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# Selective dehydration of glucose to hydroxymethylfurfural and a one-pot synthesis of a 4-acetylbutyrolactone from glucose and trioxane in solutions of aluminium salts

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## Abstract

Saturated water solutions of  $Al_2(SO_4)_3$  and  $AlCl_3$  were applied as solvent/matrices for dehydration of Glc to hydroxymethylfurfural (HMF). Addition of oxygen ligands: methanol, ethanol, THF, furan, dibutyl ether, ethyl orthoformate and trioxane influenced the yield and selectivity, the best being observed with ethanol. When Glc and trioxane were present together in reacting solution, formation of a 4-acetylbutyrolactone was observed.  $\mathbb{C}$  1999 Elsevier Science Ltd. All rights reserved.

Keywords: Glucose; Dehydration; Aluminium salts; Oxygen ligands

## 1. Introduction

The dehydration reaction of glucose in saturated aqueous solutions of  $MgCl_2$  and  $MgSO_4$  affords various amounts of hydroxymethylfurfural (HMF), other furan derivatives, the 2-acetyl propionic acid (I, levulinic acid) and humins [1]. The dehydration to HMF in solutions of sulfate probably proceeds with the participation of aquo and hydroxy complexes by intermediacy of an 'extensively hydrogenbonded species' [1]. This is a selective reaction but proceeds with low conversion. In  $MgCl_2$  solution conversion is much greater than in  $MgSO_4$ . The formation of five carbon furan derivatives in water solutions of  $MgCl_2$  is probably caused by an exocyclic  $-CH_2OH$ 

elimination, which in turn originates from an 'anions guiding rail' effect [2]. The sulfates and chlorides thereby constitute two classes of salts exerting different effects on the reactivity of glucose.

A high-yield, selective and experimentally simple, method for dehydration of glucose (partial or complete) has not so far been described. To achieve these goals there has to be a rational selection of the metallic centre and associated ligands. We limited ourselves to an application of ligands, L, which are able to offer an oxygen atom to the metal. In reaction solution one can therefore expect formation of  $\{ML_x\}A_p$  according to the reaction:

Metal salt  $MA_p + xL \rightarrow \{ML_x\}A_p$  (1)

(A, anion; p, number of associated anions). The oxygen ligands tested were the CH<sub>3</sub>OH,

EtOH, trioxane, di-n-butyl ether, furan, THF

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and triethyl orthoformate (TEOF) systems. In this paper we describe mainly the application of  $Al_2(SO_4)_3$  and  $AlCl_3$ ; in some cases  $MgCl_2$  was used.

# 2. Experimental

General.—For GC–MS analysis a Hewlett-Packard 5890 Series II gas chromatograph combined with a model 5972 mass-selective detector was used equipped with HP-5 and Innovax columns. The molecular weight was measured using LSIMS on an AMD-604 double focusing mass spectrometer (MAGD Intectra GmbH, Harpsted, Germany). <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> at 200 MHz with a Varian Gemini instrument. IR spectra were recorded on a Perkin–Elmer 1670 FT unit.

Analytical grade Glc, MeOH, EtOH Al and Mg salts were all purchased from Polskie Odczynniki Chemiczne (POCh, Gliwice, Poland). Remaining metal salts, (*n*-Bu)<sub>2</sub>O, furane, THF, trimethyl and triethylorthoformates, trimethyl and triethyl orthoacetates, were commercial products of Aldrich or E. Merck. MeOH, EtOH, water and triethyl orthoacetate were distilled but other reactants were used as received. Reactions were performed under gentle reflux with agitation by a magnetic stirrer.

