Table I. ^{1}H and ^{13}C Nmr Spectra of Chondriol[a] and Rhodophytin

^{13}C[b]		Proton (s) C no.	^{1}H[c]	
Chondriol	Rhodophytin		Chondriol acetate	Rhodophytin
12.38 (15)	12.42 (15)	1	3.04 (2)	3.05 (2)
27.71 (5,8,14)	27.08 (5,8,11,14)	2		
32.76 (5,8,14)	29.41 (5,8,11,14)	3	5.68 (4)	5.53 (4)
33.97 (5,8,14)	32.52 (5,8,11,14)	4	6.09 (8)	6.00 (8)
62.99 (1,6,7)	33.78 (5,8,11,14)	5	2.82, 2.82 (m)	2.83, 2.83 (m)
68.14 (1,6,7)	63.58 (1,6,7)	6	4.83 (8)	4.38 (8)
73.53 (1,6,7)	76.11 (1,6,7)	7	3.91 (8)	3.89 (8)
80.03 (2)	79.60 (2)	8	3.13, 2.54 (8,m)	3.09, 2.40 (8,8)
82.46 (11)	82.61 (1,6,7)	9	5.81 (m)	5.53 (m)
110.47 (3,4,9,10)	110.86 (3,4,9,10)	10	5.88 (16)	5.73 (16)
113.28 (12,13)	112.71 (12,13)	11	6.60 (2)	3.76, 2.83 (8,4)
124.54 (3,4,9,10)	124.46 (3,4,9,10)	12		
134.49 (3,4,9,10)	130.67 (3,4,9,10)	13		
140.56 (3,4,9,10)	140.09 (3,4,9,10)	14	2.82 (m)	2.60 (m)
149.83 (12,13)	148.43 (12,13)	15	1.12 (3)	1.03 (3)

[a] ^{1}H nmr values are for chondriol acetate. [b] Proton decoupled values in ppm downfield relative to internal TMS. Values in parentheses refer to potential carbon assignments. [c] ^{1}H values were recorded at 220 MHz and are expressed as ppm downfield from internal TMS (δ). Values in parentheses refer to band multiplicity.

The complete structure assignment of this unusual peroxide was facilitated by a comparison of the ^{13}C and proton nmr characteristics of this compound with those of chondriol. The 220-MHz proton nmr of rhodophytin was closely comparable to chondriol acetate for all protons except those associated with the alcohol portion of chondriol at C-11 (Table I). Comparisons of chemical shift, multiplicity, and coupling constants, together with double resonance experiments, showed 1 and 2 to be nearly identical in structure, stereochemistry, and ring confirmation. Protons on carbons 1–10 and 12–15 appear as nearly identical bands for the acetate of 1 and for 2. The extra methylene protons in rhodophytin (C-11) appear as an AB system at δ 3.76 and 2.83, respectively, the lower field band indicating deshielding from the proximal bromine on C-13.

When rhodophytin was allowed to stand in unpurified CCl$_4$, it was slowly but quantitatively converted to the conjugated diene peroxide (3), λ_{max} 220 (ϵ 10,400),

1

2   3
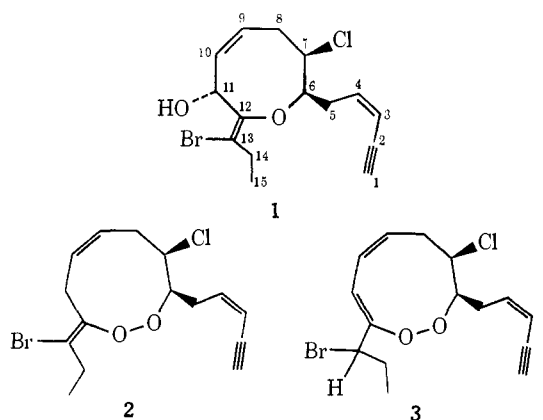
228 (ϵ 9350), and 275 nm (ϵ 7630), via an allylic rearrangement. This somewhat less stable and equally unusual peroxide[11] showed strong infrared bands at 1610 and 1640 cm^{-1}, indicative of the conjugated diene system, and also gave a strong iodide–iodine peroxide test.

