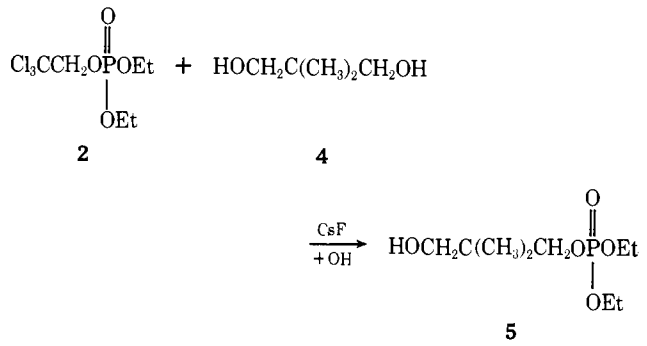
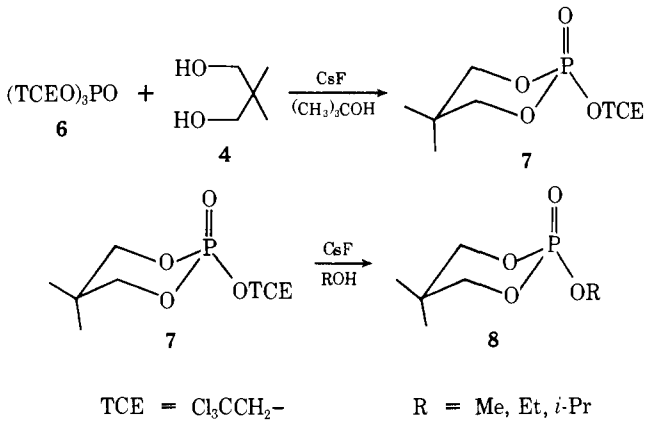
tions using a large excess of cesium fluoride.

tert-Butyl alcohol does not react with **1** even at 80 °C. Thus it makes an excellent solvent for solid alcohols. When 2,2-dimethyl-1,3-propanediol (**4**, 3.65 g) is dissolved in *t*-BuOH (20 ml) containing 10 equiv of CsF and 1 g of **2**, a quantitative yield of **5** is obtained after 2 days.



2 4 5

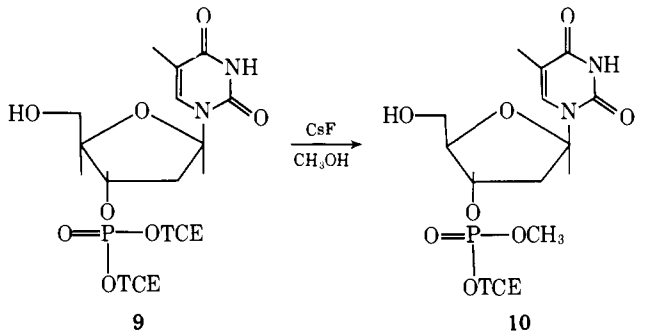
Another feature of the general reaction is the formation of cyclic phosphates from diols. For example, if one starts with tris(trichloroethyl) phosphate (**6**) and compound **4** (1 g of **6** and 4.23 g of **4**) in *t*-BuOH (20 ml) along with 10 equiv of CsF at room temperature, the cyclic phosphate (**7**) is obtained in 95% yield. The remaining trichloroethyl group of **7** can be completely exchanged to give **8** by heating **7** at 80 °C in other alcohols (1 g of **7**/20 ml) with cesium fluoride (5 equiv) for 2 days.



6 4 7 7 8

TCE = Cl_3CCH_2– R = Me, Et, *i*-Pr

As a final example, the exchange reaction occurs readily in nucleotide triesters where, for example, compound **9** is converted into **10** in 95% yield (100 mg of **8**/10 ml of MeOH and 30 equiv of CsF at room temperature for 2 days).



9 10

Thus the reaction described[9] in this report is remarkably versatile and will benefit fields ranging from pesticides to phospholipids to nucleotides.

Acknowledgment. We wish to thank the National Research Council of Canada and the Province of Quebec for financial support.

