CARBOHYDRATES AS RENEWABLE RAW MATERIALS: A MAJOR CHALLENGE OF GREEN CHEMISTRY

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A raw material as feedstock should be renewable rather than depleting wherever technically and economically practicable.

INTRODUCTION

Coal, oil, and natural gas, the fossil resources built up over eons, are not only our main energy suppliers but they are also raw materials for a large variety of man-made products ranging from gasoline and diesel oil to bulk, intermediate, and fine chemicals. However, as our fossil raw materials are irrevocably decreasing and as the pressure on our environment is building up, the progressive changeover of chemical industry to renewable feedstocks for their raw materials emerges as an inevitable necessity, that is, it will have to increasingly proceed to the raw materials basis that prevailed before natural gas and oil outpaced all other sources.

The present overreliance of the chemical industry on fossil raw materials has its foreseeable limits, as these materials are depleting and irreplaceable. The basic question today is not “When will affordable fossil fuels be exhausted?”—fossil

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oil will be around for a long time, even if it has to be isolated eventually from oliferous rocks or shale—but “When will the end of cheap oil be?” or, stated more appropriately, “When will fossil raw materials have become so expensive that biofeedstocks are an economically competitive alternative?” Experts realistically prognosticate this for 2040 at the latest.5

The transition to a more biobased production system is hampered by a variety of obstacles: Fossil raw materials are not only more economic at present, but the process technology for their conversion into organic chemicals is exceedingly well developed and basically different from that required for transforming bio-based raw materials into products with industrial application profiles. This situation originates from the inherently different chemical structures of the two types of raw materials. Compared to coal, oil, and natural gas, terrestrial biomass is considerably more complex, constituting a multifaceted array of low and high-molecular-weight products: sugars, hydroxy and amino acids, lipids, and biopolymers such as cellulose, hemicelluloses, chitin, starch, lignin, and proteins. By far the most important class of organic compounds in terms of volume produced are carbohydrates, as they represent roughly 75% of the annually renewable biomass of about 200 billion tons (Figure 2.1). Of these, only a minor fraction (ca. 4%) is used by man, the rest decays and recycles along natural pathways.

Thus, carbohydrates, a single class of natural products—aside from their traditional uses for food, lumber, paper, and heat—are the major biofeedstocks from which to develop the industrially and economically viable organic chemicals that are to replace those derived from petrochemical sources.

The bulk of the annually renewable carbohydrate biomass is polysaccharides, yet their nonfood utilization is confined to the textile, paper, and coating industries, either as such or in the form of simple esters and ethers. Organic commodity chemicals, however, are usually of low molecular weight, so they are more expediently obtained from low-molecular-weight carbohydrates than from polysaccharides. Accordingly, the constituent repeating units of these polysaccharides—glucose (cellulose, starch), fructose (inulin), xylose (hemicelluloses), or disaccharide versions thereof, most notably sucrose—are the actual carbohydrate raw materials for organic chemicals with tailor-made industrial applications: they are inexpensive, ton-scale accessible, and provide a resulting chemistry that is better worked out and more variable than that of their polymers.

![Figure 2.1 Renewable biomass (200 billion tons/year).](Q2)
2.1 AVAILABILITY OF MONO- AND DISACCHARIDES

Table 2.1 lists the availability and bulk-quantity prices of the eight least expensive sugars—all well below about $8/kg—as compared to some sugar-derived, naturally occurring compounds and basic chemicals from petrochemical sources. The result is stunning, since the five cheapest sugars, some sugar alcohols, and

<table>
<thead>
<tr>
<th></th>
<th>World Production(^a) (metric t/year)</th>
<th>Price(^b) (€ / kg)</th>
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</thead>
<tbody>
<tr>
<td><strong>Sugars</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucrose</td>
<td>140,000,000</td>
<td>0.20</td>
</tr>
<tr>
<td>D-Glucose</td>
<td>30,000,000</td>
<td>0.30</td>
</tr>
<tr>
<td>Lactose</td>
<td>295,000</td>
<td>0.60</td>
</tr>
<tr>
<td>D-Fructose</td>
<td>60,000</td>
<td>1.00</td>
</tr>
<tr>
<td>Isomaltulose</td>
<td>70,000</td>
<td>2.00</td>
</tr>
<tr>
<td>Maltose</td>
<td>3,000</td>
<td>3.00</td>
</tr>
<tr>
<td>D-Xylose</td>
<td>10,000</td>
<td>4.50</td>
</tr>
<tr>
<td>L-Sorbose</td>
<td>60,000</td>
<td>7.50</td>
</tr>
<tr>
<td><strong>Sugar Alcohols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-Sorbitol</td>
<td>650,000</td>
<td>1.80</td>
</tr>
<tr>
<td>Erythritol</td>
<td>30,000</td>
<td>2.25</td>
</tr>
<tr>
<td>D-Xyitol</td>
<td>30,000</td>
<td>5.00</td>
</tr>
<tr>
<td>D-Mannitol</td>
<td>30,000</td>
<td>8.00</td>
</tr>
<tr>
<td><strong>Sugar-Derived Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citric acid</td>
<td>1,500,000</td>
<td>1.00</td>
</tr>
<tr>
<td>D-Gluconic acid</td>
<td>100,000</td>
<td>1.40</td>
</tr>
<tr>
<td>L-Lactic acid</td>
<td>150,000</td>
<td>1.75</td>
</tr>
<tr>
<td>L-Tartaric acid</td>
<td>35,000</td>
<td>6.00</td>
</tr>
<tr>
<td>L-Ascorbic acid</td>
<td>80,000</td>
<td>8.00</td>
</tr>
<tr>
<td><strong>Amino Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-Glutamic acid</td>
<td>1,500,000</td>
<td>1.20</td>
</tr>
<tr>
<td>L-Lysine</td>
<td>740,000</td>
<td>2.00</td>
</tr>
<tr>
<td><strong>Petrochemicals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethylene</td>
<td>90,000,000</td>
<td>0.40</td>
</tr>
<tr>
<td>Propylene</td>
<td>45,000,000</td>
<td>0.35</td>
</tr>
<tr>
<td>Benzene</td>
<td>23,000,000</td>
<td>0.40</td>
</tr>
<tr>
<td>Terephthalic acid</td>
<td>12,000,000</td>
<td>0.70</td>
</tr>
</tbody>
</table>

(Continued)
TABLE 2.1 Continued

<table>
<thead>
<tr>
<th></th>
<th>World Production(^a) (metric t/year)</th>
<th>Price(^b) (€ / kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aniline</td>
<td>1,300,000</td>
<td>0.95</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>900,000</td>
<td>1.10</td>
</tr>
<tr>
<td>Adipic acid</td>
<td>1,500,000</td>
<td>1.70</td>
</tr>
</tbody>
</table>

**Solvents**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>25,000,000</td>
<td>0.15</td>
</tr>
<tr>
<td>Toluene</td>
<td>6,500,000</td>
<td>0.25</td>
</tr>
<tr>
<td>Acetone</td>
<td>3,200,000</td>
<td>0.55</td>
</tr>
</tbody>
</table>

\(^a\)Reliable data are only available for the world production of sucrose, the figure given referring to the crop cycle 2004/2005. \(^b\)All other data are average values based on estimates from producers and/or suppliers, as the production volume of many products is not publicly available.

