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MECHANISM OF LEVULINIC ACID FORMATION

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Summary: Based on the intermediates revealed by ^{13}C-NMR spectroscopy, the mechanism of levulinic acid (6) formation in acid catalysed hydrolysis of 2-hydroxymethylfurane (1) and 5-hydroxymethylfuran-2-carbaldehyde (14) is proposed.

Acid catalysed degradation of hexoses into levulinic acid (6) has been known for more than a century.[1] This reaction implies a puzzling transformation of the 6-hydroxymethyl group in hexoses into a methyl group of the final product. A plausible mechanism for the formation of the intermediary 5-hydroxymethyl-2-carbaldehyde (14) was advanced by Haworth and Jones[2]; compound 14 was quantitatively formed under anhydrous conditions.[3] An early mechanistic proposal[4] for conversion of 14 into levulinic acid (6) was later corrected[5,6] on the basis of the structures proposed (though not spectroscopically confirmed) for some isolated intermediates in the acid catalysed methanolysis of hydroxymethylfurane 1.

We revisited the mechanism of formation of 6 by monitoring the hydrolysis of 1, its 2-methyl congener 11, and 14 by ^{13}C-NMR spectroscopy. On dissolving 1 and 11 in dil. aq. hydrochloric acid, both compounds turned within 10-15 min. at ambient temperature into oils, that were separated and analysed by ^{13}C-NMR. Compound 1 gave a mixture of the unsaturated acetal 2 and its dehydration product 3, as well as a minor quantity of an unsaturated ketone derivative, presumably 5. Compound 11 transformed into a mixture of the hemiacetal 12 and the open-chain derivative 13 (Scheme 1 and 2, Table), which underwent complete polymerization above 70°C.

When the acidic solutions containing 2 and 3 were heated at the same temperature complete conversion into levulinic acid took place. Since no traces of neither a (enolic form of α-angelica lactone 4) nor 4 were observed, 4 can be eliminated as the intermediate. We found the latter compound to be stable, and completely in its carbonyl form under above conditions.[7]
Acid catalysed methanolysis of 1, under conditions described for preparative scale experiments[6], revealed accumulation of the open-chain intermediates 8 and 9 along with the final ester 10. No cyclic intermediates possessing a

Table 1. ^{13}C-NMR Chemical Shifts (in ppm) for the Compounds 1-16[a,b]

Compound	C_1	C_2	C_3	C_4	C_5	C_6
1	57.2 (t)	156.0 (s)	109.0 (d)	112.0 (d)	143.7 (d)	
2	56.8 (t)	153.3 (s)	110.3 (d)	27.3 (t)	107.1 (d)	
3	108.4 (t)	151.3	105.2	141.4 (d)	106.5 (d)	
4	13.9 (q)	153.2 (s)	99.5 (d)	34.1 (t)	170.0 (s)	
5	27.2	206.4	126.6	137.3	108[g]	
6	29.6 (q)	208.3 (s)	37.9 (t)	27.9 (t)	177.3 (s)	
7[f]	78.4	143.7	108.5	28.3	108.1	
8[f]	30.0	208[g]	39.9	66.5	108[g]	
9[f]	27.8	208[g]	128.3	135.1	110[g]	
10	29.5 (q)	206.9 (s)	38.0 (t)	28.0 (t)	173.4 (s)	51.6
11	11.9 (q)	151.1 (s)	104.6 (d)	109.5 (d)	139.9 (d)	
12	12.1 (q)	153.0 (s)	105.2 (d)	28.6 (t)	105.0 (d)	
13	27[g]	206.2[d]	35.2[c]	36.1[c]	205.5[d]	
14	58.3 (t)	153.6 (s)	113.0 (d)	128.4 (d)	163.4 (s)	181.2
15	65.2 (t)	113.4 (s)	26.9 (t)	125.4	153.5	192.2
16	26.8	207.5[e]	128.8	138.7	209.8[e]	184.6

a. Numbering of the C-atoms is exemplified on the formulas of the compounds 1, 6, 4, and 16 in the Schemes 1 and 2.

b. Multiplicities of the signals in the off resonance experiments are given in parenthesis.

c, d, e. Assignments may be interchanged.

f. The signals of the methoxy group carbons appear between 55-58 ppm.

