can be used for this calculation, but a good average can be obtained by comparing the total peak area for each perfluoropropyl group. Therefore the per cent of the *n*-propyl isomer is

$$\frac{0.69 + 0.66 + 0.95}{0.69 + 0.66 + 0.95 + 1.00 + 5.77} \times 100 = 25\%$$

The product was thus identified as a mixture of approximately 25% $CF_3CF_2CF_2OOF$ and 75% $CF_3CF(OOF)CF_3$.

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Received May 1, 1968

The Total Synthesis of Kasugamycin

Sir:

Kasugamycin, found in 1965,[1] is an antibiotic produced by *Streptomyces kasugaensis*, and exhibits a strong preventive effect against rice blast. The structure (I) was established in 1966 by chemical[2] and X-ray crystallographic[3] studies. We now wish to describe the total synthesis of kasugamycin.[4]

6-Methyl-3,4-dihydro-2H-pyran-2-one[5] (II) was treated with nitrosyl chloride in methylene chloride at −60° to give a dimer of 6-chloro-6-methyl-5-nitrosotetrahydropyran-2-one (III) (97%), mp 74–74.5°.[6] The chloronitroso dimer III was easily hydrolyzed with water at room temperature to give 4-oximino-5-oxohexanoic acid (IV) in the theoretical yield. Direct hydrogenation of III with hydrogen over Pd–C afforded only 3,6-dimethylpyrazine-2,5-dipropionic acid.[7] However, the catalytic reduction of IV with hydrogen over Pt afforded stereoselectively DL-*erythro*-4-amino-5-hydroxyhexanoic acid (V) (71%), mp 184–185°.[8] The *erythro* acid V was lactonized by treatment with Ac_2O at room temperature, affording a N-acetylated lactone (VI) (95%), bp 165–168° (0.22 mm). The lactone VI was reduced with $LiAlH_4$ to a hemiacetal[9] (VII) (70%), mp 139–141°, which by treatment with Ac_2O and pyridine at room temperature gave a dihydropyran (VIIIa) (95%), mp 60–62°, and by refluxing with Ac_2O and pyridine at 118–119° gave an N-diacetyl dihydropyran (VIIIb) (70%), bp 110–111° (3.5 mm). The stereochemistry of VIIIb was confirmed to be *trans* as expected from *erythro* isomer V by its nmr spectrum.[10] On the other hand, forosamine[11] obtained from the acid hydrolysate of spiramycin has a D-*erythro* configuration[12] and has been synthesized from the *erythro* acid V in three steps. The reductive dimethylation of V by Bowman's method[13] followed by lactonization with Ac_2O gave IX (95% over-all yield), bp 114–115° (0.5 mm), which on reduction with $LiAlH_4$ gave DL-forosamine (X). This finding not only supports the *trans* relation of the amino and methyl groups, but presents a new and useful method for the synthesis of a deoxyamino sugar from readily available chemicals.

N-Diacetyldihydropyran VIIIb was treated with nitrosyl chloride under similar conditions as in the case of III, affording the expected chloronitroso dimer XI (83%), mp 75–76°. Displacement with lower alcohols such as CH_3OH, EtOH, and *i*-PrOH in the presence of $Hg(CN)_2$ at room temperature afforded the corresponding α-glycosides of nitroso dimer XIIa, XIIb, and XIIc, respectively, in excellent yields. XIIa, mp 135–136°, mol wt 530.5, was reduced with hydrogen over Pt, followed by separation using an acidic ion-exchange resin to give mono-N-acetyl derivative XIIIa (96%), mp 203–204° as hydrochloride, which by hydrolysis with $Ba(OH)_2$ gave DL-methylkasugaminide (XIIIc) (91%), mp 164–165° as dihydrochloride, showing an nmr identical with that of methylkasugaminide.[14] This evidence indicates that the nitroso group is exclusively introduced in the axial configuration at C-2 by the addition of nitrosyl chloride.[15] Therefore, the synthesis of the deoxyamino sugar moiety of kasugamycin has been accomplished by stereoselective reactions.

The chloronitroso dimer XI was treated with excess 1:2,3:4-di-O-isopropylidene-D-inositol[16] in methylene chloride at 0° in the presence of Ag_2CO_3, $AgClO_4$, and Drielite, followed by hydrogenation over Pt in acetic acid and boiling in 50% acetic acid. The reaction product was carefully purified by chromatography using Amberlite CG-50 (ammonium form) and

(1) H. Umezawa, Y. Okami, T. Hashimoto, Y. Suhara, M. Hamada, and T. Takeuchi, *J. Antibiotics*, **18A**, 101 (1965).

