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STEREOCHEMISTRY AND MECHANISM OF CATALYTIC HYDROGENATION OF SUBSTITUTED METHYLENECYCLOHEXANES

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Abstract—Substituted alkylmethylenecyclohexanes were hydrogenated over several transition metal catalysts. The ratios of the epimeric products were almost unity over freshly prepared Raney Ni but the axial Me counterparts were favoured over aged catalyst. The axial Me products were also preferred on Pt or Rh catalysts. Pd catalysed hydrogenation gave predominantly the equatorial Me isomers at high catalyst ratio, while the axial Me counterparts were favoured at the early stage of the reaction at a catalyst-substrate ratio of 1:20. The change of the ratio of epimeric products depending on the amount of catalyst is due to the rapid migration of *exo*-cyclic double bond to the inside of the cyclohexane ring at high catalyst ratio. The mechanism of hydrogenation is discussed in terms of the modified Horiuti-Polanyi mechanism.

We have previously pointed out that the stereochemistry of the hydrogenation of cyclopentanones and methylenecyclopentanes depends on the chemical and steric structure of the substrates, catalysts and reaction conditions.[1] In this paper the hydrogenation, using a variety of catalysts, of methylenecyclohexane derivatives which have a structure similar to the corresponding cyclohexanones is reported, and the stereochemistry and mechanism of the reaction are discussed in terms of the modified Horiuti-Polanyi mechanism.

RESULTS

Raney nickel. The hydrogenation of 4-*t*-butylmethylenecyclohexane over freshly prepared Raney Ni gave the product, the epimeric isomers ratio of which was close to the unity. If the Raney Ni was aged for 15 days, the amount of the *cis* product increased significantly. Detailed products analysis showed that during the course of the reaction, migration of the *exo*-cyclic double bond to the inside of the 6-membered ring occurred to form methylcyclohexenes (Table 1). 2-Methyl-, 3-methyl-, 4-methyl-, 4-ethyl- and 4-isopropylmethylenecyclohexane were also hydrogenated. The hydrogenation over freshly prepared Raney Ni gave a ratio of the *cis* to *trans* isomer of almost unity except in the case of 2-methylmethylenecyclohexane, the epimeric product ratio of which was 60% of the *cis* and 40% of the *trans* isomer. If the catalyst was aged for 15 days, the axial Me product which is the less stable of the two possible products was always favoured. In the presence of an alkaline substance a decreasing stereoselectivity was observed on the aged catalyst, but no appreciable effects were found if freshly prepared catalyst was used.

Platinum catalyst. The hydrogenation over Pt-black† gave preferably the axial products. Even if the PtO_2 contained a small amount of alkaline substance,[2] a similar isomer distribution of products was obtained. In the hydrogenation of 4-alkylmethylenecyclohexanes in acetic acid instead of ethanol, the stereoselectivity increased and more *cis* isomer was obtained.

Rhodium catalyst. The axial Me products (the *cis* isomer from 2- and 4-substituted and the *trans* from 3-substituted methylenecyclohexane) were always favoured.

Palladium catalyst. The hydrogenation proceeded readily at a Pd-carbon-substrate ratio of 1:4, substituted methylenecyclohexanes affording 23–26% of the corresponding axial Me products. A detailed study of the hydrogenation of 4-*t*-butylmethylenecyclohexane indicated that methylcyclohexenes were formed by the double bond migration and *cis* 1-*t*-butyl-4-methyl-cyclohexane was favoured at an early stage of the reaction. As hydrogenation progressed, the amount of the *trans* product gradually increased (Table 2). In benzene solvent 54% of the *cis* isomer was obtained after 7% reaction (Table 3). In order to study the ratio of the products at an early stage of the reaction, the hydrogenation was performed at a Pd-carbon-substrate ratio of 1:30. Double bond migration was not so rapid and the product composition showed that 57% of the *cis* isomer formed after