Prices given are those attainable in early 2005 for bulk delivery of crystalline material (where applicable) based on pricing information from the sugar industry (sucrose) and the Chemical Market Reporter (2005) (acids, basic chemicals, and solvents). The listings are intended as a benchmark rather than as a basis for negotiations between producers and customers. Quotations for less pure products are, in part, sizably lower, for example, the commercial sweetener “high fructose syrup,” which contains up to 95% fructose, may readily be used for large-scale preparative purposes.

Sugar-derived acids are not only cheaper than any other natural product, but they compare favorably with basic organic bulk chemicals such as acetaldehyde or aniline. Actually, the first three of these sugars—sucrose, glucose, and lactose—are in the price range of some of the standard organic solvents.

Despite their large-scale accessibility, the chemical industry, at present, utilizes these mono- and disaccharides as feedstock for organic chemicals only to a minor extent, which is amply documented by the fact that of the 100 major organic

![Fossil Resources vs. Renewable Resources](image)

**Figure 2.2** Hydrocarbons vs. carbohydrates: more than a play on words, as their names, taken literally, reveal the basic differences in their utilization as organic raw materials.
chemicals manufactured in the United States in 1995, seven were derived from biofeedstocks, and of these only five—ethanol, sorbitol, citric acid, lysine, and glutamic acid—used sugars as the raw-materials source. The reasons, already alluded to, lie in the inherently different structure of carbohydrates and fossil raw materials, of which the essence is manifested in their structure-based names (Figure 2.2): Our fossil resources are hydrocarbons, distinctly hydrophobic, oxygen-free, and lacking functional groups; annual renewables are carbohydrates, overfunctionalized with hydroxyl groups and pronouncedly hydrophilic. Needless to say, that methods required for converting carbohydrates into viable industrial chemicals—reduction of oxygen content with introduction of C=O and C==O unsaturation—are diametrically opposed to those prevalent in the petrochemical industry.

Intense efforts within the last decade to boost the acquisition of organic chemicals from the sugars listed in Table 2.1 have, so far, failed to bridge the conceptional, technological, and economic gap between hydrocarbons and carbohydrates as organic raw materials.

2.2 CURRENT NONFOOD INDUSTRIAL USES OF SUGARS

The current utilization of carbohydrates as a feedstock for the chemical industry—be it for bulk, commodity, intermediate, fine, or high-value-added specialty chemicals—is modest when considering their ready availability at low cost and the huge as yet unexploited potential. The examples currently realized on an industrial scale are outlined briefly.

2.2.1 Ethanol

With production of about 24 million tons (300 million hectoliters (hL)), fermentation ethanol ("bioethanol") is the largest volume biobased chemical today. The principal organism for fermentation is Saccharomyces cerevisiae, an ascomycetous yeast that can grow on a wide variety carbohydrate feedstocks: sugar crops, and sugar-containing by-products, such as sugar cane, sugar beet, sorghum, molasses, and—after hydrolysis to glucose—starchy crops, such as corn, potatoes and grains, or cellulosic materials, for example, wood pulping sludges from pulp and paper mills.

The manufacturing costs are said to be roughly the same as those for its production from ethylene at a comparable plant size. The large growth in production of industrial-grade fermentation ethanol within recent years is less due to its use as a solvent and starting material for follow-up chemicals such as acetaldehyde, ethyl esters (e.g., EtOAc), and ethers (Et2O)—these mostly result from ethylene-based processing lines—but from its high potential as a fuel additive. It is either directly admixed to standard gasoline to the extent of 5%, or indirectly in the form of ETBE (ethyl t-butyl ether) in proportions of up to 15%; however, a hefty government subsidy is required (repeal of the gasoline tax) to remain competitive. The growth opportunities for fuel-grade bioethanol are enormous and are predicted to increase substantially within the next five years.
2.2.2 Furfural

With an annual production of about 250 000 tons, furfural (2-furfuraldehyde) appears to be the only unsaturated large-volume organic chemical prepared from carbohydrate sources. The technical process involves exposure of agricultural or forestry wastes, that is, the hemicelluloses contained therein consisting up to 25% of D-xylose polysaccharides (xylosans), to aqueous acid and fairly high temperatures, the xylosans first being hydrolyzed, then undergoing acid-induced cyclodehydration.\textsuperscript{14}

The chemistry of furfural is well developed, providing a host of versatile industrial chemicals by simple straightforward operations (Scheme 2.1): furfuryl alcohol (2) and its tetrahydro derivative 1 (hydrogenation), furylamine 3 (reductive amination), furoic acid 4 (oxidation), and furanacrylic acid 5 (Perkin reaction), or furylidene ketones 6 (aldol condensations). Furfural is also the key chemical for the commercial production of furan (through catalytic decarbonylation) and tetrahydrofuran 8 (hydrogenation), thereby providing a biomass-based alternative to its petrochemical production via dehydration of 1,4-butanediol.\textsuperscript{14} Additional importance of these furanic chemicals stems from their ring-cleavage chemistry,\textsuperscript{15} which has led to a variety of other established chemicals such as fumaric, maleic, and levulinic acid, the latter being a by-product of its production.\textsuperscript{16}

\begin{center}
\textbf{Scheme 2.1} Furanic commodity chemicals derived from pentosans in agricultural wastes (corn cobs, oat hulls, bagasse, wood chips).
\end{center}
2.2 CURRENT NONFOOD INDUSTRIAL USES OF SUGARS

Currently, the bulk of the furfural produced is used as a selective solvent in the refining of lubricating oil, and, together with furfurylalcohol in condensations with formaldehyde, phenol, acetone or urea to yield resins of complex, ill-defined structures, yet excellent thermostetting properties, most notably high corrosion resistance, low fire hazard, and extreme physical strength;\textsuperscript{14} they are extensively used in the foundry industry as cores for high-quality castings.

### 2.2.3 D-Sorbitol (=D-Glucitol)

Readily produced by hydrogenation of D-glucose,\textsuperscript{17} the main consumer of the sizable annual production of D-sorbitol (Table 2.1) is the food industry, primarily as a noncaloric sweetening agent; as a key intermediary for the production of ascorbic acid (vitamin C),\textsuperscript{18} it has important nonfood applications due to its moisture conditioning, softening, and plastifying properties. These entail its use in adhesives, paper, printing, textiles, cellulose-based foils, and pharmaceutical formulations.

Other nonfood applications of D-sorbitol result from etherification and polycondensation reactions providing biodegradable polyetherpolys used for soft polyurethane foams and melamine/formaldehyde or phenol resins. Sizable amounts of D-sorbitol also enter into the production of the sorbitan ester surfactants (cf. later in this chapter).