(2) (a) Y. Suhara, K. Maeda, H. Umezawa, and M. Ohno, *Tetrahedron Lett.*, 1239 (1966); (b) "Deoxy Sugars" Advances in Chemistry Series, No. 74, American Chemical Society, Washington, D. C., in press.

(3) T. Ikekawa, H. Umezawa, and Y. Iitaka, *J. Antibiotics*, **19A**, 49 (1966).

(4) A synthesis of kasuganobiosamine (XIIId) starting from glucose has recently been reported: M. Nakajima, H. Shibata, K. Kitahara, S. Takahashi, and A. Hasegawa, *Tetrahedron Lett.*, 2271 (1968).

(5) D. Vorlander and A. Knotzsch, *Ann.*, **294**, 319 (1897).

(6) Recent progress of the nitrosyl chloride addition reaction on various olefins seems to present a useful synthetic method for amino sugar containing antibiotics (M. Ohno, N. Naruse, M. Okamoto, S. Torimitsu, and I. Sakai, *Bull. Chem. Soc. Jap.*, **39**, 1119, 1125, 1129 (1966); R. U. Lemieux, T. L. Nagabhushan, and I. K. O'Neill, *Can. J. Chem.*, **46**, 413 (1968), and references contained therein).

(7) R. A. F. Bullerwell, A. Lawson, and H. V. Morley, *J. Chem. Soc.*, 3283 (1954).

(8) The stereoselectivity may reasonably be explained on the basis of kinetic control at the transition state of reduction as in the case of α-methylaminopropiophenone (E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 435).

(9) G. E. Arth, *J. Amer. Chem. Soc.*, **75**, 2413 (1953).

(10) The tetrahydropyran derivative obtained by hydrogenation of VIIIb over Pt showed a large coupling constant between the hydrogens in question ($J_{4,5}$ = 9.0 Hz).

(11) R. Paul and S. Tchelitcheff, *Bull. Soc. Chim. Fr.*, 734 (1957).

(12) C. L. Stevens, G. E. Gutowski, K. G. Taylor, and C. P. Bryant, *Tetrahedron Lett.*, 5717 (1966).

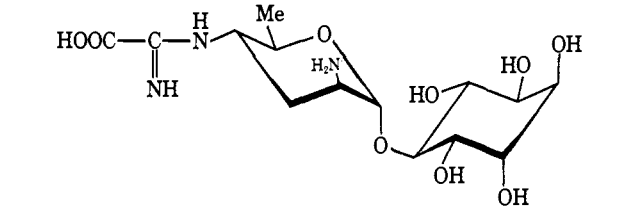
(13) R. E. Bowman and H. H. Stroud, *J. Chem. Soc.*, 1342 (1950).

(14) Originally, the methoxy group of methylkasugaminide was assigned to be β only on the basis of nmr spectrum, but now revised to be α on the basis of chemical evidence, which will be given in a full paper (Y. Suhara, *et al.*, *J. Antibiotics*, **18A**, 184 (1965)).

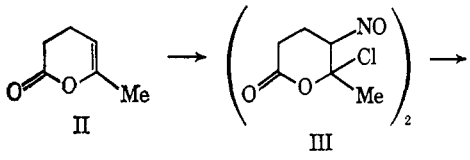
(15) Although the stereochemistry of XI was not decided by nmr methods because of its instability and insolubility in usual solvents, the steric course of NOCl addition seems to be more preferred in the *cis* manner in methylene chloride. See, for instance, M. Ohno, M. Okamoto, and K. Nukada, *Tetrahedron Lett.*, 4047 (1965). The exclusive β-side attack of NOCl can be explained by the steric hindrance of the bulky N-diacetylamino group of VIIIb.

(16) C. E. Ballou and H. O. L. Fischer, *J. Amer. Chem. Soc.*, **75**, 3673 (1953).

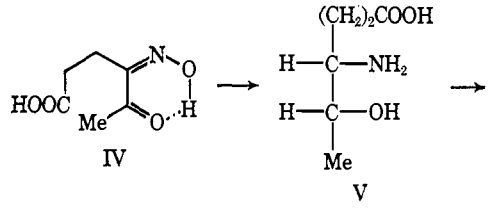
Chart I



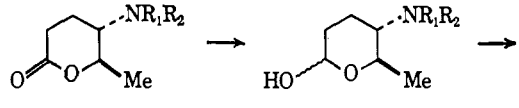
I



II III

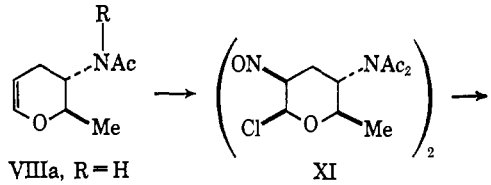


IV V



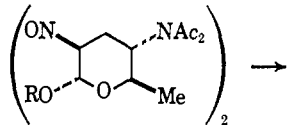
VI, R_1 = H; R_2 = Ac
IX, R_1 = R_2 = Me

