thermal polymerization are both unnecessary and unreasonable energetically.

Acknowledgment. One of us (R.C.) acknowledges a helpful discussion with Professor D. M. Lemal.

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(16) Historically, the popularity of the carbene scheme is attributable mainly to the fact that the first two x-ray structures for the polydiacetylenes yielded acetylene backbones; this backbone is arrived at with straightforward bookkeeping in the carbene scheme. However, butatriene backbones have now been observed in two cases, as well as apparent thermally induced phase transformations between the two backbone sequences.[17] Also, a carbene chain end has recently been observed in ESR experiments on PTS,[15] but *only* in the autocatalytic region where the chain propagation lengths are longer. As argued in detail elsewhere,[6] we do not believe the final bonding sequence (or, therefore, the nature of the termination) has any significant implications regarding the chain initiation event.
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A Selective Formose Reaction[1]

Sir:

The formose reaction, by which a complex mixture of sugars and sugar alcohols (the so-called formose) is produced by the base-catalyzed condensation of formaldehyde, has received much attention in connection with the prebiotic synthesis of carbohydrates and the microbial utilization of formose sugars.[2-4] The reaction using calcium hydroxide catalyst in aqueous media, which has been most widely investigated, proceeds via three distinct steps. (1) An induction period is necessary for the formation of a small amount of condensation products of C_2 and C_3 such as glycolaldehyde, glyceraldehyde, and dihydroxyacetone, which are believed to act as catalytic species by compexing with calcium ions, in the subsequent step. (2) Formose formation occurs rapidly and the yield of formose sugars reaches a maximum at the so-called yellowing point[5] at which the reaction mixture shows yellow coloration. (3) The third step includes the decomposition of the formed formose sugars under the reaction conditions. Such a complexity, especially the nonselective sugar formation (see Figure 1a), has made detailed analysis of the formose reaction very labo-
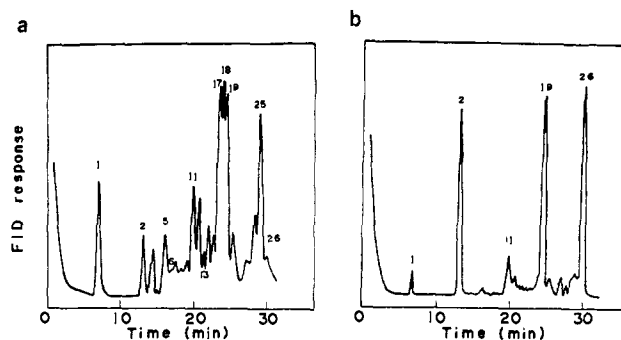

Figure 1. The GLC patterns of trimethylsilylated products obtained from (a) the usual calcium hydroxide catalyzed formose reaction starting from [HCHO] = 2.0 M and [Ca(OH)$_2$] = 0.22 M at 60 °C.[10,11] and (b) the selective formose reaction starting from [HCHO] = 1.0 M and [Ca(OH)$_2$] = 0.1 M at 60 °C followed by removing calcium ions by the addition of oxalic acid at the end of the induction period.

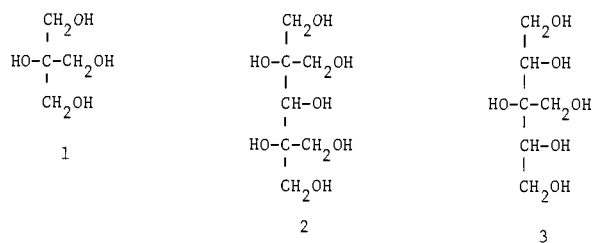rious, although kinetic approaches were recently done by Weiss et al.[6-8]

We have developed a method for analyzing the reaction course by measuring the oxidation–reduction potential (ORP) changes during the reaction, which can clearly discriminate each step by an ORP minimum (T_{min}) and maximum (T_{max}) appearing at the end of the induction period and near the yellowing point, respectively.[9-12] In continuation of our kinetic studies, it was discovered that *a number of sugar alcohols are formed with a high selectivity* when most of the dissolved calcium ions are removed at T_{min}.