Two other peroxides, ascaridole[12] and ergosterol

(11) This peroxide is very sensitive to traces of acid and cannot be stored. It is effectively reduced with sodium sulfite in aqueous methanol.
(12) H. Szmant and A. Halpern, *J. Amer. Chem. Soc.*, **71**, 1133 (1949).

peroxide,[13,14] have been reported from natural sources. Each of these structures may be formally considered the cycloaddition product of an oxygen molecule with a conjugated diene precursor. Rhodophytin differs significantly from these earlier examples in that the ring system of 2 is probably generated from a hydroperoxide intermediate. Peroxidation of a logical precursor such as laurediol,[15] followed by bromonium ion induced ring closure, would generate the cyclic peroxide structure of 2.

Rhodophytin exhibits unusual thermal and base stability. These factors provided for its isolation and structure elucidation.

(13) P. Wieland and V. Prelog, *Helv. Chim. Acta*, **30**, 1028 (1947).
(14) H. K. Adam, I. M. Campbell, and N. J. McCorkindale, *Nature (London)*, **216**, 397 (1967).
(15) E. Kurosawa, A. Fukuzawa, and T. Irie, *Tetrahedron Lett.*, 2121 (1972).

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A Nucleophilic Ethynyl Group Equivalent and Its Use in Conjugate Addition to α,β-Enones

Sir:

As a result of previous studies,[1] an excellent method is now available for the introduction of angular vinyl groups[2] in fused cyclic structures starting from a cyclic α,β-enone and the vinyl ($\hat{V}$) Gilman[3] reagent $\hat{V}_2$CuLi. An analogous process for the establishment of angular

(1) E. J. Corey and R. L. Carney, *J. Amer. Chem. Soc.*, **93**, 7318 (1971).
(2) Substituents derivable from vinyl which can be generated[1] at angular positions by a further step include C$_2$H$_5$, CH$_2$CHO, CHO, and COOH.
(3) H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952); H. Gilman and J. M. Straley, *Recl. Trav. Chim. Pays-Bas*, **55**, 821 (1936).

Scheme I
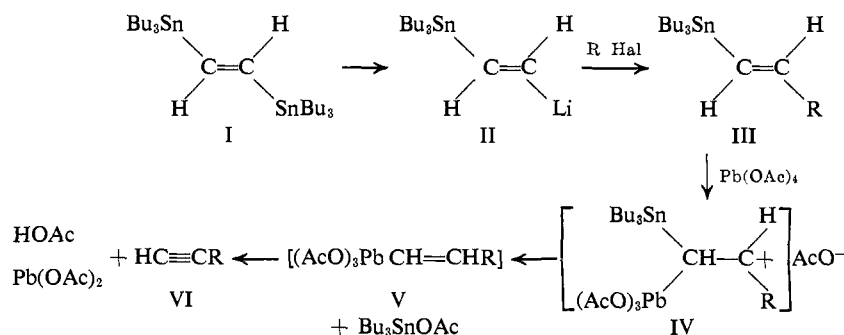
ethynyl groups is precluded by the tenacity with which copper binds ethynyl ligands[4] and the consequent unreactivity of ethynyl Gilman reagents. Further the conjugate addition of ethynyl groups from alane reagents which occurs readily with acyclic α,β-enones[5] (and presumably also cyclic s-cis α,β-enones) is not operable with cyclic enones which are configurationally s-trans. We report here a solution to this problem which was made possible by the development of a new reaction for the synthesis of acetylenes.

Reaction of the readily available *trans*-1,2-bis(tri-*n*-butylstannyl)ethylene[6] (I) with *n*-butyllithium in tetrahydrofuran at −78° for 1 hr resulted in clean generation of the lithium reagent II which underwent alkylation nearly quantitatively by reaction with a variety of alkyl halides to form *trans*-1-alkenyltri-*n*-butylstannanes (III). The alkenylstannanes, III, upon treatment with lead tetraacetate in acetonitrile (Scheme I) were smoothly converted to terminal alkynes VI. This novel route to acetylenes may be rationalized in terms of a mechanism involving intermediates IV and V. There is ample analogy for such an addition–elimination process.[7–9]

The mixed cuprate VII formed rapidly and cleanly when I was treated with 1 equiv of *n*-butyllithium followed by 1 equiv of *n*-propylethynylcopper.[4b] The reaction of the brown, soluble reagent VII with α,β-enones VIII and IX proceeded with excellent selectivity to afford the desired β-vinylstannyl ketones X and XI in 85 and 93% isolated yields, respectively (Scheme II).

