molecules within the material and agrees with the previous Mössbauer and magnetic data.[5] The ligands around Ir(1) show no disorder. (4) The bond distances of the ligands bonded to Ir(1) and Ir(2) are shown in Figure 2. The Ir–CO distances give indications of multiple-bond character. The Ir(1)–CO bond which is trans to the Cl bond is 0.071 (8) Å shorter than the cis Ir–CO distance. This is consistent with a strong trans bond and a large backbonding $d\text{-}\pi_{\pi^*}$ contribution. (5) Unlike the Pt 1-D materials where water molecules and counterions fit into holes or channels in the lattice, $Ir(CO)_3Cl$ crystallizes in a close-packed lattice where all intermolecular contacts except for the Ir–Ir bond are at normal van der Waals distances. This leaves no room for interstitial Cl^- sites as can be verified by inspection of Figure 1. This is confirmed by the final difference Fourier map which showed no electron density above $0.6\ e^-/\text{Å}^3$ where $0.4\ e^-/\text{Å}^3$ was the noise level of the map.[13] A three-dimensional model based on van der Waals distances also shows no possible Cl^- sites; thus there are no holes or channels for disordered interstitial Cl^- ions within the lattice.

Therefore, based on the above structural and analytical evidence, we conclude that the earlier chemical analyses of Hieber[2] and later of Fischer[3] were correct and that $Ir(CO)_3Cl$ is stoichiometric. This finding is highly significant in view of the considerable evidence that this material has some of the properties of a metal or semimetal, e.g., its metallic luster, high conductivity, and linear metal chains with very short metal-metal bonds. However the physical measurements made on good samples of this material are rather meager as yet and proof of metallic character is lacking. If $Ir(CO)_3Cl$ is indeed a one-dimensional metal or semimetal, it would represent the first member of a new class of 1-D materials where the metallic state is stabilized by metal-metal and metal-ligand bonding without charge transfer to the lattice. Assuming that to be true an overlapping $5d_{z^2}\text{-}6p_z$ band model offers a possible electronic description of the origin of the conduction band. Of course extensive calculations would be necessary to bear this out. Polarized reflectance measurements, x-ray diffuse scattering studies, and inelastic neutron scattering studies are being carried out to determine the metallic state of $Ir(CO)_3Cl$.

References and Notes

(1) This work was performed under the auspices of the Division of Physical Research of the U.S. Energy Research and Development Administration.

(2) W. Hieber and H. Lagally, *Z. Anorg. Allg. Chem.*, **245**, 321 (1940); W. Hieber, H. Lagally, and H. Mayr, *ibid.*, **246**, 138 (1941).

(3) E. O. Fischer and K. S. Brenner, *Z. Naturforsch. B*, **17**, 774 (1962).

(4) K. Krogmann, W. Binder, and H. D. Hausen, *Angew. Chem., Int. Ed. Engl.*, **7**, 812 (1968); *Angew. Chem.*, **80**, 844 (1968).

(5) A. P. Ginsberg, R. L. Cohen, F. J. Di Salvo, and K. W. West, *J. Chem. Phys.*, **60**, 2657 (1974).

(6) L. F. Dahl in J. S. Miller and A. J. Epstein, *Prog. Inorg. Chem.*, **20**, 1 (1976).

(7) J. S. Miller and A. J. Epstein, *Prog. Inorg. Chem.*, **20**, 1 (1976).

(8) A. H. Reis, Jr., and S. W. Peterson, *Inorg. Chem.*, **15**, 3186 (1976).

(9) J. M. Williams, *Inorg. Nucl. Chem. Lett.*, **12**, 651 (1976).

(10) K. Krogmann and H. P. Geserich in "Extended Interactions Between Metal Ions in Transition Metal Complexes", L. V. Interrante, Ed., American Chemical Society, Washington, D.C., 1974, p 350.

(11) A. P. Ginsberg, J. W. Koepke, J. J. Hauser, K. W. West, F. J. Di Salvo, C. R. Sprinkle, and R. L. Cohen, *Inorg. Chem.*, **15**, 514 (1976).

(12) Because of the large correlations between the Cl(2) and C(4) atoms, the position and anisotropic thermal parameters of C(4) were fixed. The multipliers of Cl(2), C(4), and O(4) refined to 0.25(1), 0.25(2), and 0.25(1) respectively at an R_F 0.019.

(13) The calculated peak electron density for the 0.8 Cl atoms ($Z = 8$) disordered over 16-fold general positions is $0.85\ e^-/\text{Å}^3$. This value is obtained by direct scaling from the Cl(1) peak height on the final observed Fourier map.