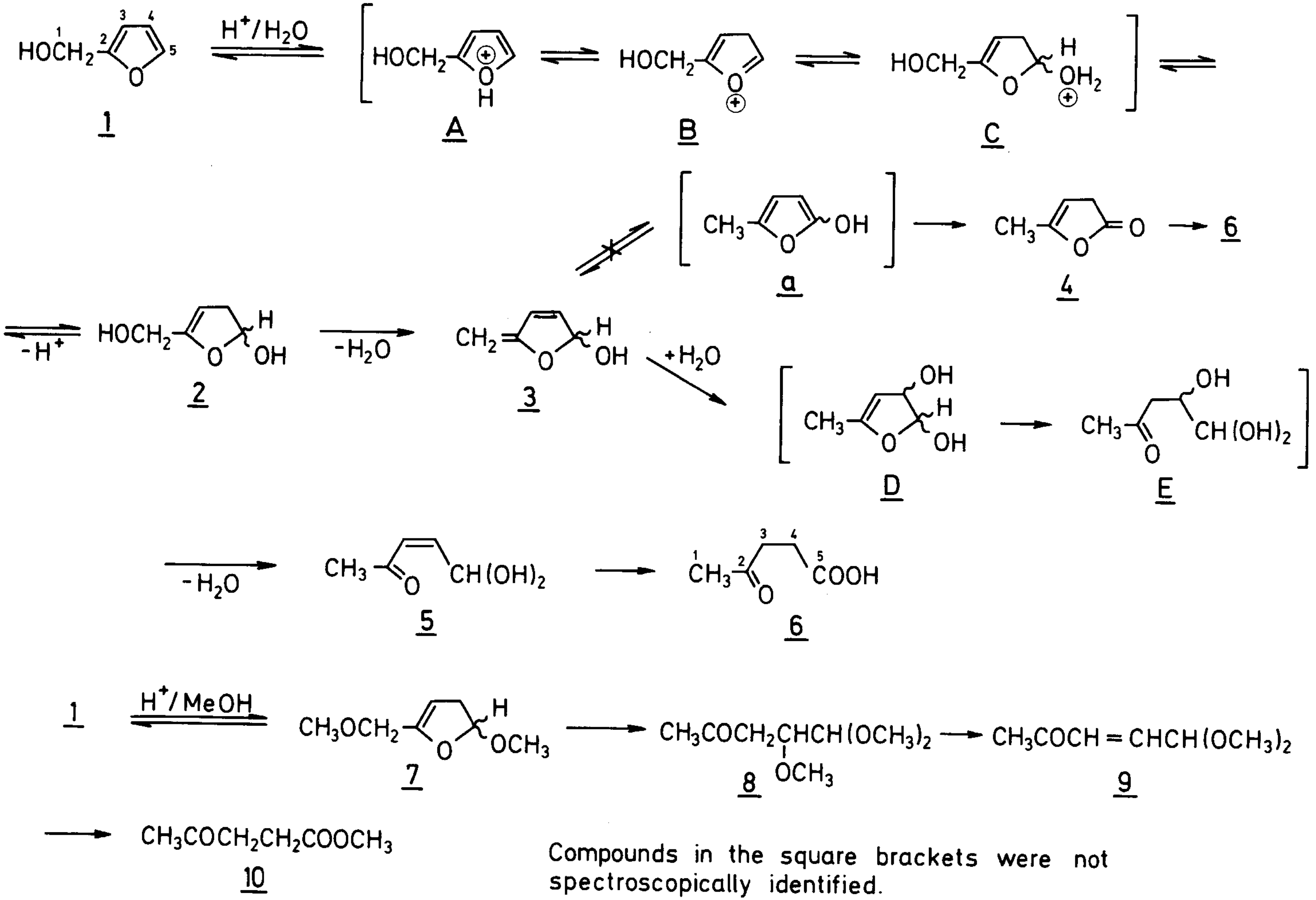
g. Assignments are ambiguous, more than one signal being present in the narrow region.

methyl group on the cyclic acetals were observed. This result indicates that the cyclic acetals isolated earlier[5,6] were formed during the distillation procedure.

