*Carbohydrate Research*, 162 (1987) c1–c3
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

**Preliminary communication**

# The favored formation of DL-*glycero*-tetrulose in the formose reaction*

YOSHIHIRO SHIGEMASA, AKIRA OKANO, HIROYUKI SAIMOTO, AND RUKA NAKASHIMA
*Department of Industrial Chemistry, Faculty of Engineering, Tottori University, Tottori 680 (Japan)*

(Received November 12th, 1986; accepted for publication, January 15th, 1987)

In our recent communication[2] on the formose reaction in *N,N*-dimethylformamide catalyzed by 2-(dimethylamino)ethanol and vitamin $B_1$ hydrochloride, it was reported that, with an increase in the formaldehyde concentration, the yield of GP-$2^{\alpha}$ and GP-10 increased instead of dihydroxyacetone decreasing. Figure 1 shows the selective formation of dihydroxyacetone at 1.1M formaldehyde concentration and the favored formation of GP-$2^{\alpha}$ at 3.0M formaldehyde concentration. We describe herein the first example of the favored formation of DL-*glycero*-tetrulose (GP-$2^{\alpha}$) in the formose reaction, and its isolation and structure elucidation.

In a typical experiment, the reaction was performed in *N,N*-dimethylformamide solution (180 mL) of 3.0M formaldehyde (17.1 g) in the presence of 0.15M 2-(dimethylamino)ethanol and 28mM vitamin $B_1$ hydrochloride at 100° under nitrogen. At various time-intervals, aliquots (5 mL) were transferred into a 10-mL flask and the reaction was quenched immediately by acidification with 9M hydrochloric acid. These aliquots were analyzed for formaldehyde by the method of Bricker and Johnson[3], except that the absorbance was measured at 579 nm. The resulting compounds were analyzed as per(trimethylsilyl)ated derivatives by g.l.c., the pattern of which (Fig. 1b) clearly indicated the favored formation of a product corresponding to peak number $2^{\alpha}$ (GP-$2^{\alpha}$) (20% by g.l.c.).

The reaction mixture was concentrated to ~50 mL under reduced pressure (25–30°, 0.13 kPa). The concentrate was added to water (~50 mL), extracted with diethyl ether, and the water layer passed through a column of active carbon. Concentration of the filtrate gave a pale-yellow syrup (GP-$2^{\alpha}$; 12.1 g, 21.3% by g.l.c.). GP-$2^{\alpha}$ was isolated by repeating the chromatography on cellulose powder with wet butanol as eluent to give GP-$2^{\alpha}$ (1.2 g), colorless syrup (purity >95% by g.l.c.), $[\alpha]_D^{28}$ 0° (*c* 0.65, methanol); $\nu_{max}$ 3300–3400 (O–H) and 1730 $cm^{-1}$ (C=O); $^1$H-n.m.r. ($CD_3OD$; int. standard, $Me_4Si$): $\delta$ 3.75 (d, 2 H, *J* 4 Hz, –HCOH–C$H_2$OH),

---

*Formose reactions. Part 23. For Part 22, see ref. 1.