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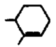
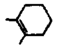
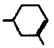
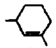
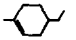
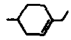
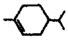
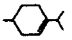
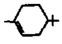
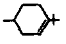
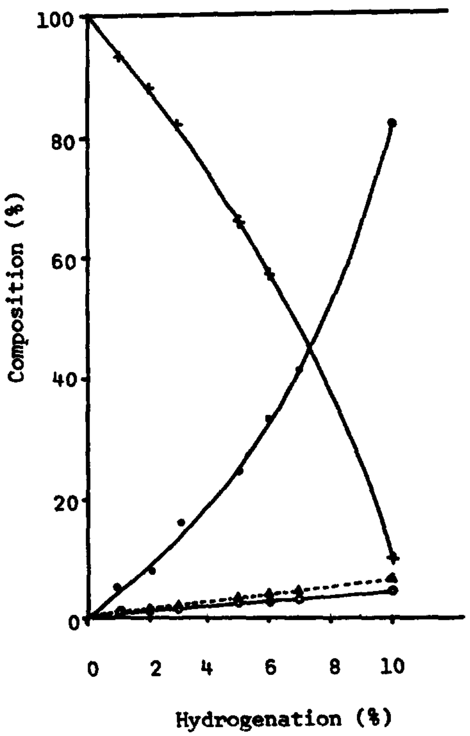
†Pt-black is the catalyst which is prepared by the hydrogen reduction of PtO_2 and is washed well with distilled water.

Table 1. Hydrogenation of substituted methylenecyclohexanes on Raney Ni

Methylene- cyclohexane	Catalyst[a]	Product composition (%)			
		Saturated product	Cyclohexene		
2-Me-					
	A	87	8	5	
	A+NaOH	87	5	4	b
	B	85	9	6	
3-Me-					
	A	86	6	2	c
	A+NaOH	84	4	2	d
	B	91	2	7	
4-Me-					
	A	96	4		
	A+NaOH	99	1		
	B	95	5		
	B+NaOH	96	4		
4-Et-					e
	A	96	4		
	A+NaOH	98	2		
	B	70	30		
	B+NaOH	74	26		
4-Iso-Pr-					
	A	94	6	0	
	A+NaOH	93	7	0	
	B	77	23	0	
	B+NaOH	97	3	t[f]	
4-*t*-Bu-					
	A	95	5	t	
	A+NaOH	72	22	6	
	B	95	3	2	
	B+NaOH	89	7	4	

[a] A, freshly prepared; B, aged for 15 days.
[b] Starting material, 4%.
[c] Starting material, 6%.
[d] Starting material, 10%.
[e] The gas chromatograph was unable to distinguish the two.
[f] Trace.

10% reaction. This composition did not change as long as *exo*-olefin was present in the reaction system (Fig 1). When 2-methylmethylenecyclohexane was hydrogenated in ethanol with Pd-carbon, the weight of which was 1/20 of that of the substrate, the apparent rate ratio of the hydrogenation and double bond migration was almost unity and the percent of the *cis* product became 85% at an early stage of the reaction (Table 4). These results indicated that the hydrogenation of



× 4-*t*-Butylmethylenecyclohexane
● 4-*t*-Butyl-1-methylcyclohexene
△ *cis* 1-*t*-Butyl-4-methylcyclohexane
○ *trans* 1-*t*-Butyl-4-methylcyclohexane

(Substrate, 150 mg; 5% Pd-carbon, 5 mg; Solvent, 5·0 ml)

Fig 1. Hydrogenation of 4-*t*-butylmethylenecyclohexane with Pd-carbon in ethanol.

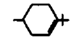
methylenecyclohexanes with Pd catalyst essentially gave the axial Me products as with Pt or Rh catalysts. The migration of the *exo*-cyclic double bond to the inside of the cyclohexane ring observed in the course of the reaction indicates that the hydrogenation of the *endo*-cyclic double bond also occurred and finally the isomer distribution became 24–26% of the axial Me compounds and 76–74% of the equatorial Me counterparts.

