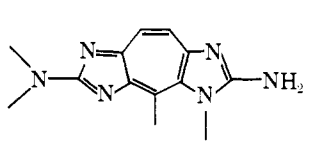
pent[*e*]azulene) group. Within the two series the metabolites differ only in the number and position of *N*-methyl groups. Zoanthoxanthin[1,2] (**1**) and paragracine[6,7] (**2**) have received most attention, and their structures were established mainly by x-ray crystallography.



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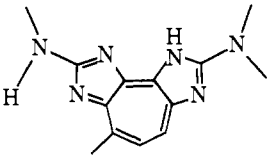
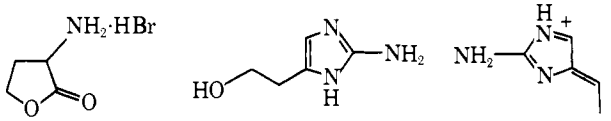


2

Experimental evidence relating to the biosynthesis of the zoanthoxanthins is lacking but the Italian workers, who deserve credit for their pioneering studies on this novel class of natural products, first postulated the intermediacy of two arginine derived C_5N_3 units.[4] We describe a short laboratory synthesis of the two simplest zoanthoxanthins that embodies this principle.

Reduction of the commercially available lactone **3** in aqueous ethanol (45:20) with 2.5% sodium amalgam[8] (12 equiv of sodium) at pH 2.5–3.5 (3–7°; 2 h), followed by addition of 4–5 equiv of cyanamide[9] at pH 4.5 (60–70°; 2 h) and exposure of the crude product to 15% aqueous hydrochloric acid (20°; 30 min) gave 2-amino-4(5)-hydroxyethylimidazole (**4**) conveniently purified as the crystalline picrate, mp 177–179° (C_2H_5OH). A standard procedure[10] was used to reconvert the picrate to the pure, yet oily hydrochloride (64% overall yield from **3**): NMR (D_2O; sodium 2,2,3,3-tetradeuterio-3-trimethylsilylpropionate) δ 6.55 (s, 1), 3.80 (t, 2, J = 7 Hz), 2.75 (t, 2, J = 7 Hz); uv(max) (C_2H_5OH) 216 nm (ϵ 8150); *m/e* 127 (M^+ of free base), 109, 97, 96. Conversion of the imidazole **4** to the two zoanthoxanthins **7** and **8** was effected simply by heating a 10% solution of the hydrochloride in concentrated sulfuric acid (90–95°; 17 h). The reaction mixture was diluted with water and basified to pH 12 with barium hydroxide. Filtration and concentration of the solution afforded crude zoanthoxanthins which were purified by thin layer chromatography (silica gel, $CHCl_3$–CH_3OH–concentrated NH_4OH (80:20:3). The more polar isomer (R_f 1.8) (15% yield) (mp >310°; NMR (CF_3COOH, Me_4Si) δ 3.30 (s, 3), 8.94 (s, 2); uv(max) (CH_3OH) 295 nm (ϵ 30 400), 403 (10 600); uv(max) (CH_3OH; HCl) 286 nm (ϵ 33 200), 381 (9450); *m/e* found 214.09556 calcd for $C_{10}H_{10}N_6$ 214.09669[11] was identical with parazoanthoxanthin A[4] (**7**) previously isolated from *Parazoanthus axinellae*. The less polar isomer (R_f 2.4) (8% yield) (mp >310°, NMR (CF_3COOH, Me_4Si) δ 3.13 (s, 3), 8.61 (AB quartet, J = 11 Hz); uv(max) (CH_3OH) 250 nm (ϵ 8600), 297 (24 000), 360 (4000), 400 (6700); uv(max) (CH_3OH; HCl) 237 nm (ϵ 6650), 286 (27 600), ~340 broad, 394 (8500); *m/e* found 214.09631) is a new compound. According to its uv and NMR spectra it belongs to the pseudo series and we propose the name pseudozoanthoxanthin A (**8**).



