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Note

Homogeneous catalytic hydrogenation of sugars

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This Note reports the first, rapid, homogeneous hydrogenation of sugars under mild conditions, in the presence of catalytic amounts of $RuHCl(PPh_3)_3$ [hydridochlorotris(triphenylphosphine)ruthenium(II)][1,2] and hydrogen chloride. The acid prevents decarbonylation of the aldehyde group and subsequent formation of the inactive complex[4] $Ru(H)(Cl)(CO)(PPh_3)_3$.

For example, the reaction of 0.5M α-D-glucose in *N,N*-dimethylacetamide (DMA) to give D-glucitol has a half-life of 20 min at 75° and 3 atm pressure of hydrogen in the presence of 10^{-2}M catalyst (Table I; experiment 8). Kinetic measurements in DMA showed that the rate is independent of hydrogen pressure above 3 atm and is first order in concentrations of substrate and catalyst (Table I). An activation energy (E_a) of 24 kcal was measured between 50 and 90°.

TABLE I

KINETIC DATA FOR THE HYDROGENATION OF α-D-GLUCOSE IN *N,N*-DIMETHYLACETAMIDE: EFFECT ON RATES OF CHANGE IN CONCENTRATIONS OF SUBSTRATE AND CATALYST, PRESSURE OF HYDROGEN, AND TEMPERATURE

Expt. no.	*Substrate conc. (M)*	*$RuCl_2(PPh_3)_3$ conc. (M)*	*Pressure of hydrogen in lb.in.$^{-2}$*	$t_{1/2}$ *(min)*	$k' \times 10^3$ *(min^{-1})*	*Temp. (°)*
1	0.75	0.01	50	20	0.35	75
2	0.5	0.01	50	20	0.35	75
3	0.25	0.01	50	20	0.35	75
4	0.125	0.01	50	20	0.35	75
5	0.5	0.015	50	14.5	0.48	75
6	0.5	0.005	50	42	0.17	75
7	0.5	0.01	10	27	0.26	75
8	0.5	0.01	30	20	0.35	75
9	0.5	0.01	50	225	0.031	50
10	0.5	0.01	50	76	0.092	60
11	0.5	0.01	50	8	0.84	90

TABLE II

EFFECT OF CHANGE IN SOLVENT ON RATE OF HYDROGENATION OF α-D-GLUCOSE[a]

Solvent	$t_{1/2}$ *(min)*
NMP[b]	100
$HCONMe_2$	65
Me_2NCOMe	20
$Me_2NCOMe:H_2O$ (25:1)	20
$Me_2NCOMe:AcOH$ (25:1)	20
$NMP:H_2O$ (25:1)	40
$NMP:MeOCH_2CH_2OH:H_2O$ (15:15:2)	30

[a]T, 75°; 0.01M in $RuCl_2(PPh_3)_3$, 0.5M in substrate, 50 lb.in^{-2} hydrogen. [b]1-Methyl-2-pyrrolidinone.

TABLE III

DEPENDENCE OF RATE ON THE Ru:PPh_3 RATIO AT 110° IN MIXED SOLVENT (15:15:2 1-METHYL-2-PYRROLIDINONE–2-METHOXYETHANOL–WATER)

Amount of catalyst	*Ratio of Ru:PPh_3*	*Amount of substrate (g)*	$t_{1/2}$
$RuCl_3$ (65 mg) + PPh_3 (69 mg)	1:1	1	150
$RuCl_3$ (65 mg) + PPh_3 (138 mg)	1:2	1	5
$RuCl_3$ (65 mg) + PPh_3 (207 mg)	1:3	1	<5
$RuCl_3$ (65 mg) + PPh_3 (610 mg)	1:9	1	8

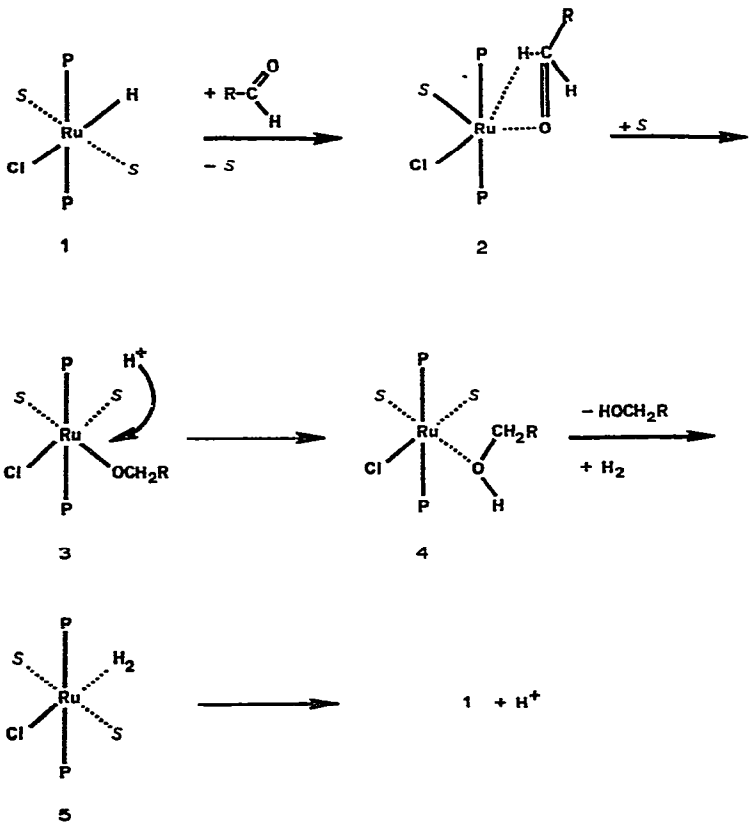
The rate of hydrogenation of α-D-glucose is solvent-dependent. The reaction half-life is 65 min in *N,N*-dimethylformamide (DMF), and 100 min in 1-methyl-2-pyrrolidinone (NMP) (Table II). The addition of water or alcohol does not increase the rate in DMF, but does so by a factor of about 3 in a 15:15:2 mixture of NMP, 2-methoxyethanol, and water. A ratio of at least 1:2 of ruthenium to triphenylphosphine is needed to obtain an active catalyst (Table III). A large excess of PPh_3 does not affect the rate, contrary to observation[2] in nonpolar solvents. On the other hand, $Ph_3PCH_2CH_2PPh_3$, added in stoichiometric amounts, strongly poisons the catalyst. This result is consistent with the assumption that, in the catalytically active species, the two bulky PPh_3 groups, as well as hydrogen and chlorine, are situated *trans* to each other[5]. The reaction of stoichiometric amounts of $RuHCl(PPh_3)_3$, formed *in situ*, with D-glucose at 80° yields a product containing 80% of D-glucitol.

