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Substituent Effects in the Hydrogenolysis of Benzyl Alcohol Derivatives Over Palladium

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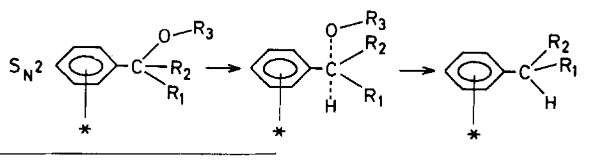
A kinetic study of substituent effects in the liquid-phase hydrogenolysis of benzyl oxygen compounds has been made using carbon-supported palladium as the catalyst. The reaction is zero order in substrate and is progressively inhibited by its product. Proton catalysis is essential for the hydrogenolysis of benzyl alcohols and alkyl benzyl ethers. For the hydrogenolysis of benzyl alcohols and 2-aryl-3-methyl-2-butanols the effects of substituents in the aromatic ring may be expressed in terms of a Hammett–Yukawa relationship with $\rho = -0.37$ and -1.43, respectively. α-Substituents retard the rate of hydrogenolysis of benzyl alcohol. The order of reactivity for different leaving groups is: OH, OAlkyl $\ll$ OAryl $<$ $^{+}$OHAlkyl $<$ $^{+}OH_2$, OAc $<$ $OCOCF_3$. It is concluded that the hydrogenolysis reaction involves hydride attack at the benzylic carbon displacing the leaving group as its anion. For primary alcohols an S_N2 mechanism is operative, whereas tertiary alcohols show S_N1 type character. The adsorbed state is discussed on the basis of deuterolysis experiments.

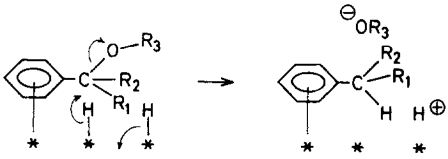
INTRODUCTION

In recent years a number of mechanistic studies concerning the stereochemistry of the catalytic hydrogenolysis of benzyl alcohol derivatives have been reported (*1–4*). However, only a few kinetic data of the hydrogenolysis reaction are available.

The hydrogenolysis over palladium was generally found to proceed with inversion of configuration. This has been explained (*3*) by an S_N2 type reaction mechanism, i.e., a one-step attack in which the reducing agent displaces the oxygen group from its attachment to the carbon atom.



However, we felt that the results also might be explained by an S_N1 type reaction mechanism, i.e., a preliminary cleavage of the carbon–oxygen bond to give a carbonium ion, which then reacts with the hydrogen on the surface of the catalyst.



For the latter mechanism high stereoselectivity is to be expected because (i) rotation around the C_{aryl}–C bond will be difficult due to steric interactions of R_1 and R_2 with the catalyst surface and (ii) exclusive hydrogen attack from the catalyst surface will result in inversion.

An important difference between these

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reaction mechanisms is the much greater electron demand of the reaction centre in the transition state of the S_N1 reaction. We, therefore, have examined the effect of substituents in the aromatic nucleus and of R_1, R_2, and R_3 on the rate of hydrogenolysis in order to obtain more information regarding the mechanism involved. In particular, the application of linear free energy relationships to ring-substituted benzyl alcohol derivatives was expected to be very valuable for the elucidation of the reaction mechanism. Furthermore, some deuterolysis experiments have been included.

EXPERIMENTAL

Materials

Palladium, 10% on carbon, was purchased from Johnson & Matthey Chemicals Ltd., London. Palladium, 1% on carbon, was prepared by hydrogenation of palladium chloride in water in the presence of carbon (*5*). Deuterized palladium, 10% on carbon, was prepared in a similar way using deuterium and deuterium oxide. Acetic acid (99.8%), trifluoroacetic acid (99.5%), and ethanol (99.5%) were Baker Analyzed Reagents. Acetic acid-*d* was prepared from acetic anhydride (Baker Analyzed Reagent) and deuterium oxide (Merck A.G.).

Most of the substrates were commercial samples or preparations made by standard procedures. The compounds were purified by repeated distillation or crystallization. Physical constants agreed with literature values.

