room temperature. Intermediate **6** was treated in turn with magnesium triflate and thiophenol to effect D-ring formation with production of the α-phenylthio amide **7**.[14] On the basis of information garnered from our studies with the related trans compound,[15] **7** was exposed to excess dimethylzinc in chloroform. *Only with this organometallic reagent were we able to achieve selective replacement of the thio substituent by methyl!* The mechanistic features of this new reaction and its extension to other sulfur-containing systems are under active study.

Having now overcome two major hurdles, creation of the proper cis relationship between the C-4 and C-11 side-chain appendages and installation of the gem-dimethyl grouping, we were ready to construct the fifth and last ring, the acyltetramic acid, a unit that may be responsible for the biological activity of αCA because of its ability to chelate trace metals. On the basis of prior methodology in the tetramic acid field,[16] we chose to accomplish this last ring forming step through an internal condensation between acetoacetamide and ester. The *N*-acetyl group of **8** was thus removed,[17] and the free amine reacted with diketene to provide

(1) Holzapfel, C. W. *Tetrahedron* **1968**, *24*, 2101. Steyn, P. S.; Wessels, P. L. *Tetrahedron Lett.* **1978**, 4707.

(2) Ohmomo, S.; Sugita, M.; Abe, M. *J. Agric. Chem. Soc. Jpn.* **1973**, *47*, 83. Luk, K. C.; Kobbe, B.; Townsend, J. M. *Appl. Environ. Microbiol.* **1977**, *33*, 212.

(3) Wilson, B. J. In "Mycotoxins in Human Health"; Purchase, I. F. H., Ed.; Macmillan: New York, 1971; pp 223–229. Wilson, B. J.; Wilson, C. H.; Hayes, A. W. *Nature (London)* **1968**, *220*, 77. Harrison, J. *Trop. Sci.* **1971**, *13*, 57.

(4) Holzapfel, C. W.; Schabort, J. C. *S. Afr. J. Chem.* **1977**, *30*, 233.

(5) Holzapfel, C. W.; Hutchison, R. D.; Wilkins, D. C. *Tetrahedron* **1970**, *26*, 5239.

(6) Holzapfel, C. W.; Gildenhuys, P. J. *S. Afr. J. Chem.* **1977**, *30*, 125.

(7) Holzapfel, C. W. In "The Biosynthesis of Mycotoxins"; Steyn, P. S., Ed.; Academic Press: New York, 1980; pp 327–355.

(8) Kozikowski, A. P.; Ishida, H.; Chen, Y.-Y. *J. Org. Chem.* **1980**, *45*, 3350.

(9) Smith, G. F. *J. Chem. Soc.* **1954**, 3842.

(10) Hellmann, H.; Teichmann, K.; Lingens, F. *Chem. Ber.* **1958**, *91*, 2417. Hengartner, V.; Valentine, D.; Johnson, K. K.; Larscheid, M. E.; Pigott, F.; Scheidl, F.; Scott, J. W.; Sun, R. C.; Townsend, J. M.; Williams, T. H. *J. Org. Chem.* **1979**, *44*, 3741. The *E/Z* nature of the amidoacrylate group of **3** and **4** has not yet been rigorously determined.

(11) Miller, R. D.; McKean, D. R. *Synthesis* **1979**, 730.

(12) (a) The introduction and subsequent removal of the sulfur substituent was crucial to the control of the relative stereochemistry between C-4 and C-11, for cyclization of the keto amide ii prepared from i led to the product
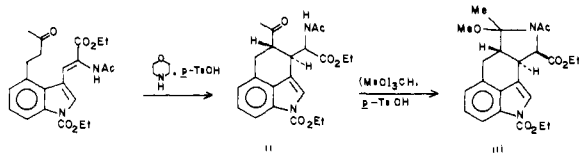
iii possessing a trans-C,D-ring fusion. Accordingly, epimerization at C-11 does not precede D-ring closure, a feature that we had counted on at the outset of our work on αCA. The assignment of trans stereochemistry to iii is based on ¹H NMR analysis ($J_{4,11}$ = 11.9 Hz) as well as a single-crystal X-ray analysis. (b) Further experimentation has revealed that the tricyclic compound corresponding to **5** but containing a cis disposition of the carbon appendages is formed in the Michael reaction as well (~1:1). This compound is also converted to **6** (but at faster rate!) upon Raney nickel hydrogenolysis.