The ratios of the epimeric saturated products in the hydrogenation of alkyl-substituted methylenecyclohexanes are summarized in Table 5. Some of these results are in good agreement with those obtained by Siegel *et al.*[3,4,5] and Hussey *et al.*[6,7]

DISCUSSION

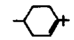
Since the product determining step of the Raney Ni hydrogenation of cyclohexenes is the adsorption of the substrate on the catalyst,[8] the product determining step of methylenecyclohexanes is considered to be the same reaction step. Since the adsorption state of methylenecyclohexane is from the less hindered equatorial side and the equatorial

Table 2. Hydrogenation of 4-*t*-butylmethylenecyclohexane with Pd-carbon in ethanol[a]

Hydrogenation (%)	Composition of resulting mixture (%) Starting material	Saturated product	Cyclohexene 		Saturated product (*cis* %)
16	1	16	82·5	0·5	32
28	0	28	70	2	27
46·5	0	46·5	50·5	3	26
66	0	66	29·5	4·5	24
76·5	0	76·5	19	4·5	24
83·5	0	83·5	13	3·5	24

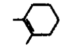
[a]Substrate, 40 μl; 5% Pd-carbon, 10 mg; Solvent, 5·0 ml.

Table 3. Hydrogenation of 4-*t*-butylmethylenecyclohexane with Pd-carbon in benzene[a]

Hydrogenation (%)	Composition of resulting mixture (%) Starting material	Saturated product	Cyclohexene 		Saturated product (*cis* %)
7·5	t[b]	7·5	92·5	0	54
23·5	0	23·5	74	2·5	32
31	0	31	64	5	29
49	0	49	41·5	9·5	29
62·5	0	62·5	24·5	13	28

[a]Substrate, 40 μl; 5% Pd-carbon, 10 mg; Solvent, 5·0 ml.
[b]Trace.

Table 4. Hydrogenation of 2-methylmethylenecyclohexane with Pd-carbon in ethanol[a]

Isomerization / Hydrogenation	Composition of resulting mixture (%) Starting material	Saturated product	Cyclohexene 		Saturated product (*cis* %)
1·3	96	1·7	1·15	1·15	85
22	54	2	24·5	19·5	53
25	8	3·5	47	41·5	51
15	1	6	46·5	46·5	45

[a]Substrate, 100 mg; 5% Pd-carbon, 5 mg; Solvent, 5·0 ml.

alkyl substituent in alkylmethylenecyclohexane is more stable than the alternative, the *cis* isomer is expected from 2- and 4-substituted methylenecyclohexane and the *trans* from 3-substituted methylenecyclohexane. In spite of the above expectation almost equal amounts of the *cis* and the *trans* products were obtained on hydrogenation with the freshly prepared Raney Ni except in the case of 2-methylmethylenecyclohexane whose substituent has relatively large catalyst hindrance.

Although the adsorption of the substrates on the catalyst was simply illustrated in the Horiuti-Polanyi mechanism,[9] we have imagined two types of adsorption state; one the π-type and the other the σ-type. The former is assumed to be the adsorption in which π-electrons of the double bond are donated to the vacant *d* orbitals of the metal with a bonding of the filled metal *d* orbitals to the antibonding π-orbitals of the olefin. Since the existence of many σ-bonded 3-membered ring transition metal complexes or those closely resembling that structure, e.g., Pt,[10] Rh,[11] Ir,[12] Ni[12] and Fe[13] complex, have been established by several workers, the π-type adsorption species may convert to the alter-

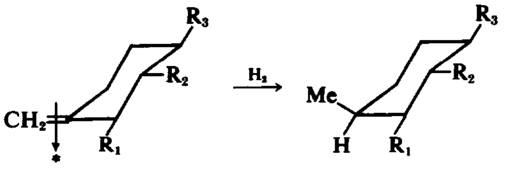
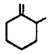
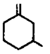
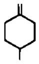
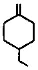
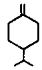
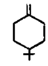


Table 5. Hydrogenation of substituted methylenecyclohexanes[a,b]

Substrate							
Catalyst	Solvent[c]	Product composition (axial methyl isomer %)					
Raney Ni (freshly prepared)	E	60	50	45	47	41	44
Raney Ni (freshly prepared) + NaOH[d]	E	59	33	44	44	50	47
Raney Ni (aged for 15 days)	E	63	82	78	68	70	81
Raney Ni (aged for 15 days) + NaOH	E	—	76	68	65	61	71
Pt-black	E	74	65	62	64	67	72
PtO_2	E	72(70)[g]	65(72)[h]	64(73)[h]	65	68(81)[i]	73(84)[h]
Pt-black	A	—	—	73	77	76	76
PtO_2	A	—	—	73	74	75	75
5% Rh-carbon	E	69	69	61	62	67	67
5% Pd-carbon[e]	E	25(26)[j]	23	26(29)[k]	26	25(21)[l]	25
5% Pd-carbon[f]	E	85[m]	—	—	—	—	—

[a] Figures in parentheses are the results reported in the literature.

