energy may be a consequence of the relatively small transfer of charge to the metal during the homolysis process.[15] Finally, we note that while the lowest energy "d-d" transition in acidopentaammine complexes may be assigned as (d_{xz}, d_{yz}, or d_{xy}) → d_{z^2}, the small energy for Co-CH_3 homolysis suggests that the 478-nm transition in Co([14]aneN$_4$)$(OH_2)CH_3^{2+}$ should be assigned as $\psi_B \rightarrow d_{x^2-y^2}$. A more traditional assignment of the weakly allowed transitions in Co([14]aneN$_4$)$(OH_2)CH_3^{2+}$ as "ligand field" transitions (analogous to those of $Co(NH_3)_6^{3+}$) is not compatible with the photochemical observations.[15]

More detailed analyses of the bonding energetics and the electronic structures of the organo-cobalt complexes will be presented elsewhere.[15,16] Consideration of our observations on Co([14]aneN$_4$)$(OH_2)CH_3^{2+}$ should lead to more correct spectroscopic assignments, since the transition energies should vary in a predictable manner with changes of the equatorial ligands.[17] Furthermore, homolysis threshold energies can be used as measures of Co-alkyl bond energies, and the limited information available suggests that cobalt-alkyl bonds are generally relatively weak.

Photochemical techniques and synthesis of compounds have been described elsewhere.[2,9,13,16] Photolyses were performed anaerobically in solutions containing 10^{-3} M $HClO_4$ and 2.5 M 2-propanol (as a $\cdot CH_3$ scavenger). The quantitative determination of Co^{II}([14]aneN$_4$) was accomplished by aerating aliquots of photolyte and determining the amount of μ-peroxodicobalt species developed, based on the absorbance at 420 nm.[18] Dark reactions of primary products were not directly detected and observed isosbestic points in spectroscopic scans of photolyte were consistent with reaction 1.[16]

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(15) The homolysis energy of CoL_5X^{2+} may be approximately partitioned into components due to ionic (I), covalent (C), and changes in ligand field stabilization energy (ΔLFSE) per the cycle:

$$Co^{3+}(g) + 5L(g) + X^-(g) \xrightarrow{IP(Co) + EA(X)} Co^{2+}(g) + 5L(g) + \cdot X(g)$$

$$\downarrow [LFSE(Co^{III}) + U_{ox}] \qquad [LFSE(Co^{II}) + U_{red}] \downarrow$$

$$M^{III}L_5(X^-)(g) \xrightarrow{\Delta H_B} \{M^{II}L_5, \cdot X\}(g)$$

Thus the homolysis energy is given by $\Delta H_B = [\Delta U_0 + IP + EA] + \Delta LFSE$, where $[\Delta U_0 + IP + EA] \simeq I + C$. In this approach, the contrast between the homolysis energies of $Co(NH_3)_5Br^{2+}$ ($\Delta H_B \simeq 236$ kJ/mol) and Co([14]-aneN$_4$)$(OH_2)CH_3^{2+}$ ($\Delta H_B < 217$ kJ/mol) would be attributed to a smaller value (by about 25% of ΔLFSE for Co–CH_3 homolysis than for Co–Br homolysis since a larger "covalent" contribution would be expected for the Co–CH_3 bond than for the Co–Br bond (J. F. Endicott, *Inorg. Chem.*, in press).
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A General Transesterification Method for the Synthesis of Mixed Trialkyl Phosphates

Sir:

The synthesis of mixed trialkyl phosphates continues to be an important goal. Such compounds are of current interest in such diverse areas as pesticides, phospholipids, and nucleic acids. There have been several recent reports on new methods of synthesis of mixed alkyl phosphates.[1-3] We wish to report on a very simple exchange reaction involving readily available starting materials which allows the synthesis of mixed trialkyl phosphates.

The general reaction is shown below where a bis(trichloroethyl) alkyl phosphate[4] (**1**) is dissolved in an alcohol and in the presence of fluoride ion (CsF) the product **2** is obtained.[5]

$$\underset{\mathbf{1}}{(Cl_3CCH_2O)_2POR} \xrightarrow[CsF]{R'OH} \underset{\mathbf{2}}{Cl_3CCH_2OPOR} \xrightarrow[CsF]{R''OH} \underset{\mathbf{3}}{R''OPOR}$$
(each O; OR′)

