zine-mediated dephthaloylation the modified trityl group could be removed via unstable 4,4',4''-triaminotrityl ethers.

Therefore, we synthesized masked pararosaniline derivatives (**1a-d**) in more than 85% yields simply by treatment of pararosaniline with several kinds of phthalic anhydrides in pyridine at 80 °C for 1-2 h followed by addition of acetic anhydride (Chart I). The carbinols **1a-d** were stable under acidic conditions such as 80% acetic acid (room temperature, 24 h), but **1d** decomposed during column chromatography, and the others were stable on silica gel. Expectedly, deacylation of **1a-d** with a 1 M hydrazine solution in pyridine-acetic acid (3:1, v/v) resulted in formation of paparosaline. The order of the deacylations observed is **1b** (t_{comp} = <5 min) ≃ **1d** (<5 min) < **1c** (15 min) << **1a** (10 h).

From these results, we prepared 4,4',4''-tris(4,5-dichlorophthalimido)trityl bromide (CPTrBr) as slightly yellowish crystals (mp > 270 °C) in 82% yield by bromination of **1b** with acetyl bromide in refluxing benzene for 7 h. Because of these simple operations, CPTrBr can be prepared on a kilogram scale.[7] This new reagent allowed facile tritylation with appropriately protected nucleoside derivatives (**2-4**) by the silver ion promoted reaction[8] in the presence of $AgNO_3$ in dimethylformamide to give 5'-tritylated nucleoside derivatives (**8-10**) (Scheme I) in high yields as shown in Table I.[9] The selective introduction of the CPTr group on the primary alcohols of other polyfunctional nucleoside and carbohydrate derivatives (**5-7**) was also achieved in high yields. The CPTr group was found to be stable in pyridine-water (2:1) and even in 80% acetic acid at room temperature for 24 h. Detritylation of compounds **8-10** by use of 1 M hydrazine in pyridine-acetic acid (3:1, v/v)[11] for 20 min followed by quenching with pyridine-acetic acid (1:3, v/v)[12] expectedly led to direct C-O bond fission of the CPTr ethers giving rise to the parent compounds **2-4** quantitatively. It is clearly shown that the N^3-pivaloyloxy)methyl (Pom)[13,14] (for U), O^6-diphenylcarbamoyl (DPC)[16] (for G), N^2-propionyl (Pro)[16] (for G), and 2'-*O*-tetrahydropyran-2-yl (THP)[17] groups (see table I) survived the hydrazine reaction.

Another facinating feature of the CPTr group is that CPTr-containing compounds can be easily detected as red spots on TLC by heating on a hot plate or by spraying 1 M hydrazine in pyridine-acetic acid (3:1, v/v). Its great lipophilicity also helps isolation of the products. CPTr-containing products are more readily eluted from a silica gel column than the DMTr derivatives. Furthermore, the degree of deprotection can be monitored visibly by the color of the liberated pararosaniline. The amount of pararosaniline formed as the result of the hydrazine treatmnet can also be measured spectrophotometrically in a neutral buffer or ethanol by using the ϵ value of 93 000 at 544 nm (λ_{max}) without using strong acids such as perchloric acid.

These results strongly suggest that the CPTr group can be used conveniently in the synthesis of oligoribonucleotides in both the liquid and solid phases. In fact, we achieved high-yield syntheses of several oligoribonucleotides containing the four common ribonucleosides according to our approach.[18] These results will be shortly reported elsewhere. In conclusion, the CPTr group is superior to the levulinyl group in several aspects and will be applicable to the synthesis of a wide variety of natural products.