[b] At an ordinary pressure and room temperature.

[c] E, ethanol; A, acetic acid.

[d] 10^{-4} mol.

[e] At a catalyst-substrate ratio of 1:4.

[f] At a catalyst-substrate ratio of 1:20.

[g] In acetic acid (ref. 3).

[h] In acetic acid (ref. 5); Sauvage, Baker and Hussey (ref. 7) report that 4-methylmethylenecyclohexane gives 75% *cis* and 4-*t*-butylmethylenecyclohexane gives 83% *cis*.

[i] In acetic acid (ref. 4).

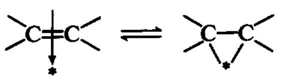
[j] Ref. 4.

[k] In acetic acid (ref. 6).

[l] Ref. 6; Sauvage, Baker and Hussey report that 4-isopropylmethylenecyclohexane gives 24% of *cis* in acetic acid.

[m] After 4% reaction. Details are shown in Table 4.

native adsorption species on the catalyst surface forming a σ-bonded 3-membered ring in which electrons from two σ-orbitals of the metal are paired with sp^3 electrons of carbon by the extreme back donation. These species can be illustrated as follows:



2 π-Type ⇌ 2′ σ-Type

SCHEME 1

We can assume some free energy of activation between these two adsorption states, so that the Horiuti-Polanyi mechanism will be modified as follows:

(i) If E_B and E_{-B} are nearly zero a resonance hybrid between these two adsorption species is assumed. (ii) If E_B and E_{-B} are sufficiently small compared to E_{-A} and E_C these two species are in equilibrium. (iii) If E_A or E_B is larger than those of any other elementary reaction step one of these two reaction steps will be product determining. It is not necessarly to imagine the presence of two types of adsorption species in two cases (i) and (ii).

Since in the case of Raney Ni hydrogenation the product determining step is the adsorption of the substrate on the catalyst, the third case can be applied. The following discussion explains the difference in the stereoselectivity between Raney Ni freshly prepared and that aged for a long time. The π-type adsorbed species was easily converted to the 3-membered σ-type adsorbed species on the freshly prepared Raney Ni and the hydrogenolysis of σ-type carbon-metal bond occurred subsequently with the adsorbed hydrogen. The decrease in the

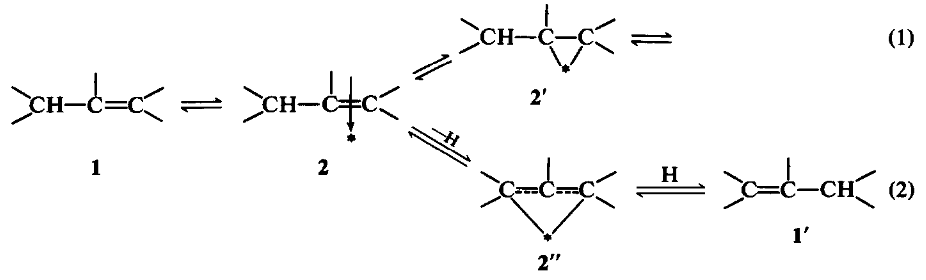
$$\text{Substrate} \underset{E_{-A}}{\overset{E_A}{\rightleftharpoons}} \begin{matrix}\pi\text{-Type}\\ \text{Adsorption}\\ \text{State}\end{matrix} \underset{E_{-B}}{\overset{E_B}{\rightleftharpoons}} \begin{matrix}\sigma\text{-Type}\\ \text{Adsorption}\\ \text{State}\end{matrix} \underset{E_{-C}}{\overset{E_C}{\rightleftharpoons}} \begin{matrix}\text{Half-}\\ \text{Hydrogenated}\\ \text{State}\end{matrix} \underset{E_{-D}}{\overset{E_D}{\rightleftharpoons}} \text{Product}$$

1 A 2 B 2′ C 3 D 4

SCHEME 2

catalytic activity of aged Raney Ni results in an increase of the free energy of activation of adsorption especially that from π-adsorbed species to σ-adsorbed one and this step may participate in the product distribution.