Treatment of X and XI with lead tetraacetate in acetonitrile at room temperature afforded the corresponding β-ethynyl ketones XII and XIII in 96 and 64% yields, respectively.[10] The structure of XIII was fur-

Scheme II
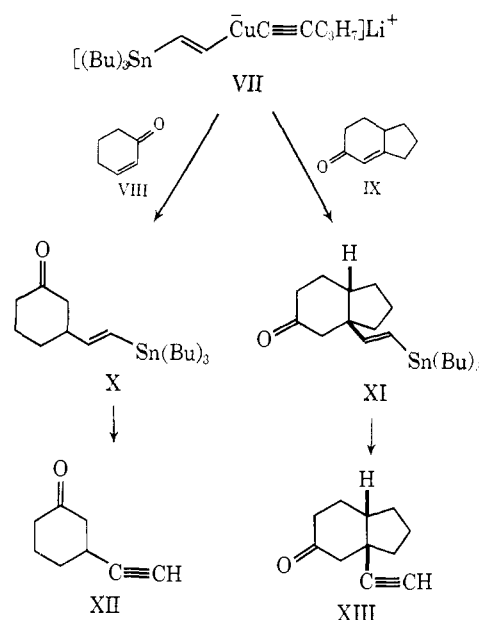
ther established by conversion to the previously reported[11] diketone XIV by treatment with mercuric acetate in ethyl acetate for 36 hr followed by precipitation of mercuric sulfide by passing hydrogen sulfide through the reaction mixture. A typical experimental procedure follows.

XIV
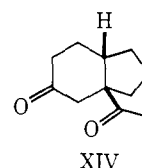
1-(*trans*-2-Tri-*n*-butylstannylethenyl)bicyclo[4.3.0]nonan-3-one (XI). To a solution of 6.04 g (10.0 mmol) of *trans*-1,2-bis(tri-*n*-butylstannyl)ethylene in 25 ml of dry THF at −78° was added 5.00 ml (10.6 mmol) of 2.13 *M* *n*-butyllithium. Following slow warming to −40° during 30 min, the clear, light yellow solution was transferred through metal tubing (18 gauge) to another flask containing a suspension of 1.61 g (10.2 mmol) of *n*-propylethynylcopper[12] in 6 ml of THF and 5.0 ml (27 mmol) of hexamethylphosphorous triamide[4b] over 30 min. After recooling to −78° the solution was stirred

(4) See (a) R. Nast, *Chem. Soc., Spec. Publ.*, No. 13, 103 (1959); (b) E. J. Corey and D. J. Beames, *J. Amer. Chem. Soc.*, 94, 7210 (1972).

(5) J. Hooz and R. B. Layton, *J. Amer. Chem. Soc.*, 93, 7320 (1971).

(6) The procedure of A. N. Nesmeyanov, A. E. Borisov, *Dokl. Akad. Nauk SSSR*, 174, 96 (1967), could be used for the preparation of this compound; however, in our hands yields were higher (88 *vs.* 74%) and more reproducible if a catalytic amount of azobisisobutyronitrile was added to the neat mixture of tri-*n*-butyltin acetylide and tri-*n*-butyltin hydride.

(7) The addition of the electrophilic lead(IV) triacetate cation to III to form the cation IV is favored by the stability of such β-metallo cations. See, for example, J. M. Jerkunica and T. G. Traylor, *J. Amer. Chem. Soc.*, 93, 6278 (1971).

(8) For modes of formation and reaction of species of type R Pb-(OAc)₃, see R. Criegee, *Angew. Chem.*, 70, 173 (1958); R. Criegee in "Oxidation in Organic Chemistry," Part A, K. Wiberg, Ed., Academic Press, New York, N. Y., 1965.