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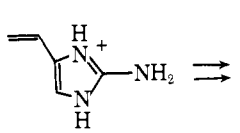

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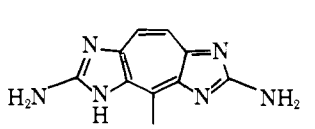

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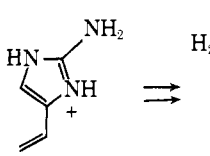

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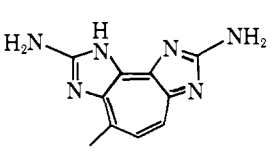

8

Sulfuric acid serves both as an oxidant and an acid catalyst in this oxidative dimerization. It may not be the agent of choice but other acids and oxidizing agents remain to be tested. 2-Amino-4(5)-vinylimidazole (**6**) undoubtedly is involved in the transformation and [6 + 4] cycloadditions[12] of **5** and **6** in the manner indicated account for the eventual formation of isomers **7** and **8**. Methods for alkylation of both ring and side chain nitrogen atoms have been devised[3] and homologous zoanthoxanthins can thus be synthesized from the prototypes **7** and **8**.

Acknowledgment. This work was supported by the National Institutes of Health (GM 09868) and the Hoffmann-La Roche Foundation.

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The Structure of the Heteropolytungstate $(NH_4)_{17}Na[NaW_{21}Sb_9O_{86}]\cdot 14H_2O$. An Inorganic Cryptate

Sir:

Although the chemistry and structure of hetero and isopolyanions have been studied for a long time,[1] new properties of known compounds and ions possessing new structural units are still being found. Thus, Jasmin and co-workers have recently shown that silico-12-tungstates have in vitro antiviral properties.[2] This study prompted a systematic screening of similar compounds and a recently prepared antimoniotungstate[3] was found whose in vitro activity was much higher than that of the silico-12-tungstates. This compound is active against a broad spectrum of viral strains and, in vivo, against Friend leukemia virus.[4] Its toxicity is extremely low.

We undertook the x-ray structure analysis of this compound in order to firmly establish its geometry and composition.

Crystals of the title compound are hexagonal with $a = b =$ 17.791 (3) Å and c = 22.709 (5) Å. The observed density is 3.72 g/cm^3; the calculated value is 3.65 g/cm^3 for Z = 2, M = 6396.6. Possible space groups are $P\bar{6}2c$ and $P6_3/mmc$. Data

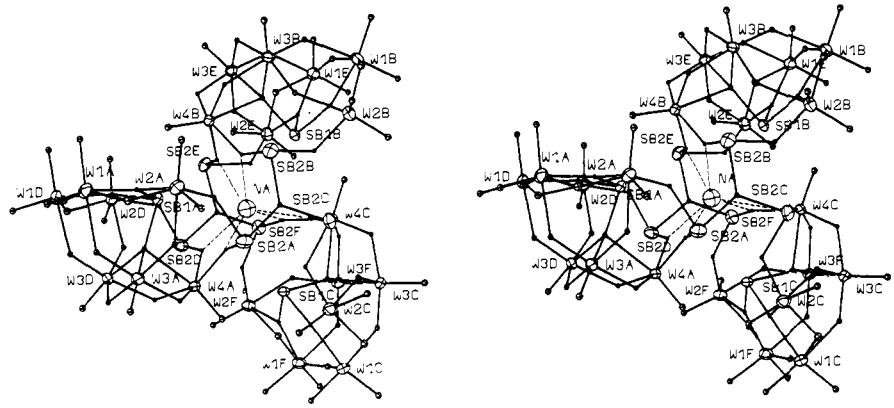

Figure 1. A stereoview of the anion. The heavy atoms ellipsoids are drawn at 0.4 probability level. For the purpose of clarity, isotropic temperature factors divided by 10 were used for the oxygen atoms.