During the hydrogenation double bond migration to form *endo*-olefin occurred even on the freshly prepared Raney Ni but more *endo*-olefin seemed to be obtained on the aged catalyst. This may mean that the higher the free energy of activation of the reaction step B in the Scheme 2, the more double bond migration will occur *via* π-allylic adsorbed species as a by-pass route (Scheme 3).

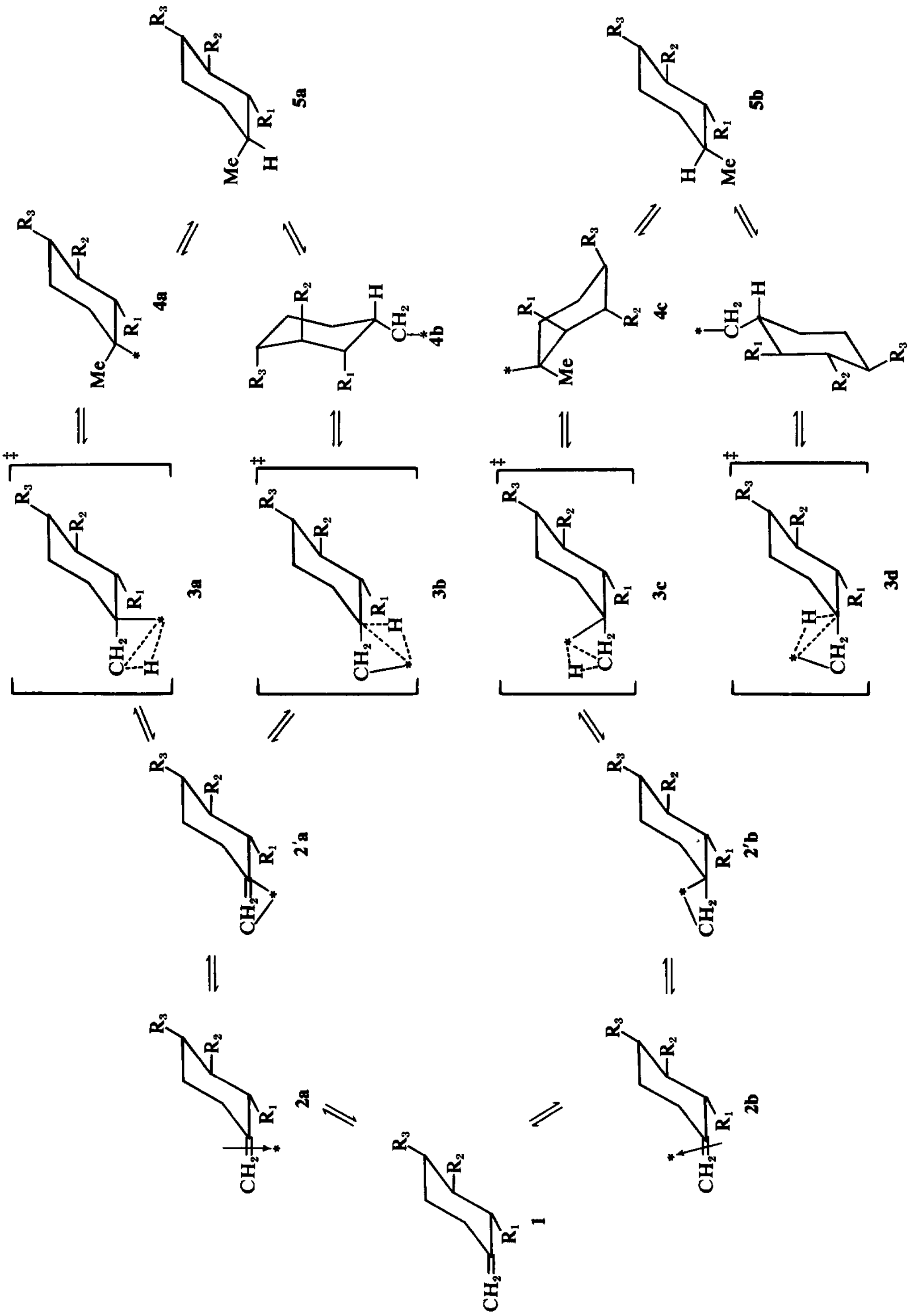


SCHEME 3

In the case of the Pt catalysed hydrogenation in ethanol, the axial Me compound was favoured. The addition of sodium hydroxide had no effect, differing from the hydrogenation of cyclohexanones.[14] This difference may be caused by the different character between the carbon-metal bond and the oxygen-metal bond in the half-hydrogenated state; the hydrogenolysis of the carbon-metal bond is easier than that of the oxygen-metal bond because of the relative stabilities between them. The hydrogenolysis of the oxygen-metal bond is restricted even by the presence of a small amount of alkaline substance, so that this reaction step may become product determining. As a consequence, the equilibrium of the two epimeric half-hydrogenated species is important and the equatorial alcohol becomes predominant. On the other hand, the hydrogenolysis of the carbon-metal bond may not be affected by the presence of the alkaline substance.

When the weight of Pd-carbon was 1/4 of the methylenecyclohexane, double bond migration as well as the hydrogenation occurred quite rapidly. The rate of double bond migration was nearly 10 times faster than hydrogenation at the early stage of the reaction and the equatorial Me product was preferably obtained. But when the ratio of the catalyst to weight of olefin was 1/20 or less, the axial Me product was favoured at the early stage of the hydrogenation. These results infer that the stereoselectivity of the product is primarily affected by the hydrogen concentration on the catalyst surface.