The preparation of a number of 2-aryl-3-methyl-2-butanols has been recently described (*6*). In the same way 2-(4-isopropylphenyl)-3-methyl-2-butanol (bp 129–131°C/8 mm, mp 46–47°C), 2-(4-t-butylphenyl)-3-methyl-2-butanol (mp 82–83°C), and 2-(3-methoxyphenyl)-3-methyl-2-butanol (bp 72°C/0.1 mm, n_D^{25} 1.5200) were obtained. 1,1,1,3,3,3-Hexadeutero-2-phenyl-2-propanol (5.89 *d*) and 2-(pentadeuterophenyl)-2-propanol (4.91 *d*) were prepared as described for the undeuterated compound (*7*) using hexadeuteroacetone (Merck A.G.) and pentadeuterobromobenzene (Fluka A.G.), respectively.

Apparatus

The hydrogenolyses were carried out with magnetic stirring in a 25-ml reaction vessel provided with a thermostat jacket, injection rubber, gas-inlet and gas-outlet tubes, and a revolving tubular device for adding solids. The gas-inlet was connected to an automatic hydrogenation apparatus as described elsewhere (*8*). Experiments were performed at atmospheric pressure. Temperature was held constant within 0.1°C.

Procedure

The catalyst and 5 ml of solvent were placed in the reaction vessel. After evacuation, hydrogen was admitted and this procedure repeated twice. The mixture was stirred for 30 min and then reaction was started by introducing the substrate (1 mmole). Reactions were followed by measuring the uptake of hydrogen. No reduction of the aromatic ring was observed. Formulations were chosen to prevent diffusion limitation.

Deuterolyses were carried out in a similar way using deuterium and deuterized palladium, 10% on carbon. The products were analyzed by NMR and mass spectrometry.

KINETICS

In all cases the hydrogenolysis of the benzyl–oxygen bond over palladium was found to proceed at a progressively decreasing rate. However, the initial rate proved to be independent of the concentration of the substrate, as is shown for benzyl alcohol and 3-methyl-2-phenyl-2-butanol in Table 1.

Clearly, the hydrogenolysis is zero order in substrate and is inhibited by the hydrocarbon as it is formed in increasing amounts (*9*). We may describe this phenomenon by the following adsorption equilibrium of the alcohol (A) and its product (B):

$$A(\text{in solution}) + B(\text{adsorbed}) \rightleftarrows A(\text{adsorbed}) + B(\text{in solution})$$

and one may write an equilibrium constant $K = \theta_A C_B/\theta_B C_A$, in which θ_A and θ_B are the fractions of the active catalyst surface, covered by A and B, and C_A and C_B are the concentrations of A and B in solution. Both the zero-order kinetics with respect to A and the retarding influence of B indicate relative strong adsorption of A and B on the catalyst, so that we may write $\theta_A + \theta_B = 1$ and $r_t = r_0\theta_A$, in which r_0 and r_t are the rates of reaction at time zero and time t, respectively. Combining these equations gives

TABLE 1

EFFECT OF THE CONCENTRATION OF THE SUBSTRATE ON THE INITIAL RATE OF HYDROGENOLYSIS

Benzyl alcohol[a,b]		3-Methyl-2-phenyl-2-butanol[a,c]	
Concentration (mole liter^{-1})	Hydrogen uptake (ml min^{-1})	Concentration (mole liter^{-1})	Hydrogen uptake (ml min^{-1})
0.15	3.0	0.13	2.1
0.26	3.2	0.22	2.2
0.77	3.2	0.69	2.0

[a] Solvent 90% AcOH (5 ml); temperature 30°C; atmospheric H_2 pressure.

[b] Pd, 1% on carbon (300 mg).

[c] Pd, 10% on carbon (100 mg).

$$C_B/C_A = Kr_0/r_t - K, \text{ or}$$

$$V/(V_{\max} - V) = K\left(\frac{dV}{dt}\right)_0 \bigg/ \left(\frac{dV}{dt}\right)_t - K,$$

in which V and $V_{\max}$ are the volume and the maximum volume of hydrogen consumed. All hydrogenolysis reactions proved to obey this relation with K values varying from 0.7 to 2.4. Both K and $(dV/dt)_0$ can be derived from the plot of $V/(V_{\max} - V)$ vs $1/(dV/dt)_t$ as is shown in Fig. 1.