### 2.2.4 Lactic Acid → Polylactic Acid (PLA)

Large amounts of D-glucose—in crude form as obtainable from corn, potatoes, or molasses by acid hydrolysis—enter industrial fermentation processes in the

\begin{center}
\begin{tikzcd}
\text{Glucose-based feedstock} \quad (\text{cornstarch, sucrose, molasses}) & \\
\rightarrow & \\
\text{Fermentation} \quad \text{with bacteria or fungi} & \\
\rightarrow & \\
\text{EtOH} & \text{Polycondensation} \\
\rightarrow & \\
\text{Ethyl lactate} & \text{Polylactic acid (PLA)}
\end{tikzcd}
\end{center}

\textbf{Scheme 2.2} Production of lactic acid and its uses.
production of lactic acid (cf. Scheme 2.2), citric acid, and various amino acids, such as L-lysine or L-glutamic acid. While the major use of these products is in food and related industries, recent nonfood uses of lactic acid have made it a large-scale, organic commodity chemical. Most of it is subsequently polymerized via its cyclic dimer (lactide) to polylactic acid,\textsuperscript{18} a high molecular weight polyester.

Due to its high strength, polylactic acid (PLA) can be fabricated into fibers, films, and rods that are fully biodegradable (→ lactic acid, CO\textsubscript{2}) and compostable, since the degrade within 45–60 days. Accordingly, PLA and copolymers of lactic and glycolic acid are of particular significance for food packaging and in agricultural or gardening applications; they are also highly suitable materials for surgical implants and sutures, as they are bioresorbable.

Since 1989, Cargill, has invested some $750 million to develop and commercialize polylactic acid (tradename: NatureWorks). Its Nebraska plant, with an annual capacity of 140,000 metric tons, opened in 2002.\textsuperscript{19–21} Thus, polylactides, combining favorable economics with green sustainability, are poised to compete in large-volume markets that are now the domain of thermoplastic polymers derived from petrochemical sources.

Another green development based on lactic acid is its ethyl ester (Vertec\textsuperscript{TM}) that has been marketed for applications in specialty coatings, inks, and straight-use cleaning because of their high performance and versatility.\textsuperscript{22} As a very benign solvent—green, readily biodegradable, and an excellent toxicology record it has the potential to displace various petrochemically based solvents such as acetone, dimethyl formamide (DMF), toluene, or N-methylpyrrolidone in industrial processes.

\begin{center}
\begin{align*}
\text{Glucose (Starch)} & \xrightarrow{n\text{-BuOH}} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \\
& + \text{C}_8\text{-C}_{14}\text{OH} \\
& \xrightarrow{\text{H}^+} \\
& \text{APGs (x = 0.3–0.7; n = 2–5)}
\end{align*}
\end{center}

\textbf{Scheme 2.3} Synthesis of alkyl polyglucosides (APGs).
2.2.5 Sugar-Based Surfactants

The use of cheap, bulk-scale accessible sugars as the hydrophilic component, and fatty acids or fatty alcohol as the lipophilic part, yields nonionic surfactants, which are nontoxic, non-irritating, and fully biodegradable. The industrially relevant surfactants of this type are fatty acid esters of sorbitol (sorbitan esters\textsuperscript{17}) and of sucrose, fatty acid amides of 1-methylamino-1-deoxy-d-glucitol (NMGAs), and, most apparent in terms of volume produced, fatty alcohol glucosides, the so-called alkyl polyglycosides (APGs).\textsuperscript{25} The latter are produced

![Chemical structures](image)

**Figure 2.3** Sugar-derived high-value-added products: antibiotics, vitamins, and pharmaceuticals.
by several companies—most notably by Cognis, with a capacity in the 50,000-t/a range—and are by far the most important nonionic surfactants. They represent fatty alcohol glucosides with an alcohol chain length normally between C₈ and C₁₄. Their industrial synthesis either comprises a direct acid-catalyzed Fischer glycosidation of glucose (in the form of a syrupy starch hydrolysate) or starch itself. The alternate process consists of two stages, the first being Fischer glycosidation with n-butanol to butyl glycosides, which are subsequently subjected to acid-promoted transacetalization.²⁵

The resulting product mixtures contain mostly α-D-glucosides, as designated in the formula (Scheme 2.3) and are marketed as such. APGs are not skin-irritating, have good foaming properties, and are completely biodegradable; hence, they are widely used in hand dishwashing detergents and in formulations of shampoos, hair conditioners, and other personal-care products.²⁴²⁵

2.2.6 Pharmaceuticals and Vitamins

Aside from the enormous amount of sugars, mostly glucose and sucrose, that flows into the fermentative production of amino and hydroxy acids (cf. Table 2.1)—a substantial part of which is for food use—a significant volume of these sugars enters into the fermentation processes of high-value-added products: antibiotics and vitamins, much too complex in their structures to be generated by chemical synthesis. Figure 2.3 lists a number of representative examples: penicillins and cephalosporins, with an estimated world production in the 75,000-t/a range, the aminoglycoside antibiotics of the kamamycin and spectinomycin type, or the recently optimized bioprocesses for the bulk-scale production of vitamins C and B₆.

Some sugar-derived drugs obtained by chemical means have also achieved some importance, for example, ranitidine (Zantac³⁶), an inhibitor of gastric acid secretion—one of the top 30 drugs based on sales—²⁶—isosorbide dinitrate, a coronary vasodilator,²⁷ or topiramate, a fructose-derived antiepileptic drug with high antiepileptic efficacy.²⁸

2.3 TOWARD FURTHER SUGAR-BASED CHEMICALS: POTENTIAL DEVELOPMENT LINES

Considering the large-scale, low-cost availability of the basic biomass-sugars listed in Table 2.1, their present nonfood use by the chemical industry is modest, that is, the huge feedstock potential of carbohydrates in general, and low-molecular-weight sugars in particular, is largely untapped. In view of the necessity of the chemical industry to somehow effect the changeover from fossil raw materials to biofeedstocks—that is, to primarily, carbohydrates as these are more accessible from agricultural crops and waste materials than any other natural products—their further development as industrial products is one of the major challenges of green chemistry. Thus, the fundamental basic and applied research
objectives of the near future—hopefully, incorporated into the European Commission’s 7th Framework Programme—must be to systematically improve existing methods for either chemical or enzymatic conversions of carbohydrates into industrially viable chemicals and materials, and to develop new ones.

The major directions that broad-scale exploratory research toward carbohydrate-based nonfood products will have to take are—as far as conceivable today—outlined in the following for the four key sugars of biomass: the “royal carbohydrate”\textsuperscript{29} (sucrose), D-glucose, D-fructose, and D-xylose.