(14) Participant in the Undergraduate Research Participation Program sponsored by the Argonne Center for Educational Affairs from Central Michigan University, Mt. Pleasant, Mich., 48859.

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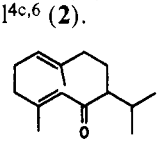
An Expeditious Route to the Germacranes. Total Synthesis of (±)-Acoragermacrone and (±)-Preisocalamendiol

Sir:

The germacranes are a class of commonly occurring medium-ring sesquiterpenes whose members include a variety of pheromones, antibiotics, cytotoxins, and antitumor agents.[1] These compounds are also known to be synthetic as well as biogenetic precursors of other important classes of sesquiterpenes.[2] Although a great deal of effort has been devoted to preparation of the requisite 1,5-cyclodecadiene ring,[3] only a few approaches have proven applicable to the synthesis of these chemically and thermally labile natural products.[4] Since existing syntheses either start from another relatively complex natural product (note exceptions[4d,e]) or suffer somewhat in terms of overall efficiency, we have conducted studies directed toward efficient new synthetic solutions to the germacranes. We wish to report (1) a concise and highly stereoselective approach to the 1,5-cyclodecadiene ring system from a simple monocyclic precursor; and (2) application of the sequence to total syntheses of (±)-acoragermacrone[5] (**1**) and (±)-preisocalamendiol[4c,6] (**2**).



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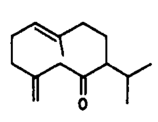

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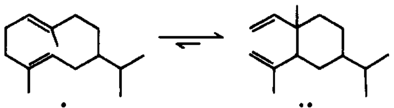
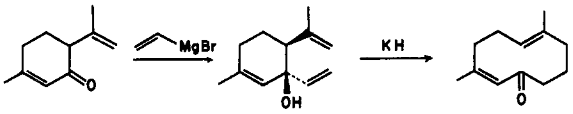
Our approach to 1,5-cyclodecadienes is based on the well-known tendency of the germacranes (i) to undergo an extemely facile Cope rearrangement to the isomeric elemane sesquiterpenes (ii).[7] Although the equilibrium usually lies toward ii, it is possible to upset the normal equilibrium and thus prepare 1,5-cyclodecadienes from appropriately substituted divinylcyclohexanes.



i ii

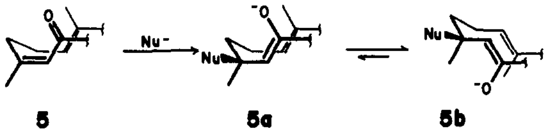
The starting point for our studies was the monoterpene isopiperitenone (**3**) which is itself readily prepared by oxidation of limonene.[8] Addition of vinylmagnesium bromide (THF, −20 °C) gave the *trans*-divinylcyclohexenol **4** (ir (neat) 3480 cm^{-1}), which was not purified but immediately subjected to the Evans modification[9] of the oxy-Cope rearrangement (KH, THF, 18-crown-6, 18 h, 25 °C).[10] Workup and short column chromatography gave a 75% overall yield of the (*Z*,*E*)-cyclodecadienone **5** (mp (pentane) 28.5–29 °C; IR (neat) 1685, 1635 cm^{-1}; NMR ($\delta^{\mathrm{CCl_4}}$) 5.93 (1 H, br s), 4.88 (1 H, br t, $J = 7$ Hz), 1.76 (3 H, d, $J = 1.2$ Hz), 1.43 (3 H, d, $J = 1.2$ Hz)). Spectral comparisons[3c] as well as NOE experiments confirmed the olefinic geometries shown. No trace of other isomers could be detected in the crude product.



3 **4** **5**

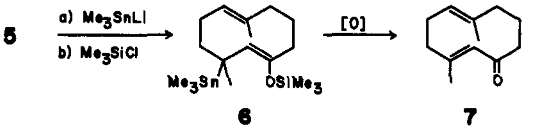
Although some germacranes incorporate the *Z*,*E* olefinic stereochemistry of **5**, most have the isomeric *E*,*E* geometry. It would therefore be desirable to have some method for isomerizing the more stable[5] *Z* enone **5** to the less stable *E* enone **6**. Although the usual procedures for olefin inversion via photoisomerization or intermediate epoxide opening proved ineffective, we felt that the conformational properties of the cyclodecadienes and the chemical reactivity of organotin compounds might merge to provide a simple solution to the isomerization problem.