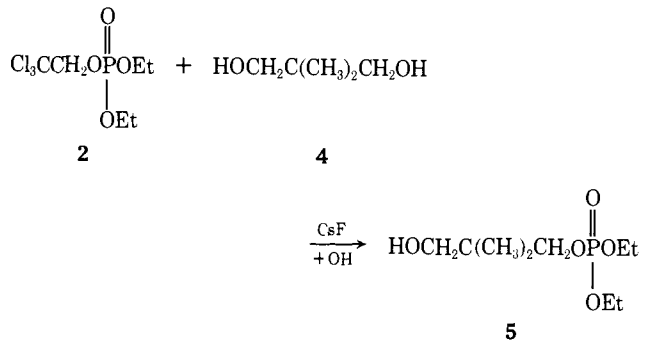
The yields of **2** range from 85 to 100%. For example, when **1** (R = Et) is dissolved in isopropyl alcohol (1 g of **1**/20 ml of *i*-PrOH) with 15 molar equiv (per mole of **1**) of cesium fluoride the product **2** (R = Et, R′ = *i*-Pr) is obtained in quantitative yield in 20 h at room temperature. If **1** (R = *i*-Pr) is dissolved in ethanol[6] (1 g of **1**/90 ml of EtOH) with 10 equiv of CsF, a 90% yield of **2** (R = *i*-Pr, R′ = Et) is obtained after 50 h at room temperature (3% of **1** remained and 7% of **3** (R = *i*-Pr, R′ = R″ = Et was obtained)). When **1** (R = Et) is treated with methanol[6] (1 g of **1**/35 ml of MeOH) using 15 equiv of CsF, an 82% yield of **2** (R = Et, R′ = Me) is obtained in 23 h along with 9% of **1** and 9% of **3** (R = Et, R′ = R″ = Me). All of the products are easily isolated by silica gel chromatography or for very large scale reactions by fractional distillation.[7]

The conversion of **2** into **3** is slower than the above exchange and reactions are usually heated at 80 °C. Thus on dissolving **2** (R = Me, R′ = Et) in isopropyl alcohol (1 g of **2**/20 ml of *i*-PrOH) with 10 equiv of CsF, a quantitative yield of **3** (R = Me, R′ = Et, R″ = *i*-Pr) is obtained after 25 h at 80 °C. This reaction when applied to **2** (R = Et, R′ = *n*-Pr) in *n*-octanol (300 mg of **2**/10 ml) with 5 equiv of CsF yielded 87% of **3** (R = Et, R′ = *n*-Pr, R″ = *n*-oct) after 6 days at 80 °C (13% of **2** was recovered).

These reactions occur equally well when tetra-*n*-butylammonium fluoride is used in place of cesium fluoride. However, the reactions do not occur in the absence of fluoride ion. In addition, ordinary alkyl groups are not displaced under these conditions. For example, trimethyl phosphate is unaffected by heating at 80 °C for extended periods of time in alcohol solu-

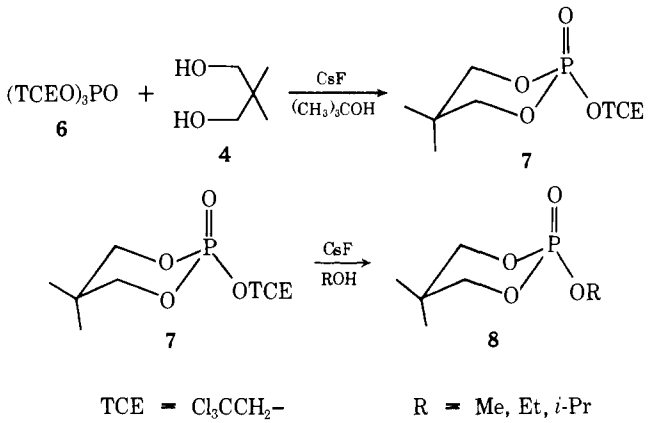
tions using a large excess of cesium fluoride.

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

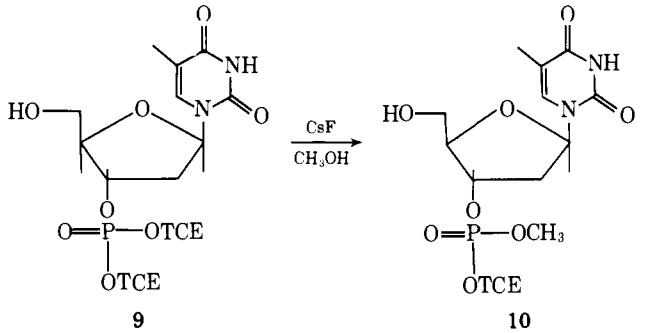
Another feature of the general reaction is the formation of cyclic phosphates from diols. For example, if one starts with tris(trichloroethyl) phosphate (**6**) and compound **4** (1 g of **6** and 4.23 g of **4**) in *t*-BuOH (20 ml) along with 10 equiv of CsF at room temperature, the cyclic phosphate (**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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(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.

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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