2.3.1 Nonfood Valorization of Glucose: Potential Development Lines

2.3.1.1 Chemical Conversions. Although D-glucose is the component sugar of cellulose and starch, only the latter is the raw material for its commercial

\begin{center}
\includegraphics[width=\textwidth]{Scheme24}
\end{center}

Scheme 2.4 Accessible, tautomERICALLY fixed D-glucose derivatives with which to embark toward versatile building blocks.\textsuperscript{32}
production. The chemistry of D-glucose is exceedingly well developed, its ensuing basic reactions going back to Emil Fischer, who in the 1890s, on the basis of oxidative and reductive conversions and on the synthesis of glucose by cyanohydrin extension of arabinose, succeeded in figuring out its (relative) configuration. As a reducing sugar, D-glucose can form pyranoid, furanoid, and acyclic tautomers, so for ensuing straightforward reactions, the tautomeric form has to be fixed first (Scheme 2.4): isopropyldenation leads to the furanoid diacetonide, mercaptalization to an acyclic dithioacetal, pyranoid structures may be effectively generated in the form of glucosides, esters of glucal, and hydroxyglucal.

Another simple, one-step entry from D-glucose to highly substituted furans involves their ZnCl₂-mediated reaction with acetylacetone. Since only the first two sugar carbons of D-glucose contribute to the formation of the furan, a distinctly hydrophilic tetrahydroxybutyl side chain is produced; this chain can be shortened oxidatively to dicarboxylic acid or a variety of other furanic building blocks (Scheme 2.5). By contrast, under mildly basic conditions D-glucose reacts with pentane-2,4-dione in an entirely different way, producing 2-C-glucosylpropanone via C-addition and subsequent retroaldol-type elimination of acetate. Because this conversion can be performed with unprotected sugar and with simple reagents in aqueous solution, it fully complies with green and sustainable principles. The procedure is equally operable with other monosaccharides, and, thus, one of the cleanest and most efficient preparative entries into the area of C-glycosides, which as stable “mimics” of the usual O-glycosides, command major interest as glycosidase inhibitors.

Despite the easy accessibility of these “entry products,” and their fairly well-developed ensuing chemistry, their development toward industrial intermediates is

\[
\begin{align*}
\text{Scheme 2.5} & \quad \text{One-pot conversions of D-glucose into hydrophilic furans or, alternatively, into C-glycosides by reaction with acetylacetone.}
\end{align*}
\]
Figure 2.4 Enantiomerically pure six-carbon building blocks accessible from D-glucose via glucal (upper half) or hydroxyglucal esters (lower entries) as the key intermediates. All products require no more than 3 to 5 straightforward steps from D-glucose.37–46

exceedingly modest. Nevertheless, to emphasize their potential toward industrial intermediates, be it as enantiopure building blocks for the synthesis of noncarbohydrate natural products36 or for agrochemicals and/or high-value added pharmaceuticals, a highly versatile array of dihydropyranols and dihydropyranones is given in Figure 2.4, all of which are derivable from D-glucose (via the glucal and hydroxyglucal esters) in no more than three to five straightforward steps. As in each of these products, at least two of the asymmetric centers of the D-glucose are retained, are enantiomerically pure, and are thus ideal six-carbon building blocks for the synthesis of pharmaceuticals in enantiopure form.

Figure 2.4 Enantiomerically pure six-carbon building blocks accessible from D-glucose via glucal (upper half) or hydroxyglucal esters (lower entries) as the key intermediates. All products require no more than 3 to 5 straightforward steps from D-glucose.37–46
Levoglucosenone, a bicyclic dihydropyranone, is accessible even more directly by vacuum pyrolysis of waste paper. \(^{47}\) Although the yield attainable is relatively low—levoglucosan is also formed, the amount depending on the exact conditions (Scheme 2.6)—relatively large amounts can be amassed quickly; levoglucosenone has been used for the synthesis of a diverse variety of natural products in enantiomeric form. \(^{48}\)

Kojic acid, a \(\gamma\)-pyrone, is readily obtained from \(\delta\)-glucose, either enzymatically by \textit{Aspergillus oryzae} growing on steamed rice, \(^{49}\) chemically via pyranoid 3,2-enolones. \(^{36,50}\) A structurally similar \(\alpha\)-pyrone can be effectively generated by oxidation of glucose to \(\delta\)-gluconic acid and acetylation. \(^{51}\) At present, both, are of little significance as six-carbon building blocks, despite a surprisingly effective route to cyclopentanoid products, \(^{52}\) which is surmised to have industrial potential:

\[
\text{D-Glucose} \xrightarrow{A. oryzae} \text{Kojic acid}
\]

\[
\text{AcO} \quad \text{AcO}
\]

\[
\text{OH} \quad \text{OAc}
\]

\[
\text{DMPA} \quad 90\%
\]

\[
\text{CO}_2\text{H}
\]

\[
\text{OH}
\]

\textit{Glucose-Derived Carboxylic Acids.} There are several carboxylic acids derivable from \(\delta\)-glucose by chemical means that have broad potential as versatile intermediate chemicals for biorefinery platforms (Scheme 2.7); \(\delta\)-gluconic acid, the large quantity produced by oxidation of glucose \(^{53}\) (cf. Table 2.1) is used in the food, beverage, and pharmaceutical industries, yet it is also used for removing calcareous and rust deposits from metals surfaces (due to its complexing properties) \(\delta\)-gluconic acid and \textit{levulinic acid}.

\(\delta\)-Gluconic acid, directly produced by nitric oxidation of glucose or starch, \(^{54}\) is usually isolated as its 1,4-lactone. The technical barrier to its large-scale production mainly includes development of an efficient and selective oxidation technology to eliminate the need for nitric acid as the oxidant. Because it represents a tetrahydroxy-adipic acid, \(\delta\)-gluconic acid is of similar use as adipic acid for the generation of polyesters and polyamides (see later in this chapter).

\textit{Levulinic acid} and formic acid are end products of the acidic and thermal decomposition of lignocellulosic material, their multistep formation from the hexoses contained therein proceeding through hydroxymethylfurfural (HMF) as
the key intermediate, while the hemicellulosic part, mostly xylans, produces furfural.\textsuperscript{55} A commercially viable fractionation technology for the specific acquisition of levulinic acid has been developed,\textsuperscript{56} rendering it an attractive option for a biorefinery platform chemical.\textsuperscript{57}

Levulinic acid is a starting material for a large number of higher-value products, because it can be converted through established procedures into higher-value products such as acrylic and succinic acids, pyrrolidines, diphenolic acid (which has the potential of replacing bisphenol A in the manufacture of polycarbonate resins), or 5-aminolevulinic acid used in agriculture as a herbicide and a growth-promoting factor for plants.

\textit{Hydrocarbons from D-Glucose}. Being a six-carbon commodity graciously provided by Nature, albeit "overhydroxylated," a full deoxygenation of glucose (or other hexoses) formally leads to \textit{n}-hexane, which is usable as a liquid fuel. If such a process could be made practically feasible—this author is well aware that some will say "Never"—it would certainly exceed glucose-derived ethanol as a biofuel (additive), inasmuch as fermentation cuts the six-carbon chain into ethanol and CO\textsubscript{2}, while deoxygenation implies full atom economy by retaining it.
Recent investigations aimed at establishing such a deoxygenation process have met with some success, yet are admittedly far from industrial implementation. Sorbitol, for example, readily accessible from glucose through catalytic hydrogenation, can be tailored to produce a mixture of alkanes consisting primarily of butane, pentane, and hexane, by exposing an aqueous solution to a metal (Pt or Pd) and solid acid catalysts (SiO₂-Al₂O₃) and hydrogen at 225°C. The process is complex, as it not only entails a series of dehydrations and hydrogenations to eventually provide n-hexane, but also dehydrogenations and C—C fissions to produce pentane and butane.

