Carbohydrate Research, 190 (1989) 23–28
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

SELECTIVE FORMOSE REACTIONS INITIATED BY γ-IRRADIATION*

SETSUKO IRIE
Osaka Prefectural Radiation Research Institute, Sakai, Osaka, 593 (Japan)

(Received June 30th, 1988; accepted for publication in revised form November 15th, 1988)

ABSTRACT

Formose reactions initiated by γ-irradiation in the presence of inorganic bases selectively produce ethylene glycol and pentaerythritol as major products at room temperature in the presence of calcium hydroxide. The yield ratio of ethylene glycol to pentaerythritol depends on the initial concentration of formaldehyde. At low concentration, the main product is ethylene glycol, whereas pentaerythritol increases at high concentration. The decomposition of formaldehyde is inhibited by ethanol, a hydroxyl-radical scavenger. These results suggest that radical reactions play an important role in radiation-initiated formose synthesis, in contrast to thermal formose reactions.

INTRODUCTION

Since the pioneering work of Butlerow in 1861, formose reactions have received much attention from two points of view. The major interest is to apply the reactions for mass production of edible carbohydrates. Reactions have also been studied as a fundamental process of chemical evolution, the prebiotic synthesis of carbohydrates[2].

Formose reactions catalyzed by metal hydroxides in aqueous solutions generally give complex mixtures containing more than thirty carbohydrate species. Selective formose reactions that yield a specific product in high yield are of high interest. A number of inorganic and organic catalysts have been examined in the search for selective formose reactions. Recently, it has been reported that triose is selectively formed from formaldehyde by using a thiazolium salt as an organic base[3]. Several inorganic bases are also reported to be useful for selective formose synthesis[4–6].

The present study sought to improve the selectivity of the formose synthesis by γ-irradiation in the presence of inorganic bases. γ-Irradiation can initiate reactions at a low temperature. The low temperature is advantageous because it diminishes side reactions.

---

*Formose Reactions. Part 2. For Part 1, see ref. 1.

0008-6215/89/$ 03.50

RESULTS AND DISCUSSION

I. Reactions in the presence of inorganic bases. — Aqueous formaldehyde solutions were irradiated at room temperature with ^{60}Co γ-rays in the absence and presence of inorganic bases. Table I summarizes the decomposition of formaldehyde. The formation of formic acid, one of the major products, is included in Table I. The normal thermal reaction of formaldehyde was not observed without irradiation at this temperature.

Effective formose reactions were observed in the presence of sodium phosphate, potassium hydroxide, and calcium hydroxide. The decomposition rate increased by a factor of ~10 on the addition of 0.3M calcium hydroxide at a formaldehyde concentration of 1.0M, as shown in Fig. 1. When the concentration of formaldehyde was decreased from 1.0 to 0.1M, the decomposition of HCHO reached 100%.

The addition of calcium carbonate and magnesium hydroxide did not accelerate the γ-ray-induced decomposition of formaldehyde; these bases were not effective catalysts for the formose reaction initiated by γ-irradiation.

II. Products of the reactions. — An aqueous solution of formaldehyde was irradiated with a total dose of 5×10^6 rads in the absence of catalyst at 25°. Although the yield was very low, a small amount of formose mixture was obtained. A gas chromatogram of the trimethylsilylated formose mixture gave five peaks, including ethylene glycol and pentaerythritol, with equal intensities. The reaction selectively was poor, but slightly better than the selectivity of the thermal reaction catalyzed by calcium hydroxide[4], in which >30 products were detected by the same analytical procedure.

The radiation-induced decomposition of formaldehyde (Table I) and the yield of the formose mixture was increased remarkably by the addition of potassium

TABLE I

FORMOSE REACTION INITIATED BY γ-IRRADIATION IN THE PRESENCE OF VARIOUS INORGANIC BASES AT 25°

Inorganic base catalyst[a]	*HCHO*[b] *Decomposition (%)*		*HCO_2H Formation (%)*	
	0.4 Mrads	*5 Mrads*	*0.4 Mrads*	*5 Mrads*
None	1	7	0	2
Calcium carbonate	1	8	0	2
Magnesium hydroxide	5	15	1	5
Sodium hydroxide	6	42	2	23
Sodium carbonate	15	34	5	11
Potassium hydroxide	18	46	12	24
Sodium phosphate, tribasic	23	76	11	20
Calcium hydroxide	28	50	10	12

[a][Catalyst] = 0.3M. [b][HCHO] = 1.0M.