(13) van Tamelen, E. E.; Grant, E. A. *J. Am. Chem. Soc.* **1954**, *81*, 2160. Pettit, G. R.; van Tamelen, E. E. *Org. React. (N.Y.)* **1962**, *12*, 356.

(14) Corey, E. J.; Shimoji, K. *Tetrahedron Lett.* **1983**, *24*, 169.

(15) The α-methoxy amide iii[12] could be converted to the corresponding α-phenylthioamide iv on reaction with magnesium triflate and thiophenol.
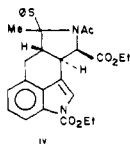
Both iii and iv were treated with a wide variety of methyl metallics in an effort to replace the exocyclic-heteroatom substituent by methyl. Dimethylzinc was the only reagent capable of bringing about the desired transformation, and this reagent worked only with iv.

(16) Harris, S. A.; Fischer, L. V.; Folkers, K. *J. Med. Chem.* **1965**, *8*, 447. Yuki, H.; Kariya, K.; Hashimoto, Y. *Chem. Pharm. Bull.* **1967**, *15*, 727. Lee, V. J.; Branfman, A. R.; Herrin, T. R.; Rinehart, K. L. *J. Am. Chem. Soc.* **1978**, *100*, 4225.

(17) Kozikowski, A. P.; Ishida, H. *J. Am. Chem. Soc.* **1980**, *102*, 4265.

the acetoacetamide **9**. Surprisingly, when this intermediate was exposed to methanolic sodium methoxide in benzene and the resulting enolate mixture brought to a pH of 4, iso-α-cyclopiazonic acid was isolated. The conversion of αCA to the iso compound has been reported by Holzapfel employing 0.3 N sodium hydroxide as base; however, after 10 h, the reaction mixture consisted primarily of αCA (ratio αCA:iso-αCA ≅ 1.5:1). Epimerization of the ester-bearing center may thus precede ring closure in the present instance. To complete the synthesis, the iso compound was isomerized with triethylamine in chloroform at 100 °C (sealed tube) to a 2.5:1 mixture of αCA and the iso compound. These could be separated by formamide–oxalic acid impregnated paper chromatography to provide the pure product.[1] The αCA obtained in this manner was identical with the natural product by UV, IR, NMR, and mass spectral analysis. In summary the synthesis scheme presented herein provides a fairly straightforward route to αCA which should prove valuable in analogue construction.[18] The zinc chemistry discovered in the context of this synthesis is unique and is certainly amenable to other important synthetic applications.[19,20]

(18) For a recent report concerning synthetic studies directed toward αCA, see: Somei, M.; Tokutake, S.; Kaneko, C. *Chem. Pharm. Bull.* **1983**, *31*, 2153.

(19) The structures of all of the materials reported herein are supported by satisfactory ¹H NMR, IR, high-resolution mass spectral data, and elemental analysis. Experimental procedures will be provided in a full paper to be published at a later date.

(20) Phenylthio glycosides are transformed, for example, to C-glycosides in high yield by using organozinc reagents. Ritter, A., unpublished results.

Copper(I) and Silver(I) Diiridium Polyhydrides

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Received January 20, 1984

In the course of our study of chemical oxidation (e.g., Ag⁺) of transition-metal polyhydrides, we have isolated adducts of the related oxidant (electrophile) Cu⁺.[1] It is known that one-electron oxidation of the 18-electron species $M(CO)_2(P\sim P)_2$ (M = Cr, Mo, W)[2] and $MX(CO)_3P_2$[3] (M = Mn and Re) greatly enhances the rate of (intramolecular) isomerization. Since *fac*- and *mer*-$IrH_3(PMe_2Ph)_3$ comprise a stereoisomeric pair whose thermal equilibrium (~70:30 in benzene) is established only slowly at 25 °C, we have used these polyhydrides to probe the degree to which our proposed "redox intermediates" mimic the behavior expected of true Ir(IV) radical cations (e.g., Cu⁺ catalysis of eq 1).

$$\textit{fac}\text{-IrH}_3\text{P}_3 \underset{?}{\overset{\text{Cu}^+}{\rightleftharpoons}} \textit{mer}\text{-IrH}_3\text{P}_3 \qquad (1)$$
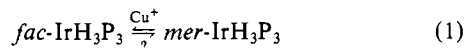
(1) Rhodes, L. J.; Zubkowski, J. D.; Folting, K.; Huffman, J. C.; Caulton, K. G. *Inorg. Chem.* **1982**, *21*, 4185–4192.