(4) Sekine, M.; Hata, T. J. *Org. Chem.* **1983**, *48*, 3112.
(5) We also reported a similar 5'-OH protecting group, 4,4',4''-tris(levulinyloxy)trityl.[6] However, this group was removed by the impractical procedure involving successive hydrazinolysis, extraction, and heating in a pyridine-acetic acid medium.[6] Its introducing agent, [4,4'-tris(levulinyloxy)-trityl]carbinol, was isolated only by inconvenient silica gel column chromatography.
(6) Sekine, M.; Hata, T., unpublished results.
(7) 4,5-Dichlorophthalic acid is commercially available from Aldrich Co. Ltd. and is converted quantitatively to the acid anhydride by heating with acetic anhydride in CCl_4.
(8) Ogilvie, K. K.; Cheriyan, U. O.; Radatus, B. K. *Can. J. Chem.* **1982**, *60*, 3005.
(9) The CPTr group can also be introduced onto the 5'-hydroxyls of the other 2'-*O*-tetrahydropyranylribonucleoside derivatives in high yields (unpublished data).
(10) Footnote deleted in proof.
(11) This cleavage mode has been reported by Letsinger et al. (Letsinger, R. L.; Caruthers, M. H.; Miller, P. S.; Ogilvie, K. K. *J. Am. Chem. Soc.* **1967**, *89*, 7146, who first used β-benzoylpropionyl as a hydrazine-labile protecting group in nucleotide chemistry.
(12) This quenching workup is very effective for the complete conversion of the last traces of the intermediates to the parent ribonucleosides.
(13) The Pom group has been used as a protecting group of adenine by: Rasmussen, M.; Leonard, N. J.; *J. Am. Chem. Soc.* **1967**, *8*., 5439.
(14) The anisoyl group has been used for protecting the N^4-amino function of uridine in this lab.[15] However, this was somewhat sensitive to the hydrazine treatment. We found that the Pom group was resistant to hydrazine. The details of this group will be reported elsewhere.
(15) Kamimura, T.; Masegi, T.; Urakami, K.; Honda, S.; Sekine, M.; Hata, T. *Chem. Lett.* **1983**, 1051.
(16) Kamimura, T.; Tsuchiya, M.; Koura, K.; Sekine, M.; Hata, T. *Tetrahedron Lett.* **1983**, *24*, 2775.
(17) Griffin, B. E.; Jarman, M.; Reese, C. B. *Tetrahedron* **1967**, *24*, 639.
(18) Kamimura, T.; Tsuchiya, M.; Urakami, K.; Koura, K.; Sekine, M.; Shinozaki, K.; Miura, K.; Hata, T. *J. Am. Chem. Soc.*, in press.

Biosynthesis of Elaiomycin. 2. An Unusual Origin for the (Methoxyamino)butanol Moiety

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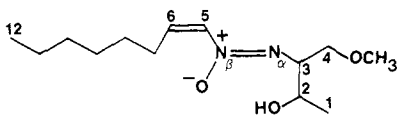
The antibiotic elaiomycin (**1**) is a naturally occurring azoxy compound isolated from the fermentation broth of *Streptomyces gelaticus*.[1] Elaiomycin exhibits novel biological activity since



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it inhibits axenic multiplication of *Mycobacterium tuberculosis*.[2] The antibiotic has also been found to induce tumors in rats.[3] As a naturally occurring azoxy compound, elaiomycin is a member of a small class of unusual natural products that includes (*p*-carboxyphenyl)azoxy cyanide,[4] the cycad toxins macrozamin and cycasin,[5] and the antifungal agent LL-BH872α.[6] Previous experiments in our laboratory have demonstrated[7] that C-5 to C-12 of elaiomycin and the β-nitrogen atom of the antibiotic are derived from *n*-octylamine. We now report experiments which establish that the (methoxyamino)butanol moiety of the antibiotic is biosynthesized in an unusual manner.

