tion-state structure and obviously higher (CPK molecular models) rotational barriers, stereospecificity was not observed.

Using molecular models, it is easy to convince oneself that conformational selection should occur in enolate formation from **1f** and **1g**. Apparently steric retardation of protonation increases the lifetime of the derived enolates and allows conformational equilibration to occur, resulting in a loss of stereospecificity. This strongly suggests that the pivalyl carbonyl oxygen in **1b**, probably by complexation with potassium ion, lowers the transition-state energy enough to allow protonation to compete with conformational change.[7,8] Thus bulky substituents (to increase the barrier to conformational change) and a participating functional group (to allow penetration of the concomitant barrier to reaction) are important in producing the observed stereospecificity. We would not claim to have unequivocally demonstrated a unique explanation for the stereochemical course of this reaction. We hope, however, that this analysis will direct us to related systems in which the stereospecificity is enhanced and that such studies will lead to increasingly detailed understanding of the transition states in chemical reactions.

Acknowledgment. We thank the National Science Foundation for a grant (GP-42837-X) which helped to support this work.

(7) The effect of crown ether addition is consistent with this interpretation, although crown ether could simply be reducing the protonation rate. See: Guthrie, R. D.; Weisman, G. R.; Burdon, L. G. *J. Am. Chem. Soc.* **1974**, *96*, 6955.

(8) In this discussion, we have avoided dealing with the possiblity of protonation on oxygen to give an enol. This may occur but has no bearing on the arguments presented.

Dimethylpentatetraenylidene

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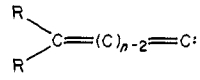
We report the capture of the title intermediate, which is the fifth member in the series of cumulenylidenes, or "extended unsaturated carbenes",[1] with the formula R_2C_n and structure I. The



I

trapping of even members up to $n = 6$ has been described;[2] that of the odd members has not progressed beyond $n = 3$,[3] although this is not for lack of effort.[4] Part of the difficulty is that the cumulenic products to be expected from trapping by means of olefins are generally unstable[5] and subject to prototropic rearrangements,[5,6] methylenecyclopropane rearrangements,[7] and dimerizations.[8] In addition, there may be a systematic difference in stability between the odd and even carbenes. Thus, the theoretical treatments[9] of these species seem to agree that the odd members have a much larger dipole moment, presumably because of a substantial contribution from structure II; our own previous

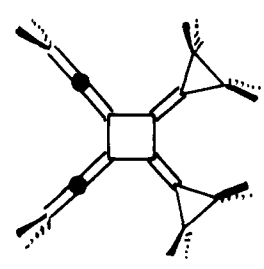
$$R_2C^+—(C\equiv C)_{(n-3)/2}—C\equiv C^-$$

II

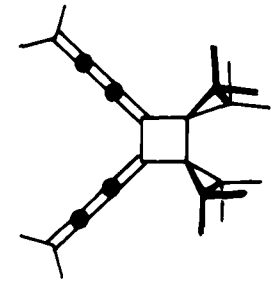
experimental work in this area tends to support this description.[10] The successes by Stang[2] and Gore[11] have led us to search for the fifth member ($n = 5$). After numerous vain attempts, we have found the following procedure to furnish reproducible results. 5-Chloro-5-methylhexa-1,3-diyne[12] (20 mmol) dissolved in 10 mL of well-dried glyme is added dropwise (45 min) into a magnetically stirred solution of 21 mmol of freshly sublimed *tert*-BuOK in 20 mL of glyme containing a 10-fold excess of tetramethylethylene at −30 °C. The temperature is thereafter allowed to rise slowly (several hours) to ambient temperature; a nitrogen atmosphere is maintained throughout. The volatile components are flash evaporated, and the dark brown residue is extracted several times with 50 mL of hexane; the resulting red solution upon flash evaporation leaves a dark red wax. Trituration with 50 mL of methanol leads to the appearance of a tan solid in 15% yield; mp 120–124 °C dec. Sublimation at 80 °C (10^{-5} torr) slowly produces a light yellow solid, mp 129–130 °C dec.;[13] most of the product was obtained in somewhat less pure form by column chromatography (silica gel and benzene–dichloromethane–ethyl acetate).