C₄–C₆ Alkanes are highly volatile and, hence, of low value as a transportation fuel or a fuel additive. Since high-quality fuels require the generation of liquid hydrocarbons, the fructose-derived HMF and acetone have been converted into their mono- (C₆) and bis-aldols (C₁₃), which on SiO₂-Al₂O₃/Pt-catalyzed dehydration/hydrogenation produce C₆–C₁₅ alkanes (Scheme 2.8). A major drawback of this approach, however, is the fact that HMF, de facto, is a fructose-derived product, and is not producible in an industrially viable price frame at present (vide infra, Section 2.3.2).
2.3 TOWARD FURTHER SUGAR-BASED CHEMICALS

Scheme 2.8 Effectuation of the deoxygenation of D-glucose (or other sugars) to hydrocarbons.\textsuperscript{58,59}

2.3.2.1 Valorization of D-Glucose Through Microbial Conversions. Some experts predict that biotechnology will produce up to 20\% of the industrial chemicals by 2010—from currently 5\%.\textsuperscript{61,62} Undoubtedly, such an increase will receive its major thrust from the various genetically engineered bioprocesses currently in industrial pipelines, most notably those that involve the bioconversion of D-glucose—Nature’s principal sugar for essentially any biotransformation—into industrially important C\textsubscript{3}–C\textsubscript{5}-carboxylic acids apart from those already exploited (cf. Table 2.1) or into alcohols other than ethanol.\textsuperscript{63}

Intense research and development efforts currently appear to go into the following chemicals:

- 3-hydroxypropionic acid
- 1,4-diacids (malic, fumaric, succinic)
- itaconic acid
- 1,3- and 1,2-propanediol

of which the carboxylic acids—currently petroleum-based bulk commodities—are on the list of the 12 future sugar-derived platform chemicals\textsuperscript{57} of the U.S. Department of Energy. If low-cost D-glucose-based fermentation routes can be developed and implemented on an industrial scale, there is a good chance of their production process being replaced along petrochemical channels.

3-Hydroxypropionic Acid (3-HPA). As it did with the structurally isomeric lactic acid, a three-carbon building block with the potential of becoming a key
intermediate for a variety of high-volume chemicals—malonic and acrylic acids, methacrylate, acrylonitrile, 1,3-propanediol, and so forth\textsuperscript{57b}. Cargill is developing a low-cost fermentation route by metabolic engineering of the microbial biocatalyst that produces 3-HPA under anaerobic conditions,\textsuperscript{64a} yet it will take another one or two years for the process to reach commercial viability:\textsuperscript{64b}

\[
\begin{align*}
\text{Lactic acid (LA)} & \quad \text{3-Hydroxypropionic acid} \\
(2-\text{Hydroxypropionic acid}) & \quad \text{(3-HPA)}
\end{align*}
\]

Unlike a product such as lactic acid, another of 3-HPA’s appeals is that, at present, it is not manufactured commercially, either by chemical or biological means.

1,4-Diacids. The microbial generation of malic, fumaric, and succinic acid essentially implies Krebs cycle pathway engineering of biocatalytic organisms to overproduce oxaloacetate as the primary four-carbon diacid that subsequently undergoes reduction and dehydration processes (Scheme 2.9). The use of these four-carbon diacids as intermediate chemicals and the state of their desirable microbial production is briefly outlined.

The major portion of malic acid currently produced at an approximate 10,000 t/a is racemic, because it originates from petrochemically produced fumaric acid. The l-form can also be generated from fumaric acid by its hydration with immobilized cells of \textit{Brevibacterium} or \textit{Corynebacterium}.

\textit{Fumaric acid}, a metabolite of many fungi, lichens, moss, and some plants, and mainly used as the diacid component in alkyd resins,\textsuperscript{65} is produced commercially

\[
\begin{align*}
\text{d-Glucose} & \quad \text{Pyruvic acid} \\
& \quad \text{NAD\textsuperscript{+} NADH + H\textsuperscript{+}} \\
& \quad \text{Pyrurate carboxylase} \\
& \quad \text{CO}_2 \\
& \quad \text{Oxaloacetic acid} \\
& \quad \text{Malate dehydrogenase} \\
& \quad \text{NADH NAD\textsuperscript{+}} \\
& \quad \text{Succinic acid} \quad \text{Fumarate reductase} \\
& \quad \text{Fumaric acid} \quad \text{Fumarase} \\
& \quad \text{l-Malic acid}
\end{align*}
\]

\textbf{Scheme 2.9} Glycolytic pathway leading to the l-malic, fumaric, and succinic acids.
to some extent by fermentation of glucose in *Rhizopus arrhizus*, yet productivity improvements appear essential for the product to be an option for replacing its petrochemical production by catalytic isomerization of maleic acid.

Succinic acid is used in producing food and pharmaceutical products, surfactants and detergents, biodegradable solvents and plastics, and ingredients to stimulate animal and plant growth. Although it is a common metabolite formed by plants, animals, and microorganisms, its current commercial production of 15,000 t/y is from petroleum, that is, by hydrogenation of fumaric or maleic acid. The major technical hurdles for succinic acid as a green, renewable, bulk-scale commodity chemical—1,4-butanediol, THF, γ-butyrolactone, or pyrrolidones are industrially relevant follow-up products—include the development of a very low-cost fermentation route from sugar feedstocks. Currently available anaerobic fermentations of glucose (Scheme 2.9) include a genetically cloned form of *Aspergillus succinoperucens*, an engineered *E. coli* strain developed by DOE laboratories, and a number of others—processes that are currently under active development. Production costs are to be brought to or below $0.25/pound in order to match those via petrochemical channels.

Itaconic Acid. Structurally an α-substituted methacrylic acid, itaconic acid constitutes a C₅ building block with significant market opportunities. It is currently produced via fungal fermentation at about 10,000 t/a and mainly used as a specialty comonomer in acrylic or methacrylic resins, as incorporation of small amounts of itaconic acid into polyacrylonitrile significantly improve their dyeability.

![Itaconic acid](image)

To become a commodity chemical, though, productivity improvements with the currently used fungi *Aspergillus terreus* and *Aspergillus itaconicus* are required, and promising ameliorations appear to be in the making. To be competitive to analogous commodities, the crucial production price of about 0.25 $/lb has to be reached—a significant technical challenge still to be solved.

1,3-Propanediol. Both the diol and the dicarboxylic acid components of polytrimethylene-terephthalate, a high performance polyester fiber with extensive applications in textile apparel and carpeting, are currently manufactured from petrochemical raw materials.

