solvent (path b). The fact that *trans*-3-hexene, the thermodynamically more stable isomer,[18] always predominates in the reaction mixture suggests that the former alternative (path a) is adopted. Vinyl free radicals generated by perester decomposition and trapped by reaction with hydrogen atom donors (*e.g.*, cumene) invariably lead to products which, relative to the equilibrium mixture, are markedly enriched in the thermodynamically less stable olefin.[6,7] This is readily explained in terms of increased steric interaction between the donor and acceptor molecules in the transition state for hydrogen atom donation to the *trans* radical as compared with the *cis* radical.[7] The transition state for electron transfer from radical anion to the vinyl radical presumably need not be so highly oriented or so intimate as that for hydrogen atom donation. Thus transfer should take place with equal ease to either the *cis*- or *trans*-vinyl radical.

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(18) $\Delta G_f°_{298}°K$(*trans*-3-hexene(g)) = 18.86 kcal/mole; $\Delta G_f°_{298}°K$(*cis*-3-hexene(g)) = 19.66 kcal/mole: F. D. Rossini, *et al.*, "Selected Values of the Properties of Hydrocarbons," National Bureau of Standards Circular C461, U. S. Government Printing Office, Washington, D. C., 1947.

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The Reaction of Phenyl(trihalomethyl)mercurials with Hexamethylditin. The First Case of Dihalocarbene Insertion into a Metal–Metal Bond to Give a Stable MCX_2M System

Sir:

In a recent communication[1] we described the reaction of phenyl(bromodichloromethyl)mercury with bis(trimethylsilyl)mercury and bis(trimethylgermyl)mercury. We proposed that an intermediate formed in these reactions was the product of dichlorocarbene insertion into the Si–Hg and Ge–Hg bonds, $Me_3MCCl_2HgMMe_3$ (M = Si and Ge), and that further reactions of this intermediate led to the observed products. This explanation in terms of dihalocarbene insertion into metal–metalloid bonds suggested to us that other such insertions into covalent metal–metal bonds should be possible and that in favorable cases the initial M–CX_2–M systems could be both thermally stable and kinetically stable with respect to further attack by CX_2 and thus capable of isolation. We have found this to be the case with hexamethylditin in its reaction with phenyl(bromodichloromethyl)mercury and phenyl(dibromochloromethyl)mercury (eq 1).

$$C_6H_5HgCXClBr + (CH_3)_3Sn\text{–}Sn(CH_3)_3 \longrightarrow (CH_3)_3SnCXClSn(CH_3)_3 + C_6H_5HgBr \quad (1)$$
$$X = Cl \text{ or } Br$$

As an example, we describe the reaction between $PhHgCCl_2Br$ and hexamethylditin. A mixture of 0.10 mole each of the mercurial[2] and hexamethylditin in 250 ml of dry benzene was stirred and heated at reflux under nitrogen for 3.5 hr. The reaction mixture was filtered to remove 30.6 g of gray solid, mp 276–286° (phenylmercuric bromide contaminated with some metallic mercury). Concentration of the orange filtrate at 10 mm resulted in crystallization of 3.64 g of diphenylmercury. Trap-to-trap distillation at 0.8 mm (pot temperature to 100°) removed the remaining solvent and minor amounts of trimethyltin halides; further distillation at 2×10^{-4} mm at room temperature gave small amounts of trimethyltin halides and phenyltrimethyltin,[3] leaving a liquid identified as bis(trimethyltin)dichloromethane, $(CH_3)_3SnCCl_2Sn(CH_3)_3$, bp 48–50° ($2 \times 10^{-4}$ mm), $n^{25}D$ 1.5326, analysis for all elements satisfactory, in 53% yield. Its nmr spectrum (CS_2) showed a sharp singlet at 0.3 ppm downfield from internal tetramethylsilane, with the expected tin satellites ($J_{Sn^{119}-H^1}$ = 53.5 cps; $J_{Sn^{117}-H^1}$ = 51.5 cps), and the infrared spectrum (pure liquid) showed bands at 2980 (s), 2915 (s), 1191 (s), 770 (vs), 725 (s), 667 (m), 632 (s), 527 (s), and 507 (sh) cm^{-1}. The mass spectroscopically determined molecular weight was 410 (calculated 410); the major fragment was Me_3Sn^+.