The parent peak of the mass spectrum of this compound is at m/e 348; this alone constitutes proof of capture of the pentatetraenylidene by tetramethylethylene followed by dimerization. The spectrum also exhibits the multiple families of peaks normally associated with the loss of as many methyl groups. Brief exposure of the product to the atmosphere quickly leads to the uptake of oxygen. Repeated elemental analyses showed it then to contain variable amounts of oxygen to as much as 22%; however, all samples gave the correct C/H ratio (to ±2%).

The oxygen sensitivity made it difficult to obtain a crystal of quality sufficient for X-ray analysis. Although, consequently, the structure assignment can presently not be made with complete certainty, the choice appears limited to the C_{2v} structures III and IV. The pertinent data are as follows.



III



IV

The ^1H NMR spectrum reveals three sharp singlets of equal intensity at δ 1.76, 1.18, and 1.06; this rules out any head-to-tail (D_{2h}) structures for the dimer. The IR spectrum in chloroform shows a weak band at 1995 cm^{-1}. the UV spectrum in *n*-hexane shows maxima at 337 (ϵ 2000), 318 (3000), 303 (3300), 256 (14000), 243 (15000), 225 (49000) and 214 (52200) nm in close similarity to Hartzler's D_{4h} dimer of tetra-*tert*-butylhexapentaene.[8] The ^{13}C NMR (^1H decoupled, measured with 7 mg in the mi-

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(13) It may be that our ability to sublime this high molecular weight dimer rests on reversible dissociation. Such reversion has been observed, for example, with the tetraphenylbutatriene photodimer; R. O. Uhler, H. Shechter, and G. V. D. Tiers, *J. Am. Chem. Soc.*, **84**, 3397 (1962).

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croprobe of an 80-MHz Varian CFT-20 in hexadeuteriobenzene, 35 000 scans with 5-s delay) showed nine peaks at δ 195.14, 135.09, 102.14, 24.60, 22.53, 22.14, 21.32, 21.03, and 20.35. Structure III would be expected to have three proton NMR signals in the regions indicated. Structure IV should have four signals, but the trienylmethyls are so similar that they are quite likely to be accidentally isochronous. Cumulenes typically have a band at about 2010 cm^{-1} in the IR spectrum, whereas allenes are generally seen to absorb at 1995 cm^{-1}. The δ 195 carbon peak is in the range invariably encountered for the sp carbon atom in allenes;[14] on these various grounds, one might favor structure III. On the other hand, the presence of six high field and three low field peaks in the ^{13}C NMR spectrum seems in better accord with structure IV (expected;[15] six and four, respectively) than with III (five and five). The missing 10th peak must be attributed to isochronous signals or unusual relaxation characteristics of one of the carbon atoms. Our present work focuses on the *tert*-butyl substituted carbene; it is hoped that this type of substitution will lead to more stable derivatives.

In any case, proof that the title carbene (or some loosely bound complex mimicking it) has been captured seems unassailable. This opens further possibilities for experimental study, among them the question whether it has the same dipolar characteristics as dimethylallenylidene and whether extension to still longer chains is possible, perhaps with *tert*-butyl group stabilization. Our work continues along these lines.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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Studies of Nitrogen Metabolism Using ^{13}C NMR Spectroscopy. 2. Incorporation of L-[*guanido*-^{13}C,$^{15}N_2$]Arginine and DL-[*guanido*-^{13}C,2-^{15}N]Arginine into Streptothricin F[1]

