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A High Cis-Stereoselectivity in the Hydrogenation of 6-*t*-Butyltetrahydropyran-3-one and 2-*t*-Butyl-1,3-dioxan-5-one

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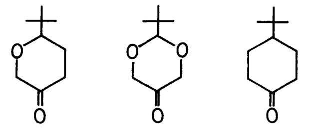
Stereochemistry in the hydrogenation of 4-*t*-butylcyclohexanone and the corresponding oxa- and dioxacyclohexanone was examined. A high cis selectivity was observed in the latter two compounds regardless of the catalyst metals used here. These results were explained in terms of intramolecular n_O–π_{CO} interaction, which was supported by ^{13}C NMR chemical shifts of the carbonyl carbons and CNDO/2 calculation.

The stereochemistry of hydrogenation of an unsaturated bond is frequently controlled by a heteroatom in a molecule. For instance, in allylic alcohols and ethers, hydrogens come into the unsaturated bond from the same side as the oxygen atom of the hydroxyl or the alkoxyl group. This is attributed to an interaction of the oxygen atom through the lone pair with the catalyst surface. This is called as the "directing effect" or "anchor effect".[1] However, in some cases, this effect does not necessarily appear. For methylene-1,3-dioxanes in which oxygen atoms and the double bond are placed at an appropriate position, the stereochemistry of the hydrogenation is such that the hydrogens add from the side opposite to the oxygen lone pair. This is interpreted in terms of intramolecular interaction between the nonbonding orbital of the oxygen and the olefinic π-orbital.[2]

Table 1. Hydrogenation[a] and Complex Metal Hydride Reduction[b] of 6-*t*-Butyltetrahydropyran-3-one (**1**), 2-*t*-Butyl-1,3-dioxan-5-one (**2**) and 4-*t*-Butylcyclohexanone (**3**)



Catalyst	Weight/mg	(**1**)	(**2**)	(**3**)
Raney Co	1000	80	91	56
Raney Ni	1000	89	97	71
Ru-black	20	90	91	77
Rh-black	20	94	100	—[c]
Pd-black	20	96[d]	100	—[e]
Os-black	20	66	67	55
Ir-black	20	70	88	58
Pt-black	20	81	90	32
$LiAlH_4$		8	7	7
$NaBH_4$		9	6	15

a) Values are cis% of alcohols produced when 50% of substrates were consumed. Substrate; 0.5 mmol, solvent (ethanol); 3 ml, ambient temperature under atmospheric pressure of hydrogen. b) Values are cis% of alcohols. Substrate 1 mmol, complex metal hydride; 0.25 mmol, solvent (ether with $LiAlH_4$ and 2-propanol with $NaBH_4$); 10 ml at 0 °C. c) Acetal, 98%. d) Acetal, 85%. e) Acetal and ethers, 100%.

In this paper, in order to investigate how the effect of an oxygen atom appears in the hydrogenation of cyclic ketones, 6-*t*-butyltetrahydropyran-3-one (**1**) and 2-*t*-butyl-1,3-dioxan-5-one (**2**) were hydrogenated in ethanol over several Group VIII transition metal catalysts and the stereochemistry was compared with that of 4-*t*-butylcyclohexanone (**3**). The results of the hydrogenation are tabulated in Table 1.

In the hydrogenation of **1** and **3**, Pd and Rh black catalysts behaved somewhat differently from other metal catalysts used in the present study. The main products of hydrogenation from **3** were saturated alcohol on Rh catalyst (Fig. 2) and saturated ether on Pd catalyst (Fig. 3) similar as the results obtained by Nishimura et al.[3] On the contrary, the saturated alcohol was the main products of hydrogenation from **1** on Pd catalyst under the same reaction conditions (Fig. 1).

