EXTENDED ABSTRACT

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Drugs and high-value-added materials from agricultural leftovers

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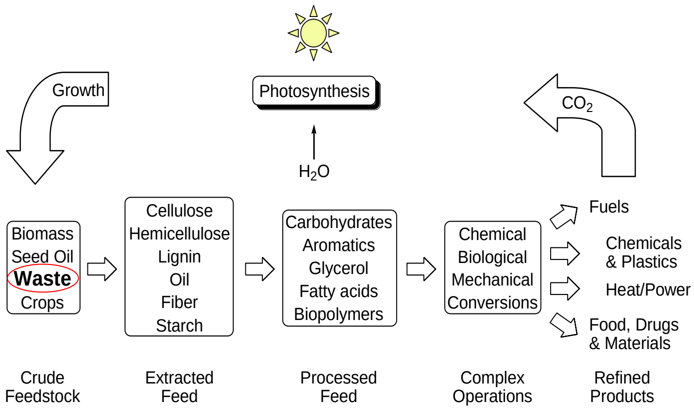
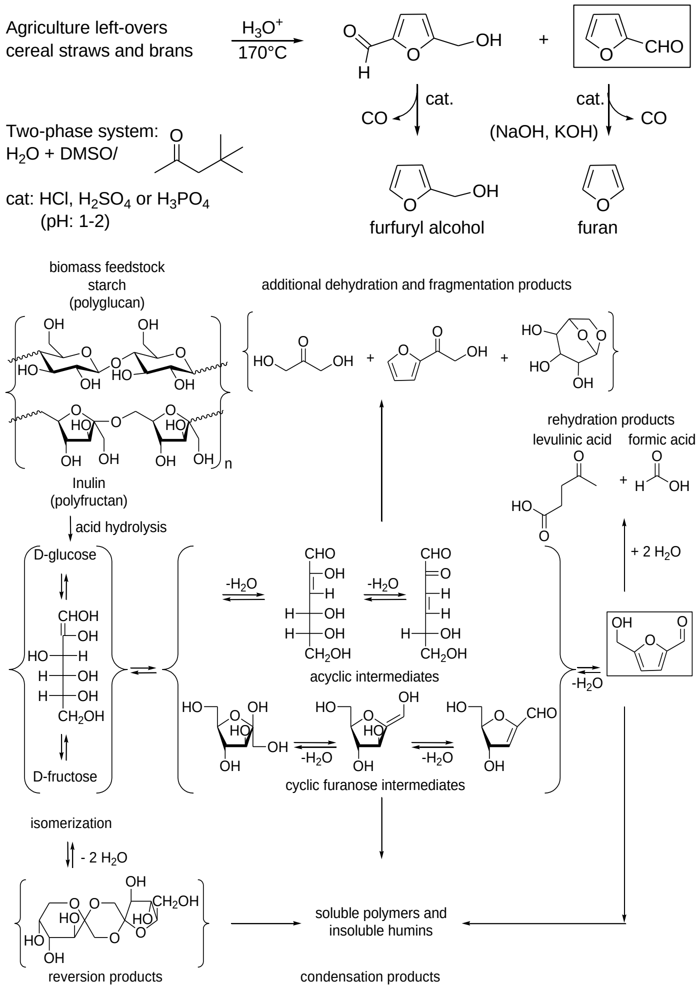
Introduction. – With the future exhaust of petroleum and coal that represent our raw materials for material sciences, crop protecting agents and drugs our civilization is confronted with the urgent need to find new sources of carbon containing raw materials. Vegetable biomass, generated from CO_2, H_2O and using sunlight as the energy source producing O_2 as a subproduct, is the best alternative to oil, gas and coal. Plants have to be used to feed men. To divert them into fuel and fine chemical production cannot be done at this moment, unless new plants are found that can have a better photochemical yield for the conversion of CO_2 in carbohydrates and other compounds, and would not require huge amount of water. Thus as long as one cannot grow biomass in the desert, only the left-overs (mainly straw) can be used as a sources of fuel and fine chemicals.[1] For many years our laboratory has developed synthetic methodology permitting to convert furans into high value added chemicals such as drugs. Furans are inexpensive, non-toxic compounds obtained by acidic treatment of agriculture left-overs (e.g. straw).[2]