*Methods.*—The composition of the reacting solution defined as a reference reaction was as follows: 9 cm<sup>3</sup> of saturated water solution of an aluminium sulfate (containing 8.33 mmol of Al<sub>2</sub>(SO<sub>2</sub>)<sub>4</sub>, 8.33 mmol of Glc and 324 mmol of EtOH). This reference reaction mixture was then modified: (a) at a constant concentration of Glc; the molar ratio  $Glc/Al_2(SO_4)_3$  varied from 9 to 0.67; the molar ratio EtOH/Glc 286-6.1; in such a range of conditions the highest yield of HMF  $\sim 7\%$  was observed for  $Glc/Al_2(SO_4)_3$  0.67 and EtOH/Glc 6.1 (data concerning yields  $\pm 1.5\%$ ); and (b) at a constant EtOH/Al<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub> ratio of 40; the Glc/  $Al_2(SO_4)_3$  varied from 9 to 0.67; the highest yield of  $\sim 8\%$  was observed for the range 1.3-0.67. Reactions performed only in water gave no products. Isolation of crude products and their GC analysis were performed as described in Ref. [1]. The retention times span up to 1.7 min because the experiments were done over a period of about 2 years, which caused changes in the column properties. The identity of chromatographic peaks was always established by complementary MS data.

Isolation and purification of a methyl ether of HMF was by column chromatography as follows: crude reaction products (1.7 g) were chromatographed on silica gel (E. Merck, 30 g) with 1:4 acetone-CHCl<sub>3</sub>. The chromatography was repeated on the intermediate fraction (the one which was least contaminated as assessed by TLC) with toluene on silica gel to give 0.007 g of V. NMR data:  $\delta$  4.45 (s. 3H, -OCH<sub>3</sub>); 4.50 (s, 2H, OCH<sub>3</sub>); 6.53 (d, 1H, =CH); 7.22 (d, 1H, =CH); 9.63 (s, 1H, -CHO). MS: MW 140; m/z (relative intensity):140 (32), 139 (6), 112 (6), 111 (100), 109 (40), 81 (18), 80 (6), 68 (6), 55 (11), 53 (45), 52(14), 51(12), 50(8), 45(6), 39(14). The molecular weight was confirmed by an LSIMS technique, using *m*-nitrobenzyl alcohol as a matrix. IR: no -OH band; 1690 cm<sup>-1</sup> vs. (C=O). HMF ethyl ether (III) was identified by MS spectrum: MW 154; m/z (relative intensity) 154 (27), 125(86), 111 (13), 109(100), 97 (93), 81 (44), 69(24), 53(48), 52(29), 51(17), 50 (10), 41 (25), 38(20) and by measurement of the molecular weight by LSIMS. Separation of 2-acetylbutyrolactone (VI) from crude reaction products was performed as follows: the crude product (0.09 g) was chromatographed on silica gel (E. Merck,  $\sim 2.0$  g) with CHCl<sub>3</sub>. NMR data of combined TLC pure fractions:  $\delta$  2.26 (s, 3H, CH<sub>3</sub>CO), 2.60–2.87 (m, 2H), 3.48-3.62 (m, 1H), 4.33-4.55 (m, 2H). Our NMR data agree with those of Muller [3]. The NMR data of other papers [4,5] show minor differences. MS: MW 128; m/z (relative intensity: 128(6), 100(5), 86(30), 71(9), 55(22), 43(100), 42(11), 38(8.); IR (film): 1780, 1718  $cm^{-1}$ . The reference conditions for synthesis of VI were: 10 cm<sup>3</sup> of saturated water solution of AlCl<sub>3</sub> ( $\sim 29.6$  mmol), 0.5 g of Glc (2.7 mmol), 1.0 g of trioxane (11.1 mmol), and 2 cm<sup>3</sup> of TEOF (12 mmol). The pH of the reacting systems was always assessed by litmus paper, to within pH 3-6 without addition of an acid, so that reactions were always performed in slightly acidic solutions except when alkaline reagents had been added.

## 3. Results

When Glc reacts in saturated water solution of  $Al_2(SO_4)_3$ , after 3–4 h a dark heterogeneous mixture with coke-like material is produced.



