Carbohydrate pyrolysis mechanisms from isotopic labeling
Part 4. The pyrolysis of D-glucose: The formation of furans

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The use of ^{13}C isotopically labeled D-glucose has led to an improved understanding of the mechanisms of pyrolytic formation of furan and 15 of its derivatives. The cyclic Grob fragmentation of 1,3-diols as applied to D-glucose leads to rationalizations of important observed labeling patterns among the 11 furans that resulted from carbon-loss during the pyrolytic sequence. A copyrolysis of [13]carbo-ubiquilog and naturalomer D-glucose established that the preponderance of each of the furans arose in unimolecular fashion. Copyrolysis of [13]carbo-ubiquilog D-glucose and naturalomer D-fructose provided relative product formation ratios consistent with the involvement of fructose in some of the mechanistic pathways. Formation of nine of the furans from D-glucose (furfural, 5-hydroxymethylfurfural, furan, 3-[2H]-furanone, hydroxymethyl furyl ketone, furfuryl alcohol, alpha-angelica lactone, "Miyazaki's substance", and furan-3-carboxaldehyde) can be rationalized without need to invoke oxidation–reduction steps. Prospective mechanistic schemes are presented for most of these. Six of the furans (5-methylfurfural, 2-methylfuran, 3-methylfuran, 2,5-dimethylfuran, 2-(1,2-dihydroxyethyl)furan, and butyrolactone) need the intervention of redox chemistry to account for their formation, and their relation to similar products that can form without need for redox chemistry is discussed.

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1. Introduction

The pyrolysis of carbohydrates dates back into geological prehistory [1]. It occurs in the course of the pyrolysis or combustion of biomass [2–4], during the cooking of foods [5], and during the smoking of tobacco [6,7]. Despite this long history, much remains to be learned about the mechanistic details of the process. Thus, in an effort to better understand the chemistry of carbohydrate pyrolysis, particularly as it may occur under smoking conditions, we have been examining the flash pyrolysis of D-glucose (**1**), isotopically labeled with [13]C [8–10].

In the first paper in this series [8], we found by the use of isotopic labeling that glycerin afforded acetaldehyde as a pyrolysis product by two different mechanisms. To explain one of the labeling patterns, which arises in unimolecular fashion, we hypothesized a cyclic version of the Grob fragmentation [11,12]. This mechanism involved a hydrogen-bonding interaction between the terminal hydroxyl groups (1 and 3) of glycerin. By concerted electron migration, this arrangement fragments into water, formaldehyde and enol-acetaldehyde (ethenol). Similar 1,3-diol interactions are ubiquitous among carbohydrates. The

participation of such interactions in the homologous mechanism could therefore be expected to rationalize important aspects of carbohydrate pyrolysis. In particular, the mechanism provides a low-energy means of effecting initial carbon–carbon bond breakage at varying positions along the carbon chain, each distinct mode leading to a different family of products. The preceding two papers [9,10] extended the cyclic Grob fragmentation to an explanation of important labeling patterns found among many of the carbonyl-compounds that result from the pyrolysis of the prototypical monosaccharide, D-glucose. The involvement of fructose (**2**) was frequently invoked in the explanation of mechanistic pathways, and this involvement could be probed by isotopically labeled pyrolysis of glucose–fructose mixtures. The following paper [13] will cover the formation of the light gases. Part 1 [8] also presents the nomenclature that we have introduced to further distinguish types of isotopic labeling and which will be used in this series of papers.

This paper extends the cyclic Grob fragmentation further, to explain the formation of several of the C_4 or C_5 furans observed from the pyrolysis of D-glucose. Information as to the C_6 furans, the major proportions of which arose directly without need to invoke carbon–carbon bond-breaking fragmentation reactions, will also be presented.

The earliest application of isotopic labeling to the pyrolysis of D-glucose addressed the formation of furfural (**3**) [14,15] and 5-

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hydroxymethylfurfural (**4**) [14]. This work will be discussed in more detail below with the discussion of the formation of the individual furanic products.

2. Experimental

Isotopically labeled D-glucose was obtained from Cambridge Isotope Laboratories, Inc., and used as received. Microgram (80–100) sample quantities of α-D-glucose (naturalomer [8]) or its six $^{13}C_1$-isotopologs, or of an approximately-equimolar homogeneous blend of naturalomer ($^{98.9\%}$ $^{12}C_6$-) and ^{13}carbo-ubiquilog ($^{\sim 100\%}$ $^{13}C_6$-) D-glucose (to probe reaction unimolecularity) were loaded into a capillary tube and pyrolyzed in air, using a CDS Analytical, Inc. Pyroprobe 2000 pyrolysis unit. Temperatures were ramped up at the maximum rate, going from ambient to about 1000 °C in about 2 s. The data were extracted from the same GC/MS runs as provided the data for parts 2 and 3 [9,10]. To evaluate the relative importance of fructose in glucose pyrolysis mechanisms, an equimolar blend of ^{13}carbo-ubiquilog ($^{\sim 100\%}$ $^{13}C_6$-) D-glucose and naturalomer ($^{98.9\%}$ $^{12}C_6$-) D-fructose was pyrolyzed, and the ratio determined as to relative product yield from each. In some cases, interferences from impurities, or other vagaries of GC/MS precluded the determination of unimolecularity or glucose–fructose product formation ratios for certain products, from the experiments as run. The further experimental details are provided in the first paper in this series [8].