Processing of crude feed-stocks to refined products in a sustainable biorefinery1

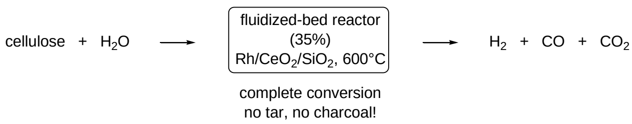


Acid-catalyzed dehydration of polysaccharides: ***gold from garbage***[3]



Formation of levulinic acid and formic acid is suppressed when fructose or glucose is heated (80-100°C) in ionic liquid methylimidazolium chloride with $CrCl_2$ as catalyst.[4]

Energy efficient production of H_2 and Syngas from biomass[5]



Further method: droplets of sugar, H_2O, soy oil hit a porous ceramic

[1] Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* **2007**, *107*, 2411-2502.
[2] Chheda, J. N.; Huber, G. W.; Dumesic, J. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 7164-7183.
[3] Chheda, J. N.; Roman-Leshkov, Y.; Dumesic, J. A. *Green Chem.* **2007**, *9*, 342-350 (Univ. Wisconsin-Madison).
[4] Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. *Science* **2007**, *316*, 1597-1600 (Pacific Northwest Nat. Lab.).
[5] Asadullah, M.; Ito, S.i.; Kunimori, K.; Yamada, M.; Tomishige, K. *Environ. Sci. Technol.* **2002**, *36*, 4476-4481.

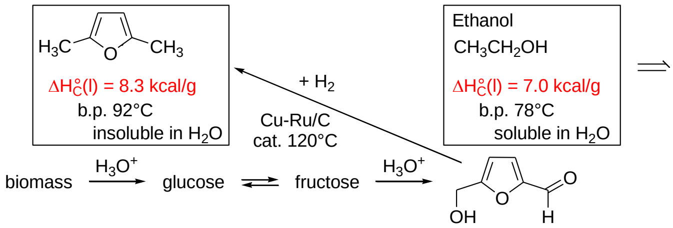
catalyst heated to 1000°C ⇒ maximum yield in H_2 + CO.[6]

Pyrolysis of wood and bark → bio-oil.[7]

Pyrolysis of biomass → CO + H_2 + CH_4.[8]

2,5-Dimethylfuran: the liquid fuel of the future?

Has a higher energy density (+40%) than ethanol.[9]



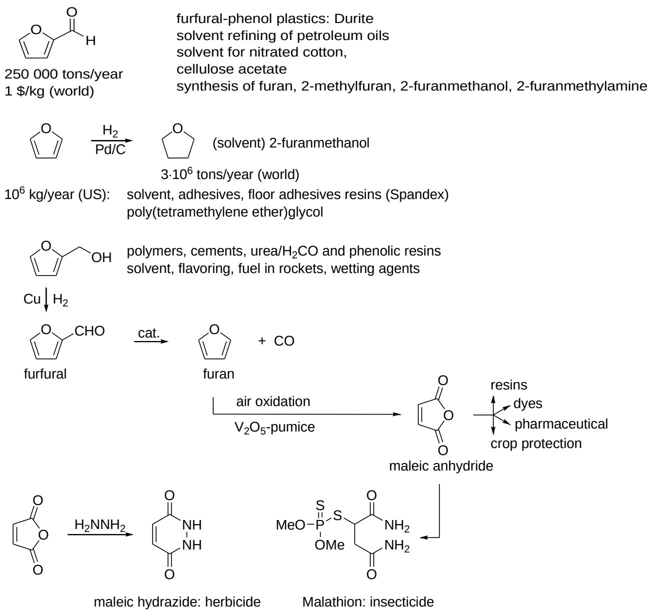
1862: ***N. A. Otto invents the internal combustion engine working with ethanol.***