(1) (a) Haskell, T. H.; Ryder, A.; Bartz, Q. R. *Antibiot. Chemother. (Washington, D.C.)* **1954**, *4*, 141. (b) Stevens, C. L.; Gillis, B. T.; French, J. C.; Haskell, T. H. *J. Am. Chem. Soc.* **1956**, *78*, 3229. (c) Stevens, C. L.; Gillis, B. T.; French, J. C.; Haskell, T. H. *Ibid.* **1958**, *80*, 6088. (d) Stevens, C. L.; Gillis, B. T.; Haskell, T. H. *Ibid.* **1959**, *81*, 1435. (e) Taylor, K. G.; Riehl, T. *Ibid.* **1972**, *94*, 250.
(2) (a) Ehrlich, J.; Anderson, L. E.; Coffey, G. L.; Feldman, W. H.; Fisher, M. W.; Hillegas, A. B.; Karlson, A. G.; Kaudsen, M. P.; Weston, J. K.; Youmans, A. S.; Youmans, G. P. *Antibiot. Chemother. (Washington, D.C)* **1954**, *4*, 338. (b) Karlson, A. G. *Ibid.* **1962**, *12*, 446.
(3) Baroni, C. D.; Ward, E. N. *Nature (London)* **1969**, *221*, 765.
(4) Gasco, A.; Serafino, A.; Mortarini, V.; Menziani, E. *Tetrahedron Lett.* **1974**, 3431.
(5) (a) Lythgoe, B.; Riggs, N. V. *J. Chem. Soc.* **1949**, 2716. (b) Langley, B. W.; Lythgoe, B.; Riggs, N. V. *Chem. Ind. (London)* **1951**, 75. (c) Riggs, N. V. *Ibid.* **1956**, 926. (d) Korsch, B.; Riggs, N. V. *Tetrahedron Lett.* **1964**, 523.
(6) (a) McGahren, W. J.; Kunstmann, M. P. *J. Am. Chem. Soc.* **1969**, *91*, 2808. (b) McGahren, W. J.; Kunstmann, M. P. *Ibid.* **1970**, *92*, 1587. (c) McGahren, W. J.; Kunstmann, M. P. *J. Org. Chem.* **1972**, *37*, 902.
(7) Parry, R. J.; Rao, H. S. P.; Mueller, J. *J. Am. Chem. Soc.* **1982**, *104*, 339.

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Table I. Incorporation of Labeled Precursors into Elaiomycin

expt no.	precursor ($^3H/^{14}C$)	incorpn, %	labeling pattern
1	(3-^{13}C)-DL-serine		9-fold enhancement of C-4
2	[3(*R*,*S*)-^3H,U-^{14}C]-L-serine (4.91)	0.02, $^3H/^{14}C$ = 4.86	
3	(2-^{13}C,^{15}N)-DL-serine		16-fold enhancement of C-3; C-3 a doublet, J_{CN} = 3.3 Hz
4	(*methyl*-^{13}C)-L-methionine		40-fold enhancement of OMe
5	sodium (1,2-$^{13}C_2$)acetate		C-1, C-5–C-12 labeled; 4-fold enhancement of C-12, 6-fold enhancement of C-1
6	sodium (2-^{13}C)acetate		C-1, C-6, C-8, C-10, C-12 labeled; 4-fold enhancement of C-12 and C-1

Our initial efforts to elucidate the biosynthesis of the (methoxyamino)butanol moiety explored the possibility that this portion of the antibiotic was derived from the amino acid threonine. The specific incorporation of this amino acid was never observed, however. A second likely candidate as a precursor appeared to be serine. Accordingly, (3-^{13}C)-DL-serine was synthesized[8] and administered to cultures of *S. gelaticus*. Examination of the noise-decoupled ^{13}C NMR spectrum of the resulting antibiotic revealed a high degree of enrichment at C-4 (70.4 ppm) (Table I, experiment 1). The specific incorporation of C-3 of serine having been established, an experiment was carried out with [3(*R*,*S*)-^3H,U-^{14}C]-L-serine to determine whether the entire carbon skeleton of the amino acid was incorporated into elaiomycin. The results of this experiment (Table I, experiment 2) clearly show that C-2–C-4 of elaiomycin are derived from serine. This result led in turn to the question of the source of the α-nitrogen atom of elaiomycin. The question was answered by administration of (2-^{13}C,^{15}N)-DL-serine[9] to *S. gelaticus*. Examination of the noise-decoupled ^{13}C NMR spectrum of the elaiomycin produced in this experiment revealed that C-3 (64.8 ppm) of the antibiotic was coupled to ^{15}N (Table I, experiment 3) thereby proving that the α-nitrogen atom of elaiomycin is derived from the amino group of serine.