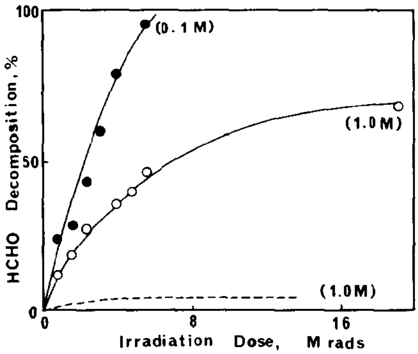


Fig. 1. Formose reaction initiated by γ-irradiation in the absence (— — —) and presence (——) of calcium hydroxide at 25°. Effect of formaldehyde concentration. ● 0.1M, ○ 1.0M. $[Ca(OH)_2] = 0.3M$.

or calcium hydroxides. The formose mixture was trimethylsilylated and analyzed by gas chromatography. Fig. 2 shows the retention times of the products obtained from aqueous solutions containing calcium hydroxide. The major products, 1 and 2, were isolated by liquid chromatography and identified as ethylene glycol and pentaerythritol, respectively, by direct comparison of the ^{1}H-n.m.r., ^{13}C-n.m.r., g.l.c.–m.s. and i.r. spectra with those of authentic compounds[1].

The number of products depended on the initial concentration of formaldehyde. At low concentration, the main product was ethylene glycol, whereas the yield of pentaerythritol increased with concentration of formaldehyde. Table II summarizes the dependence of the ratio of ethylene glycol to pentaerythritol on the initial formaldehyde concentration, and the decomposition of formaldehyde.

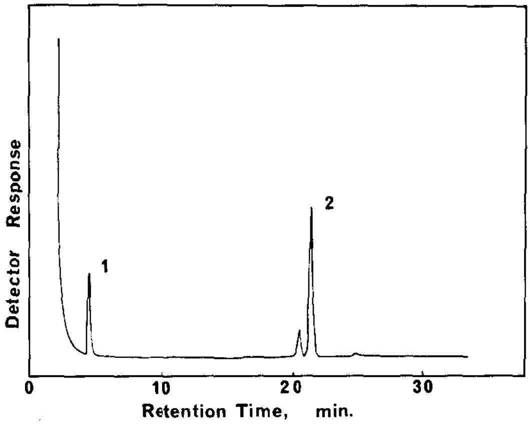
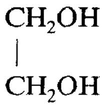
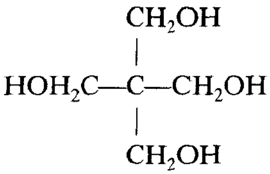


Fig. 2. The gas chromatogram of the Me_3Si derivatives of the products obtained by γ-irradiation in the presence of calcium hydroxide. The initial concentration of formaldehyde was 0.1M. Peak 1 corresponds to ethyene glycol, peak 2, pentaerythritol.



$$CH_2OH-CH_2OH$$

ethylene glycol



$$C(CH_2OH)_4$$

pentaerythritol

The addition of calcium hydroxide increased not only the product yield but also the selectivity of the formose reactions. The selectivity obtained by γ-irradiation in the presence of calcium hydroxide was much better than the thermal formose reaction in the presence of calcium hydroxide. In the thermal reaction, the number of products was not dependent on the initial concentration of formaldehyde, in contrast to the γ-ray-induced reaction. The addition of potassium hydroxide also improved the selectivity of the γ-ray-induced formose reaction, although the selectivity was lower than that in the presence of calcium hydroxide.

III. Reaction mechanism. — The mechanism of the radiation-induced formose reaction is considered to be different from that of the thermal reaction. The characteristics of the reaction are the following:

(*i*) The formose reaction is initiated by the radiolysis products of water; (*ii*) the γ-ray-induced formose reactions take place even at room temperature, at which temperature thermal formose reactions are negligible; (*iii*) the reaction selectivity depends on the initial concentration of formaldehyde.

In order to clarify the initiation mechanism of formose synthesis, the effect of radical and electron scavengers was examined. The addition of ethanol (0.02M), a good hydroxyl-radical scavenger, decreased the decomposition of formaldehyde by as much as 52%, at a formaldehyde concentration of 0.1M, although the addition of N_2O, which is a scavenger for hydrated electrons, increased it. The result clearly indicates that the formose reaction induced by γ-irradiation is initiated by hydroxyl radicals produced by the radiolysis of water.