Furthermore, hydrogenolyses were found to be first order with respect to catalyst. Assuming reactions to be also first order with respect to hydrogen pressure, the re-

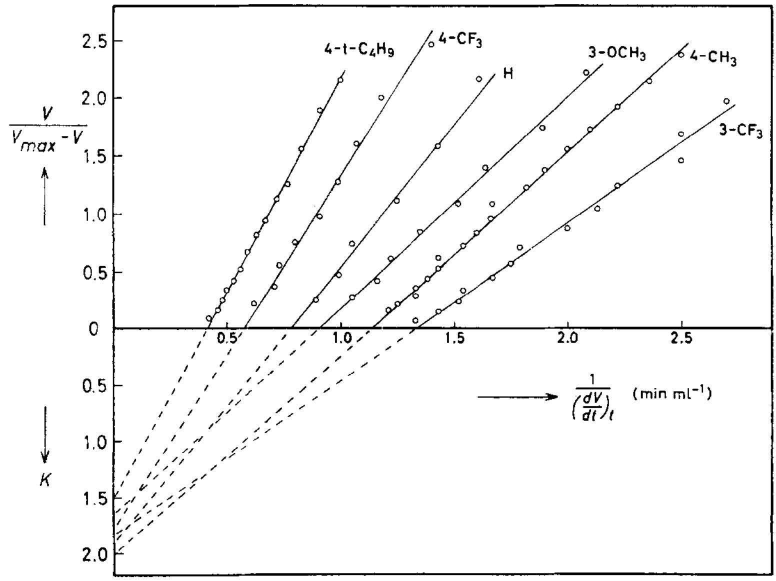


FIG. 1. Plots of $V/(V_{\max} - V)$ vs. $[1/(dV/dt)t]$ for a number of substituted benzyl alcohols.

action rate constant k(mole s^{-1} g catalyst^{-1}) was calculated from

$$k = 203 \times 10^{-6} \frac{p}{(p - p_s)\, Tw} \left(\frac{dV}{dt}\right)_0,$$

in which p is the pressure in mm, p_s is the vapour pressure of the solvent, w is the amount of catalyst in g, and $(dV/dt)_0$ is the uptake of hydrogen (ml min^{-1}) at p mm and T °K. It may be noted that a deviation from first-order kinetics with respect to the hydrogen pressure will affect the results only to a slight extent, since $p - p_s$ is fairly constant in all cases (cf. Table 4).

RESULTS

The results are given in Table 2 for a series of substituted benzyl alcohols and of 2-aryl-3-methyl-2-butanols. The data show that the hydrogenolysis is retarded by electron-withdrawal and accelerated by electron-donation by substituents. The effects are more pronounced for the tertiary alcohol. The K values show that the primary alcohol is more strongly adsorbed than its product, while the strength of adsorption of the tertiary alcohol and of its product is roughly the same.

The introduction of α-substituents retards the rate of hydrogenolysis of benzyl alcohol (Table 3). In the alkyl series the rate is strongly dependent on the size of the alkyl group. In some cases the retarding effect is caused by an unfavourable entropy of activation as compared with that of benzyl alcohol. The activation parameters were calculated from the Arrhenius plots, which are presented in Fig. 2.

Table 4 shows the results of the hydrogenolysis of various benzyl oxygen compounds in acid and in basic medium. The hydrogenolysis of benzyl alcohol and alkyl benzyl ethers is strongly inhibited by adding base. In contrast, the rate of reaction of aryl benzyl ethers and benzyl esters is hardly influenced. The reaction rate is strongly dependent on the nature of the leaving group OR_3, especially in basic medium.