Our approach to the task was based on the following working hypothesis. Conjugate addition of some very bulky nucleophile to **5** should yield adducts existing largely in the kinetic conformation **5a** or in what appears to be the thermodynamic conformation **5b**.[11] Once thermodynamic equilibrium has been established, preferential elimination from **5b** leading to the desired *E* enone **7** would be expected if the elimination transition state geometry were reactant-like or if its energy of activation were small relative to the conformational interconversion barrier leading back to **5a**.[12]



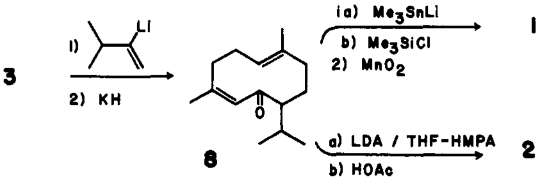
5 **5a** **5b**

Based on the above analysis, we have developed a kinetic 1,4 addition/elimination sequence for the isomerization of **5** to **7**. Conjugate addition of trimethylstannyllithium (THF, −78 °C) and silylation of the resulting enolate gave the stannyl enol silyl ether **6**.[13] Conversion to the desired (*E*,*E*)-cyclodecadienone **7** was easily accomplished by mild oxidation. Although a variety of oxidants[14] could be used, we found that the Attenburrow[15] manganese dioxide (1.5 g of MnO_2/mmol of **6**, CH_2Cl_2, 30 min, 25 °C) was particularly effective for smooth preparation of **7** (70% yield from **5**; ir (neat) 1680, 1610 cm^{-1}; NMR (δ^{CCl_4}) 5.44 (1 H, br s), 4.78 (1 H, br t, J = 7.5 Hz), 1.89 (3 H, br s), 1.20 (3 H, br s)).[5] No starting *Z*,*E* dienone could be detected by TLC or NMR.



6 **7**

To illustrate the potential of our approach we have applied the above procedures to the total synthesis of (±)-acoragermacrone (**1**) (four steps) and (±)-preisocalamendiol (**2**) (three steps). Addition of 2-lithio-3-methyl-1-butene[16] (THF, −78 °C) to isopiperitenone (**3**) followed by oxy-Cope rearrangement as before gave the known isoacoragermacrone[3c,5] (**8**) in 73% yield. Isomerization via the above organotin addition/oxidation sequence yielded (±)-acoragermacrone (**1**, 71% yield, mp 26 °C) and approximately 5% **8**. Alternatively, **8** could be deconjugated by kinetic enolate protonation[17] to yield (±)-preisocalamendiol (**2**, 76% yield).[18] These racemic materials had spectroscopic properties identical with those reported for the naturally occurring substances.[19]



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References and Notes

(1) A partial listing of germacranes: T. K. Devon and A. I. Scott, "Handbook of Naturally Occurring Compounds", Vol. II, Academic Press, New York, N.Y., 1972, pp 77–83. Review: F. Sŏrm, *J. Agric. Food Chem.*, **19**, 1081 (1971).

(2) Sesquiterpene biogenesis, review: G. A. Cordell, *Chem. Rev.*, **76**, 425 (1976). Synthetic studies: cf., inter alia, (a) E. D. Brown, M. D. Solomon, J. K. Sutherland, and A. Torre, *J. Chem. Soc. Chem. Commun.*, 111 (1967); (b) E. D. Brown and J. K. Sutherland, *ibid.*, 1060 (1968); (c) K. Yoshihara, Y. Ohta, R. Sakai, and Y. Hirose, *Tetrahedron Lett.*, 2263 (1969); (d) T. W. Sam and J. K. Sutherland, *J. Chem. Soc., Chem. Commun.*, 970 (1971); (e) T. C. Jain and J. E. McCloskey, *Tetrahedron Lett.*, 5139 (1972); (f) M. Iguchi, M. Niwa and S. Yamamura, *ibid.*, 4367 (1973); (g) M. Niwa, M. Iguchi and S. Yamamura, *Bull. Chem. Soc. Jpn.*, **49**, 3137, 3148 (1976).

(3) (a) P. S. Wharton, Y. Sumi, and R. A. Kretchmer, *J. Org. Chem.*, **30**, 234 (1965); (b) E. J. Corey and E. A. Broger, *Tetrahedron Lett.*, 1779 (1969); (c) M. Iguchi, A. Nishiyama, S. Yamamura, and Y. Hirata, *ibid.*, 4295 (1969); (d) J. A. Marshall, *Synthesis*, 229 (1971); (e) J. A. Marshall, W. F. Huffman, and J. A. Ruth, *J. Am. Chem. Soc.*, **94**, 4691 (1972); (f) G. L. Lange, M.-A. Huggins, and E. Neidert, *Tetrahedron Lett.*, 4409 (1976); (g) P. A. Wender and J. C. Lechleiter, *J. Am. Chem. Soc.*, **99**, 267 (1977).