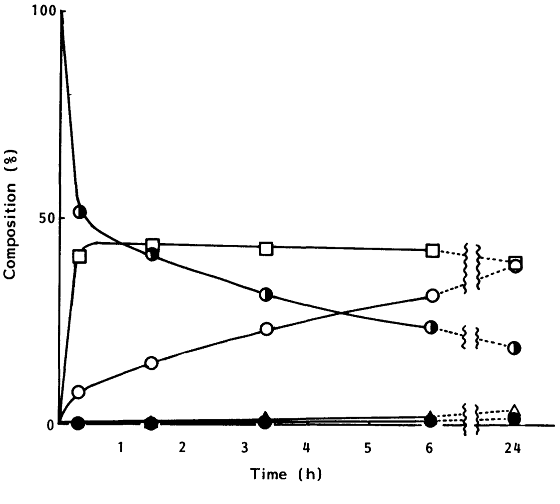


Fig. 1. Hydrogenation of 6-*t*-butyltetrahydropyran-3-one (**1**) over Pd-black catalyst: ◑; **2**, □; 6-*t*-butyltetrahydropyran-3-one diethyl acetal, △; *cis*-6-*t*-butyl-1-ethoxytetrahydropyran, ○; *cis*-6-*t*-butyltetrahydropyran-3-ol, ●; *trans*-6-*t*-butyltetrahydropyran-3-ol.

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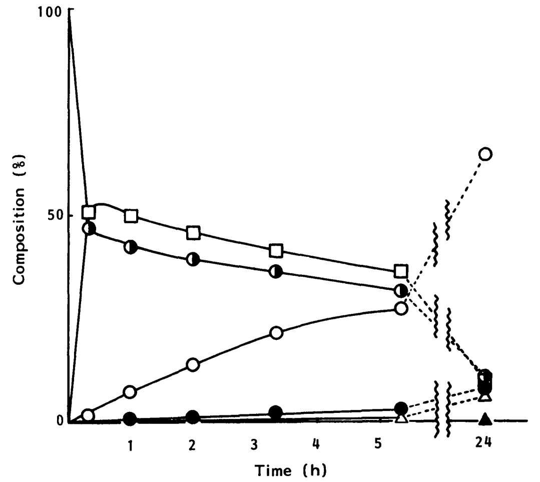


Fig. 2. Hydrogenation of 4-*t*-butylcyclohexanone (**3**) over Rh-black catalyst: ◑; **3**, □; 4-*t*-butylcyclohexanone diethyl acetal, △; *cis*-1-*t*-butyl-4-ethoxycyclohexane, ▲; *trans*-1-*t*-butyl-4-ethoxycyclohexane, ○; *cis*-4-*t*-butylcyclohexanol, ●; *trans*-4-*t*-butylcyclohexanol.

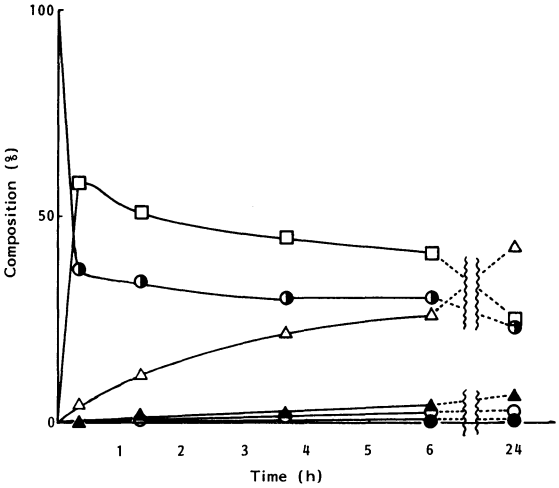
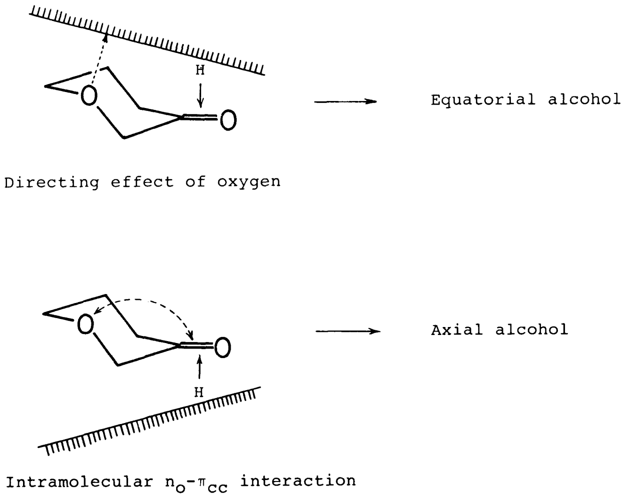