House *et al.* reported that the stereoselectivity of the hydrogenation is controlled by the amount of the Pd catalyst.[15] Augustine also reported that when a large amount of catalyst was used, the amount of hydrogen available is spread over a large surface area of catalyst, decreasing the probability of interaction with the reactant. This permits equilibriation between the *cis* and the *trans* half-hydrogenated states or the *cis* and the *trans* adsorbed species, thus resulting in decreased stereoselectivity of the reaction.[16] When a large reactant to catalyst ratio is employed the hydrogen transfer to the adsorbed species is relatively easy. Therefore, such a decreasing stereoselectivity was not observed. The probable reaction sequence is considered to be not only course I but course II in which π-allylic adsorbed intermediate (2″) is assumed. 2″ is converted to the isomeric olefin (1′). Since probability to take the reaction course II is more likely in a condition of low hydrogen availability, more equatorial Me compound, which was obtained by the hydrogenation of methylcyclohexene derivatives,[3] is supposed to form. Siegel and Smith indicated that the product determining step of Pd catalysed reaction was the hydrogen transfer from the catalyst surface to the half-hydrogenated intermediate in terms of the Horiuti-Polanyi mechanism.[3] They considered, therefore, that the isomerization occurs between two epimeric half-hydrogenated intermediates. From the study of the effect of the quantity of catalyst on the stereoselectivity of the reaction, the product determining step of the hydrogenation of *exo*-cyclic double bond with Pd catalyst is not the hydrogen transfer to the half-hydrogenated species but essentially the substrate adsorption on the catalyst as with Raney Ni or the hydrogen transfer to the adsorbed species as with the Pt or Rh catalysts. The rapid migration of the *exo*-cyclic double bond to the inside of the cyclohexane ring may be characteristic of the Pd metal[17] on which a π-allylic complex is easily formed and the double bond



SCHEME 4

migration occurs *via* π-allylic complex as well as the half-hydrogenated state. This assumption is supported by double bond migration on the Raney Ni catalyst where the product determining step of the hydrogenation is the adsorption of the substrate on the catalyst.

The hydrogenation of methylenecyclohexane derivatives over Pt, Rh and Pd where a large amount of hydrogen is available, the axial Me product is preferably formed.