Fig. 1. Capillary gas chromatograms: (A) products of a reaction in 9 cm<sup>3</sup> of saturated aqueous solution of  $Al_2(SO_4)_3$  (8.33 mmol), 19.3 cm<sup>3</sup> of EtOH (324 mmol) and of Glc (8.33 mmol). (B) Products of reaction with 10 ml of a saturated aqueous solution of AlCl<sub>3</sub>, 8 cm<sup>3</sup> of MeOH (197 mmol) and 8.33 mmol of Glc. In this system, HMF methyl ether and levulinic acid methyl ester are formed.

#### Table 1

Influence of acidification and of the presence of alkaline reagents on yield of products in the reference system

Acid or alka- line reagent	Molar ratio (Glu:acid, Glu:alk)	$\Sigma$ yield of all products (%)
HCl HBr H <sub>2</sub> SO <sub>4</sub>	40:1	8
HCl HBr H <sub>2</sub> SO <sub>4</sub>	4:1	6
NaOH CaO MgO NEt <sub>3</sub>	40:1	4
NaOH CaO MgO NEt <sub>3</sub>	4:1	2

The same was observed in saturated aqueous solutions of  $MgCl_2[1]$ . However, upon addition of EtOH to saturated aqueous solutions of magnesium chloride (10 cm<sup>3</sup> of  $MgCl_2$  solution, 3 cm<sup>3</sup> of EtOH and 8.33 mmol of Glc) a clean reaction mixture without tar and coke was observed [1]. The presence of MeOH or EtOH here also made the reaction more selective and cleaner. Capillary gas chromatograms of reaction products formed in systems containing water solutions of  $Al_2(SO_4)_3$  and of  $AlCl_3$  with alcohols are shown in Fig. 1.

Consequently, reactions were performed in the presence of EtOH. There were four main products in the presence of EtOH in the range of conditions studied: HMF, 2-acetylpropionic acid (I), the ethyl ester of 2-acetylpropionic acid (II) and HMF ethyl ether (III). With MeOH, 2-acetylpropionic acid methyl ester (IV) and HMF methyl ether (V) formed in place of II and III.

Mass spectra of HMF ethers are not in the Wiley Library so the ethers were isolated and identified by known methods (Section 2). The remaining products were identified using the Wiley Library (1993) with a PBM search algorithm and by comparison with authentic samples. In the reference reaction humins were not formed. Other compounds detected by GC were present in minor quantities, so the reference system produced HMF (together with compounds of its subsequent reactions) rather selectively. In a previous paper [1] we described the existence of a dehydration product of Glc in the presence of EtOH having a retention time of 55.8 min and called a '154' product. Contrary to our preliminary assumptions that this product was a carbocyclic substance, we found it to be the ethyl ether of HMF (Section 2). Also observed was formation of this ether with aqueous MgCl<sub>2</sub>. The reference system was than modified by several procedures: acidification or making the solution alkaline (Table 1), and by introducing salts of cations considered as hard (or borderline [6]) Lewis acids (Table 2). Conversion of Glc in saturated aqueous solutions of sulfates of Ag(I), Fe(II), Fe(III), Cu(II), Zn(II), Cr(III) and of 'RuSO<sub>4</sub>' was negligible except sulfates of Fe(III) and Cr(III), where the HMF and its ether were formed with  $\sim 8\%$ yield (with EtOH; concentrations as in the

### Table 2

Influence of selected metal salts and complexes on yield of products

Salt or complex	System	Molar ratio	Yield (%)
Sulfates of Ag(I), Fe(III), Cu(II), Zn(II), Cr(III), 'RuSO <sub>4</sub> ' [1]	Reference system	Glu:sulfate = 10	10–20% decrease in yield compar- ing to the reference system
Chlorides of Al(III), Ti(III), Fe(III); nitrates of Al(III) and of Fe(III)	Reference system	Glc:salt = 10	10–40% decrease
PdCl <sub>2</sub>	Saturated aq solution of AlCl <sub>3</sub> + MeOH or EtOH (50–300 mmol) Glc conc as in ref system	Glc:Pd = 10–50	HMF and its ethers 3–14, levulinic acid and its esters 3–22
H <sub>2</sub> IrCl <sub>6</sub>	Saturated aq solution of MgCl <sub>2</sub> + MeOH or EtOH; Glc conc as in ref system	Glc:Ir = 10–50	HMF and its ethers 3, levulinic acid and esters 0.5