![Poly-trimethylene-terephthalate](image)

Sorona® (DuPont)  Corterra® (Shell)
For the polyester’s 1,3-propanediol portion, however, biobased alternatives have been developed, relying on microbial conversions of glycerol, a by-product of biodiesel production, or of corn-derived glucose. For the latter conversion, DuPont has developed a biocatalyst, engineered by incorporating genes from baker’s yeast and *Klebsiella pneumoniae* into *E. coli*, which efficiently converts corn-derived glucose in 1,3-propanediol. The bioprocess, currently being implemented on an industrial scale in a Tennessee manufacturing plant by a DuPont/Tate & Lyle joint venture, will provide bulk quantities from 2006 on.

\[
\begin{align*}
\text{d-Glucose} & \xrightarrow{E. coli} \text{HO} & \text{Fermentation} & \text{OH} \\
\end{align*}
\]

1,2-Propanediol. In its racemic form, 1,2-propanediol is a petroleum-based high-volume chemical with an annual production of over 500,000 t, mostly used to manufacture the unsaturated polyester resins, yet also featuring excellent anti-freeze properties. Enantiomerically pure (R)-1,2-propanediol accumulates along two different pathways via DAHP (3-deoxy-d-arabino-heptulosonic acid 7-phosphate) and methylglyoxal, which then is reduced with either hydroxyacetone or lactaldehyde as the intermediates. Both routes have been examined for their microbial production from glucose by means of genetically engineered biocatalysts, obtained by expressing glycerol dehydrogenase genes or by overexpressing the methylglyoxal synthase gene in *E. coli*. Another approach implies inoculating silos with chopped whole-crop maize with *Lactobacillus buchneri*; after storing for four months, yields of 50 g/kg were reported. Thus, prospects for elaborating an economically sound bioprocess look promising.

### 2.3.2 d-Fructose: Potentials for Nonfood Uses

The substantial amounts of this ketohexose are mainly prepared by base-catalyzed isomerization of starch-derived glucose, yet may also are generated by hydrolysis of inulin, a fructooligosaccharide. An aqueous solution of fructose—consisting of a mixture of all four cyclic tautomers (Figure 2.5), of which only the β-β-pyranose (β-1,2) form present (about 73%) at room temperature is sweet—about 1.5 times sweeter than an equimolar solution of sucrose; hence, it is widely used as a sweetener for beverages ("high fructose syrup").

The nonfood utilization of fructose is modest—not surprising, since its basic chemistry is more capricious and considerably less developed than that of glucose. Nevertheless, there are various “entry reactions” into simple pyranoid derivatives (Scheme 2.10) with which to exploit their industrial application potential.

Equally simple entries—in fact, one-pot reactions each—lead from d-fructose to N-heterocycles of the imidazol, pyrrole, and pyridine type (Scheme 2.11), all of which, due to their hydrophilic substitution patterns, are considered useful building blocks to pharmaceuticals.
By far the highest industrial potential for a fructose-based compound is to be attributed to HMF, which has been termed “a key substance between carbohydrate chemistry and mineral-oil-based industrial organic chemistry.” Like the bulk-scale commodities hexamethylenediamine and adipic acid, HMF represents a six-carbon compound with broad industrial application profiles. It is readily accessible from fructose or inulin hydrolysates by acid-induced elimination of three moles of water. Even a pilot-plant-size process has been elaborated.

HMF as such has been used for the manufacture of special phenolic resins, as acid catalysis induces its aldehyde and hydroxymethyl group to react with phenol. Of equally high industrial potential as intermediate chemicals are the various HMF-derived products for which well-worked-out, large-scale adaptable production protocols are available. Of these, the 5-hydroxymethyl-furoic acid, the 2,5-dicarboxylic acid, the 1,6-diamine, and the respective 1,6-diol (framed in Scheme 2.12) are the most versatile intermediate chemicals of high industrial potential, as they represent six-carbon monomers that could replace adipic acid, alkyl diols, or hexamethylenediamine in the production of polyamides and polyesters.

Indeed, an impressive series of furanic polyesters and polyamides has been prepared in which the furan-dicarboxylic acid replaces terephthalic and isophthalic
acid in the present industrial products (cf. Figure 2.6), yet none has proved economically competitive to existing products. Thus, as of now, HMF, is not produced on an industrial scale. A tentative assessment of its economics as compared to petrochemical raw materials clearly unfolds the reasons underlying: ton prices of naphtha and ethylene are in the 150–400 € range, that of aniline (500 €/t), and of fructose in particular (~1000 €/t) are substantially higher, entailing an HMF-marketing price of at least 2500 €/t—too expensive at present for a bulk-scale industrial product. Accordingly, as long as the economic situation favors fossil raw materials, applications of HMF lie in high-value-added products, such as pharmaceuticals or special niche materials.

2.3.3 Potential Industrial Chemicals from D-Xylose

D-Xylose, also referred to as “wood sugar” because it is, in the form of its polysaccharide xylan, widely distributed in woods, straw, and other fibrous tissues, usually in close association with cellulose. Acid hydrolysis of such xylans in
agricultural wastes (corn cobs,\textsuperscript{89} cottonseed bulks, or other woody materials) split their \( \beta(1 \rightarrow 4) \)-glycosidic linkages to \( \alpha \)-xylose (Scheme 2.13). When more forcing acidic conditions are applied, furfural is the product due to dehydratizations (cf. see earlier in this chapter). Although \( \alpha \)-xylose can thus be made cheaply (cf. Table 2.1 for its estimated present production), as insufficient uses have unfolded yet to make the manufacture of the sugar of commercial interest.

Like \( \beta \)-glucose and \( \beta \)-fructose, however, \( \alpha \)-xylose can be utilized—chemically or microbially—to generate a variety of interesting five-carbon chemicals other than furfural (\textit{vide supra}) or xylitol, a noncaloric sweetener,\textsuperscript{100} both being directly produced from xylan hydrolysates, that is, without the actual isolation of the sugar. Other readily accessible intermediate products of high preparative utility (Scheme 2.14) are the open-chain fixed dithiaoacetol,\textsuperscript{101} the \( \alpha \)-xylal,\textsuperscript{102} and \( \alpha \)-hydroxy-xytal esters,\textsuperscript{103} or pyrazol or imidazol \( \alpha \)-heterocycles with a hydrophilic trihydroxypropyl side chain.\textsuperscript{89}

Another entry into useful five-carbon building blocks from \( \alpha \)-xylose encompasses the expeditious four-step protocol for the 1-phenylpyrazol-3-carboxaldehyde with a 5-hydroxymethyl substituent (Scheme 2.15) and the various follow-up reactions feasible.\textsuperscript{104}
Scheme 2.12  Versatile intermediate chemicals from HMF.$^{93-97}$

Figure 2.6  Furanolic polyesters and polyamides of potential industrial significance.
Aside from the multifaceted chemical conversions, there are sources to develop into industrially viable microbial conversions. 1,2,4-Butanetriol, for example, used as an intermediate chemical for alkyd resins and rocket fuels, is currently prepared commercially from malic acid by high-pressure hydrogenation or hydride reduction of its methyl ester. In a novel environmentally benign approach to this chemical, wood-derived D-xylose is microbially oxidized to D-xylonic acid, followed by a

Scheme 2.14 Readily accessible five-carbon building blocks from D-xylose.
multistep conversion to the product effected by a biocatalyst specially engineered by inserting *Pseudomonas putida* plasmids into *E. coli*:106

Although further metabolic engineering is required to increase product concentration and yields, the microbial generation of 1,2,4-butanetriol is a clear alternative to its acquisition by chemical procedures.