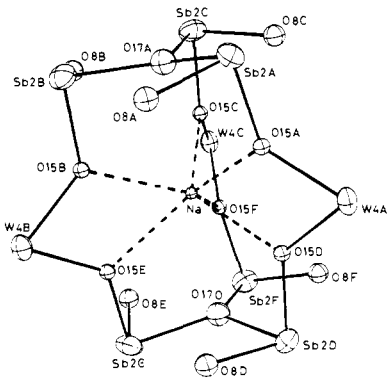

Figure 2. A view of the central cavity showing the coordination of sodium to the six prismatic oxygen atoms. The weak interaction between Na and O_{17} is not represented on this drawing.

were collected using Mo Kα radiation with a Picker diffractometer. Statistical tests indicated that the structure is noncentrosymmetric and the structure was solved and refined in space group $P\bar{6}2c$ using 1266 observed reflections. Data collection, structure solution, and refinement were conducted as previously described.[5] Oxygen scattering factors were assigned to an atom found at special position ($\frac{2}{3}$, $\frac{1}{3}$, $\frac{1}{4}$). Upon refinement, all positional and thermal parameters converged to acceptable values, except for the temperature factor of the latter atom, which became negative. This behavior indicates the need for a larger electron density, and sodium form factors were tentatively ascribed to this atom. With this hypothesis, refinement converged to acceptable values for all atoms. Using anisotropic temperature factors for all atoms, the final R value is 0.068.[6] The presence of sodium was confirmed by atomic absorption analysis: expected 0.33%, found 0.66% ± 2 (average of six determinations). In view of this result it is suggested that the correct formula for the compound is $(NH_4)_{17}Na|NaW_{21}Sb_9O_{86}|\cdot 14H_2O$. It has not been possible to distinguish between ammonium cations and water molecules; similarly, it is not possible to locate the second sodium atom since it probably occupies an ammonium site.

The asymmetric unit contains four crystallographically independent tungsten atoms and two antimony atoms. The anion contains a C_3 axis perpendicular to a crystallographic symmetry plane. The letters A through F used in Figure 1 and in the discussion refer to the first six equivalent positions as listed in the "International Tables for X-Ray Crystallography."[7] The plane is illustrated in the stereoview by tungsten atoms W4 A, B, and C and antimony atoms Sb1 A, B, and C. The threefold axis passes through the sodium atom and the oxygen atoms shared by Sb2 A, B, C and Sb2 D, E, F. The assemblage of WO_6 octahedra is most clearly seen in the upper right part of the stereoview, (equivalent atoms denoted B and E). The other two lobes are equivalent through the threefold axis.

The WO_6 edifice is conveniently described using two $W_3O_{10}^{2-}$ groups and the Sb1 antimony atom. The first such group is formed by W1, W2, and W3B. The oxygen atoms involved are the five terminal atoms, the three that bridge these tungsten atoms and one atom shared by W1 and W2 B and Sb1B. The tenth oxygen atom is that shared by W1B and W1E or W3E, respectively. It is readily seen that this assemblage and its mirror equivalent around the E tungsten atoms form half a Keggin structure with two important differences.[8] First, there are two more terminal oxygen atoms per $W_3O_{10}^{2-}$ group than in the Keggin structure. Second and most important, the antimony atom is oxygen deficient. So are the "internal" tungsten atoms W2B, W3B, W3E, and W2E. Since the antimony atoms bear only three oxygen atoms, a normal Keggin structure is precluded.