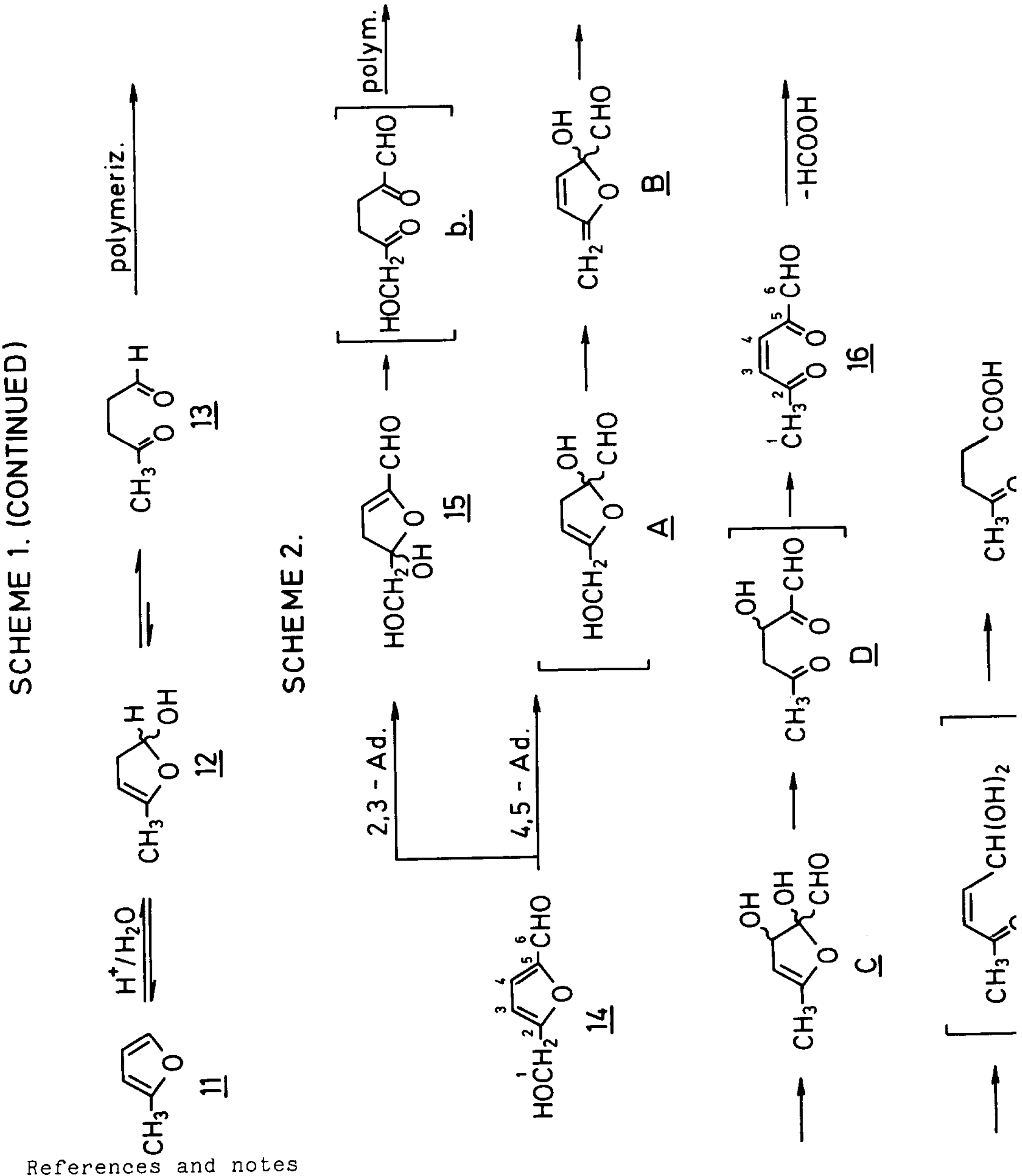
Finally, during the hydrolysis of 14 which required somewhat higher temperature (∼100°C), the formation of the two intermediates (15 and 16) was demonstrated (Scheme 2, Table). Obviously, the first one (15) resulted from the regioselective 2,3-addition of water on 14 and presumably polymerized via b. (similarly as 11 polymerized via 12 and 13). The "correct" 4,5-addition of water on 14 should give A which then undergoes a similar sequence of transformations as 2, including the decarboxylation step of the detectable intermediate 16.

Full account of the present work will appear in a forthcoming paper.

SCHEME 1.



Compounds in the square brackets were not spectroscopically identified.



SCHEME 1. (CONTINUED)

SCHEME 2.

References and notes

1. R. Grote and W. Tollens, Liebigs Ann. Chem. 175 (1876) 183; ibid. 206 (1880) 226.
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7. This finding contradicts the earlier one (based on UV-spectroscopic data) that 6 exists in the enolic form.[8]
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