Fig. 3. Hydrogenation of 4-*t*-butylcyclohexanone (**3**) over Pd-black catalyst: ◑; **3**, □; 4-*t*-butylcyclohexanone diethyl acetal, △; *cis*-1-*t*-butyl-4-ethoxycyclohexane, ▲; *trans*-1-*t*-butyl-4-ethoxycyclohexane, ○; *cis*-4-*t*-butylcyclohexanol, ●; *trans*-4-*t*-butylcyclohexanol.

The stereochemistry of the hydrogenation of **3** over Group VIII transition metal black catalysts has been investigated in detail and was interpreted in terms of the Horiuti–Polanyi mechanism which is one of the most satisfactory theories.[4] The change in the product-controlling step depending on the catalysts coincides with a change in the ratio of the product. The Horiuti–Polanyi formulation of the mechanism of hydrogenation of unsaturated bonds may be represented by four elementary reactions, dissociation of hydrogen, adsorption of the substrate on the catalyst, first hydrogen transfer to the adsorbed species, and second hydrogen transfer to the half-hydrogenated intermediate. The proportion of the stereoisomeric products will depend upon which of the elementary reactions is a product controlling step, because the geometry and/or composition of the several possible transition states differ from one another. When the product controlling step is the adsorption of the substrate on the catalyst or the first hydrogen transfer from the catalyst to the adsorbed species, the stereochemistry of the reaction is controlled by the interaction between the substrate and the catalyst. On the other hand, when the product controlling step is the second hydrogen transfer from the catalyst to the half-hydrogenated species, the stereochemistry is controlled by the relative stabilities of the two epimeric half-hydrogenated species.



Scheme 1.

The hydrogenation of **3** gave an excess cis product (55—77%) except in the case of Pt black on which the more stable one of the two possible products was predominant. This indicates that the stereochemistry is controlled by the steric interaction between the substrate and the catalysts other than Pt black catalysts.[5] Significantly high cis stereoselectivity was observed in the hydrogenation of **1** and **2** which contain the oxygen atom/atoms in the *β*-position with respect to the carbonyl carbon. Since geometries of the 1,3-dioxane and the tetrahydropyran skeleton are similar to the cyclohexane ring, formation of the trans products (equatorial alcohol) is expected by the introduction of the oxygen atom/atoms (Scheme 1).[1] The reaction, however, proceeded selectively to give cis saturated products. Such a high cis selectivity in the oxygen-containing substrates has been found in the hydrogenation of 2-*t*-butyl-5-methylene-1,3-dioxane and 2-*t*-butyl-5-methylenetetrahydropyran.[2]

In order to obtain information on the structure of these molecules, the substrates were subjected to ^{13}C NMR spectroscopy. The chemical shifts were tabulated in Table 2. The chemical shifts of the

Table 2. Carbon-13 Chemical Shifts of 6-*t*-Butyltetrahydropyran-3-one (**1**), 2-*t*-Butyl-1,3-dioxan-5-one (**2**), 4-*t*-Butylcyclohexanone (**3**) and the Hydrogenation Products of **1** and **2** in $CDCl_3$ (δ)

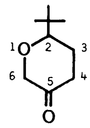
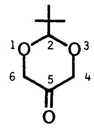
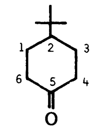
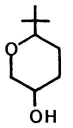
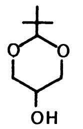
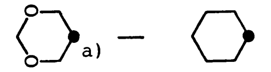
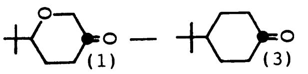
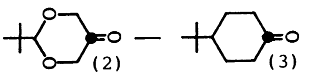
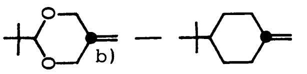
							