The results of the deuterolysis of benzyl alcohol and 2-phenyl-2-propanol over

TABLE 2

HYDROGENOLYSIS OF SUBSTITUTED BENZYL ALCOHOLS[a] AND OF 2-ARYL-3-METHYL-2-BUTANOLS[b] OVER PALLADIUM

	Benzyl alcohols		2-Aryl-3-methyl-2-butanols	
Substituent	10^6k (mole s^{-1} g catalyst^{-1})	K^c	10^6k (mole s^{-1} g catalyst^{-1})	K^c
H	6.7	1.9	13.9	0.8
2-CH_3	4.4	1.9		
3-CH_3	7.1	2.1	12.6	0.7
4-CH_3	8.0	2.0	23.1	1.0
4-C_2H_5			22.4	0.7
4-i-C_3H_7			20.5	0.8
4-t-C_4H_9	7.1	1.5	10.4	0.7
2-NH_3^+	0.5	2.2		
3-OCH_3	5.8	1.7	6.3	1.0
4-OCH_3	12.4	1.9	100	0.8
4-OC_2H_5	10.0	2.0		
3-CF_3	4.4	1.8	2.45	1.2
4-CF_3	4.2	1.8		

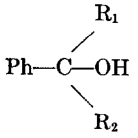
[a] Temperature 30°C; atmospheric H_2 pressure; solvent 90% AcOH; Pd, 1% on carbon.

[b] Idem, Pd, 10% on carbon.

[c] Adsorption equilibrium constant, see text.

TABLE 3

EFFECT OF α-SUBSTITUTION ON THE HYDROGENOLYSIS OF BENZYL ALCOHOLS OVER PALLADIUM[a]



R_1	R_2	10^6k (mole s^{-1} g catalyst^{-1})	K^c	ΔH (kcal mole^{-1})	$\Delta\Delta S^b$ (eu)
H	H	6.7	1.9	9.8	0.0
CH_3	H	2.61	1.0	9.2	−3.9
C_2H_5	H	1.22	1.0		
i-C_3H_7	H	0.080	0.8		
t-C_4H_9	H	<0.003			
CH_3	CH_3	1.14	1.2	7.9	−7.3
CH_3	i-C_3H_7	0.063	0.8		
CH_3	COOH	<0.002			
CH_3	$COOC_2H_5$	<0.002			
C_6H_5	H	0.78	1.7	8.0	−10.2
4-$CH_3OC_6H_4$	H	4.6	1.0		
C_6H_5	C_6H_5	1.92	0.8	12.3	+3.5

[a,c] See legend Table 2.

[b] Relative to benzyl alcohol.

palladium are collected in Table 5. Acetic acid-*d* was used as the solvent, since slow exchange occurs between the acidic proton of the solvent and deuterium (*10*). Isotopic dilution due to the rapid exchange of the alcoholic proton of the substrate and the acidic proton of the solvent will be less than 7%. In another experiment 1,1,1,3,3,3-hexadeutero-2-phenyl-2-propanol was subjected to deuterolysis in acetic acid-*d* resulting in 0.94 *d* at the α-position. Clearly, the rather low deuterium content at the α-position of cumene from the deuterolysis of 2-phenyl-2-propanol is due to the attack of exchanged β-hydrogen atoms. Under the same reaction conditions and times toluene and cumene showed only a small H/D exchange at the α-position (0.2 and 0.1 *d*, respectively). In all cases deuterium incorporation in the aromatic ring was not observed. This was further confirmed by hydrogenolysis of 2-(pentadeuterophenyl)-2-propanol (4.91 *d*) in acetic acid yielding 2,3,4,5,6-pentadeuterocumene with almost the same isotopic labeling (4.87 *d*).

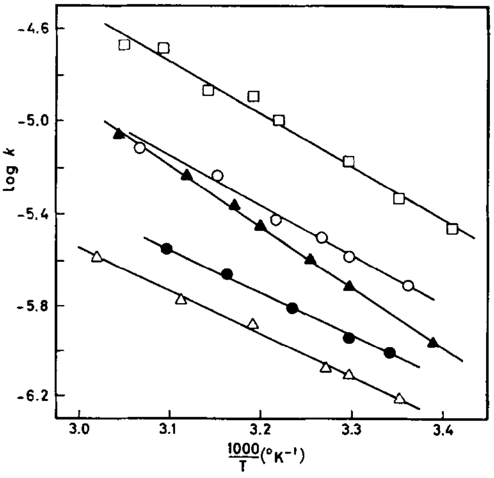


FIG. 2. Arrhenius plots for the hydrogenolysis of benzyl alcohol (□), 1-phenylethanol (○), 2-phenyl-2-propanol (●), diphenylcarbinol (△), and triphenylcarbinol (▲) over palladium.