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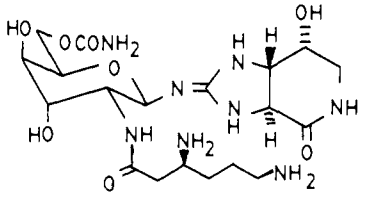
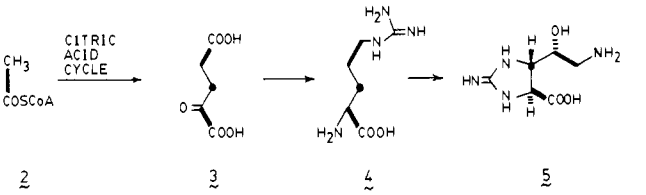
We have recently reported the labeling of streptothricin F (**1**), a broad-spectrum antibiotic produced by various *Streptomyces*, by sodium [1,2-$^{13}C_2$]acetate.[3] As shown in Scheme I, the labeling



1

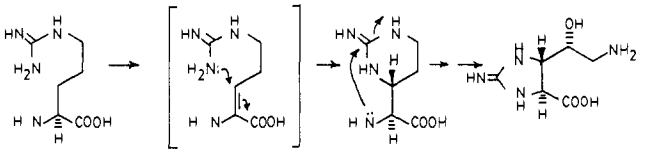
pattern of the heterocyclic (streptolidine) portion of the antibiotic was consistent with the incorporation of acetyl-CoA (**2**) via α-ketoglutarate (**3**) and arginine (**4**). This interpretation eliminated

Scheme I



2 **3** **4** **5**

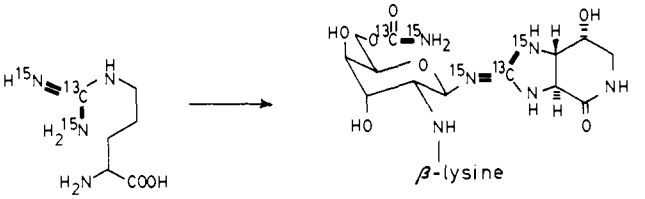
Scheme II



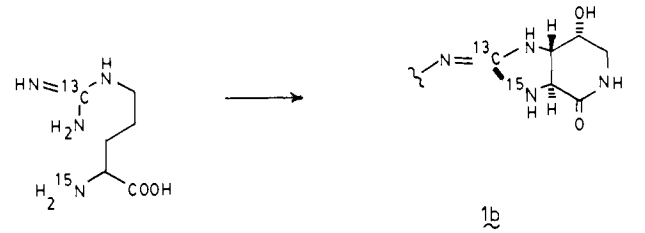
4 **5**

the need to invoke two fundamentally different metabolic pathways for the formation of the streptolidine moiety (**5**), as had been claimed by previous workers.[4,5]

We now report direct, conclusive evidence for **4** as the primary precursor of **5**, as well as evidence supporting Bycroft and King's proposal (Scheme II) for the biogenesis of **5** from **4**.[6] L-[*guanido*-^{13}C,$^{15}N_2$]Arginine (**4a**) and DL-[*guanido*-^{13}C,2-^{15}N]arginine (**4b**) now have each been incorporated into the antibiotic, yielding **1a** and **1b**, respectively. The presence and locations of both ^{13}C and ^{15}N labels were revealed in the ^{13}C NMR spectra from the heteronuclear spin couplings.[7]



4a **1a**



4b **1b**

Arginine **4a** (48.8 mg as the hydrochloride, 232 μmol, 92 atom % ^{13}C, 94 atom % ^{15}N), mixed with DL-[1-^{14}C]arginine (4.9 μCi), was added aseptically to each of two 250-mL production broths 12 h after innoculation with a vegetative seed culture of *Streptomyces* L-1689-23.[3] Standard workup[3] 36 h later afforded 126 mg of the crystalline, radiochemically pure helianthate salt of streptothricin F.

(1) This is part 2 in the series "The Biosynthesis of Streptothricin F".
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