tant absorbs appreciably in the region photolyzed. In the case of reaction 5, $\Delta G^{\circ\prime} = 1.45$ V, which means that 69% of the excited state energy of $Ru(bpy)_3^{2+*}$ has been converted into chemical energy. Scheme I represents a useful inorganic model for photosynthesis. Ultimately, a related sequence of reactions may lead to the permanent storage of light energy as chemical energy.

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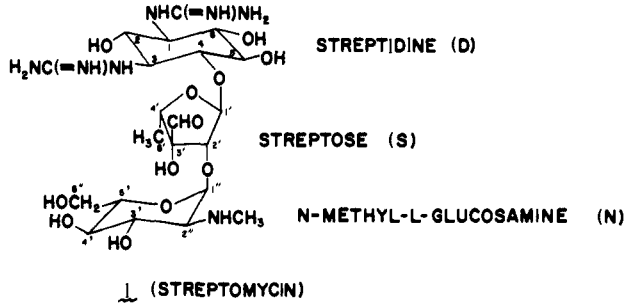
Carbon-13 Evidence for the Stereochemistry of Streptomycin Biosynthesis from Glucose[1,2]

Sir:

Streptomycin (**1**), the antibiotic produced by *Streptomyces griseus*, remains a medically important antibiotic. Studies in recent years[3] have argued for glucose as the precursor of all three subunits of streptomycin–streptidine, streptose, and *N*-methyl-L-glucosamine. Extensive chemical degrada-



tions of the latter two ^{14}C-labeled units of streptomycin indicate direct conversion of all carbons of glucose to like-numbered carbons of *N*-methyl-L-glucosamine[4] and conversion of carbons 1, 2, 4, 5, and 6 of glucose to carbons 1′, 2′, 3′, 4′, and 5′, respectively, and carbon-3 to the formyl carbon, of streptose.[5] However, the only reported degradation of ^{14}C-labeled streptidine involved periodate cleavage of *N,N′*-dibenzoylstreptamine following labeled glucose feeding.[6] These studies indicated that a majority (68,[6a] 83%[6b]) of the label was lost as formic acid, presumably from C-5 of streptidine, when [1-^{14}C]glucose was administered and that a majority of the label was retained in the cyclic dialdehyde hydrate when [2-^{14}C]-, [3,4-^{14}C]-, or [6-^{14}C]glucose was employed. This labeling pattern has been used in support of a biosynthetic pathway involving conversion of glucose to *scyllo*-inosose (**2**, Figure 1). Subsequent steps from **2** have been shown to involve its transamination, phosphorylation, and transamidination to guanidodeoxyinositol, and repeti-

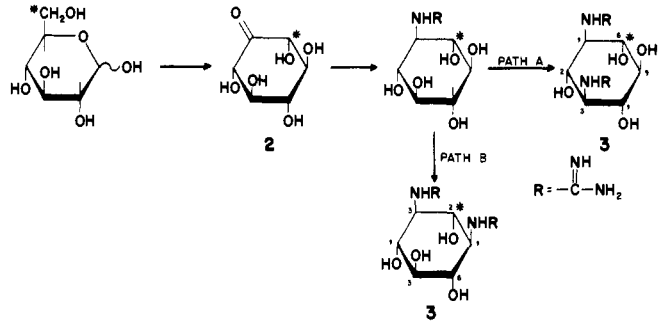
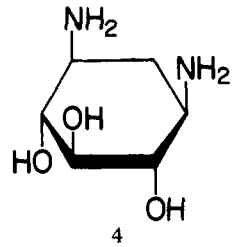


Figure 1. Biosynthetic conversion of glucose to streptidine via *scyllo*-inosose (**2**), with C-6 of glucose labeling C-6 of streptidine by path A, that apparently employed by *S. griseus*. Path B is not followed for streptidine formation but would be analogous to the pathway employed for deoxystreptamine formation by *S. fradiae*.[2b] The asterisks indicate the carbons expected to arise in each pathway from C-6 of glucose.

tion of the keto → guanido steps at the β-carbon in the counterclockwise direction (path A), yielding streptidine (**3**).[7]

Unfortunately, no other carbons of streptidine have been correlated with its glucose precursor. For example, even if [1-^{14}C]glucose gives [5-^{14}C]streptidine, [6-^{14}C]glucose could label either C-4 or C-6 of streptidine. Moreover, we have recently found[2b] that deoxystreptamine (**4**) is formed



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in *Streptomyces fradiae* by an alternative to pathway A which apparently involves oxidation at the β-carbon in the clockwise direction (Figure 1, path B) followed by transamination. With pathway B operative in a closely related aminocyclitol, and in view of the occasional unreliability[8] of periodate oxidation[6] as a structural tool, it seemed advisable to define further the conversion of glucose to streptidine by reinvestigating the biosynthesis of streptidine using a ^{13}C-labeled precursor. We report here our results with [6-^{13}C]-D-glucose, which we have now shown to label carbon-6 of streptidine (pathway A).