In a typical run, the reaction was started with 1.0 M aqueous formaldehyde solution in the presence of calcium hydroxide (0.1 M) at 60 °C. The progress of the reaction was followed by the ORP measurement. At T_{min} (the time that the induction period is terminated) an equivalent amount of oxalic acid (0.1 M) was added to precipitate the dissolved calcium ions as oxalates. After adjusting the pH to 12.0 with an aqueous potassium hydroxide and the temperature to 60 °C, formose formation occurred, though at a slower rate than that under the usual conditions. At T_{max} (the time that the sugar yield becomes maximum), the reaction was stopped by acidifying the mixture, which was then analyzed for total sugar (24%)[13] and product distribution was determined by GLC of trimethylsilylated products. The GLC pattern shown in Figure 1b indicated dramatic selective formation of products corresponding to peaks 2, 19, and 26.[14]

Addition of potassium dihydrogen phosphate or a calcium-chelating agent such as ethylenediaminetetraacetic acid (EDTA) and nitrilotriacetic acid (NTA) at T_{min} was also found to cause the similar selectivity.[15] In these cases, the total GLC peak percent of peaks 2, 19, and 26 amounted to 50-67%. However, addition of sulfuric acid and formic acid in a similar manner resulted in the usual nonselective formose formation. Based on a comparison of solubilities of calcium sulfate (3.4 × 10⁻² mol L⁻¹) and calcium formate (5.2 × 10⁻²) with those of calcium oxalate (5.2 × 10⁻⁴) and potassium calcium phosphate (1.0 × 10⁻⁴) and also with stability constants of calcium–EDTA (1.2 × 10⁻⁶) and –NTA (1.66 × 10⁻⁴) complexes,[16] it is suggested that the effective concentration of the dissolved calcium ions should be lower than 10⁻³ mol L⁻¹ for causing the selective formose reaction.

It was also found that the removal of calcium ions with oxalic acid followed by addition of a certain metal salt such as $Mg(OH)_2$, $Fe(OH)_3$, FeO, and Al_2O_3 (0.1 M) resulted in the similar selective reaction with an increase of the total sugar yield (32-46%) and the total GLC peak percent of peaks 2, 19, and 26 (65-89%),[17] but that addition of barium hydroxide resulted in nonselective formose formation.[18]

Products corresponding to GLC peaks 2, 19, and 26 were

$$
\begin{array}{ccc}
\text{CH}_2\text{OH} & \text{CH}_2\text{OH} & \text{CH}_2\text{OH}\\
| & | & |\\
\text{HO–C–CH}_2\text{OH} & \text{HO–C–CH}_2\text{OH} & \text{CH–OH}\\
| & | & |\\
\text{CH}_2\text{OH} & \text{CH–OH} & \text{HO–C–CH}_2\text{OH}\\
& | & |\\
\mathbf{1} & \text{HO–C–CH}_2\text{OH} & \text{CH–OH}\\
& | & |\\
& \text{CH}_2\text{OH} & \text{CH}_2\text{OH}\\
& \mathbf{2} & \mathbf{3}
\end{array}
$$

isolated by fractionations with ion-exchange chromatography.[19] Peak 2 product was identified as 2-hydroxymethylglycerol (**1**) by a direct comparison with authentic sample.[20] Peak 26 product was obtained in a crystalline form, mp 117.0 °C.[21] Its ^{13}C NMR spectrum[22] showed a pair of two equivalent CH$_2$s, a CH, and two equivalent tertiary carbons. The mass spectrum[23] of its trimethylsilyl derivative showed an intense peak at m/e 307 compared with peaks at m/e 103 and 205 supporting the presence of $-(\text{OH})\text{C}(\text{CH}_2\text{OH})_2$ group(s) in the parent compound.[24] The results led us to assign structure **2** (2,4-bis(hydroxymethyl)-1,2,3,4,5-pentanepentol) for peak 26 product. Peak 19 product appeared to be a mixture of at least three components. Based on the spectral data,[25] we tentatively assigned this to be a mixture of three diastereomers of 3-hydroxymethyl-1,2,3,4,5-pentanepentol (**3**).