(2) Bond, A. M.; Grabaric, B. S.; Jackowski, J. J. *Inorg. Chem.* **1978**, *17*, 2153 and references therein.

(3) Bond, A. M.; Colton, R.; McDonald, M. E. *Inorg. Chem.* **1978**, *17*, 284i and references therein.
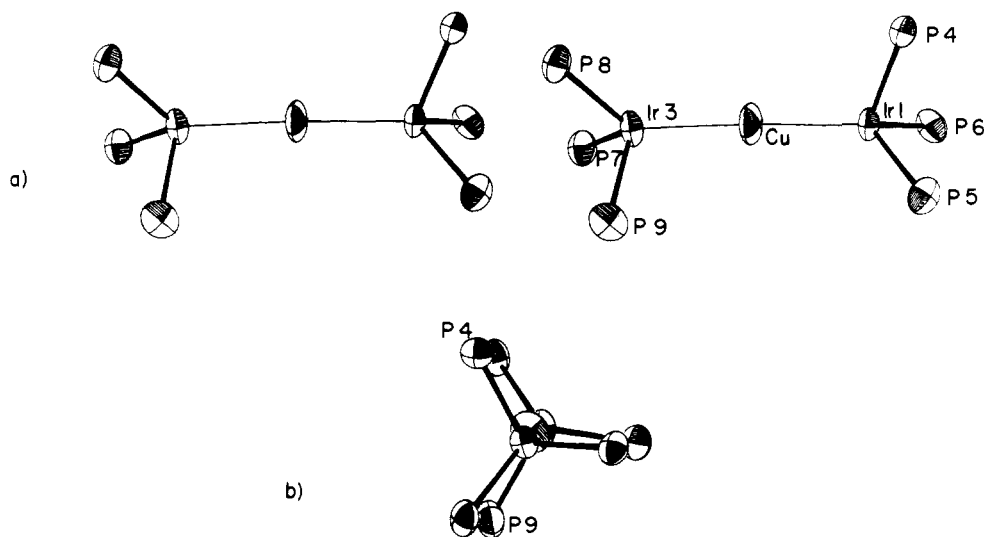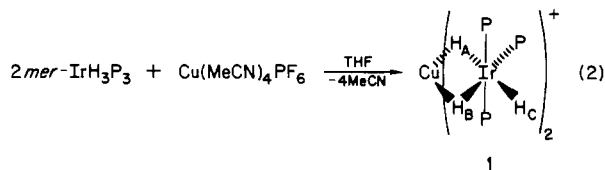
Figure 1. (a) Stereo ORTEP drawing of the inner coordination sphere of $(fac\text{-IrH}_3P_3)_2\text{Cu}^+$, looking down an idealized (non-crystallographic) twofold axis of symmetry. (b) View along the Ir–Cu–Ir line, showing eclipsing of the phosphorus nuclei. Selected bond lengths: Cu–Ir1 = 2.502 (4) Å; Cu–Ir3 = 2.529 (4) Å; Ir1–P4 = 2.308 (9) Å; Ir1–P5 = 2.300 (9) Å; Ir1–P6 = 2.316 (9) Å; Ir3–P7 = 2.277 (8) Å; Ir3–P8 = 2.295 (9) Å; Ir3–P9 = 2.319 (10) Å. Angles: Ir1–Cu–Ir3 = 176.0°; Cu–Ir1–P4 = 109.6 (2)°; Cu–Ir1–P5 = 123.2 (3)°; Cu–Ir1–P6 = 122.2 (2)°; Cu–Ir3–P7 = 123.4 (2)°; Cu–Ir3–P8 = 127.9 (3)°; Cu–Ir3–P9 = 101.3 (3)°. All angles P–Ir–P fall in the narrow range 98.8 (3)–100.0 (3)°.
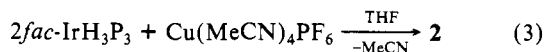
Herein, we report the unexpected outcome of the reaction between Cu(I) and the *mer* and *fac* isomers of IrH_3P_3 (P ≡ PMe_2Ph) and the first example of a transition metal/silver(I) adduct multiply bridged by hydrides.[4]