1892: ***R. Diesel: Carnot heat engine powered by coal dust.***

1900: ***R. Diesel: engine powered by peanut oil (biodiesel).***

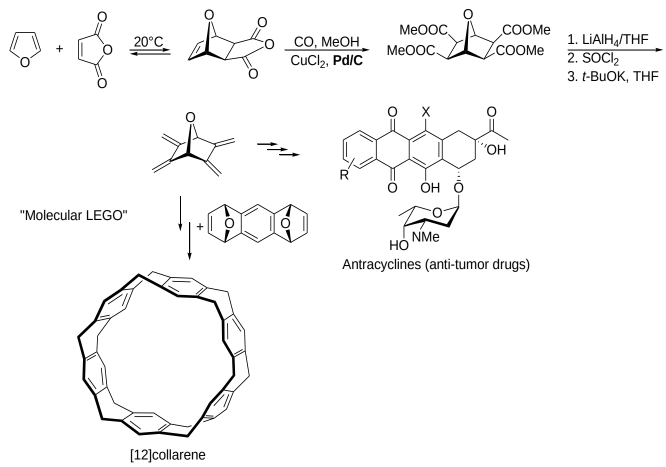
1903: ***H. Ford, Model T (1903-1926) ran on biofuel.***

Industrial uses of furfural (gold from garbage)

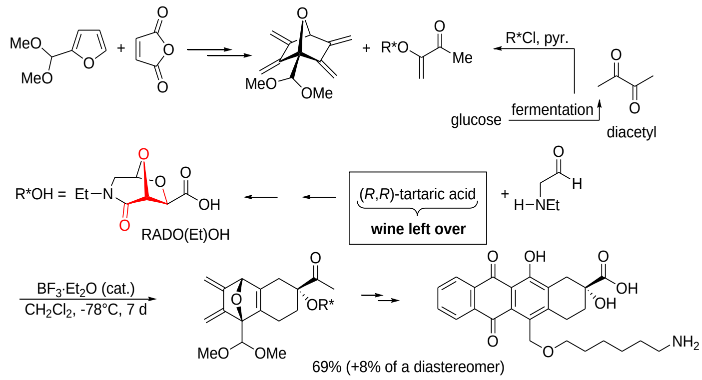


From furan to nanomaterials and anti-cancer drugs[10]

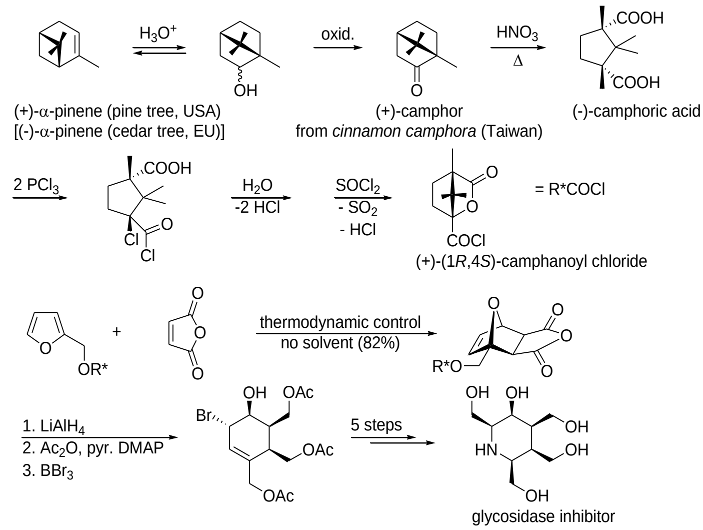
[6] McGee, T. *Science & Technology*, Nov. 7, **2006**.
[7] Ingram, L. et al. *Energy Fuels* **2008**, *22*, 614-625.
[8] Müller-Hagedorn, M.; Backborn, H. *J. Anal. Appl. Pyrolysis* **2007**, *79*, 136-146.
[9] Roman-Leshkov, Y.; Barrett, C. J.; Liu, Z. Y.; Dumesic, J. A. *Nature* **2007**, *447*, 982-985.