### 2.3.4 Nonfood Valorization of Sucrose

Sucrose, affectionately called “the royal carbohydrate,”30 is a nonreducing disaccharide, because its component sugars, D-glucose and D-fructose, are glycosidically linked through their anomeric carbon atoms. Hence, it constitutes a β-D-fructofuranosyl α-D-glucopyranoside (Figure 2.7). It is widely distributed throughout the plant kingdom, is the main carbohydrate reserve and energy source, and an indispensable dietary material for humans. For centuries, sucrose
has been the world’s most plentifully produced organic compound of low molecular mass (cf. Table 2.1). Due to the usual overproduction, and the potential to be producable on an even higher scale if required, it is, together with cellulose- or starch-derived glucose, the major carbohydrate feedstock of low molecular weight, from which to elaborate organic chemicals.
The resulting chemistry of sucrose is capricious.\textsuperscript{111} The pronounced acid sensitivity of the intersaccharic linkage excludes any reaction that requires acidic conditions, and, featuring eight hydroxyl groups with only subtle reactivity differences, reactions with high regioselectivity for one or two of the OH-groups are few, in fact, mostly enzymatic.

2.3.4.1 Oxidation Products of Sucrose. The essentially regiospecific oxidation by \textit{Agrobacterium tumefaciens}, whose dehydrogenase exclusively generates 3\textsuperscript{\text{b}}-ketosucrose,\textsuperscript{112} is the prototype of an entry reaction into modified sucroses. This ready access opened the way to manifold modifications at the 3\textsuperscript{\text{a}}-carbonyl function (Scheme 2.16).\textsuperscript{113} Chemical oxidation proceeds less uniformly, for example agitation of an aqueous solution of pH 6.5–7.0 at 35°C with air in the presence of 0.5% Pt/C gave a 9.9:1 ratio of the 6\textsuperscript{\text{b}}-, 6\textsuperscript{\text{c}}-, and 1\textsuperscript{\text{a}}-saccharonic acids.\textsuperscript{114} On further oxidation, particularly when using large amounts of the Pt catalyst and higher temperature (80–100°C), the preferred formation of the 6\textsuperscript{\text{b}}-6\textsuperscript{\text{c}}-dicarboxylic acid has been observed,\textsuperscript{115} which may be isolated in up to a 70% yield by continuous electrodialytic removal.\textsuperscript{116}

Extended catalytic oxidation finally yields the 1\textsuperscript{\text{c}}-, 6\textsuperscript{\text{c}}-, 6\textsuperscript{\text{b}}-tricarboxylic acid, that is, all primary hydroxyl groups have yielded to oxidation.\textsuperscript{117} An alternate useful oxidant to the tricarboxylate is the NaOCl/TEMPO system, which, on applying high-frequency ultrasound, produces the tricarboxylate in up to a 70% yield.\textsuperscript{118}

These sucrose-derived carboxylic acids have potential as the acid components of polyesters and polyamides. On amidation of the methyl ester of sucrose-6\textsuperscript{\text{b}}-6\textsuperscript{\text{a}}-dicarboxylic acid with fat-amines, for example, surface-active diamides (left formula) with remarkable tensiometric properties are obtained, whereas reaction with hexamethylenediamine produces an interesting, highly hydrophilic polyamide (right).\textsuperscript{119}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{sucrose_ox_products.png}
\caption{(n = 1–4)}
\end{figure}

2.3.4.2 Sucrose Esters. Sucrose esters have industrial interest in the area of surfactants,\textsuperscript{122} bleaching boosters, cosmetics,\textsuperscript{120} and fat substitutes.\textsuperscript{131} Synthetically prepared\textsuperscript{122} octa-fatty acid esters of sucrose have similar properties as the normal triglycerides, yet are not degraded by lipases, which determined their marketing
as noncaloric fat substitutes—after being approved by the U.S. Food and Drug Administration\textsuperscript{123} under the name Olestra\textsuperscript{68} or Olean\textsuperscript{81}.

Less highly esterified sucroses, usually mixtures with a high proportion of either mono-, di-, or tri-esters of variable regiosomeric distribution over the 2\textsuperscript{\textdegree}, 6\textsuperscript{\textdegree}, 6\textsuperscript{\textdegree}, as well as other hydroxyls (see arrows in Figure 2.8), are cosmetic emulsifiers and have favorable surfactant properties, combining low toxicity, skin

\textbf{Figure 2.8} Sucrose monoesters and monoethers with useful surfactant properties.
compatibility, and biodegradability. Currently, they are produced at an estimated 5000 t/a level, mainly in Japan,\textsuperscript{24b} yet have the potential of becoming viable alternatives to the APG biodetergents if they become more selectively producible.

2.3.4.3 Sucrose Ethers. Because they are next to the anomeric center and intramolecularly hydrogen-bonded, the $2^\alpha$-OH of sucrose is the most acidic, which means it is deprotonated first under alkaline conditions, and thus preferentially yields to etherification. Benzylaion with NaH/benzylbromide in DMF, for example, results in an 11:2:1 mixture of $2^\alpha$-O-benzyl-sucrose (Figure 2.8) and its 1-$O$- and 3-$O$-isomers.\textsuperscript{124} Because the former is readily accessible, it proved to be a versatile intermediate for the generation of $2^\alpha$-modified sucroses, for example, the $2^\alpha$-keto and $2^\alpha$-deoxy derivatives as well as sucrosamine (2$\delta$-amino-2$\delta$-deoxy-sucrose),\textsuperscript{124} whose application profiles remain to be investigated.

Of higher interest industrially is the etherification of sucrose with long-chain epoxides such as 1,2-epoxydecane\textsuperscript{125} or 1,2-epoxydecan-3-ol,\textsuperscript{126} which are performable as one-pot reactions in dimethyl sulfoxide (DMSO) and the presence of a base to provide sucrose monoethers with preferred regioselectivities of the $2^\alpha$-O- and 1$\alpha$-O-positions. Unlike sucrose esters, the long-chain esters are resistant to alkaline conditions, which considerably extends their potential applications as nonionic surfactants. They also have promising liquid crystalline properties, their mesophases depending on the point where the fatty chain attaches to the sucrose.

The only large-scale application of sucrose ethers appears to be to use poly-$O$-(hydroxypropyl) ethers, generated by alkoxlation with propylene oxide, as the polyol component for rigid polyurethanes—sucrose itself gives only brittle ones—which are used primarily in cushioning applications. The structures of these products, that is, the positions at which sucrose is alkoxylated and then carbamoylated with diisocyanates, and the type(s) of cross-linking involved, are not well defined though.

