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EFFECT OF SODIUM HYDROXIDE IN THE PLATINUM-CATALYZED STEREOSELECTIVE HYDROGENATION OF ALKYL-SUBSTITUTED CYCLOHEXANONES

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The cis/trans ratio of the products was studied for the platinum catalyzed hydrogenation of 4-methyl-, 4-isopropyl-, and 4-t-butyl-cyclohexanone in the presence of bases. Contrary to both the von Auwers-Skita rule and the results for platinum oxide catalyst already reported, addition of sodium hydroxide promoted the formation of cis-isomer.

It has been shown that the cis/trans ratio of stereoisomers produced in the catalytic hydrogenation of alkyl-substituted cyclohexanones is influenced by reaction conditions such as the catalyst, additive, and solvent, as well as by the structure of the substrate (1). In most cases, the relationship between the stereochemistry and the additive has been explained by the empirical von Auwers-Skita rule (2) or improved Barton rule (3). Namely, formation of cis isomer (axial alcohol) predominates in the catalytic hydrogenation of hindered or unhindered cyclohexanones in acidic media, while for unhindered cyclohexanones the formation of trans isomer (equatorial alcohol) is favored in neutral or basic madia. Wicker (4) and Mitsui and co-workers (5) have also reported that the hydrogenation of unhindered alkyl-substituted cyclohexanones over platinum oxide (PtO_2) containing an alkaline substance gives the trans isomer preferentially.

However, we have found that in the presence of sodium hydroxide, 4-methylcyclohexanone (I), 4-isopropylcyclohexanone (II), and 4-tert-butylcyclohexanone (III) in ethanol, cyclohexane, or water as solvent are hydrogenated over a platinum catalyst at 30° and 80°C under a hydrogen pressure of 20 kg/cm^2 to products richer in cis isomer than in the absence of sodium hydroxide. Table 1 summarized the unexpected stereoselectivity in the presence of small amounts of sodium hydroxide on hydrogena-

Table 1. Effect of Bases on Stereoselectivity in the Hydrogenation of Unhindered Alkyl-Substituted Cyclohexanones over Platinum Catalysta)

Compound	React.Temp. (°C)	Additive (mmol)	Solventb)	Conversionc) (%/60min.)	Cis isomerc) (%)
I	80	-	E	61	32
I	80	NaOH, 4.0	E	76	52 (34)d),(26)e
II	80	-	E	57	32
II	80	NaOH, 4.0	E	71	64
III	30	-	E	25	22
III	30	NaOH, 4.0	E	23	68 (38)d),(35)f
III	80	-	E	18	35
III	80	-	E	42	28g)
III	80	NaOH, 0.0625	E	34	60
III	80	NaOH, 0.125	E	46	59
III	80	NaOH, 0.25	E	19	69
III	80	NaOH, 0.5	E	39	65
III	80	NaOH, 1.0	E	27	70
III	80	NaOH, 2.0	E	37	68
III	80	NaOH, 4.0	E	48	72
III	80	C_6H_5N, 0.5	E	21	31
III	80	C_6H_5N, 4.0	E	7	37
III	80	-	C	15	33
III	80	NaOH, 0.1	C	2	50
III	80	-	Wh)	11	40
III	80	NaOH, 0.5	Wh)	2	61
III	80	NaOH, 4.0	Wh)	2	73

a) The substrates ($1x10^{-2}$mol) were hydrogenated with 20 mg of the platinum catalyst in 10 ml of solvent and additive (0.5 ml of $NaOH_{aq.}$), in a 30 ml autoclave of the electromagnetically stirred type, at 30 and 80°C and a hydrogen pressure of 20 kg/cm^2.

b) E:Ethyl alcohol; C:Cyclohexane; W:Water.

C) The conversion and yield of cis isomer were found by gas chromatography.

d) Reaction at 30°C and 1 atm of hydrogen over PtO_2 containing alkaline substance (cf. Ref. 5).

e) Reaction at 20°C and 1 atm of hydrogen over PtO_2 (cf. Ref. 4).

f) M. Muhlstadt, R. Borsdorf, and F. J. Strber, Tetrahedron Letters, 1966, 1879.

g) PtO_2 catalyst.

h) A very small amount of hydrocarbon was observed in the reaction mixture when water was used as solvent.

tion of the unhindered cyclohexanones I, II, and III. In the hydrogenation of III, the cis isomer was obtained in 60% yield by the addition of only 6.25 X 10^{-2} mmol of sodium hydroxide per 20 mg of catalyst, whereas without addition of sodium hydroxide the yield was about 35%. Though the percentage of cis isomer increased slightly with increasing concentration of sodium hydroxide, it was unchanged between 1 and 4 mmol of the alkali. The platinum used in this study was prepared by hydrogen reduction of platinum hydroxide in water (20 ml) under a pressure of 80 kg/cm^2 of hydrogen at 80°C, followed by thorough washing with water (6). When platinum oxide was used, III gave substantially more of the trans isomer, as reported by the Muhlstadt and Mitsui groups (see Table 1).

Although the stereoselectivity is unconnected with the kind of 4-alkyl substituent in the absence of sodium hydroxide, the formation of cis isomer increased in the order methyl$<$i-propyl$\leq$t-butyl in the presence of sodium hydroxide. Thus, the presence of sodium hydroxide enhances the formation of cis isomer and the effect of sodium hydroxide was independent of the solvent used. The results obtained here is contrary to the rule proposed by von Auwers and Barton.

On the other hand, hydrogenation of III in the presence of pyridine gave a product rich in trans isomer, as in the case of additive-free solvent. Thus, the stereochemical effect of bases in the hydrogenation of unhindered cyclohexanones differs in inorganic and organic bases.

We suggest that the sodium hydroxide promotes the formation of cis isomer over platinum metal, and that the stereoselective function of the alkalis is different from that of the alkaline substance involved in platinum oxide catalyzed hydrogenation.

Further studies of the hydrogenation of unhindered and hindered alkyl-substituted cyclohexanones in the presence of alkalis and acids are in progress. Variation of the stereoselectivity by the additivies is expected to shed more light on the reaction mechanism.

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