New class of DNA-intercalators and human topoisomerase II inhibitors[11]

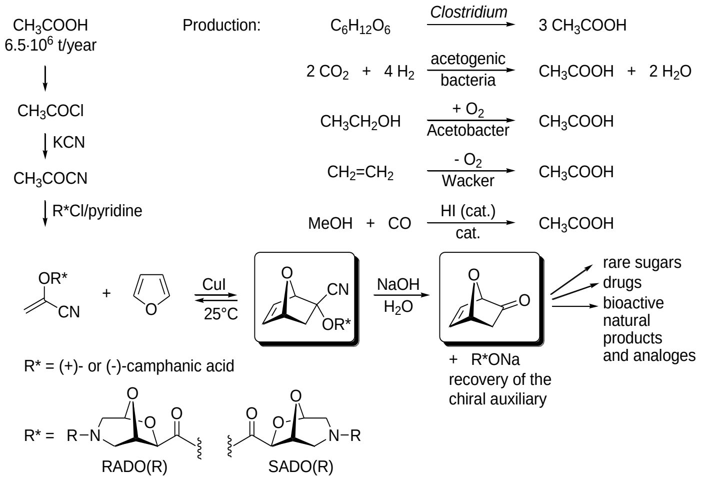


Chiral auxiliaries from the biomass[12]

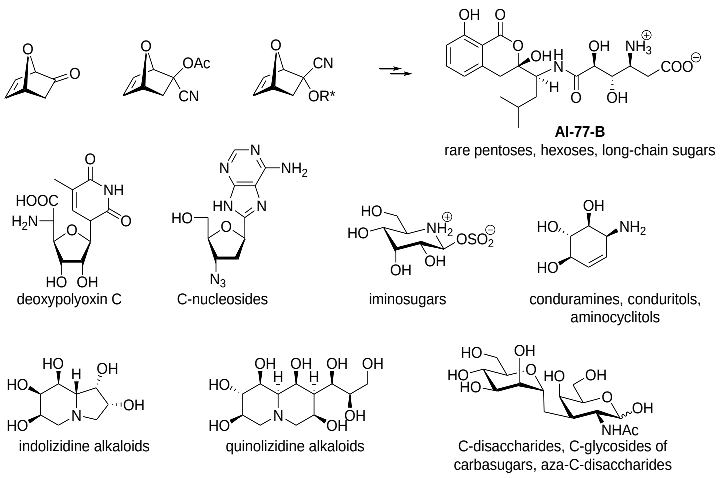


[10] Vogel, P.; Carrupt, P.-A.; Patent ref. RAN 4060/100 (**1979**); Vogel, P. *Curr. Org. Chem.* **1998**, *2*, 255-280; Stoddart, J. F. and coll. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1261-1263; *J. Am. Chem. Soc.* **1992**, *114*, 6330-6353; Pollmann, M.; Müllen, K. *J. Am. Chem. Soc.* **1994**, *116*, 2318-2323.
[11] Dienes, Z.; Vogel, P. *J. Org. Chem.* **1996**, *61*, 6958-6970.
[12] Theurillat-Moritz, V.; Vogel, P. *Tetrahedron:Asymmetry* **1996**, *7*, 3163-3168; Jotterand, N.; Vogel, P. *J. Org. Chem.* **1999**, *64*, 8973-8975.

The "naked sugar" methodology[13]

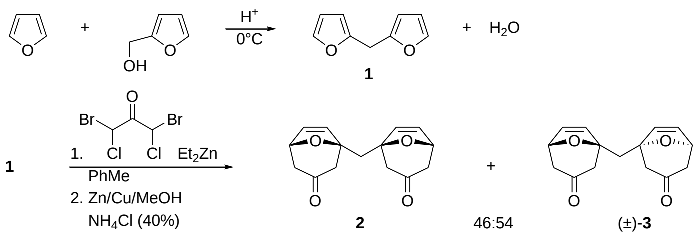


"Naked sugars of the first generation" (chirons from furan)[14]

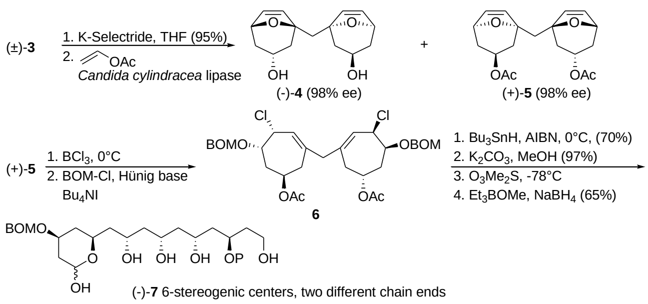


Furan + furfuryl alcohol → 2,2'-methylenebis(furan): a synthon for the synthesis of bioactive compounds.