Addition of $\text{Cu(MeCN)}_4\text{PF}_6$ to a cooled (−70 °C) THF solution of 2 equiv of *mer*-IrH_3P_3 yields a pale yellow solution upon warming to room temperature. The ^1H NMR[5] of the reaction mixture indicated a quantitative yield of a product consistent with the formulation $[(mer\text{-IrH}_3P_3)_2\text{Cu}]\text{PF}_6$ (**1**) (eq 2). The IR[6] and

$$2\,mer\text{-IrH}_3P_3 \;+\; \text{Cu(MeCN)}_4\text{PF}_6 \xrightarrow[\text{−4MeCN}]{\text{THF}} \left[\text{Cu} \underset{H_B}{\overset{H_A}{\underset{P}{\overset{P}{\left\langle \text{Ir} \right\rangle}}}} H_C \right]_2^+ \quad (2)$$

1

high-field (146 MHz) $^{31}\text{P}\{^1\text{H}\}$ NMR[7] spectra of **1** also agree with the product formulation and suggest a structure containing four bridging hydrides ligating copper and stereochemically rigid at iridium in solution over a period of hours at 25 °C. Such rigidity by itself indicates the inapplicability of a dative-bonding model ($P_3H_3\text{Ir}{\rightarrow}\text{Cu}^+$) for **1**, since seven-coordinate hydrides are without exception fluxional.

The addition of $\text{Cu(MeCN)}_4\text{PF}_6$ to a cooled THF solution of 2 equiv of *fac*-IrH_3P_3 gives a colorless solution at room temperature which exhibits $^{31}\text{P}\{^1\text{H}\}$ and ^1H NMR[8] spectra consistent with a quantitative yield of a single product formulated as $[(fac\text{-}\text{IrH}_3P_3)_2\text{Cu}]\text{PF}_6$ (**2**) (eq 3). There is no conversion of **2** to **1** over

$$2\,fac\text{-IrH}_3P_3 \;+\; \text{Cu(MeCN)}_4\text{PF}_6 \xrightarrow[\text{−MeCN}]{\text{THF}} \mathbf{2} \quad (3)$$

a period of hours in acetonitrile at 25 °C. Even though the IR[9] of **2** indicates the presence of bridging and terminal hydride ligands, the $^{31}\text{P}\{^1\text{H}\}$ and ^1H NMR of **2** are temperature independent (to −80 °C) and are characterized by a single hydride and a single phosphine chemical shift. However, a single-crystal X-ray study[10] of **2** (Figure 1a) reveals a linear trimetallic chain in which the phosphines adopt an eclipsed rotational conformation (Figure 1b). Although the hydrides were not found crystallographically, a hydride-coupled ^{31}P NMR spectrum of $\mathbf{2}^{11}$ shows an apparent doublet ($J = 50$ Hz); this proves that each phosphine is trans to a hydride in a stereochemically rigid octahedral arrangement about Ir. The X-ray structure also reveals two types of P–Ir–Cu angles, two small (105° average) and four large (124° average). These features, along with the IR data, lead uniquely to the conclusion that the copper in **2** binds to only four of the sterically available six hydride ligands and that the CuH_4 stereochemistry is not planar but better represented by the following sketch. Since two hydride ligands remain terminal on iridium

2
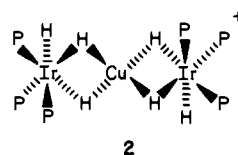
facile fluxionality at copper is required by the NMR spectral data. This result is wholly unanticipated since $(\text{ReH}_5P_3)_2\text{Cu}^+$ contains two facial ReH_3 units which provide octahedral geometry (six coordination) to copper.[12] Taken together, these results appear to rule out facile formation of fully oxidized $\text{IrH}_3P_3^+$ species from **1** or **2** (cf. eq 1).

Suspecting that the oxidative stability of IrH_3P_3 might allow isolation of an adduct with stronger oxidant, the silver(I) adduct of *fac*-IrH_3P_3 was synthesized in 100% spectroscopic yield (eq 4).