reference reaction). Upon diluting the reference system with water the conversions were negligible; and similarly in a saturated solution of sodium sulfate and in aluminium sulfate with different amounts of 30% H<sub>2</sub>O<sub>2</sub> in the presence of Fe(II) sulfate (Fenton reagent). Saturated aqueous solutions of MgCl<sub>2</sub> with MeOH (50-300 mmol), produced HMF and V in 4–10% yield (concentrations as in the reference system), whereas saturated aqueous solutions of AlCl<sub>3</sub> with MeOH produced only levulinic acid (28%) and its ester (2%). HMF and I-V were sometimes accompanied by other furane derivatives such as 2-furancarboxaldehyde, methoxy furan 1-(2-furanyl)ethanone, albeit in minor quantities. A series of reactions of the reference system were performed with prolonged reaction times. Results are given in Table 3. Gas chromotograms of extractable products indicated the existence of other minor products in comparison to those observed in the '24 h' reaction. Yields reached maximum with time but than decreased. In addition to MeOH and EtOH, THF, furane, (*n*-Bu)<sub>2</sub>O, TEOF and

Table 3

Dependence of product yields upon reaction time using the ratios of reactants as in the reference system

Reaction time (h)	Yield of HMF and III (%)	Yield of I and II (%)
24	7	
72	13	2
124	20	4
144	22	6
168	15	3

trioxane were used as ligands in aqueous solutions of Al salts. The presence of THF completely inhibited any reaction of Glc; tar and coke-like materials were also not formed. With furane and  $(n-Bu)_2O$  only I was formed with 24–26% yield. Addition of furan produced considerable amounts of humins. When trioxane and TEOF were present together in solution, it was observed that one compound appeared as the most abundant component of a crude extract (retention time 62.4 min. Innovax column). This compound was unknown to the Wiley Library, and after isolation was identified as 4-acetylbutyrolactone VI. We studied the influence of several variables on this reaction and found that a molar ratio of trioxane/glucose = 4 was the best. With a higher trioxane/glucose ratio, reactions become very non-selective, and with trioxane/glucose = 7-8VI was not formed at all. In 10 mL of saturated aqueous solution of AlCl<sub>3</sub> there are  $\sim 29.6$ mmol of AlCl<sub>3</sub> and  $\sim 479$  mmol of water, so the AlCl<sub>3</sub>/H<sub>2</sub>O ratio was ~ 16. A reaction performed with this ratio gave a negligible yield of lactone and is non-selective. Increasing the water/AlCl<sub>3</sub> ratio by addition of water gave the results shown in Table 4. The effect of the  $(\text{TEOF}/\text{AlCl}_3)$  ratio was also studied: when it was > 0.6 formation of VI was inhibited. For a ratio up to 0.2, formation of VI was negligible and the reaction was not selective. The best results were obtained for TEOF/AlCl<sub>3</sub> = 0.3-0.4 with other conditions summarised in Table 4. Application of other orthoesters such as triethyl orthoacetate, trimethyl orthoformate or acetate did not ameliorate either selectivity or the yield. These esters were studied in condiTable 4

Influence of water added to the reference system on yield of  $\ensuremath{\mathbf{VI}}$ 

Amount of added water (cm <sup>3</sup> ; mmol)	Molar ratio water/AlCl <sub>3</sub>	Yield of VI (%)
None	16.1	Negligible
1; 55.5	18.0	4.8
2; 111.1	19.9	3.7
3; 166.6	21.8	11.3
4; 222.2	23.7	2.0

tions as indicated in Table 4. Formation of VI was also observed in the systems which did not contain TEOF, but consisted of saturated aqueous solutions of  $AlCl_3$  diluted with variable proportions of water and (or) MeOH or EtOH. In such systems, yields were inferior to those indicated in Table 4; also the crude products always contained variable amounts of methyleneglucoses [7].