VII, R_1 = H; R_2 = Ac
X, R_1 = R_2 = Me

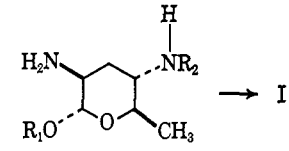


VIIIa, R = H
b, R = Ac

XI



XIIa, R = Me
b, R = Et
c, R = *i*-Pr



XIIIa, R_1 = Me; R_2 = Ac
b, R_1 = residue of D-inositol; R_2 = Ac
c, R_1 = Me; R_2 = H
d, R_1 = residue of D-inositol; R_2 = H

by recrystallization from a mixed solvent of methanol and acetone, affording N^4-acetyldiamino sugar XIIIb, mp 139–142°, in low yield.[17] The synthetic material XIIIb was confirmed to be identical with the N-acetyl derivative[18] of natural kasuganobiosamine in all respects, including nmr, ir, optical rotation, and mixture melting point. The treatment of XIIIb with $Ba(OH)_2$ afforded kasuganobiosamine (XIIId). It is noteworthy that not only the displacement but also the resolution of XI has been carried out by the reaction with 1:2,3:4-di-O-isopropylidene-D-inositol, yielding the product stereochemically conforming with natural kasuganobiosamine, which is successfully crystallized in a pure state without any other procedure for the separation of the diastereoisomers. The synthesis of XIIId completes the total synthesis of kasugamycin, since kasuganobiosamine (XIIId) was previously converted to kasugamycin (I) by treatment with the diethyl ester of oxalimidic acid and subsequent mild hydrolysis with HCl in our structural studies.[2,19] (See Chart I for structures.)

(17) Although the yield of the crude material was 10.5% based on XI, the most purified material with $[\alpha]^{20}D$ +116° (*c* 1.3, H_2O) was obtained in *ca.* 1% yield.

(18) Y. Suhara, K. Maeda, and H. Umezawa, *J. Antibiotics*, **18A**, 187 (1965).

(19) Satisfactory elemental analyses were obtained for all the compounds for which melting point or boiling point values were given. All the compounds cited showed reasonable spectral data. In the chart, compounds V to XIII are all racemic except XIIIb and XIIId, but only one member of the pairs is shown. The homogeneity of V and XIIa was confirmed by a combination of tlc, paper chromatography, and nmr methods.

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The Photochemical Synthesis of Thiocyanatobis(triphenylphosphine)copper(I)

Sir:

Organic azides are known to undergo several types of reactions. For example, organic azides react with olefins by 1,3 cycloaddition to form heterocyclic compounds which may decompose thermally or photolytically to yield a variety of products.[1,2] In analogy to organic azides, azido complexes of transition metals might be expected in some cases to undergo the same types of reaction. We therefore have undertaken a detailed study of the photochemistry of coordinated azides. Here we wish to report the photochemical synthesis of the thiocyanatobis(triphenylphosphine)copper(I) complex by the addition of CS_2 to azidobis(triphenylphosphine)copper(I) and its subsequent photolysis.

$((C_6H_5)_3P)_2CuN_3$[3] was prepared by the addition of a methanolic solution of NaN_3 to a chloroform solution containing cuprous chloride and excess $(C_6H_5)_3P$. The compound, mp 185° dec, has been compositionally identified by elemental analysis and a molecular weight determination in $CHCl_3$.[4] *Anal.* Calcd for $((C_6H_5)_3P)_2CuN_3$: C, 68.5; H, 4.75; N, 6.65; P, 9.75. Found: C, 68.3; H, 5.1; N, 6.75; P, 9.32. The N–N stretching[5] frequency of the azide is at 2045 cm^{-1}; mol wt: calcd, 629.5; found, 644. Judging from its composition and monomeric nature in solution we

(1) R. Huisgen, *Angew. Chem. Intern. Ed. Engl.*, 565 (1963).
(2) R. F. Bleiholder and H. Shecter, *J. Amer. Chem. Soc.*, 90, 2131 (1968).
(3) W. Beck, M. Bauder, W. P. Fehlhammer, P. Pollmann, and H. Schachl, *Inorg. Nucl. Chem. Letters*, 4, 143 (1968).
(4) Molecular weights were determined with a Mechrolab osmometer, Model 301A.
(5) Infrared measurements were made on a Beckman IR-5A using KBr disks.