.*, *41*, 3571 (1970).
(10) U. Niedballa and H. Vorbrüggen, *J. Org. Chem.*, **39**, 3654 (1974).
(11) A. Piskala and F. Sörm, *Collect. Czech. Chem. Commun.*, **29**, 2060 (1964).
(12) U. Niedballa and H. Vorbrüggen, *Angew. Chem.*, **9**, 461 (1970).
(13) B. Bannister, 10th International Symposium on the Chemistry of Natural Products, Dunedia, New Zealand, Aug., 1976, Abstr C-28.
(14) D. Duchamp, B. Bannister, and C. Chidester, unpublished data.
(15) U. Niedballa and H. Vorbrüggen, *J. Org. Chem.*, **41**, 2084 (1976).
(16) M. Prystas, J. Farkas, and F. Sörm, *Collect. Czech. Chem. Commun.*, **30**, 3123 (1965).
(17) A. K. Bhattacharya, R. K. Ness, and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 428 (1963).
(18) H. Zinner and M. Pfeyer, *Chem. Ber.*, **94**, 2792 (1961).
(19) A. Szabolcs, *J. Carbohydr., Nucleosides, Nucleotides*, **2(3)**, 197 (1975).
(20) W. Zorbach and R. Tipson, "Synthetic Procedures in Nucleic Acid Chemistry", Vol. 2, Wiley, New York, N.Y., 1973.
(21) K. A. Watanabe, D. H. Hollenberg, and J. J. Fox, *J. Carbohydr., Nucleosides, Nucleotides*, **1**, 1 (1974).
(22) A. Piskala and J. Gut, *Collect. Czech. Chem. Commun.*, **27**, 1562 (1962).
(23) Yields were determined by making a 1 mg/mL (H_2O) solution of the crude, hydrolyzed (25% CH_3ONa/CH_3OH) reaction mixture, saturating a 12.7 mm disk (No. 740-S, Schlercher and Schuell Inc.) with this solution, assaying against *Klebsiella pneumonia*, and comparing the results to those obtained with known concentrations of the antibiotic. The α anomer was shown to be devoid of any antibacterial activity.

C_{15} Halogenated Compounds from the Hawaiian Marine Alga *Laurencia nidifica*. Maneonenes and Isomaneonenes

Sigmund M. Waraszkiewicz, Hao H. Sun, and Karen L. Erickson*

Jeppson Laboratory, Clark University, Worcester, Massachusetts 01610

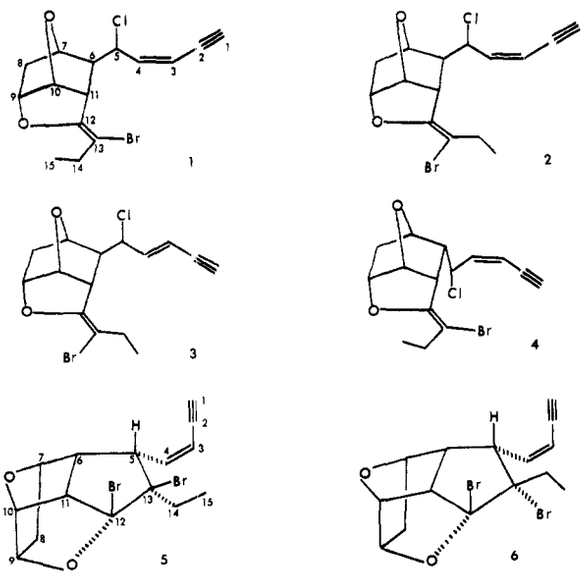
Janet Finer and Jon Clardy*

Ames Laboratory-USERDA and Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received September 30, 1977

Six C_{15} nonterpenoid halo ethers from a green variety of the Hawaiian marine alga *Laurencia nidifica* have been isolated and characterized by chemical and spectroscopic methods. The maneonenes (**1–4**) have one carbocyclic ring and the isomaneonenes (**5** and **6**) possess two carbocyclic rings, an unusual feature for C_{15} nonterpenoid ethers of *Laurencia*. The structure of isomaneonene-B is confirmed by X-ray analysis.

Marine algae of the genus *Laurencia* have been extensively investigated in recent years and a variety of terpenoid and nonterpenoid metabolites have been isolated and characterized.[1] The Hawaiian alga *Laurencia nidifica* has been divided into two pink varieties, one elaborating laurinterol, aplysin, and pacifenol[2] and the second elaborating nidifidiene, nidificene,[2] nidifidienol,[3] and nidifocene,[4] and a green variety, containing sesquiterpenoid alcohols[5] and halogenated nonterpenoid C_{15} compounds, the maneonenes **1–4** and the isomaneonenes **5** and **6**.[6–8] This paper describes the details of the structural work on the latter two groups of compounds together with X-ray confirmation of structure for isomaneonene-B.



Collections of the alga were made in January and June 1975 and January 1976 at Diamond Head and Black Point reefs on the island of Oahu, Hawaii. The alga is bright green in color and grows in patches on the reef where the wave action is substantial. Although its color and habitat are different from other varieties of *L. nidifica*, this alga has been classified as the same species.[9]

Ether extracts of the air-dried alga were chromatographed on silica gel columns. The benzene fraction afforded the *cis*-maneonenes **1**, **2**, and **4** and benzene–ether fractions gave *trans*-maneonene-B (**3**) together with the isomaneonenes **5** and **6**. *cis*-Maneonene-B (**2**) was consistently the major component, but amounts of the other compounds varied, apparently with the season; *trans*-maneonene-B (**3**) was found only in the January 1976 collection. Separation of the isomers was achieved by repeated thin layer chromatography on silica gel with multiple developments (Scheme I).

High resolution mass spectroscopy established the formula of $C_{15}H_{16}BrClO_2$ for the maneonenes **1–4**. All of the spectral and chemical data suggested that these four compounds were very closely related, consequently the component of greatest abundance, *cis*-maneonene-B (**2**), and its isomer, *cis*-maneonene-A (**1**), were investigated first. These two compounds differ only in the configuration of the C-12 double bond.

cis-Maneonene-A displays an acetylenic C–H stretch (3310 cm^{-1}) in the IR spectrum. The UV (225 nm) and ^1H and ^{13}C NMR spectra (Table I, C_1, C_3, and C_4) established the *cis*-enyne portion of the C-5 side chain. Downfield absorptions in the ^{13}C NMR (δ 58.3) and in the ^1H NMR spectra (δ 5.08) were ascribed to a halogen-bearing carbon with one proton attached. This proton is coupled by 10.5 Hz to the C-4 vinylic

0022-3263/78/1943-3194$01.00/0