In catalytic hydrogenation at first stage the substrate **1** is adsorbed on the catalyst surface to form π-type adsorption species, two types of which are expected; one, **2a** will give the axial Me compound and the other, **2b** will give the equatorial Me compound. The π-type adsorption species then subsequently converts to σ-type one, **2′a** and **2′b**, whose structures are assumed to be the 3-membered ring including a metal atom. The shape of these species is an olefin-like molecular geometry like an epoxide ring.[18] The adsorbed species, **2′a** and **2′b** are hydrogenolysed by the adsorbed hydrogen on the catalyst surface to form the half-hydrogenated species, **4a** ~ **4d**, through the transition states, **3a** ~ **3d**; the ring C atom C_1 ~ metal bond remains in **4a** and **4c** when terminal methylene carbon ~ metal bond is hydrogenolysed and terminal methylene C atom ~ metal bond remains in **4b** and **4d** when C_1 ~ metal bond is hydrogenolysed. The second hydrogen transfers to the half-hydrogenated species and the epimeric products, **5a** and **5b** will be obtained (Scheme 4).

It has been suggested that the LAH reduction of cyclohexanones[19] and the hydroboration of methylenecyclohexanes[20] have a reactant-like transition state. If it is possible to extend the above assumption to the hydrogenation, the transition state of the hydrogen transfer to the adsorbed species may be reactant-like and the relative stabilities of the two epimeric adsorbed species reflect on those of the transition states. As a consequence, the axial Me compound will be preferred to the equatorial on Pt or Rh catalysts as on Raney Ni on which the product determining step of the hydrogenation is considered to be the adsorption of the substrate on the catalyst. These results show the sharp contrast compared to the hydrogenation of methylenecyclopentane derivatives in which the stereoselectivity over Raney Ni is inversed relative to that over Pt.[1] This is because of the difference in the shape of the transition state that the hydrogen transfer to the adsorbed species is considered to be product-like in 5-membered ring compounds and reactant-like in 6-membered ring compounds.

EXPERIMENTAL

Materials. Alkylmethylenecyclohexanes were prepared by the method of Corey *et al.*[21] NaH, 2·0 g and 20 ml DMSO was heated for 1 hr at 70° in a N_2 atmosphere and then cooled in an ice bath, and a soln of 20 g methyltriphenylphosphonium bromide in 50 ml DMSO was added. The red soln was stirred for 15 min at room temp; then 5·0 g 2-methylcyclohexanone was added. The mixture was stirred for an additional hr and the product was distilled directly from this soln with DMSO at 40–80° (20 mm). The distillate was digested with pentane and was washed 3 times with water. Distillation gave 1·3 g (28%) 2-methylmethylenecyclohexane: b.p. 118–120°. 3-Methylmethylenecyclohexane was obtained by a similar procedure; yield 2·2 g (48%), b.p. 118°. Other olefins were prepared as follows; after the Wittig reaction was over, the mixture was poured into a large volume of ice water (400 ml) and the solid separated was filtered off. The soln was extracted 3 times with pentane. Distillation gave 4-methylmethylenecyclohexane, yield 3·3 g (65%), b.p. 40–43° (46 mm); 4-ethylmethylenecyclohexane, yield 3·5 g (71%), b.p. 55–57° (35 mm); 4-isopropylmethylenecyclohexane, yield 3·0 g (61%), b.p. 91–93° (66 mm); 4-*t*-butylmethylenecyclohexane, yield 3·1 g (63%), b.p. 98–102° (65 mm). Compounds which had earlier been prepared agreed in physical constants with those reported in the literature. All compounds were also checked by gas chromatography and NMR and IR spectra.

Catalytic hydrogenation. The following general procedure was used. A known amount of substrate and catalyst in the solvent was stirred with H_2 at an ordinary temp. After the reaction was over the catalyst was removed by the centrifugal method and the mixture was analysed by gas chromatography.

Gas chromatographic analyses. Hitachi F-6 and K-53 gas chromatograph equipped with flame ionization detector was used with Infortonics digital integrator. The products were analysed on a 45 m × 0·25 mm Goley column of PEG 400 at 40° (the hydrogenation products from 2-, 3- and 4-methylmethylenecyclohexane and from 4-ethylmethylenecyclohexane) or 90° (the hydrogenation products from 4-isopropyl- and 4-*t*-butylmethylenecyclohexane.

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