(9) Vinylstannanes of type III undergo rapid tin–bromide exchange at −78° upon treatment with bromine in carbon tetrachloride, to form in high yield *trans*-1-bromoalkenes: *cf.* D. Seyferth, *J. Amer. Chem. Soc.*, 79, 2133 (1957) and S. D. Rosenberg, A. J. Gibbons, Jr., *J. Amer. Chem. Soc.*, 79, 2138 (1957). In addition, *trans*-1-bromoalkenes are formed rapidly at room temperature by treatment of compounds of type III with *N*-bromosuccinimide. This substitution reaction presumably occurs by an addition–elimination analogous to the change III → V.

(10) Satisfactory infrared, proton magnetic resonance, and mass spectral data were obtained for all new substances reported herein.

(11) H. O. House, S. G. Boots, and V. K. Jones, *J. Org. Chem.*, 30, 2519 (1965).

(12) C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, 31, 4071 (1966).

for 45 min and 0.727 g (5.34 mmol) of enone IX[1] in 5.0 ml of THF was added over 12 min. After stirring for 30 min at this temperature, the reaction mixture was warmed to $-40°$ during 15 min and then quenched by pouring into ice-cold saturated aqueous ammonium sulfate. The organic layer was separated and the aqueous layer was extracted with ether. The combined ethereal layers were extracted with 2% (v/v) sulfuric acid, filtered through a pad of hyflo super cel, and dried (MgSO₄) to afford, after removal of solvent, 7.77 g of yellow-brown oil. Column chromatography on alumina with hexane as eluent gave 3.14 g (91%) of tetra-n-butyltin. Further elution with CHCl₃ yielded 4.07 g (93%) of the desired ketone XI: ir (neat, partial) 3.39, 5.84, 6.30, 10.1, and 10.4 μ; nmr (CCl₄) δ 0.27–2.85 (br m with s at 2.25, total 40 H) and 5.84 (s, 2 H); m/e, 452.2255 (calcd for C₂₃H₄₂O¹¹⁸Sn, 452.2253).

1-Ethynylbicyclo[4.3.0]nonan-3-one (XIII). A solution of 0.233 g (0.50 mmol) of 1-($trans$-2-tri-n-butylstannylethenyl)bicyclo[4.3.0]nonan-3-one (XI) in 5 ml of dry acetonitrile was treated with 0.232 g (0.52 mmol) of lead tetraacetate. The reaction mixture became homogeneous after 3 min and then began forming a brown precipitate. After stirring at room temperature for 3 hr, tlc analysis (CHCl₃) showed no starting material. Dilution of the crude product with pentane and filtration through Celite and alumina (each pad washed twice with pentane and once with methylene chloride) afforded almost pure 1-ethynylbicyclo[4.3.0]nonan-3-one (XIII) (51 mg, 64%), homogeneous by tlc analysis (R_f 0.44, CHCl₃): ir (neat, partial) 3.03, 3.38, 4.74, and 5.85 μ; nmr (CCl₄) δ 0.50–2.57 (br m with s at 1.96, 2.10, and 2.38); m/e 162.1045 (calcd for C₁₁H₁₄O, 162.1049).

The methodology reported here leads to compounds which are otherwise relatively inaccessible. Numerous applications can be foreseen in addition to the synthesis of angularly substituted polycyclic structures.[13]

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Received May 24, 1974

Resonance Raman Studies of "Blue" Copper Proteins

Sir:

"Blue" copper proteins[1] have at least one copper which gives rise to unusually intense visible absorption bands and low hyperfine coupling constants. Although these atypical properties have prompted many spectroscopic, magnetic, and theoretical investigations, little is known about the specific ligands bound to copper. We report herein the resonance Raman[2] (RR) spectra between 1700 and 200 cm⁻¹, of "blue" copper in human ceruloplasmin and in *Rhus vernicifera* stellacyanin and laccase. RR spectra of copper ovotransferrin as well as vibrational spectra of amino acids and copper complexes are used to interpret the protein spectra and formulate a molecular basis for copper–ligand bonding in the "blue" copper proteins.