Cis	(**1**)	(**2**)	(**3**)	Cis	Trans	Cis	Trans
C-1	—	—	27.6	—	—	—	—
C-2	83.6	105.8	46.8	86.1	85.4	108.0	107.4
C-3	24.3	—	27.6	20.0	24.6	—	—
C-4	74.8	73.3	41.3	73.2	73.2	71.9	71.7
C-5	208.8	204.9	212.2	64.8	66.3	64.1	61.5
C-6	37.1	73.3	41.3	30.3	33.0	71.9	71.7
$(CH_3)_3\underline{C}$	34.3	35.3	32.5	34.3	33.8	35.0	29.6
$(\underline{C}H_3)_3C$	25.9	26.9	27.6	25.9	26.2	24.5	24.8

Table 3. Differences in β-Carbon Resonances between Oxygen Containing Heterocycles and the Corresponding Carbocyclic Compounds (ppm)

	β
	−1.1
	−1.0
	−3.4
	−7.3
	−5.2
	−10.0

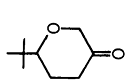
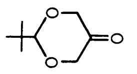
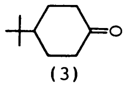
The chemical shifts were taken from a) J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press Inc., New York (1972). b) Ref. 2.

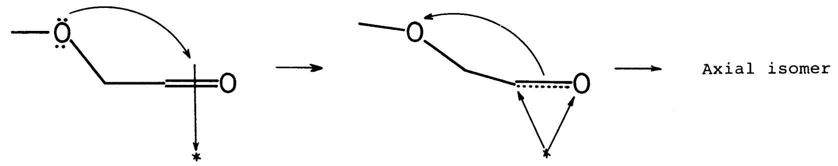
carbonyl carbons were compared with those of the carbo-cyclic carbonyl compounds. When the oxygen atom/atoms were introduced in the cyclohexane ring, the shift effect of the oxygen on the β carbon was found to be −1.1 ppm for tetrahydropyran and −1.0 for 1,3-dioxane. Much larger high field shifts of carbonyl carbons which are β to the oxygen atom were practically observed in **1** and **2** (−3.4 ppm for **1** and −7.3 ppm for **2**, respectively) as shown in Table 3. Experimentally it has been found that the effects of substituents on ^{13}C chemical shifts are largely additive. Such high field shifts of the carbonyl carbons in an unsaturated system compared to a saturated one by the introduction of an oxygen atom/atoms indicate electron delocalization of π-electrons similar to those with 2-*t*-butyl-5-methylene-1,3-dioxane[2] and 2-*t*-butyl-5-methylenetetrahydropyran (Table 3). This implies an interaction between the oxygen lone pair and the carbon–oxygen double bond.

The semi-empirical calculations of **1**, **2**, and **3** were performed to compare the electron density of the carbonyl group by the CNDO/2 method which was successful in predicting the electron density of the double bond. Total and π-electron densities of the carbonyl group in each of the most stable chair conformations were obtained and the difference in electron densities can be calculated between compounds containing oxygen and the corresponding cyclohexanone. The δD_T (difference in the total electron density) values for carbonyl carbon are +0.0211 for **1** and +0.0425 for **2**, and for carbonyl oxygen are −0.0157 for **1** and −0.0301 for **2** compared to **3**. The δD_π (difference in the π-electron density) values for carbonyl carbon are +0.0103 for **1** and +0.0193 for **2**, and for carbonyl oxygen are −0.0203 for **1** and −0.0375 for **2** compared to **3** (Table 4). A good correlation was found between the δD values of the electron density and the $\Delta\delta$ values of the ^{13}C NMR chemical shifts. The carbonyl carbon resonances moved to a higher field with an increase in the electron density. Such calculations also support the presence of intramolecular orbital interaction between the oxygen atom and the unsaturated bond.

A high cis (axial alcohol) selectivity observed in the hydrogenation of **1** and **2** implies significant control exerted by the oxygen participation on the transition state of the adsorption of the substrate. The non-bonded electrons of the oxygen can stabilize any incipient charge which might result from a π-donation of an unsaturated carbon–oxygen bond on the metal surface. The enhanced effective electronegativity of the oxygen, therefore, induces the back-donation from the metal surface to the π*-orbital of the carbonyl.