The formation of these branched sugar alcohols may be rationalized by a conventional mechanism[2-4] involving cumulative aldol condensations of formaldehyde followed by cross-Cannizzaro reaction of their aldose precursors. The predominant formation of sugar alcohols instead of aldoses is probably due to enhancement of cross-Cannizzaro reaction at higher pH than that in the usual calcium hydroxide catalyzed formose reaction (near pH 11). To our best knowledge, no one has succeeded to obtain selective formation of particular sugars or sugar alcohols in the formose reaction, except our previous report on the selective formation of **1** and pentaerythritol in a photochemical formose reaction.[20] At moment there is no reasonable explanation for the occurrence of the present selective formose formation. We are undertaking studies toward mechanistic elucidation of the selective formose reaction and a search of other types of selectivity.

Acknowledgment. The authors are indebted to Professor K. Shimizu, Medical School, Tottori University, for mass spectral measurements and their assignment.

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(18) In a preliminary experiment to search other types of selective reaction, it was found that addition of Pb$_2$O(OH)$_2$ (lead(II) oxydihydroxide) after the removal of calcium ions at T_{min} resulted in a different selective reaction giving peak 18 product with a GLC PEAK AREA OF 35% and in a total sugar yield of 51%.
(19) The supernatant from the reaction mixture was passed through a IR120(H$^+$) column and the eluate was repeatedly fractionated on a IRA400(OH$^-$) column being eluted successively with water and 0.1, 0.5, and 1.0 N KOH.
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(21) Satisfactory microanalytical data for C$_7$H$_{16}$O$_7$ were obtained for this compound.
(22) ^{13}C NMR (chemical shifts given in parts per million from Me$_4$Si and the multiplicities based on an off-resonance spectrum and number of carbon are given in parenthesis): 63.25 (t, 2), 64.71 (t, 2), 72.85 (d, 1), 77.50 (s, 2).
(23) Mass spectrum of the trimethylsilylate: m/e 307 (rel intensity 69), 217 (100), 205 (17), 103 (59).
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(25) ^{13}C NMR (see note 22): 62.88 (t), 63.31 (t), 63.73 (t), 64.09 (t), 64.29 (t), 64.76 (t, 3), 70.70 (d), 71.36 (d), 74.47 (d, 2), 76.87 (s), 77.06 (s), 77.85 (s, 1). These signals may be analyzed as those of a mixture of three diastereomers, two meso and a *dl*, of **3**. ^{1}H NMR of the acetate: δ 2.0–2.2 (m, 18 H), at least 7 CH$_3$CO peaks), 4.0–4.7 (m, 6 H; CH$_2$OAc), 5.31 (br t, 2 H, $J \approx 3.5$ Hz, –CH(OAc)CH$_2$–). Mass spectrum (rel intensity) of the trimethylsilylate: m/e 307 (34), 217 (78), 205 (57), 103 (100).

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Received April 30, 1977

Correlation of Electronic Spectra of Metalloporphyrins and Metalloproteins

Sir:

The visible and ultraviolet spectra of metalloporphyrins and metalloproteins have been extensively used in structural determinations and to follow conformational and chemical transformations. There have been several studies concerning the effect of axial ligation on the optical transitions.[1-3] Of the three kinds of interactions—metal–porphyrin, metal–ligand, and ligand–porphyrin—the stereoelectronic effect of ligand on the π orbitals of porphyrin is thought to be most important. The result is a red shift of the Soret band while the effect on the α and β bands is either a hyposochromic or bathochromic one. However, these studies are often complicated by not knowing with certainty whether the metalloporphyrin has one or two axial ligands.

Recently, several laboratories have synthesized and characterized metal-substituted hemoglobins.[4-10] The reduced state metal ion is five coordinated with His F8 as the axial ligand; the metal ion is six coordinated in the oxidized state with either H_2O or an anion as the second axial ligand. We have now synthesized many metal-substituted cytochromes *c*. The cobalt,[11,12] copper,[13] nickel,[14] and zinc[15] derivatives are all six coordinated; one of the axial ligand in these compounds is His 18 while the second axial ligand is Met 80.[12,16] The only exception in this series appears to be the manganese cytochrome *c*[17] which is five coordinated. The purpose of this communication is to show definitive correlation of electronic transition energies with axial ligation in metalloporphyrins.