The incorporation experiments just outlined revealed the origin of a major portion of the (methoxyamino)butanol moiety of elaiomycin. However, the source of C-1 remained unclear. Administration of (*methyl*-^{13}C)-L-methionine to *S. gelaticus* led to antibiotic that exhibited a high level of enrichment in the *O*-methyl group (58.7 ppm), but no enrichment was discernible at C-1 (Table I, experiment 4). A clue to the origin of the C-1 carbon atom was obtained serendipitously. A precursor incorporation experiment was carried out with sodium (1,2-$^{13}C_2$)acetate to confirm the fatty acid origin of C-5–C-12 of the antibiotic. As expected, C-5–C-12 of the elaiomycin appeared as enhanced doublets in the noise-decoupled ^{13}C NMR spectrum. Unexpectedly, the signal for C-1 of the antibiotic (20.3 ppm) appeared as a strongly enhanced singlet (Table I, experiment 5). This result suggested that C-1 of elaiomycin is derived from one of the two carbon atoms of acetate. On chemical grounds, it seemed more likely that C-2 of acetate should serve as the source for C-1 of elaiomycin. Administration of sodium (2-^{13}C)acetate to *S. gelaticus* proved this to be the case (Table I, experiment 6). The donation of a methyl group from C-2 of acetate is an unusual process whose only precedents appear to be in the biosynthesis of pactamycin and virginiamycin M_1.[10] In the case of virginiamycin M_1, the methyl group is believed to be introduced by aldol condensation of malonyl-CoA with a preformed polyketide chain followed by decarboxylation. The introduction of C-2 of acetate into elaiomycin is probably best visualized as a Claisen condensation between an activated form of serine and malonyl-CoA to yield a β-keto ester, which is hydrolyzed, decarboxylated, and reduced.

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Registry No. 1, 23315-05-1; L-serine, 56-45-1; acetic acid, 64-19-7; L-methionine, 63-68-3.

(8) King, J. A. *J. Am. Chem. Soc.* **1947**, *69*, 2738.
(9) (2-^{13}C,^{15}N)-DL-Serine was prepared by the methods used to obtain (1-^{13}C,^{15}N)-DL-serine: Murray, R., III; Williams, D. L. "Organic Synthesis with Isotopes, Pt. I"; Interscience: New York, 1958; p 175.
(10) (a) Weller, D. D.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 6757. (b) Kingston, D. G. I.; Kolpak, M. X.; LeFevre, J. W.; Borup-Grochtmann, I. *J. Am. Chem. Soc.* **1983**, *105*, 5106.

*Book Reviews**

Developments in Polymer Photochemistry. Volume 2. Edited by Norman S. Allen (Manchester Polytechnic). Applied Science Publishers, London. 1981. x + 278 pp. $63.00.

This second volume of the series on polymer photochemistry together with Volumes 1 and 3 provide the interested reader with an excellent introduction to this area of polymer science. The editor has succeeded in collecting contributions from authors who have been actively involved in the field of photochemistry of synthetic or natural polymers for several years. The book begins with a review of photoinitiated cationic polymerization by sulfonium salts, including specific methods for the preparation of these compounds, the mechanism of photolysis, and the use of photosensitizers. This is followed by an extensive table listing general processes and applications of photografting of monomers onto polymer substrates. A detailed discussion of the photooxidation reactions of phenolic antioxidants is then presented, paying particular attention to reaction mechanisms that should be of interest to organic photochemists in this field. The remaining topics in the book deal with the photocatalytic (TiO_2 or ZnO) oxidation and photodegradation of synthetic (polypropylenes and polyundecanoamides) and natural polymers (cellulose), the latter including an interesting discussion on the singlet oxygen theory vs. the hydrogen-abstraction theory for dye-sensitized photooxidation, a subject of considerable debate for many years. Photostabilization of polymers and its mechanisms are also discussed in considerable detail. This book and its companion volumes should provide photochemists and polymer chemists with pages of stimulating material. We should expect the appearance of future volumes in this series dealing with other interesting areas in the field of polymer photochemistry.

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Compendium of Organic Synthetic Methods. Volume V. By Leroy G. Wader, Jr. (Colorado State University). John Wilcy and Sons, New York. 1984. xvi + 552 pp. $37.50.

This hard-bound volume, modestly priced for its size, surveys the years 1980, 1981, and 1982 with respect to practical synthetic methods for

*Unsigned book reviews are by the Book Review Editor.