2.3.4.4 Sucrose Conversion to Isomaltulose. As a 6-$O$-(a-$d$-glucosyl)-d-fructose, isomaltulose is isomeric with sucrose, from which it is produced at an industrial level (cf. Table 2.1)—for food reasons, as it is hydrogenated to an equimolar mixture of glucosyl-$\alpha$($1 \rightarrow 6$)-glucitol—and mannitol,\textsuperscript{127} the low caloric sweetener isomalt.\textsuperscript{129} As illustrated in Scheme 2.17, the industrial process involves a glucosyl shift from the 2$\alpha$-O of sucrose to the 6$\alpha$-OH, effected by action of an immobilized \emph{Pseudomonas rubrum}-derived $\alpha$($1 \rightarrow 6$)-glucosyltransferase. Having become most readily accessible in this way, isomaltulose developed into a lucrative target for generating disaccharide intermediates of industrial potential. Particularly relevant in this context are oxidative conversions, hydrogen peroxide as the oxidant leading to shortening of the fructose chain by four carbons to provide the glucoside of glycolic acid (carboxymethyl $\alpha$-$d$-glucoside, $\alpha$-CMG) in 40% yield.\textsuperscript{130} Air oxidation in strongly alkaline solution (KOH), is less rigorous, however, affording the potassium salt of the next lower aldonic acid, that is, glucosyl-$\alpha$($1 \rightarrow 5$)-$d$-arabinonic acid ("GPA") (Scheme 2.17), isolable as such, or upon neutralization, as the GPA-lactone in high yields each.\textsuperscript{131}
Another, industrially relevant resulting reaction of isomaltulose comprises its ready conversion into 5-(α-D-glucosyloxyethyl)-furfural ("α-GMF") by acidic dehydration of its fructose portion under conditions (acidic resin in DMSO, 120°C) that retain the intersaccharide linkage (Scheme 2.17). As this process can also be performed in a continuous-flow reactor, a most versatile building block is available from sucrose in two steps, of which the first is already industrially realized, and the second simple enough to be performed on a large scale.

Various products with industrial application profiles have been prepared from GPA and α-GMF (Scheme 2.18): Amidation of GPA-lactone with long-chain amines, for example, the C₈- and C₁₂- "fat amines," provided the GPA-amides.

Scheme 2.17 Generation of isomaltulose from sucrose, and the resulting products with industrial potential.
which not only exhibit promising detergent profiles but also surprising liquid crystalline properties, such as \( S_{\alpha} \)-phases over a broad temperature range.\(^{133}\) As a glucosylated HMF, \( \alpha \)-GFM provides a particularly rich accompanying chemistry.\(^{132,134}\) aldol-type condensations provide derivatives with polymerizable double bonds that are expected to yield novel, hydrophilic polymers; oxidation and reductive amination generate the \( \alpha \)-GMF-carboxylate and \( \alpha \)-GMF-amine, respectively, which on esterification with long-chain alcohols or N-acylation with fatty acids afford a novel type of liquid crystals,\(^{133}\) as the hydrophilic glucose part and the hydrophobic fat-alkyl residue are separated by an quasi-aromatic spacer; and they combine high surface activity with biocompatibility, making them promising candidates for biomedical applications.

2.3.4.5 Linear C–C-Polymers with Pendant Sucrose Residues. The synthesis of sugars carrying \( O \)-linked residues with polymerizable double bonds ("vinyl-saccharides") and their radical or cationic copolymerization has been extensively pursued over the last 70 years,\(^{135}\) with major emphasis on suitable derivatives of glucose and sucrose—the first example, the polymerization of 1,2:5,6-di-\( O \)-isopropylidene-3-\( O \)-vinyl-d-glucosurano dating back to Reppe and Hecht in the 1930s.\(^{136}\) Thus, a large series of mono-\( O \) and di-\( O \)-substituted derivatives of sucrose—with polymerizable C=C double bonds in ester or ether moieties attached—have been prepared,\(^{137,138}\) usually as mixtures with average degrees of substitution: esters of acrylic or methacrylic acid, or vinylbenzyl ethers mostly. Their polymerization as such, or copolymerization with the standard petroleum-based monomers (methyl methacrylate, methyl acrylate, acrylonitrile, styrene, etc.), have led to a variety of interesting linear and cross-linked polymers with "sucrose anchors" attached to the polymeric carbon chain(s),\(^{137,138}\) as schematically represented in Figure 2.9. Various surface modifications of polymers by graft
polymerizations with vinyl-sucrases have also been reported, for example, grafting of sucrose acrylate on polyvinyl chloride (PVC) films.\textsuperscript{139}

Despite the highly versatile application profiles of polymers with adjunct sucrose (or other sugar) residues—their major asset is enhanced hydrophilicity as compared to their hydrophobic petroleum-derived counterparts—interest appears to be restricted to biomedical uses. Currently none is produced commercially, as the generation of vinyl-sucrases and their often capricious polymerization have made their use as commodity plastics uneconomical. Another reason is their limited biodegradability: only the sugar portion is biodegradable, with a polymeric carbon chain left over. Because biodegradability is a major issue today,\textsuperscript{140} these polyvinylsaccharides are unlikely to become petrochemical substitution options in the near future.

### 2.4 CONCLUSION

The utilization in nonfoods of inexpensive, bulk-scale-accessible, low-molecular-weight carbohydrates—sucrose, glucose, xylose, and fructose being the most readily accessible—is at a rather modest level in terms of large-scale manufactured commodities currently on the market. The unusually diverse stock of readily accessible products described in this chapter, which covers a wide range of industrial application profiles, is mostly unexploited in its potentialities. The reasons are mostly economic as equivalent products based on petrochemical raw materials are simply cheaper. Nevertheless, a basic change in this scenario is clearly foreseeable. As depletion of our fossil raw materials is progressing, petrochemicals will inevitably increase in price, such that biobased products will eventually become competitive. Realistic prognoses\textsuperscript{5} expect to occur by the middle of this century at the latest.

In the meantime, it is imperative that carbohydrates be used systematically to achieve efficient, environmentally benign, and economical processes for their large-scale conversion into industrially viable products, be it bulk or intermediate
chemicals, pharmaceuticals, or polymeric organic materials. In this endeavor, national and supranational funding institutions—in Europe, the corresponding EU bodies (in the European Commission’s seventh framework program, hopefully) and/or the European Renewable Resources & Materials Association—will have to play a much more dynamic role than heretofore. One decisive action, of course, is the generous funding not only of applied but of basic research activities in this area, and this over a considerably longer time frame—5–10 years for promising projects, rather than expecting that marketable products be delivered within 3–5 years. Impatience with the development of renewable resources for high-value-added products is futile if they are harvested too early.

Another key issue is the development of a concise, long-term strategy that takes hold in academia and chemical industry. This strategy should not to be directed toward generating the very same basic chemicals from carbohydrates that are easily accessible from petrochemical sources, but toward the development of products with analogous industrial application profiles, with as little alteration of the carbohydrate structural framework as possible. Only then will economically sound biobased alternatives to petrochemicals—various potential examples are contained in this chapter—become available.

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