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(4) Prepared by reaction of the bis(2,2,2-trichloroethyl) phosphorochloridate with the alcohol in pyridine.
(5) Reactions can be conveniently monitored by gas chromatography. The instrument used was a Hewlett-Packard Model 5711A gas chromatograph equipped with a 10 ft × ⅛ in. o.d. stainless steel column packed with 10% OV-1 on chromasorb W-HP. The off-column injector had a glass liner which must be changed frequently to prevent buildup of cesium fluoride resulting in incorrect analyses.
(6) The presence of water in the alcohol slows the reactions to some extent. However, to make the synthesis as practical as possible the results reported here are based on laboratory grade absolute alcohol and spectrograde methanol (American Chemicals Ltd.).
(7) All new products have been fully characterized including mass spectrometry on an AEI 902 high resolution instrument.
(8) It is possible to exchange one group in **6** with other alcohols as well. For example, **1** (R = Et) is obtained in 77% yield after 4 days at room temperature when **6** is dissolved in ethanol (1 g/200 ml) along with 1 equiv of CsF. After this time 15% of **6** was unchanged and 8% of **2** (R = R′ = Et) was obtained.
(9) The reactions apparently occur via initial attack of fluoride ion on phosphorus followed by rapid reaction of the phosphorofluoridate with the alcohol. The intermediate fluoridate from **7** can be detected in *t*-BuOH. This aspect will be dealt with later in a full report.

Kelvin K. Ogilvie,* Serge L. Beaucage
Nicole Theriault, Douglas W. Entwistle
Department of Chemistry, McGill University
Montreal, Quebec, Canada H3C 3G1
Received September 16, 1976

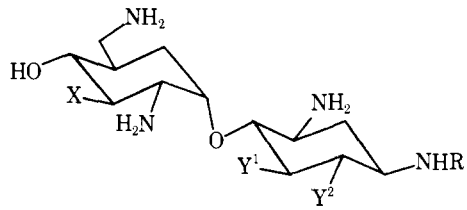
Conversion of Aminoglycosidic Antibiotics: Novel and Efficient Approaches to 3′-Deoxyaminoglycosides via 3′-Phosphoryl Esters

Sir:

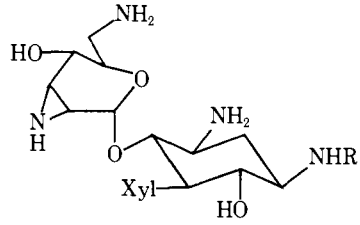
Semisynthetic 3′-deoxyaminoglycosidic antibiotics, including 3′,4′-dideoxy derivatives, are remarkably effective against resistant strain bacteria producing phosphotransferases.[1,2]

We now report new, simple methods for the selective dehydroxylation of aminoglycosides by a combination of enzymatic and chemical reactions; the former is phosphorylation of aminoglycosides by using enzymes from resistant strains,[1,3] while the latter involves transformation of phosphates into 3′-deoxyaminoglycosides by treatment with silylating agents and subsequent hydrogenation. The procedures present a conceptionally new and promising approach to modifications of polyfunctional antibiotics. Typical experimental procedures for the transformations are available; see paragraph at end of paper regarding supplementary material.

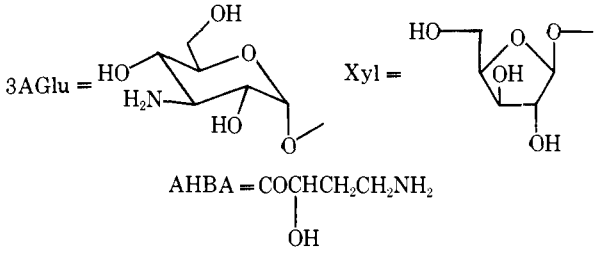
Kanamycin B (**1**) was phosphorylated with the enzyme from *Pseudomonas aeruginosa* GN 573[4] in the presence of ATP and $MgSO_4$ to its 3′-phosphate (**2**), mp 220-230 °C dec, $[\alpha]_D$ +106° (*c* 0.5, H_2O), in 99% yield.[5] Reaction of **2** with trimethylchlorosilane (TMCS)-hexamethyldisilazane (9:4 by volume) in a mixture of pyridine and HMPA in the presence of triphenylphosphine[6] in a sealed tube (120 °C, 30 h) yielded after hydrolysis, 3′-chloro-3′-deoxykanamycin B (**3**), mp 190-195 °C dec (from C_2H_5OH), $[\alpha]_D$ +126° (*c* 1.0, H_2O). The chloride **3** was hydrogenated with Raney nickel in the presence of triethylamine in water to afford 3′-deoxykanamycin B (**4**), identical with a natural product (tobramycin), in an overall yield of 47% based on **2**.[2,7] Similarly, 3′-deoxyneamine (**6**, nebramine),[2,7] 3′-deoxyxylostasin (**9**),[8] mp 134-135 °C dec (from CH_3OH), $[\alpha]_D$ +28° (*c* 0.5, H_2O), 3′-deoxyribostamycin,[9] 3′-deoxyparomomycin I (lividomycin B),[10] and 3′-deoxyneomycin B[2] were obtained from the corresponding aminoglycosides. The chlorination of butirosin A