TABLE II

FORMOSE REACTION INITIATED BY γ-IRRADIATION AT 25° [a]

HCHO concentration (M)	*HCHO decomposition (%)*	*Ethylene glycol/pentaerythritol ratio*
0.01	99	Ethylene glycol only[b]
0.02	95	10
0.05	75	1.2
0.1	68	0.57
0.5	52	0.35
1.0	38	0.1[c]

[a] With 0.3M calcium hydroxide. [b] The amount of ethylene glycol obtained was 13 mg. [c] Ethylene glycol obtained, 45 mg.

The mechanism of the γ-ray-induced formose reaction is considered to be as follows: The initiation process is the reaction of formaldehyde with a hydroxyl radical produced by the radiolysis of water. This process is followed by the conventional thermal processes, such as the acyloin condensation, aldol condensation, and crossed-Cannizzaro reaction. When the concentration of formaldehyde is very low, the aldol condensation cannot follow the initiation process and the main product is ethylene glycol. On the other hand, when the concentration of formaldehyde is high, the second thermal process proceeds to some extent and the main product becomes pentaerythritol. This mechanism explains the concentration dependence of the product selectivity.

EXPERIMENTAL

Preparation of sample solutions. — Aqueous solutions of formaldehyde were prepared by dissolving commercial paraformaldehyde in pure boiling water, and insoluble material was removed by filtration. The inorganic bases used as catalysts were of reagent grade. Helium was passed through the aqueous formaldehyde solutions containing the catalyst (0.3M) for 30 min prior to γ-irradiation in order to exclude air. γ-Irradiation was performed with ^{60}Co γ-rays (10,000 Ci).

Analysis. — The consumption of HCHO was determined by using chromotropic acid and u.v. analysis with a Hitachi 323 spectrophotometer[7]. An aliquot of the mixture was made neutral with HCl and passed successively through columns of Amberlite IR-120B (H^+) and Amberlite IRA-410 (OH^-) resins to remove cations and Cl^-. The eluate was evaporated to dryness *in vacuo* at 35° to remove unreacted HCHO. The resulting syrup was trimethylsilylated conventionally[8] and the products were extracted with $CHCl_3$. The extract was subjected to g.l.c. with a Shimadzu GC-5A chromatograph equipped with a hydrogen flame-ionization detector under the following conditions: coiled glass column of 3 m × 3 mm o.d.; adsorbent, 5% silicone gum SE-30 on 60–80 mesh Chromosorb-W; nitrogen flow-rate, 50 mL/min; temperature, 100–250°, rising at 4°/min; injection port and detector temperature, 280°.

The products were separated by high-performance liquid chromatography (Yanaco L-4000s) using a column of Shodex Ionpak KC-811, with a u.v. monitor and a refractive-index monitor (Shodex RI SE-51), connected in series.

The two main products separated were identified by direct comparison of their ^{1}H-n.m.r., ^{13}C-n.m.r., g.l.c.–m.s. and i.r. spectra with those of the authentic compounds[1]. The ^{1}H- and ^{13}C-n.m.r. and g.l.c.–m.s., and i.r. spectra were recorded on JEOL JNM-MH-100, a JEOL FX-100, LKB-9000, and a JASCO DS-701G, instruments, respectively.

REFERENCES

1 S. Irie, *Chem. Lett.*, (1984) 2153–2156.
2 N. W. Gabel, and C. Ponnanperuma, *Nature (London)*, 216 (1967) 453–455.

3 T. MATSUMOTO, H. YAMAMOTO, AND S. INOUE, *J. Am. Chem. Soc.*, 106 (1984) 4829–4832.
4 Y. SHIGEMASA, O. NAKAE, C. SAKAZAWA, R. NAKASHIMA, AND T. MATSUURA, *J. Am. Chem. Soc.*, 100 (1978) 1309–1310.
5 Y. SHIGEMASA, Y. SASAKI, N. UEDA, AND R. NAKASHIMA, *Bull. Chem. Soc. Jpn.*, 57 (1984) 2761–2767.
6 V. A. LIKHOLOBOV, A. H. WEISS, AND M. M. SAKHAROV, *React. Kinet. Catal. Lett.*, 8 (1978) 155–166.
7 M. LAMBERT, A. C. NEISH, *Can. J. Res.*, 28B (1950) 83–89.
8 C. C. SWEELEY, R. BENTLEY, M. MAKITA, AND W. W. WELLS, *J. Am. Chem. Soc.*, 85 (1963) 2497–2507.