When $RuHCl(PPh_3)_3$ was isolated[1], the half-life time of reaction was 45 min at 110° in the mixed solvent of NMP, 2-methoxyethanol, and water, considerably longer than the half-life period for $RuHCl(PPh_3)_3$ prepared *in situ*. In the former case, the deep red color of the mixture, caused by $RuHCl(PPh_3)_3$, changed to yellow within 10 min, indicating that the ruthenium complex had been carbonylated to the less-active[4] $RuHCl(CO)(PPh_3)_2$. This change was also shown by the i.r. absorption of the

isolated complex in the C=O region at 1920 cm^{-1}, and in the Ru–H region at 2005 cm^{-1}.

D-Fructose is hydrogenated at the same rate as D-glucose, giving 58% of D-mannitol and 42% of D-glucitol. This stereoselectivity of 16% disappeared when 2.5% of water was added to the solvent (DMA). The stereoselectivity did not change when (*S*)-(+)-(2-methylbutyl)diphenylphosphine was used as ligand, indicating that its asymmetric carbon atom is too far away from the reaction center to be influential.

Pentoses, 1,3-dihydroxy-2-propanone, and 1,3-dichloro-2-propanone react about 3 times as fast as α-D-glucose. Acetone is not hydrogenated by this system, indicating that the activation of carbonyl groups by electronegative substituents is necessary with this catalyst.



1 2 3 4 5

P = triphenylphosphine

We propose the following mechanism for this system: RCH=O denotes the acyclic tautomer of the substrate, and *S* the solvent. The rate-determining, hydrogen-transfer step (**1**→**2**) occurs via a four-centered transition state (**2**) in which hydrogen is transferred from the active species (**1**) to the carbonyl carbon atom. This is followed

by the formation of an intermediate, alkoxide complex (**3**). The ruthenium–oxygen bond is split in a fast, second, proton-transfer step forming an alcoholate (**4**). This proton arises from the heterolytic[8] H_2 splitting (**5**→**1**) or alternatively from a homolytic[1] splitting; we favor the former route. Dissociation of the product (**4**→**5**) and fast heterolytic activation of H_2 complete the catalytic cycle. A Ru–H bond and a proton are re-formed in this last step of the cycle.

EXPERIMENTAL

Materials. — All solvents used in this study were purified by distillation. *N,N*-Dimethylacetamide (DMA, Spectral Grade from Eastman Kodak) was used as received. $RuCl_3 \cdot nH_2O$ (containing 40% of ruthenium) was obtained from Engelhard Industries, Inc. All phosphines (Strem), sugars (Pfanstiehl), 1,3-dihydroxy-2-propanone, and 1,3-dichloro-2-propanone (Aldrich) were reagent grade and were used as obtained.

Catalyst. — $RuCl_2(PPh_3)_3$ was prepared from $RuCl_3 \cdot nH_2O$ and an excess of triphenylphosphine in boiling methanol[3]. $RuHCl(PPh_3)_3$ was prepared *in situ* from $RuCl_2(PPh_3)_3$ dissolved in 1-methyl-2-pyrrolidinone (NMP) or DMA under 1 atm pressure of hydrogen. The product was isolated by the procedure of Wilkinson *et al.*[1] or from DMA solution[2].

Procedure. — All kinetic experiments were conducted by the "pop bottle" technique[6]. The reactions were monitored at constant pressures (up to 50 lb. $in.^{-2}$ of hydrogen) and temperatures ($\pm 0.2°$) by removing samples with a syringe at various intervals. These samples were prepared for g.l.c. analysis by acetylation with acetic anhydride–pyridine[7] and separated on a 152-cm column of 5% of XE-60 on acid-washed Chromosorb W. The kinetic experiments were monitored either by an increase in the peak area for the alditol or by a decrease in the peak area for the starting sugar. Dehydration products never exceeded 1% of the total product. The catalyst could be precipitated with water and reused. The catalyst is sensitive to oxygen only in solution.

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