(4) Spencer, J. L. (Bristol, U.K.) has informed us of unpublished work on $\text{Ag[ReH}_7(\text{PPh-}i\text{-Pr}_2)_2]_2^+$.
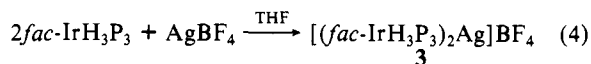
(5) ^1H NMR (CD_3CN, 20°C): δ +7.00-8.00 (m, 15 H), +1.88 (br t, 6 H), +1.83 (br t, 6 H), +1.24 (d, $J = 8.5$ Hz, 6 H), −9.36 (br s, H_A, 1H), −11.28 (d (93 Hz) of t (18 Hz), H_B, 1 H), −11.69 (q, $J_{\text{PH}} = 15.5$ Hz, H_C, 1 H).

(6) IR (KBr): $\nu(\text{IrH}_C)$ 2035 cm^{-1} (s); $\nu(\text{IrH}_B\text{Cu})$ 1886 (s, br); $\nu(\text{IrH}_A\text{Cu})$ 1624 (vs, br).

(7) $^{31}\text{P}\{^1\text{H}\}$ (CD_3CN, 146 MHz): δ −33.45 (t, 19 Hz), −34.03 (d, 23 Hz), −144 (septet, PF_6).

(8) ^1H NMR (CD_3CN, +16 °C): δ +7.57 (m, 6 H), +7.36 (m, 9 H), +1.66 (d, $J = 8$ Hz, 18 H), −11.89 (symmetrical second-order multiplet indicative of AA′A″XX′X″ spin system, 3 H). $^{31}\text{P}\{^1\text{H}\}$ (CD_3CN, 40.5 Mz): δ −37.3 (s), −144 (septet, PF_6).

(9) IR (KBr): $\nu(\text{IrH})$ 1990 cm^{-1} (s, br); $\nu(\text{IrHCu})$ 1865 (s, br).

(10) Crystallographic data (−162 °C) for $[\text{H}_3\text{Ir}(\text{PMe}_2\text{Ph})_3]_2\text{CuPF}_6\cdot$0.5THF·0.5toluene: $a = 17.833$ (6) Å, $b = 20.876$ (8) Å, $c = 18.630$ (6) Å, $\beta = 105.36$ (2)°, $Z = 4$, in space group $P2_1/c$; $R_w(F) = 8.7\%$ with Cu, Ir, P, F, and C refined anisotropically. Disorder in the PF_6^- and partial occupancy of the two solvent molecules made it impossible to locate the hydride ligands.

(11) $^{31}\text{P}\{\text{hydride coupled}\}$ (CD_3CN, 40.5 MHz): δ −37.7 (d, $J_{\text{P-trans-H}} = 50$ Hz).

(12) Rhodes, L. F.; Huffman, J. C.; Caulton, K. G. *J. Am. Chem. Soc.* **1983**, *105*, 5137–5138.

$$2fac\text{-}IrH_3P_3 + AgBF_4 \xrightarrow{\text{THF}} \underset{\mathbf{3}}{[(fac\text{-}IrH_3P_3)_2Ag]BF_4} \quad (4)$$

The hydride resonance of **3** appears as a doublet of doublets at $\delta -11.59$ ($J_{P-trans-H} = 72$ Hz; $J_{AgH} = 49.5$ Hz; separate couplings to ^{107}Ag and ^{109}Ag were not resolved). The $^{31}P\{^1H\}$ NMR spectrum consists of a doublet at $\delta -37.3$ ($J_{AgP} = 23$ Hz) with additional structure ($J_{P-trans-H} = 72$ Hz) evident upon selectively coupling the hydrides. The infrared spectrum[13] of **3** exhibits two bands, indicative of bridging and terminal hydrides. The shape and intensity of these bands are almost identical with those observed for **2**. This strongly suggests that compound **3** has a structure similar to **2** (four μ-H contacts to Ag(I)) but executes an intramolecular fluxional process about Ag. A tetrahydride coordination sphere has not previously been seen for Ag(I).[14]

Supplementary Material Available: A list of positional and thermal parameters and bond lengths and angles for [*fac*-IrH$_3$-(PMe$_2$Ph)$_3$]$_2$CuPF$_6$·O.5THF·0.5toluene (8 pages). Ordering information is given on any current masthead page.