(1) R. Malkin and B. G. Malmström, *Advan. Enzymol. Relat. Subj. Biol.*, 33, 177 (1970).
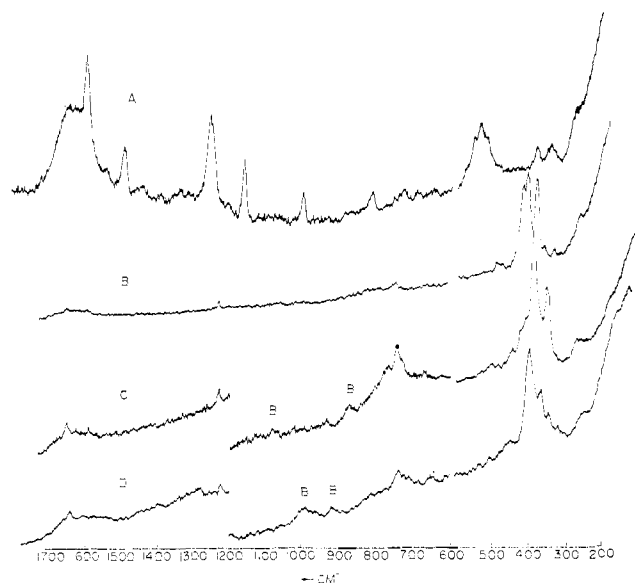(2) J. Behringer, *Raman Spectrosc.*, 1, 168 (1967).

Figure 1. Resonance Raman spectra of Cu(II) ovotransferrin, 44.6 mg/ml of protein, in 0.03 M NaHCO₃, pH $\sim$8.0 (A); laccase, 10.9 mg/ml, in 0.05 M phosphate buffer, pH 5.5 (B); stellacyanin, <600 cm⁻¹, 3.3 mg/ml, >600 cm⁻¹, 8.4 mg/ml, in 0.05 M phosphate buffer, pH 5.5 (C); and ceruloplasmin, 11.6 mg/ml, in 0.05 M acetate buffer, pH 5.5 (D). Experimental conditions (time constant, 5 sec; scan rate, 30 cm⁻¹/min)

	Excitation (nm)	Power (mW)	Slit width (cm⁻¹)	Sensitivity (counts/sec)
A	488.0	70	8.6	1000
B	647.1	70	6.4	1000
C	647.1	80	7.0	1000
D	647.1	80	10.0	2000

Broad bands near 880, 920, 1000, and 1080 cm⁻¹ marked with a B are due to buffer.

Standard methods were followed for the isolation of stellacyanin[3] and laccase,[3] further purification of ceruloplasmin[4] (Schwartz–Mann), and conversion of apo-ovotransferrin (three times crystallized, provided by Dr. D. H. Morris) to the Cu(II) complex.[5]

Excitation into the $\sim$600-nm electronic absorption band with the 647.1-nm Kr⁺ (or 568.2-nm Ar⁺) laser line yields Raman spectra (Figure 1) showing intensity-enhanced vibrations (depolarization ratios, 0.3–0.4) below 450 cm⁻¹ from "blue" copper. Some weakly enhanced ligand vibrations are detected in the region from 450 to 1700 cm⁻¹. The RR spectrum of Cu(II) transferrin irradiated within the 440-nm electronic absorption band by the 488.0-nm Ar⁺ line shows intense resonance-enhanced ligand modes above 450 cm⁻¹ as well as some less intense low-frequency bands.

Tyrosine oxygen and imidazole nitrogen (from histidine) bonding to Fe(III) has been established in Fe(III) ovotransferrin.[5] In the region 600–1700 cm⁻¹, the RR spectrum of Cu(II) transferrin has the same features (including intense ligand vibrational bands of tyrosine) as the Fe(III) complex.[6] In contrast, low-frequency metal–ligand vibrations dominate the RR spectra of

(3) S. Osaki and O. Walaas, *Arch. Biochem. Biophys.*, 123, 638 (1968).
(4) H. F. Deutsch, C. B. Kasper, and D. A. Walsh, *Arch. Biochem. Biophys.*, 99, 132 (1962).
(5) R. Aasa, B. G. Malmström, P. Saltman, and T. Vänngård, *Biochim. Biophys. Acta*, 75, 203 (1963).
(6) (a) Y. Tomimatsu, S. Kint, and J. R. Scherer, *Biochem. Biophys. Res. Commun.*, 54, 1067 (1973); (b) P. R. Carey and N. M. Young, *Can. J. Biochem.*, 52, 273 (1974).