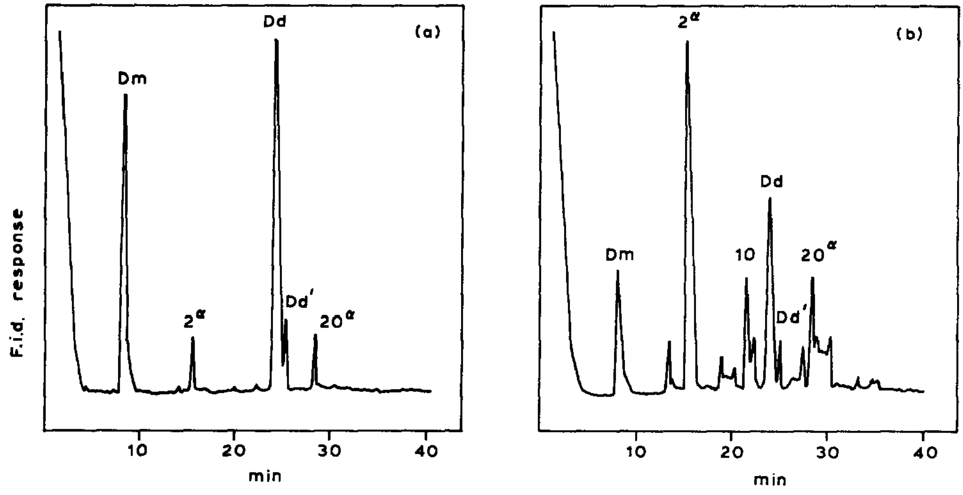

Fig. 1. G.l.c. elution patterns of per(trimethylsilyl)ated compounds obtained from selective formose reactions in *N,N*-dimethylformamide in the presence of 28mM vitamin $B_1$: (a) 1.1M formaldehyde and 0.1M 2-(dimethylamino)ethanol at 60°, (b) 3.0M formaldehyde and 0.15M 2-(dimethylamino)ethanol at 100°. Dm, Dd, and Dd', monomer and diastereomeric dimers of dihydroxyacetone; $20^\alpha$, 2-(1,2-dihydroxyethyl)-5-(2-hydroxyethyl)-4-methylthiazole.

4.23 (t, 1 H, *J* 4 Hz, $\mathrm{O{=}C{-}C}H\mathrm{OH{-}}$), and 4.48 (s, 2 H, $\mathrm{O{=}C{-}C}H_2\mathrm{OH}$); $^{13}$C-n.m.r. ($\mathrm{CD_3OD}$; int. standard, $\mathrm{Me_4Si}$); $\delta$ 64.8(t), 67.6(t), 77.8(d), and 212.8(s), corresponding to 2 $\mathrm{CH_2}$ and 1 CH groups, and a carbonyl C atom; m.s. (acetyl derivative; 70 EV); *m/z* 203 (1, $M^+ - \mathrm{O{=}CCH_3}$), 173(1), 145(6), 131(2), 103(12), 101(13), 86(2), 73(6), and 43(100, $\mathrm{O{=}CCH_3}$); lit.[4] $^1$H-n.m.r. of L-*glycero*-tetrulose ($\mathrm{D_2O}$): $\delta$ 3.85 (d, 2 H, *J* 4 Hz, $\mathrm{-HCOH{-}C}H_2\mathrm{OH}$), 4.42 (t, 1 H, *J* 4 Hz, $\mathrm{O{=}C{-}C}H\mathrm{OH{-}}$), and 4.54 (s, 2 H, $\mathrm{O{=}C{-}C}H_2\mathrm{OH}$). After reduction with sodium borohydride and trimethylsilylation with hexamethyldisilazane and trimethylchlorosilane, the gas chromatogram of the per(trimethylsilyl)ated derivatives showed two peaks, the retention times of which coincided with the peaks of per(trimethylsilyl)ated DL-threitol and *meso*-erythritol, respectively. These results indicate that the compound corresponding to peak number $2^\alpha$ (GP-$2^\alpha$) is DL-*glycero*-tetrulose.

At the present time, we are undertaking the isolation and identification of GP-10. We suppose, however, that DL-*glycero*-tetrulose (GP-$2^\alpha$) and GP-10 are formed from dihydroxyacetone (Dm, Dd, and Dd') in the presence of a sufficient amount of formaldehyde. In spite of the selective formations of dihydroxyacetone, DL-*glycero*-tetrulose, or 2-hydroxymethylglycerol in the formose reaction, it is particularly interesting that glycolaldehyde has not been detected among the formose products even in the initial stages of the reaction[2].

## ACKNOWLEDGMENTS

The authors thank Dr. Seiki Saito, Department of Synthetic Chemistry, School of Engineering, Okayama University, for recording the n.m.r. spectra.

## REFERENCES

1 Y. SHIGEMASA, A. MATSUBA, N. UEDA, R. NAKASHIMA, K. HARADA, N. TAKEDA, M. SUZUKI, AND S. SAITO, *Carbohydr. Res.*, 134 (1984) c4–c6.

2 Y. SHIGEMASA, Y. SASAKI, N. UEDA, AND R. NAKASHIMA, *Bull. Chem. Soc. Jpn.*, 57 (1984) 2761–2767: *J. Carbohydr. Chem.*, 2 (1983) 343–348.

3 C. E. BRICKER AND H. R. JOHNSON, *Ind. Eng. Chem.*, 17 (1945) 400–402; M. LAMBERT AND A. C. NEISH, *Can. J. Res., Sect. B*, 28 (1950) 83–89.

4 K. IMADA, K. INOUE, AND M. SATO, *Carbohydr. Res.*, 34 (1974) c1–c2.