A similar reaction using phenyl(dibromochloromethyl)mercury gave bis(trimethyltin)bromochloromethane, $(CH_3)_3SnCBrClSn(CH_3)_3$, bp 61° ($2 \times 10^{-4}$ mm), $n^{25}D$ 1.5502, in 39% yield. A satisfactory analysis and mass spectroscopic molecular weight were obtained. The trimethyltin resonance occurred at 0.3 ppm, and the infrared spectrum showed absorption at 2970 (m), 2900 (m), 1190 (m), 768 (vs), 720 (s), 674 (sh), 659 (s), 580 (s), and 526 (vs) cm^{-1}. It is of interest to note that the reaction of phenyl(bromodichloromethyl)mercury with hexamethylditin in benzene for 6 days at room temperature gave bis(trimethyltin)dichloromethane in 52% yield.

Attempts to utilize these bis(trimethyltin)dihalomethanes as sources of the carbene $(CH_3)_3SnCCl$[4] have thus far been unsuccessful, mostly because of the thermal stability of these compounds. Bis(trimethyltin)dichloromethane was not decomposed on being heated in a sealed tube at 145° for 40 hr. Attempted reaction with tetramethylethylene at 180° for 4 days gave trimethyltin chloride as the only identifiable organotin product. Similarly, bis(trimethyltin)bromochloromethane survived 20 hr of heating at 130° in the presence of tetramethylethylene without decomposition, but at 190–200° (24 hr) both trimethyltin bromide and chloride were formed.

We have found that nucleophilic attack by iodide ion at the metal in a trihalomethylmercury or -tin compound provides another procedure for the release of CX_2 from such reagents.[5] In the case of bis(trimethyl-

(1) D. Seyferth, R. J. Cross, and B. Prokai, *J. Organometal. Chem.* (Amsterdam), 7, P20 (1967).

(2) D. Seyferth and J. M. Burlitch, *ibid.*, **4**, 127 (1965).

(3) By-product formation can be rationalized in terms of a reaction between phenylmercuric bromide and hexamethylditin to give trimethyltin bromide and $PhHgSnMe_3$. Decomposition of the latter then gives $PhSnMe_3$ and metallic mercury in one mode, diphenylmercury, metallic mercury, and hexamethylditin in another. This point is being examined.

(4) Note analogous release of CCl_2 from Me_3SnCCl_3 and Me_3SnCCl_2Br in this connection: D. Seyferth, F. M. Armbrecht, Jr., B. Prokai, and R. J. Cross, *J. Organometal. Chem.* (Amsterdam), **6**, 573 (1966).

(5) (a) D. Seyferth, J. Y.-P. Mui, M. E. Gordon, and J. M. Burlitch, *J. Am. Chem. Soc.*, **87**, 681 (1965); (b) D. Seyferth, M. E. Gordon, J. Y.-P. Mui, and J. M. Burlitch, *ibid.*, **89**, 959 (1967); (c) D. Seyferth, H. Dertouzos, R. Suzuki, and J. Y.-P. Mui, *J. Org. Chem.*, in press.

tin)bromochloromethane, however, attack of iodide occurred at carbon (eq 2). The product, obtained in

$$(CH_3)_3SnCBrClSn(CH_3)_3 + Na^+I^- \xrightarrow{DME} (CH_3)_3SnCIClSn(CH_3)_3 + NaBr\downarrow \quad (2)$$

63% yield, was unstable in air, turning bright orange-red on exposed surfaces. Its combustion analysis, mass spectroscopic molecular weight, and infrared spectrum were in agreement with the structure shown.

We recognize that our discovery of the first case of dihalocarbene insertion into a metal–metal bond to give a stable $-M-CX_2-M-$ system opens up a broad new field of research in the organometallic aspects of carbene chemistry. The study of compounds containing covalent metal–metal bonds has received much attention in the past few years, as the many papers on this subject show.[6] We currently are investigating reactions of phenyl(trihalomethyl)mercurials with compounds containing main group metal–main group metal bonds, main group metal–transition metal bonds, and transition metal–transition metal bonds with the aim of preparing and studying new $M-CX_2-M$ systems.

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(6) *Cf.* D. Seyferth and R. B. King, "Annual Surveys of Organometallic Chemistry," Vol. 1 and 2, Elsevier Publishing Co., Amsterdam, 1965 and 1966, for recent references.

(7) Alfred P. Sloan Foundation Fellow, 1962–1966.
(8) National Institutes of Health Predoctoral Fellow, 1964–1967.

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The Presence of Dehydroalanine in the Antibiotic Nisin and Its Relationship to Activity

Sir:

When the peptide antibiotic nisin[1,2] was treated with cyanogen bromide[3] (0.1 *N* HCl, 37°, 24 hr) in order to cleave the methionyl peptide bonds, a product of low molecular weight (fractions 91–110; 22 ml) was isolated by gel chromatography on a Sephadex G-25 column (6 × 120 cm; 0.2 *N* CH_3COOH).

