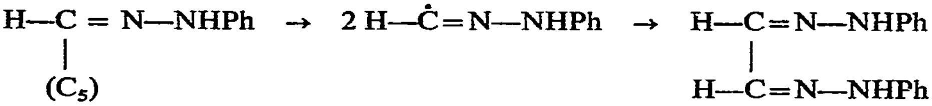
Note

The reaction of D-glucose benzoylhydrazone with base

It was reported by Pinkus[1] that D-glucose reacts with benzoylhydrazine in aqueous alkali to yield glyoxal bis(benzoylhydrazone) (**1**) and pyruvaldehyde bis(benzoylhydrazone). Diels and coworkers[2] obtained glyoxal bis(phenylhydrazone) in high yield when D-*arabino*-hexulose phenylosazone was refluxed in 1% alcoholic potassium hydroxide for 5 h. Simon and Moldenhauer[3] observed that hot 0.1M alcoholic potassium hydroxide converts D-*arabino*-hexulose phenylosazone into glyoxal bis(phenylhydrazone) in 85% yield, and into 2,4-dihydroxybutyric acid in about 45% yield. Wolfrom and coworkers[4] obtained glyoxal bis(phenylhydrazone) when either D-galactose phenylhydrazone or D-arabinose phenylhydrazone was heated with methanolic or ethanolic pyridine at 120–130°. These investigators suggested that homolytic fission occurs, followed by the union of two C_1 fragments to yield the osazone.



$$\begin{array}{l} \mathrm{H{-}C=N{-}NHPh} \\ \quad | \\ \quad (\mathrm{C_5}) \end{array} \rightarrow 2\,\mathrm{H{-}\dot{C}=N{-}NHPh} \rightarrow \begin{array}{l} \mathrm{H{-}C=N{-}NHPh} \\ \quad | \\ \mathrm{H{-}C=N{-}NHPh} \end{array}$$

We have observed that, when D-*arabino*-hexulose benzoylhydrazone (**2**) is refluxed in 1% potassium hydroxide in ethanol for 1 h, the solution is acidified with acetic acid, and sufficient water is added to dissolve the brown residue, glyoxal bis(benzoylhydrazone) (**1**) separates in low yield. In order to determine the source of the glyoxal carbon atoms, D-glucose-*1*-^{14}C benzoylhydrazone (**2a**) and D-glucose-*2*-^{14}C benzoylhydrazone (**2b**) were prepared, and subjected to the same alkaline decomposition. The results are described in Table I.

The results indicate that, in forming osazone **1**, a labeled entity derived from C-1 and C-2 of **2** competes with glycolaldehyde fragments derived from the nonlabeled atoms C-3 to C-6 of **2** for reaction with the benzoylhydrazone groups. Dilution of the product from the labeled fragment with that from the nonlabeled fragments accounts for the specific activity observed. The fragmentation could result from a reversed-aldol mechanism[5].

Supporting this approach is our observation that the reaction of **2** with glyoxal in the presence of acetic acid produces **1** in good yield. Simon and coworkers[6] reported the conversion of 2-(phenylhydrazino)acetaldehyde phenylhydrazone ($PhNHNHCH_2{-}CH{=}N{-}NHPh$) into the osazone in high yield in nonaqueous medium in the presence of acetic acid and the absence of phenylhydrazine. They also reported the ready conversion of glycolaldehyde into glyoxal bis(phenylhydrazone) in the presence of phenylhydrazine in methanolic acetic acid.

TABLE I

RADIOACTIVITY DATA

Ratio of activity of glyoxal bis(benzoylhydrazone) to that of D-*glucose benzoylhydrazone*	*Activity, dpm/mg*	
	Reactant	*Product* *Glyoxal bis(benzoylhydrazone)* *(Mol. wt.* 294)
	D-*glucose*-1-^{14}C *benzoylhydrazone (Mol. wt.* 298)	
0.333	61,8000	20,500
0.284	78,000	22,000
0.288	111,500	32,000
	D-*glucose*-2-^{14}C *benzoylhydrazone*	
0.319	64,000	20,400
0.308	62,400	19,200
0.269	101,500	27,300

EXPERIMENTAL

Materials and methods. — D-Glucose-*1*-^{14}*C* and -*2*-^{14}*C* were purchased from Nuclear Chicago. Radioactivity was measured with a Nuclear Chicago Liquid Scintillation Counter.

D-*Glucose benzoylhydrazone* (**2**, **2a**, *and* **2b**). — A solution of D-glucose (1.00 g) and benzoylhydrazine (1.00 g) in 95% ethanol (10 ml) was refluxed for 8 h, and then cooled to give **2**, as colorless crystals; yield 1.19 g (71%), m.p.[7] 185–187° (dec.), that could be recrystallized from 95% ethanol.

Reaction of **2**, **2a**, *and* **2b** *with base.* — A solution of D-glucose benzoylhydrazone (100 mg) in 1% ethanolic potassium hydroxide was refluxed. The mixture turned dark brown almost immediately. After 1 h, the solution was acidified with glacial acetic acid, and water was added to dissolve the brown residue. Yields of 1–4 mg of **1** were obtained in different experiments. Compound **1** was identified by its i.r. spectrum, m.p. and mixed m.p.

Samples (1–2 mg) for counting were solubilized with Nuclear Chicago NBS (10 drops), scintillation solution (5 ml)* (Nuclear Chicago Liquafluor diluted 25:1 with toluene) was added, and then acetic acid was added until the yellow color had been discharged or until the solution was acidic, and the milky sample was immediately counted. Compounds **1** and **2** were counted at the same time in the same way.

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*Samples were counted with 5 ml and 10 ml of scintillation solution to maximize the counts.

REFERENCES

1 G. Pinkus, *Chem. Ber.*, 31 (1898) 31.
2 O. Diels, R. Meyer, and O. Onnen, *Ann.*, 525 (1936) 94.
3 H. Simon and W. Moldenhauer, *Chem. Ber.*, 100 (1967) 3121.
4 H. El Khadem, M. L. Wolfrom, Z. M. El Shafei, and S. H. El Ashry, *Carbohyd. Res.*, 4 (1967) 225.
5 W. L. Evans, *Chem. Rev.*, 31 (1942) 537.
6 H. Simon, G. Heubach, and H. Wacker, *Chem. Ber.*, 100 (1967) 3106.
7 B. Holmberg, *Arkiv Kemi*, 7 (1954) 50.

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