The originality of the structure arises from the way in which the deficiencies are filled. In order to do this, a $Sb_2WO_8^{4-}$ group is required: oxygen atoms linked to tungsten and antimony are used to complete the "internal" tungsten atoms octahedra. The coordination of W4B seems unusual in that two edges of the same octahedron face are shared with W3B and W3E. Moreover, the same apical oxygen atom is used to complete the coordination of Sb1B, thus giving rise to a tetrahedrally coordinated oxygen atom. It is important to notice that the coordination requirements around W4B lead to the formation of a Sb-O-W-O-Sb chain. Finally, two oxygen atoms located on the threefold axis are used to complete the coordination polyhedra of the Sb2 atoms and to link the three lobes of the anion. Consequently, the Sb-O-W-O-Sb chains form a bicyclic ring and surround a large cavity in the anion. The most interesting feature of the anion is the presence of a sodium atom inside the crypt. Moreover, as shown in Figure 2, sodium interacts strongly with the six O_{15} oxygen atoms and to a lesser extent with the O_{17} atoms. The Na-O_{17} distance of 2.91 (8) Å is indeed indicative of a weak interaction with the central atom. Because of crystallographic requirements, the coordination polyhedra around sodium is a perfect bicapped trigonal prism (D_{3h}). The bicyclic cavity and coordination of sodium by the six prismatic oxygen atoms bear striking similarity to bicycloazapolyoxaalkali metal complexes.[9] As in these compounds the Na-O_{15} distance equals 2.44 (5) Å. The faces of the bicyclic cavity surrounding sodium are fairly large and, despite possible interaction of the Sb1 lone pair with sodium, it might be possible to exchange it through the faces. Unfortunately, the low solubility of the salt prevents an unambiguous demonstration of this behavior by use of NMR techniques.

With the exception of group 1a and 2a elements, most ele-

ments in the periodical table are known to occur as heteroelements[5] in molybdenum and tungsten polyanions. The present structure is the first example of inclusion of a group 1a element into a heteropolyanion and represents a hitherto unsuspected structural type in this field. It is hoped that the present study will aid in understanding the remarkable antiviral properties of this compound.

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Supplementary Material Available: Fractional and thermal parameters and observed and calculated structure factor parameters (5 pages). Ordering information is given on any current masthead page.

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Side-Chain Substituted 2,2,5,5-Tetramethylpyrrolidine-*N*-oxyl (Proxyl) Nitroxides. A New Series of Lipid Spin Labels Showing Improved Properties for the Study of Biological Membranes

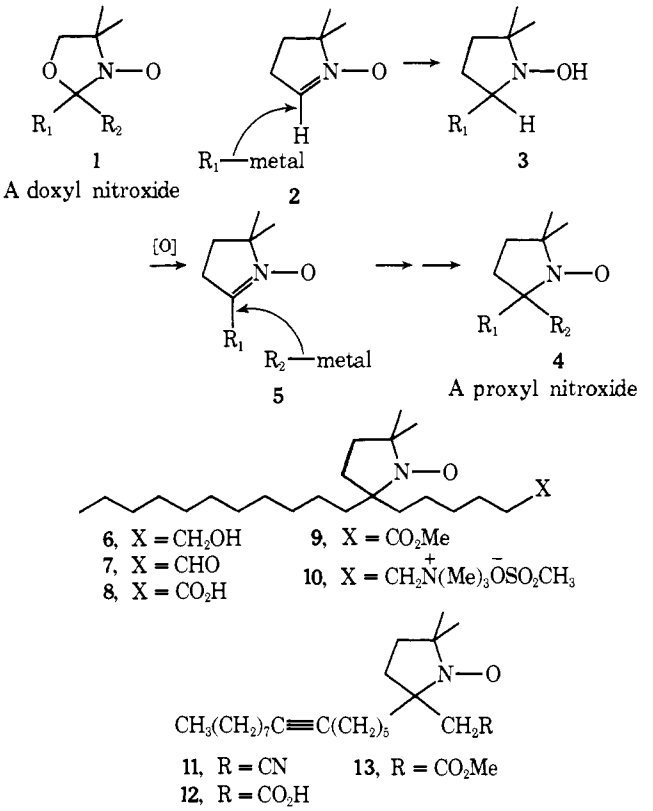
Sir:

Doxyl nitroxides **1**[2] have enjoyed wide application in the study of biological membranes by spin labeling techniques.[3] Yet in comparison with the pyrrolidine-*N*-oxyl ring system **4,** doxyl nitroxides show at times two shortcomings. Firstly, the presence of the ring oxygen atom opens up alternative pathways for decomposition, limiting the nature of subsequent chemical reactions on remote portions of doxyl containing molecules[4,5] and also giving rise to irreversible loss of ESR signal in some spin labeling studies[5] (probably via reduction to the hydrolytically unstable *N*-hydroxy derivative). Secondly, the oxygen atom within the ring renders the doxyl group quite polar, an important consideration when the label is to probe hydrophobic regions of the membrane. In response to these points we now describe the first members of a new series of nitroxide lipid spin labels based on the pyrrolidine-*N*-oxyl ring system.