The same product was isolated from control experiments in the absence of the reagent, indicating a bond which is labile under mildly acidic conditions. Aliquots of the pooled and lyophilized fractions from both experiments were analyzed directly using the accelerated system[4] of an amino acid analyzer.[5] A single substance was eluted from the 0.9 × 60 cm column at an effluent volume of 172–182 ml. Lysine was the only amino acid found in the total hydrolysate. The hydrolysate of the dinitrophenylated product contained only N^ϵ-dinitrophenyllysine, thus indicating the presence of an N^α-substituted derivative of lysine.

The product of the reaction of this lysine derivative with ninhydrin showed optical densities at 570 and 440 mμ which were reminiscent of those of free lysine. We therefore concluded that the N^α substituent is labile under the conditions of the ninhydrin reaction.

Similar observations had been made earlier with pyruvylamino acids formed during cleavage of the aminoacyl bond of N-aminoacyl-S-alkylcysteine peptides.[6]

The isolated product was treated with *o*-phenylenediamine.[7] Lysine was liberated in a yield of 50% after 4 hr of reaction at 37°. The fragment thus appeared to be pyruvyllysine. Since dehydroalanine peptides are cleaved with the formation of pyruvyl peptides it is implied that the COOH-terminal sequence[8] of nisin is *dehydroalanyllysine*. The release of pyruvyllysine in dilute acid is, however, slow (2%/24 hr; *cf.* below, conditions for the quantitative cleavage).

The molecular weight of nisin was determined by the method of partial substitution.[9] Monodinitrophenylnisin was isolated and purified[10] by countercurrent distribution in the system butan-1-ol–acetic acid–water, 4:3:1.

A molecular weight value of 3510 was calculated for this derivative, which is one-half that reported earlier.[2] It is, however, in agreement with the minimum molecular weight determined from the amino acid analyses of nisin (micromoles/0.5 mg; 92% recovery without dry weight correction) and *monodinitrophenylnisin* (micromoles/0.5 mg; quantitative recovery after desiccation): lysine (0.382; *0.267*), histidine (0.255; *0.265*), ammonia (0.425; *0.459*), aspartic acid (0.139; *0.144*), serine (0.119; *0.113*), lanthionine + β-methyllanthionine (0.740; *0.760*), proline (0.130; *0.129*), glycine (0.400; *0.421*), alanine (0.260; *0.270*), valine (0.134; *0.138*), methionine (0.253; *0.261*), isoleucine (0.376; *0.393*), leucine (0.257; *0.268*); mol wt (nisin), 3290; mol wt (mono-DNP-nisin), 3460.

These data indicate clearly that only one residue of lysine has been dinitrophenylated. Dinitrophenylation did not take place at the COOH-terminal lysine, since pyruvyllysine is still released from mono-DNP-nisin.

The above partial structure of the antibiotic is supported by: (a) the addition of mercaptoacetamide to the double bond of dehydroalanine at pH 4.5 and room temperature (with 1.6 m*M* nisin solution, the following values were determined for carboxymethylcysteine in the addition product: 0.24 residue, 24 hr, 1.6 m*M* mercaptan; 1.2 residues, 24 hr, 28 m*M* mercaptan; 1.2 residues, 72 hr, 56 m*M* mercaptan; the test for free sulhydryl groups with maleimide was negative and the hydrolysate was free of cystine); (b) a comparison

(1) From Aplin & Barrett Ltd., Yeovil, England. The purification of the antibiotic by gel chromatography and countercurrent distribution will be published separately by E. Gross, J. L. Morell, and P. Q. Lee.
(2) G. C. Cheeseman and N. J. Berridge, *Biochem. J.*, **71**, 185 (1959).
(3) E. Gross and B. Witkop, *J. Biol. Chem.*, **237**, 1856 (1962).
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(5) D. H. Spackman, W. H. Stein, and S. Moore, *Anal. Chem.*, **30**, 1190 (1958).
(6) E. Gross, C. H. Plato, J. L. Morell, and B. Witkop, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., 1965, Abstract 125, p 60C.
(7) H. B. T. Dixon and V. Moret, *Biochem. J.*, **94**, 463 (1965).
(8) Contrary to earlier reports (*cf.* ref 2) on the absence of free end groups, nisin also contains a free terminal amino group, namely, that of isoleucine.
(9) A. R. Battersby and L. C. Craig, *J. Am. Chem. Soc.*, **74**, 4023 (1952).
(10) E. Gross, J. L. Morrell, and P. Q. Lee, unpublished data.