1, X = OH; Y^1 = OH; Y^2 = 3AGlu; R = H
2, X = OPO_3H_2; Y^1 = OH; Y^2 = 3AGlu; R = H
3, X = Cl; Y^1 = OH; Y^2 = 3AGlu; R = H
4, X = H; Y^1 = OH; Y^2 = 3AGlu; R = H
5, X = Cl; Y^1 = OH; Y^2 = OH; R = H
6, X = H; Y^1 = OH; Y^2 = OH; R = H
7, X = Cl; Y^1 = Xyl; Y^2 = OH; R = H
9, X = H; Y^1 = Xyl; Y^2 = OH; R = H
10, X = OH; Y^1 = Xyl; Y^2 = OH; R = AHBA
11, X = OPO_3H_2; Y^1 = Xyl; Y^2 = OH; R = AHBA
13, X = H; Y^1 = Xyl; Y^2 = OH; R = AHBA



8, R = H
12, R = AHBA



3′-phosphate (**11**)[11] proceeded in lower yield, presumably owing to an undesired side reaction on the acyl moiety. Kanamycin A 3′-phosphate[1] possessing a hydroxy group at the 2′-position was recovered unchanged in the chlorination reaction. The equatorial configuration of the chlorine atom at the 3′-position was established on the basis of the proton-proton coupling constants observed in **3** and 3′-chloro-3′-deoxyneamine (**5**) ($J_{2',3'}$ = 10 and 11 Hz, respectively).

Another dehydroxylation procedure is the one involving aziridine derivatives. Treatment of **11** with bistrimethylsilylacetamide (BSA)-TMCS (5:1 by volume) in pyridine in a sealed tube (105 °C, 30 h) afforded, after hydrolysis, 2′,3′-epimino-2′-deamino-3′-deoxybutirosin A (**12**), mp 212–214 °C (from CH_3OH), $[\alpha]_D$ +36° (c 0.5, H_2O), in 58% yield with 80% conversion of **11**. The assigned structure for **12** was confirmed by the comparison of ^{13}C NMR spectra of butirosin A (**10**)[12] and **12**. The signal of C-2′ and C-3′ forming the aziridine ring in **12** appeared at the higher field[13] (chemical shifts for C-2′ and C-3′: 33.7–34.9 ppm in **12**; 56.4 and 74.0 ppm in **10**).[14] Hydrogenation of **12** with Raney nickel in water at 70 °C, followed by separation by ligand exchange chromatography[15] (Amberlite CG-50, Cu-NH_3 form) gave 3′-deoxybutirosin A (**13**), mp 204–208 °C (from CH_3OH), $[\alpha]_D$ +22° (c 0.5, H_2O), in 57% yield in preference to the isomer (product ratio, 5:1). The structure of **13** was confirmed by hydrolysis leading to **6** and **9**. This method was successfully applied to 3′-phosphates of **1**, neamine,[1] xylostasin,[16] and butirosin B[17] to obtain **4**, **6**, **9**, and 3′-deoxybutirosin B,[18] respectively, via the corresponding 2′,3′-epiminoaminoglycosides.

3′-Chloro- and 2′,3′-epiminoaminoglycosides thus obtained are interconvertible. For example, 2′,3′-epimino-2′-deamino-3′-deoxyxylostasin (**8**) was converted into 3′-chloro-3′-deoxyxylostasin (**7**) in high yield under the chlorination condition, while treatment of **7** with BSA in pyridine in a sealed tube (120 °C, 25 h) gave **8** in moderate yield.[19]

These results, together with the aforementioned observation obtained in both the substitutions (**2** → **3**, **11** → **12**), indicate that silylated epiminoglycosides are intermediates in the chlorination reaction.

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Supplementary Material Available: Typical experimental procedures for the transformations (4 pages). Ordering information is given on any current masthead page.

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(14) The δ values are from spectra of D_2O solutions containing dioxane as an internal standard. They were recorded in parts per million downfield from Me_4Si (dioxane, 67.4 ppm). Four peaks due to C-2′, C-3′, C-2, and C-β (N^1-acyl part) appeared at 33.7, 34.0, 34.7, and 34.9 ppm, but the exact assignment has not yet been established.
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Tetsuya Okutani, Tsunehiko Asako, Kouichi Yoshioka
Kentaro Hiraga,* Makoto Kida
Central Research Division, Takeda Chemical Industries, Ltd.
Yodogawa-ku, Osaka 532, Japan
Received August 23, 1976

Intrinsic Basicity Determination Using Metastable Ions

Sir:

We report a new method for the determination of intrinsic relative proton affinities. The procedure is sensitive to small differences in base strength and is simple in concept and in practice. It appears to be capable of generalization to the determination of affinities toward other ions. Present mass