A seed culture of *Streptomyces griseus* (MA-4583) was produced in the following medium: corn steep liquor, 30 g/l.; brewer's yeast, 1 g/l.; NZ-Amine, 0.5 g/l.; distilled water to 1 l. (final pH 7.3). Growth was carried out for 2 days at 28°, at which time the seed was used to inoculate six 250-ml erlenmeyer shakeflasks, with each flask containing 40 ml of the following synthetic medium: 31.86 g/l. of glucose (containing 3.86 g/l. of [6-^{13}C]glucose[2b] (64 atom %)); diammonium citrate, 10 g/l.; monosodium glutamate, 2.0 g/l.; K_2HPO_4, 0.5 g/l.; NaCl, 2.5 g/l.; $CaCO_3$, 1.0 g/l.; $MgSO_4 \cdot 7H_2O$, 1.0 g/l.; $FeSO_4 \cdot 7H_2O$, 0.02 g/l.; $ZnSO_4 \cdot NH_2O$, 0.01 g/l.; distilled water to 1 l. (pH 7.3). The culture was incubated on a rotary shaker (220 rpm) for 6 days at 28°, then filtered and acidified with phosphoric acid. The total filtered broth (205 ml) was diluted and passed through a CG-50 column in the NH_4^+ form. Elution with 1 *N* formic acid gave crude labeled streptomycin which was purified via the Reineckate salt.[9]

The ^{13}C NMR spectra of streptomycin show resonances for each of the 21 carbons, which will be assigned in a following communication.[10] The ^{13}C NMR spectrum of the

streptomycin isolated displayed three enhanced resonances at 13.4 (2.3 times natural abundance), 61.2 (6.5 times natural abundance), and 72.4 (4.5 times natural abundance) ppm from tetramethylsilane, which are the respective signals for carbon-5′ of streptose, carbon-6″ of *N*-methylglucosamine, and carbon-6 of streptidine.[10] The labeling of C-5′ of streptose and C-6″ of *N*-methyl-L-glucosamine is consistent with earlier work.[4,5] Labeling of C-6 of streptidine by [6-^{13}C]glucose provides definitive evidence for the stereochemistry of streptidine formation from glucose (pathway A, Figure 1).

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A Kinetic Study of a Friedel–Crafts Ethylation Reaction in Nonpolar Solvent

Sir:

Little has been reported concerning the kinetics of Friedel–Crafts alkylation reactions in nonpolar solvents. Some of the data which has been published appears to be at variance with currently accepted theories.[1] In hopes of clarifying the situation we have determined the kinetics of the $AlBr_3$ catalyzed reaction of ethyl bromide with benzene or toluene in *n*-hexane, using vacuum line procedures to optimize the exclusion of water.[2]

High purity commercially available *n*-hexane and ethyl bromide were dried over CaH_2, degassed, and stored *in vacuo* in break-tip ampoules.[2] $AlBr_3$ was synthesized, purified, and also stored in break-tip ampoules.[3] Known amounts of these reagents were condensed at −196° in a thoroughly flamed reaction flask using usual vacuum line procedures. After the addition of dry nitrogen, the reaction mixture was sealed from the line and brought to reaction temperature (15°) and stirred (spin bar). Reactions were initiated by injecting 15° previously dried (CaH_2) toluene or benzene through a rubber septum on an angled side arm of the reaction flask. Aliquots were periodically removed with a syringe, quenched with H_2O, and analyzed by flame ionization GC.[4]

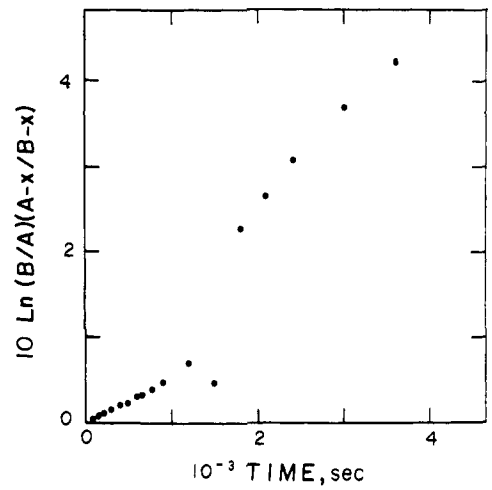

Figure 1. Typical second-order plot for reaction of benzene and ethyl bromide with $AlBr_3$ catalyst in hexane at 15°, mole ratios, 10.37:2.77:0.52:100, respectively.

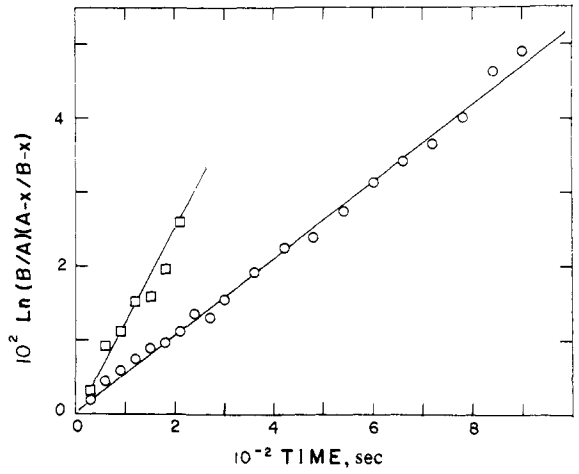

Figure 2. Typical second-order plots at short times for reaction of aromatic and ethyl bromide with $AlBr_3$ catalyst in hexane at 15°: mole ratios, circles, 10.37 (benzene):2.77:0.52:100; squares, 9.91 (toluene): 0.58:0.42:100.

In both systems, layer separation occurred and was heralded by a moderately fast color change followed by a swift change from clear to slightly turbid. The colored, separated phase then finally formed either tiny droplets on the inside of the reaction walls or a very small puddle beneath the spin bar, either of which was difficult to detect. It is significant that this phenomenon occurred in either system within 30 min.

Pseudo-second-order rate plots were obtained in both systems assuming

$$d[\text{product}]/dt = k_{app}[\text{aromatic}][\text{ethyl bromide}]$$

where $k_{app} = k[AlBr_3]_0^n$. A typical graph of $\ln (B/A)(A - x/B - x)$ plotted against time is presented in Figure 1. The plot is fairly linear at short times, i.e., up to the time of layer separation, and then monotonic albeit nonlinear for long times, i.e., after the time of layer separation.

Typical data for benzene and toluene systems at short