DISCUSSION

Effect of the Medium and of the Leaving Group

Proton catalysis proved to be essential for the hydrogenolysis of benzyl alcohol and the alkyl benzyl ethers. Apparently,

TABLE 4
HYDROGENOLYSIS OF $C_6H_5CH_2OR_3$[a] IN ACID AND IN BASIC MEDIUM

		10^6k (mole s^{-1} g catalyst^{-1})			
R_3	Solvent: $p - p_s$ (mm)	CF_3COOH 737	90% AcOH 735	0.56 M NH_3 in 96% EtOH 673	K^c
H		27	6.7	0.00070[b]	1.9
CH_3		15	2.4	0.00098[b]	1.8
$CH_2COOC_2H_5$			0.38	0.00154[b]	1.8
$CH_2C_6H_5$			0.64	0.00037[b]	
C_6H_5			0.41	0.76	2.4
4-$CH_3OC_6H_4$		4.6	0.80	0.87	2.0
4-$CH_3OCOC_6H_4$			0.60	2.00	2.4
CH_3CO		24	7.9	10	2.2
CF_3CO			70	90	2.0

[a] Temperature 30°C; atmospheric H_2 pressure; Pd, 1% on carbon.
[b] From experiments over Pd, 10% on carbon, by comparison with benzyl phenyl ether.
[c] Adsorption equilibrium constant in 90% AcOH.

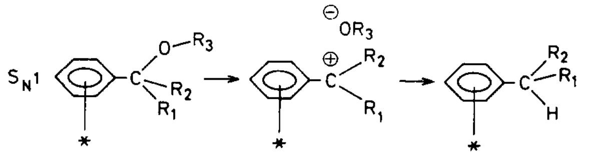
in this way a better leaving group is formed in acid medium, i.e., $^+OHR_3$ instead of OR_3. On the other hand, proton catalysis is of much less importance in the hydrogenolysis of aryl benzyl ethers and of benzyl esters.

Summarizing the results of Table 4, we may formulate the following order of reactivity: $OR_3 = OH$, OAlkyl $\ll$ OAryl $<$ $^+$OHAlkyl $<$ $^+OH_2$, OAc $<$ $OCOCF_3$. The ease of displacement clearly parallels the ability of the leaving group to bear a negative charge. This suggests a hydride displacement of the leaving group as its anion. McQuillin *et al.* (*4*) discarded such a mechanism because of the rapid hydrogenolysis of benzyl esters in apolar media. However, in apolar solvents the reaction may proceed in a more concerted fashion without the formation of the free anion:

TABLE 5
DEUTEROLYSIS OF BENZYL ALCOHOL AND 2-PHENYL-2-PROPANOL[a]
ISOTOPIC CONTENT (%) AT 60% CONVERSION

Compound:	Benzyl alcohol	Toluene	2-Phenyl-2-propanol	Cumene
d_0	84	25	100	16
d_1	12	54		47
d_2	4	17		13
d_3		4		9
d_4				7
d_5				4
d_6				3
d_7				1
$\bar{D}$	0.20	1.00	0.00	1.76
α-$\bar{D}$	0.20	1.00	0.00	0.69
β-$\bar{D}$			0.00	1.07

[a] Pd-D, 10% on carbon; temperature 30°C; atmospheric D_2 pressure; concentration of substrate 1.5 mole/liter; solvent AcOD (90% in D_2O).



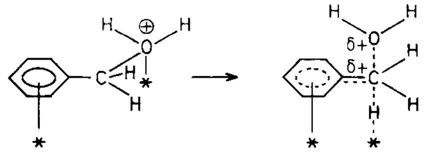
Effects of Substituents in the Aromatic Ring

The effects of substituents in the 3- and 4-position of the aromatic ring on the rate of hydrogenolysis of benzyl alcohols and of 2-aryl-3-methyl-2-butanols (Table 2) may be correlated in terms of the Hammett equation (*11*). However, since electron-donating 4-substituents were found to deviate, the Yukawa extension of the Hammett equation (*12*) was applied.