Table 4. Total and π-Electron Densities (D_T, D_π) of Carbonyl Group in 6-*t*-Butyltetrahydropyran-3-one (**1**), 2-*t*-Butyl-1,3-dioxan-5-one, and 4-*t*-Butylcyclohexanone (**3**) by CNDO/2 Calculation

		C=O				C=*O*		
 (1)	D_T	3.7673	δD_T	0.0211	D_T	6.2529	δD_T	−0.0157
	D_π	0.8288	δD_π	0.0103	D_π	1.2335	δD_π	−0.0203
 (2)	D_T	3.7887	δD_T	0.0425	D_T	6.2385	δ_T	−0.0301
	D_π	0.8378	δD_π	0.0193	D_π	1.2163	δD_π	−0.0375
 (3)	D_T	3.7462			D_T	6.2686		
	D_π	0.8185			D_π	1.2538		



Scheme 2.

This results in a predominant adsorption from the equatorial side of the molecule (Schemes 1 and 2). Similarly, anchimeric assistance by long-range oxygen participation has also been found in the solvolytic reaction of 9-oxabicyclo[4.2.1]nonan-2-yl brosylates[6] and in some electrophilic reactions of 8-oxabicyclo-[4.3.0]non-3-enes.[7]

Chemical reduction with $LiAlH_4$ and $NaBH_4$ was also examined, and its stereochemistry made a sharp contrast with that of the hydrogenation (Table 1). Stereoselective formation of equatorial alcohols from **1** and **2** was consistent with the reduction of 2-phenyl-1,3-dioxan-5-one which was reported by Jochims et al.[8]

Experimental

6-*t*-Butyltetrahydropyran-3-one (1). The compound, **1** was prepared following two methods. (I) According to the method of Ancelmi et al.[9] by using trimethylacetaldehyde and 3-buten-1-ol as starting materials. (II) The hydroboration of 2-*t*-butyl-5,6-dihydro-4*H*-pyran which was prepared by the method of Anderson and Sepp[10] followed by the oxidation with pyridinium chlorochromate; bp 92—94 °C (12 mmHg; 1 mmHg≈133.322 Pa); ^{1}H NMR ($CDCl_3$) δ=0.95 (9H, s), 1.6—3.4 (5H, m), 3.95 (1H, bs), 4.05 (1H, bs). Found: C, 68.92; H, 10.37%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

2-*t*-Butyl-1,3-dioxan-5-one (2).[11] 2-*t*-Butyl-5-hydroxymethyl-5-nitro-1,3-dioxane[12] was converted to **2** by the hydrogenation of nitro group followed by sodium periodate oxidation.

Metal Black Catalyst. The metal black catalysts were prepared from the corresponding metal chloride or metal oxides by the methods reported in the literature.[13,14]

Catalytic Hydrogenation. The substrate (0.5 mmol) was stirred under hydrogen atmosphere in 3 ml ethanol at room temperature over a weighed catalyst. The reaction was followed gas chromatographically by analyzing aliquots of the reaction mixture at appropriate time intervals. The cis products from **1** and **2** over Rh catalyst were subjected to ^{13}C NMR analysis (the epimeric purity was 94 and 100%, respectively).

Metal Hydride Reduction. To a solution of 0.25 mmol of complex metal hydride in ether ($LiAlH_4$) or in 2-propanol ($NaBH_4$), ketone (1 mmol) was added at 0 °C. After the reaction mixture had been stirred for 30 min, water was added and the solution was subjected to gas chromatography. The trans products from **1** and **2** on $LiAlH_4$ reduction were subjected to ^{13}C NMR analysis (the epimeric purity was 92 and 93%, respectively).

NMR and Gas Chromatographic Analyses. ^{1}H NMR spectra were obtained with a JEOL JNM-MH-100 spectrometer and ^{13}C NMR spectra were obtained with a JEOL JNM-FX-60-Q spectrometer. Gas chromatographic analyses were performed with Hitachi 164 with a Goley column of PEG 4000 (45 m×0.25 mm for the products from **1** and **3**, and 30 m×0.25 mm for the products from **2**) at 130 °C.

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