(4) Dihydrocostunolide: (a) E. J. Corey and A. G. Hortmann, *J. Am. Chem. Soc.*, **87**, 5736 (1965); (b) Y. Fujimoto, T. Shimizu, and T. Tatsuno, *Tetrahedron Lett.*, 2041 (1976). Preisocalamendiol: (c) K. Kato, Y. Hirata, and S. Yamamura, *J. Chem. Soc., Chem. Commun.*, 1324 (1970). Hedycaryol: (d) P. S. Wharton, C. E. Sundin, D. W. Johnson, and H. C. Kluender, *J. Org. Chem.*, **37**, 34 (1972); (e) M. Kodama, Y. Matsuki, and S. Itô, *Tetrahedron Lett.*, 1121 (1976). Dihydronovanin: (f) M. Watanabe and A. Yoshikoshi, *J. Chem. Soc., Chem. Commun.*, 698 (1972).

(5) M. Niwa, A. Nishiyama, M. Iguchi and S. Yamamura, *Bull. Chem. Soc. Jpn.*, **48**, 2930 (1975).

(6) S. Yamamura, M. Iguchi, A. Nishiyama, M. Niwa, H. Koyama, and Y. Hirata, *Tetrahedron*, **27**, 5419 (1971).

(7) For a recent study, see K. Takeda, *Tetrahedron*, **30**, 1525 (1974).

(8) G. O. Schenck, K. Gollnick, G. Buchwald, S. Schroeter, and G. Ohloff, *Justus Liebigs Ann. Chem.*, **674**, 93 (1964); G. O. Schenck, O.-A. Neumüller, G. Ohloff, and S. Schroeter, *Ibid.*, **687**, 26 (1965); W. G. Dauben, M. Lorber, and D. S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969). See also B. D. Sully, *Chem. Ind.* (*London*), 263 (1964).

(9) D. A. Evans and A. M. Golob, *J. Am. Chem. Soc.*, **97**, 4765 (1975).

(10) Cf. E. N. Marvell and W. Whalley, *Tetrahedron Lett.*, 509 (1970).

(11) The parallel double-bond conformation for 1,6-cyclodecadienes has been suggested previously.[2c,3e] Molecular models suggest that both torsional and Van der Waals interactions would favor conformation **5b**.

(12) In this regard, barriers to conformation interconversion of the closely related 1,5-cyclodecadienes are known to be large based on peak coalescence temperatures in the NMR; *e.g.*, I. Horibe, K. Tori, K. Takeda, and T. Ogino, *Tetrahedron Lett.*, 735 (1973), and references cited therein.

(13) Cf. W. C. Still, *J. Am. Chem. Soc.*, in press.

(14) These agents included *m*-chloroperbenzoic acid, *p*-periodic acid, and anhydrous ferric chloride.

(15) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

(16) Prepared from the corresponding bromide by exchange with *tert*-butyllithium; cf. D. Seebach and H. Neumann, *Chem. Ber.*, **107**, 847 (1974).

(17) Cf. M. W. Rathke and D. Sullivan, *Tetrahedron Lett.*, 4249 (1972).

(18) It is interesting that the major by-product in this operation is **1** (10–20% yield). The result can be explained by a mechanism analogous to that used to rationalize the isomerization of **5** to **7**.

(19) Structures were confirmed by IR, NMR, and TLC comparison with authentic **8** and by IR comparison with authentic **1**. I wish to thank Professor Shosuke Yamamura of Meijo University for a sample of authentic isoacoragermacrone and for an IR spectrum of natural acoragermacrone.

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Resonance Raman Study of Oxyhemocyanin with Unsymmetrically Labeled Oxygen

Sir:

We wish to report the results of a resonance Raman spectroscopic investigation of the reaction between hemocyanin, a copper-containing respiratory protein, and a mixed isotope molecular oxygen. Recently, we determined that the O–O stretching vibration of the protein-bound O_2 occurs at 744 cm^{-1} in *Cancer magister* hemocyanin and at 749 cm^{-1} in *Busycon canaliculatum* hemocyanin and shifts to 704 and 708 cm^{-1}, respectively, when >90 atom % $^{18}O_2$ is employed in place of atmospheric oxygen.[1] These frequencies indicate that oxygen is bound as a peroxide ion in oxyhemocyanin and that oxygen binding is an oxidative addition process in which O_2 is reduced and the two Cu(I) centers of colorless deoxyhemocyanin are converted to the blue Cu(II) state. Magnetic susceptibility measurements on oxyhemocyanin place the lower limit of exchange coupling at 625 cm^{-1} for the antiferromagnetically coupled cupric dimers.[2]