Computer calculations showed optimal correlation (correlation coefficient 0.98) with resonance parameters of 0.71 and 0.64 for the hydrogenolysis of benzyl alcohols and of 2-aryl-3-methyl-2-butanols, respectively. The corresponding ρ values proved to be —0.37 and —1.43, respectively, and were in excellent agreement with the ρ values derived from the Hammett relation without the 4-alkoxy and 4-alkyl substituents (viz., —0.38 and —1.40). The Hammett–Yukawa relations are shown in Fig. 3.

The negative ρ values and the high resonance parameters are consistent with an electron deficient transition state, which will be stabilized by electron donation by the aromatic system.

The small ρ value of —0.37 for substituted benzyl alcohols indicates that no highly charged structure will be involved during the reaction. This implies a direct displacement of the hydroxyl group by the hydride, i.e., and S_N2 type reaction mechanism. At first approximation, the transition state may be described by II, on the analogy of homogeneous displacement reactions (*14*).



I II

From the deuterolysis experiments we may conclude that the aromatic ring will be π-bonded on the catalyst, while at

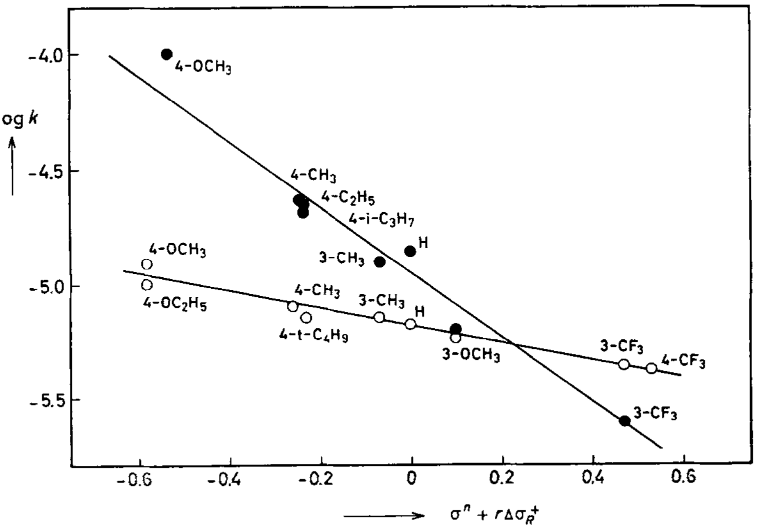


FIG. 3. Hammett–Yukawa relations for the hydrogenolysis of substituted benzyl alcohols (○, $r = 0.71$) and 2-aryl-3-methyl-2-butanols (●, $r = 0.64$) over palladium. σ^n and $\Delta\sigma_R^+$ values derived from references (*12, 13*).

least in part dissociative adsorption occurs at the benzylic carbon. The somewhat stronger adsorption of benzyl alcohol with respect to toluene points to a weak contribution of the oxygen to the adsorption of benzyl alcohol in the initial state (I). Such a geometry is rejected for the transition state in view of both the high resonance parameter and the inversion of configuration generally found for the hydrogenolysis over palladium (*1–4*).

The ρ value of -1.43 for the hydrogenolysis of the tertiary alcohol series implies a more substantial charge at the benzylic carbon in the transition state. However, a benzylic cation will not be involved, because then a ρ value of -3 to -4 had to be expected (*6*). Although the reaction will not proceed via a real S_N1 mechanism, we may ascertain that the C–O bond will be at least partly broken before the hydride attacks the benzylic carbon.

Finally, it may be noted that the observed substituent effects for the hydrogenolysis reaction are opposite to those found for the hydrogenation of acetophenones to the corresponding 1-arylethanols over palladium (*15*). In the latter case reaction occurs via an $sp^2 \rightarrow sp^3$ change in hybridization at the benzylic carbon. The present picture for the hydrogenolysis reaction involves an $sp^3 \rightarrow sp^2$ change, in accordance with the conclusion of McQuillin *et al.* (*4*).

Effects of Substituents at the Benzylic Carbon

Further support for a transition state with an electron deficient benzylic carbon in the hydrogenolysis reaction is found by the low reaction rate of atrolactic acid (Table 3: $R_1 = CH_3$ and $R_2 = COOH$) and of its ethyl ester, due to the electron-withdrawing carboxyl group. This is also shown by the rate-enhancing effect of the 4-methoxy group on the hydrogenolysis of diphenyl carbinol.