## 4. Discussion

In aqueous solutions of Al salts in the presence of MeOH or EtOH (ROH) many equilibria are possible. Examples are (An, an anion):

$$AlAn + H_2O \rightleftharpoons Al(H_2O)_6^{3+} + An(H_2O)_x \qquad (6)$$

 $\mathrm{Al}(\mathrm{H}_{2}\mathrm{O})_{6}^{3+} \rightleftharpoons \{(\mathrm{H}_{2}\mathrm{O})_{4}[\mathrm{Al}(\mathrm{H}_{2}\mathrm{O})_{2}]_{x}\mathrm{Al}(\mathrm{H}_{2}\mathrm{O})_{4}$ 

with or without An}<sup>*p*+</sup> (7)

 $Al(H_2O)_6^{3+} + ROH \rightleftharpoons Al(H_2O)_z(ROH)_w^{3+},$ z + w = 6 (8)

 $Al(H_2O)_z(ROH)_w^{3+}$ 

$$\rightleftharpoons \{(H_2O)_4[Al(ROH)_2]_kAl(H_2O)_4\}$$

with or without An}<sup>*p*+</sup>, etc.

 $Al(H_2O)_z(ROH)_w^{3+}$ 

 $\neq \{(\text{ROH})_a(\text{H}_2\text{O})_b[\text{Al}(\text{ROH})(\text{H}_2\text{O})]_c\text{Al}(\text{H}_2\text{O})_d$ 

# $(\text{ROH})_e$ with or without an An} (10)

Similiar equilibria involving ethers  $R_2O$  could also be suggested. All such compounds could be in equilibrium with glucose, therefore a description of the composition of the reaction solution and of the accurate mechanism of Glc transformation would be extremely difficult.



Fig. 2. Mechanism of Glc dehydration under influence of  $M^{n+}$  and of  $H^+$  according to Krupienskii [8].

Besides, as we always observed a certain acidity of these systems, protons may also be produced. Interaction of Glc with components of such systems and its transformations can be described by a scheme suggested by Krupienskii [8], Fig. 2.

This indicates that Glc reactions are perhaps accelerated by complexes of the type mentioned above and that reaction is 'resistant' to a wide variety of additives. When the 'standard' reaction time of 24 h was increased, the yield initially increased and then decreased with time. Such behaviour may indicate that a possible catalyst is deactivated by side reactions. At present it is not possible to say whether the Glc reaction is 'promoted' by a salt effect or catalysed by a genuine catalyst probably existing in small concentrations.

## References

(9)

- S.K. Tyrlik, D. Szerszeń, M. Olejnik, W. Danikiewicz, J. Mol. Catal. A: Chem., 106 (1996) 223.
- [2] S.K. Tyrlik, D. Szerszeń, S. Szymański, New J. Chem., 19 (1995) 1019.
- [3] R.D. Muller, G.N. Ficks, J. Org. Chem., 50 (1985) 2375.
- [4] J. Rothe, H. Zimmer, J. Org. Chem., 24 (1959) 586.
- [5] Z. Hori, Y. Ozaki, K. Nagao, S. Kin, *Tetrahedron Lett.*, 50 (1978) 5015.
- [6] (a) F. Basolo, R.G. Pearson, Mechanisms of Inorganic Reactions, Wiley, New York, 1967. (b) S. Kobayashi, S. Nagayama, T. Busujima, J. Am. Chem. Soc., 120 (1998) 8287.
- [7] W. Danikiewicz, M. Olejnik, J. Wójcik, S.K. Tyrlik, B. Nalewajko, J. Mol. Catal. A: Chem., 106 (1997) 223.
- [8] W.I. Krupienskii, Khim. Drev., 1 (1978) 72 (in Russian).