3. Results and discussion

Fig. 1 depicts the furans to be discussed: none are novel to carbohydrate pyrolysis. For example, of these products, Van der Kaaden et al. [16] reported the formation from amylose (starch) pyrolysis (in order of increased GC retention time): furan (**5**), 2-methylfuran (**7**), 2,5-dimethylfuran (**8**), furfural (**3**), furfuryl alcohol (**14**), alpha-angelica lactone (**15**), 2-acetylfuran, 5-methyl-furfural (**6**), 2-furyl hydroxymethyl ketone (**10**), and 5-hydroxymethylfurfural (**4**). Although we also observed 2-acetylfuran among the products, the material was not chromatographically pure enough to allow reliable or self-consistent calculations of isotopic content, particularly among its mass-spectral fragments, so it will not be discussed further in detail.

Isotopic distribution in the molecular ions was determined by use of the "pattern algorithm" [8] at M + 1, summarized overall in Table 1, and reported as percentages. As is usual in this series of papers, the reported numbers reflect the proportion of the product formed that bears (a single) label from the glucose isotopolog in question – and are not product yields. Tables 2–6 and 8–18 present the isotopic incorporation from the $^{13}C_1$ isotopologs of D-glucose into the various mass-spectral fragment ions of **3–10** and **13–20**, as estimated by the pattern algorithm [8] (which calculates mole-fractions, that we report as percentages). *Numbers outside the range of 0–1 mol fraction represent breakdowns in the assumptions underlying the algorithm, most typically interference from alternative fragmentation modes that by mass occur adjacently to, or super-imposed on, the fragments resulting from the process under scrutiny.* Also contributing would be changes in fragmentation probabilities brought on by the magnetic isotope effect [17]. Whenever the spectra were excessively congested due to interference, the normalized spectra were consulted to provide guidance as to the reliability of the algorithmic calculations.

Also reported in the tables are the proportions of unlabeled, singly-labeled and doubly-labeled product as determined by direct deconvolution (D.D.) [9], whenever that method succeeded in yielding meaningful, self-consistent results. However, direct deconvolution tends to fail, in part due to intervention by the

magnetic isotope effect [17], whenever strong M–H fragmentation is observed. The magnetic isotope effect usually enhances M–H fragmentation whenever the carbon losing the proton is ^{13}C instead of a non-magnetic isotope such as ^{12}C or ^{14}C. This has the effect of causing under-estimation of single-label content in the product, by a magnitude (on the order of 5%) comparable to the quantities of multiply-labeled products being sought.

In the cases where deconvolution succeeded in producing self-consistent results, calculated double-labeling of products tended to be maximal for C-1, C-2 and sometimes C-3. This is consistent with the existence of an important class of intermolecular product formation (pyrosynthesis) mechanisms involving aldol-condensation of two open-chain glucose and/or fructose moieties. The products of such condensations will be variously joined at C-1, C-2 or C-3 for the most part, with respect to each of the reacting partners. If the resulting species succumb to the usual fragmentation reactions, products may arise that *simultaneously* contain pairs of carbons originating from C-1 and C-2 (and occasionally C-3).

As usual, the extent of unimolecularity for product formation was determined by the copyrolysis of the homogeneous approximately equimolar blend of $^{12}C_6$- and $^{13}C_6$-D-glucose, and the ostensible percentages of multimolecularity are included in Table 1 (as "percent scrambled"). The scrambling experiments did not reveal significant preferences for any particular ratio of the two isotopes within the isotopic cross-products. The reported numbers were not adjusted to reflect fortuitous recombination of fragments of like isotopic content.

To assess the possible involvement of D-fructose in D-glucose pyrolysis mechanisms, a copyrolysis of $^{13}C_6$-D-glucose and $^{12}C_6$-D-fructose was also performed. For those products whose formation from glucose *required* transformation to fructose as an intermediate, it would be expected that the relative yield of product would be higher from fructose than from glucose. This is a consequence of fewer steps being needed to form the product, glucose having further alternatives available to it than merely forming fructose. An important corollary is that if fructose can be reasonably established as an intermediate for the formation of any one product (or else detected as such as a glucose pyrolysis product), then all possible products of fructose pyrolysis must also be available to be formed from glucose. For all such products, the formation from glucose would be at attenuated levels relative to fructose, if better routes were not directly available from glucose. Indeed, since fructose has been reported as a pyrolysis product of glucose [18] it is reasonable to routinely invoke its participation in the pyrolysis process, whenever an especially convenient pathway is revealed. For a wide range of products, furans or otherwise, the observed glucose–fructose product formation ratio or its inverse, whichever was greater than unity, rarely exceeded a factor of four, under our pyrolysis conditions.

3.1. Furans in general

Furans formed by the pyrolysis of D-glucose consist of C_4, C_5, and C_6 species; higher carbon-counts require intermolecular pyrosynthesis. Under conditions of locally maintained carbon–carbon bond connectivity, unsymmetrical C_4 species can be formed by six mechanistic classes, involving the first four, the last four, or the middle four carbons of D-glucose, each with two possible orientations. Given that the first four carbons or the last four carbons can be split off from D-glucose by a single carbon–carbon bond-breakage, these are the two most important fragmentation modes. The middle four carbons only arise as a result of two such carbon–carbon bond breakage steps (two high energy barrier reactions instead of one), thereby greatly reducing the importance of this fragmentation mode.