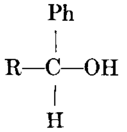
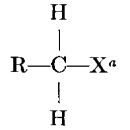
The series with $R_2 = H$ and R_1 varying from methyl to t-butyl in Table 3 shows a remarkable decrease in rate of reaction with increasing number of β-methyl groups. Comparison of this phenomenon with the effects of β-methyl groups on the rates of homogeneous S_N2 displacement reactions reflects a striking resemblance (Table 6).

At first sight, one would conclude that the hydrogenolysis will be an S_N2 type reaction. Nevertheless, the rate of reaction of 2-phenyl-2-propanol is much higher than has to be expected for an S_N2 reaction. Apparently, an S_N1-like mechanism becomes more important going from the primary to the tertiary alcohol as has been concluded before.

α-Alkyl substitution results mainly in a decrease in the entropy of activation. Probably, the freedom of motion in the transition state is decreased by the inter-

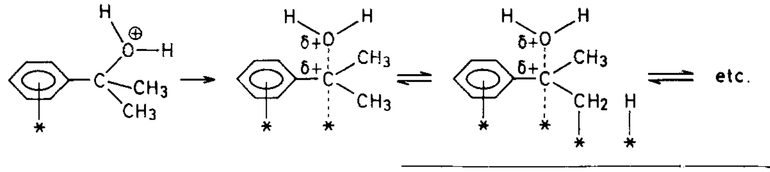
TABLE 6

EFFECT OF β-METHYL SUBSTITUTION ON THE RELATIVE RATES OF HYDROGENOLYSIS AND S_N2 DISPLACEMENT REACTIONS

R		CH_3	C_2H_5	i-C_3H_7	t-C_4H_9
Hydrogenolysis of	 $R-\overset{\displaystyle Ph}{\underset{\displaystyle H}{C}}-OH$	1.0	0.47	0.031	<0.0011
S_N2 displacement of	 $R-\overset{\displaystyle H}{\underset{\displaystyle H}{C}}-X^a$	1.0	0.4	0.03	0.00001

[a] Average relative rates of alkyl halides (*14*).

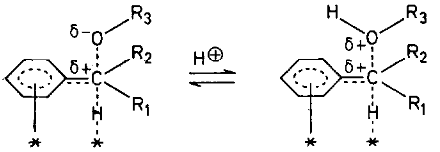
action of the alkyl substituents with the catalyst surface. This is supported by the high degree of exchange of the β-hydrogens upon deuterolysis of 2-phenyl-2-propanol. The very close approach of the α-methyl groups to the catalyst surface in the transition state will result in a contribution of dissociative adsorption of the alkyl group.



This formation of an α,β-diadsorbed species leads to a lower entropy of the transition state as compared to the initial state. The more substantial decrease of the entropy of activation for diphenyl carbinol will be due to the stronger adsorption of the molecule by its extension of the π-system with a second phenyl group. The reverse in activation parameters for triphenyl carbinol suggests that the reaction occurs via another pattern avoiding the unfavourable entropy of activation. Perhaps an S_Ni-type mechanism (*3*) is involved, in which just one phenyl group is adsorbed on the catalyst.

CONCLUSIONS

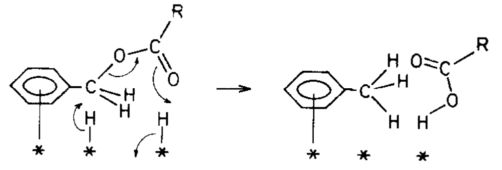
The transition state of hydrogenolysis may be generally described by



in which important overlap occurs between the electron deficient p-orbital of the benzylic carbon and the π-orbitals of the benzene ring.

For primary alcohols displacement occurs in a concerted fashion, i.e., an S_N2 type mechanism. Tertiary alcohols show a greater degree of bond-breaking than of bond-making at the transition state, i.e., somewhat S_N1-type character.

The leaving group is displaced as its anion by hydride attack from palladium at the benzylic carbon. Simultaneously, a neighbouring hydrogen atom adsorbed on the catalyst goes into solution as a proton.



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