(13) IR (CH$_2$Cl$_2$): ν(IrH) 1964 (s, br); ν(IrHAg) 1888 (s, br).
(14) For singly hydride bridged Ag(I) complexes: Green, M.; Orpen, A. G.; Salter, I. D.; Stone, F. G. A. *J. Chem. Soc., Chem. Commun.* **1982**, 813–814. Hutton, A. T.; Pringle, P. G.; Shaw, B. L. *Organometallics* **1983**, *2*, 1889–1891.

Additions and Corrections

Mechanistic Investigation of Olefin Insertion into the Rhodium Hydrogen Bond [*J. Am. Chem. Soc.* **1983**, *105*, 7770–7771]. D. C. ROE

Page 7771, eq 4 should be replaced by

$$k_2 = \frac{3}{2}\left(\frac{K+1}{K}\right)k \quad (4)$$

Insertion rates are thus faster than indicated by a factor of 1.40. Estimates of the activation parameters are insignificantly affected by this change.

*Book Reviews**

Antimicrobials in Foods. Edited by Alfred Larry Branen (University of Idaho) and P. Michael Davidson (University of Tennessee). Marcel Dekker, Inc., New York. x + 465 pp. $69.75.

This book assembles for the first time in a concise fashion a survey of those antimicrobial substances which are either added to or naturally present in foods and which contribute significantly to extending shelf life by retarding or inhibiting microbial growth. Fourteen prominent scientists review the state-of-the-art in the area of use of antimicrobials in essentially all types of food products.

The book contains 13 chapters, the first of which introduces the use of antimicrobials in foods, describing the role of chemical preservatives and rationale for selecting them based on the food product in question. This is followed by chapters singularly devoted to specific chemicals, compounds, and groups of compounds which exhibit antimicrobial properties when added to or naturally present in foods. A chapter describing the antimicrobial effects of sodium benzoate and benzoic acid is followed by chapters on phenolic compounds, organic acids, and medium-chained fatty acids and their esters.

Sorbates, sulfur dioxide and sulfites, and nitrite are covered in separate chapters. The halogens and surface-active agents are then reviewed followed by chapters devoted to dimethyl and diethyl dicarbonate, nisin, and other inhibitory substances from lactic acid bacteria, antibiotic residues, and naturally occurring and miscellaneous food antimicrobials.

The editors have done an outstanding job in molding presentations from 14 authors into a fluid text. Particularly valuable are a large number of tables listing articles on various antimicrobials, solubility characteristics, effective and legal limits in foods, and activity against specific microorganisms.

"Antimicrobials in Foods" is highly recommended as a reference for professional food microbiologists, toxicologists, and personnel working in microbiological quality assurance laboratories in food and allied industries. The book will also find use as a valuable supplementary reference for students taking food microbilogy, toxicology, and pharmacology courses at the advanced undergraduate and graduate levels.

Larry R. Beuchat, *University of Georgia*

Organic Reactions. Volume 31. Edited by W. G. Dauben. John Wiley and Sons, New York. 1984. vi + 376 pp. $44.50.

Except for the traditional fore pages and indexes to previous volumes, this is a book titled "Addition and Substitution Reactions of Nitrile-stabilized Carbanions", by S. Arseniyadis, K. S. Kyler, and D. S. Watt. The subject was previously reviewed in "Organic Reactions" in 1957 by Cope, Holmes, and House.

The subject of this review is not quite what the title might suggest, for it is concerned with carbanions stabilized by an attached cyano group, rather than those that might be stabilized by nitrile solvents, and it intentionally omits carbanions stabilized by two electron-withdrawing groups, such as those from cyanoacetic esters and malononitriles. The topic is so large that the tabular survey of examples accounts for 80% of the length, and there are no less than 927 references.

The discussion of mechanism occupies 15 pages, and is largely concerned with the generation of carbanions (including dianions) and the relation between the method of generation and subsequent reactions. The next 45 pages are devoted to the scope of the reactions; eight pages of experimental examples complete the text. Procedures for the preparation of the important strong-base reagents, lithium diisopropylamide, lithium diethylamide, and sodium bis(trimethylsilyl)amide, are included.