Advantage is taken of the ready addition[2,6,7] of Grignard reagents to pyrroline nitrone **2** (Chart I) leading to *N*-hydroxy intermediate **3.** Since an α-hydrogen atom is present in **3,** cupric acetate–air oxidation[2,8] leads to a new nitrone **5,** itself capable of undergoing reaction with a different Grignard reagent. Oxidation then produces a stable pyrrolidine-*N*-oxyl (proxyl)[9] nitroxide **4.**

The synthesis of 7-proxylstearyl alcohol **6** is representative. To a stirred solution of 3.52 g of nitrone **2**[8] in 10 ml of THF was

Chart I



added dropwise at reflux (N_2) 45.6 ml (1.5 equiv) of a 1.0 M solution of undecylmagnesium chloride in THF. After 1 h at reflux the reaction was quenched with saturated NH_4Cl. The usual workup afforded the corresponding crude *N*-hydroxy compound which was immediately taken up with 170 ml of MeOH–concentrated NH_4OH (15:2) and stirred under air in the presence of 12.9 g of $Cu(OAc)_2 \cdot H_2O$[2,8] for 1 h, affording 7.07 g (85%, based on **2**) of nitrone **5** ($R_1 = CH_3(CH_2)_{10}$–) (bp 118–121° (0.005 mm); *m/e* 267.257). The reaction of **5** ($R_1 = CH_3(CH_2)_{10}$–) (500 mg) in THF (10 ml) at 25° (N_2) with 2.8 ml (1.5 equiv) of a 1.0 M THF solution of $THPO(CH_2)_6MgCl$ was quenched after 18 h by dropwise addition (0°) of 10 ml of MeOH and 5 ml of 3 N HCl. The quenched mixture was stirred for 1.5 h at 0° in order to hydrolyze the tetrahydropyranyl ether grouping.[10] The usual workup provided the crude *N*-hydroxy alcohol which was dissolved in MeOH (10 ml) containing 5 mg of $Cu(OAc)_2 \cdot H_2O$[2] and stirred under air for 1 h. Preparative TLC over silica gel gave 154 mg (22%) of 7-proxylstearyl alcohol **6** (*m/e* 368.354).

Reaction of nitrone **2,** on the other hand, with the Grignard reagent derived from 1-bromopentadec-6-yne[11] led, after oxidation, to nitrone **5** ($R_1 = CH_3(CH_2)_7C{\equiv}C(CH_2)_5$–) (*m/e* 319.285) (89%). Addition of lithium acetonitrile in THF to this substance (−78° → 25°) followed by oxidation afforded a mixture (47%) of nitroxide **11** (*m/e* 359.305) and the corresponding lactone (by ir). Base hydrolysis of the mixture followed by chromatography over silica gel gave 9,10-dehydro-3-proxyloleic acid (**12**) (30%, based on **5**). Esterification of **12** with diazomethane afforded ester **13** (70%) (*m/e* 392.319).

The chemical stability of the proxyl ring system in these spin labels parallels that of simple pyrrolidine-*N*-oxyl nitroxides.[5] For example, oxidation of alcohol **6** with *N*-chlorosuccinimide–dimethyl sulfide[12] afforded aldehyde **7** (78%) (*m/e* 366.338). Two phase oxidation of an ether solution of **7** with Tollen's reagent gave 7-proxylstearic acid (**8**) (*m/e* 382.330) (70%) which was also converted (CH_2N_2) to the methyl ester **9** (*m/e* 396.348). Alternatively, reaction of **6** with methan-