A great variety of natural products of biological interest include polyketide (1,3-polyoxo, 1,3-polyols, aldols) components.[15] Inspired by the work of Lautens[16] and Hoffmann and co-workers,[17] who have converted 8-oxabicyclo[3.2.1]oct-6-en-3-one into seven-carbon chain 1,3-polyols and analogues,[18] and by that of Kaku et al.,[19] who have transformed cyclohept-3-ene-1,6-diol into 1,3-polyols, we have proposed a new, non-iterative asymmetric synthesis of long-chain 1,3-polyols starting from the now readily available 2,2'-methylenebis(furan) (**1**).[20, 21]



Enzymatic (lipase) kinetic optical resolution[22,23]



Apart from the reductive dechlorination step which at this moment, has been realized under standard conditions (Bu_3SnH as reducing agent), the conversion of (±)-**3** into (-)-**7** is environment friendly. Pozzi and Renaud have shown recently that organoboranes and water can substitute tin hydrides in radical reduction.[24]

Conclusion – Leftovers from agriculture provide inexpensive chemicals (**gold from garbage**) such as furan, furfural, (2-furan)methanol, 5-hydroxymethylfurfural, 2,5-dimethylfuran, maleic anhydride, tetrahydrofuran, diacetyl and carbon monoxide + hydrogen (syn-gas). These products will substitute petroleum-derived chemicals that are now necessary for our civilization (energy, crop protection, health, materials, telecommunication, etc.). This presentation gives applications of furan chemistry. We have demonstrated that furan and its readily available derivatives can be used to construct highly sophisticated compounds of biological interest such as anti-tumoral anthracyclines and polyketide

[13] Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1983**, *66*, 1865-1871; Reymond, J.-L.; Vogel, P. *Tetrahedron:Asymmetry* **1990**, *1*, 729-736.
[14] Vogel, P. *Curr. Org. Chem.* **2000**, *4*, 455-480; *Organic Chemistry of Sugars*, Levy, D. E. ed., CRC Press, Boca Raton, FL. **2006**, 629-725.
[15] Muhammad, S. et al. *Nat. Prod. Rep.* **2007**, *24*, 1142-1153; Asakawa, Y. *Pure Appl. Chem.* **2007**, *79*, 557-580; Kobayashi, J.-i.; Kubota, T. *J. Nat. Prod.* **2007**, *70*, 451-460; Mayer, A. M. S.; Gustafson, K. R. *Eur. J. Cancer* **2006**, *42*, 2241-2270; Cragg, G. M.; Newman, D. J. *Cancer Investigation* **1999**, *17*, 153-163.
[16] Lautens, M.; Ma, S.; Yee, A. *Tetrahedron Lett.* **1995**, *36*, 4185-4188.
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[18] Montaña, A. M.; Garcia, F.; Grima, P. M. *Tetrahderon* **1999**, *55*, 5483-5504.
[19] Kaku, H.; Tanaka, M.; Norimine, Y.; Miyashita, Y.; Suemune, H.; Sakai, K. *Tetrahderon:Asymmetry* **1997**, *8*, 195-201.
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[22] Csáky, A. G.; Vogel, P. *Tetrahedron:Asymmetry* **2004**, *11*, 4935-4944.
[23] Gerber-Lemaire, S.; Vogel, P. *Eur. J. Org. Chem.* **2003**, 2959-2963.
[24] Darmency, V.; Renaud, P. *Top. Curr. Chem.* **2006**, 71-106; Pozzi, D.; Renaud, P. *Chimia* **2007**, *61*, 151-154.

antibiotics. Enantiomerically pure compounds have been obtained from readily available leftovers such as tartaric acids (from wine) or from camphor derived from trees. The chemistry shown here contributes toward **sustainable development**.