to dissolve the green precipitate and the acetone was removed by evaporative distillation *in vacuo* in a 35° bath. The aqueous solution was washed with ether and saturated with sodium chloride and extracted repeatedly with methylene chloride. The extract was washed with saturated brine, dried with sodium sulfate, filtered through a pad of Norit, and evaporated to 190 mg (56%) of crude **20** as a colorless oil: ir spectrum (film), ketone C=O at 1698, lactam C=O at 1660 cm^{-1}.

***dl*-Deethylibogamine Lactam (21).**—A solution of 60 mg of **20**, 50 mg of phenylhydrazine hydrochloride, and 30 mg of anhydrous sodium acetate in 10 ml of water and 1 ml of 95% ethanol was stirred for 1 hr, chilled in an ice bath, and filtered to give 40 mg (46%) of the crude phenylhydrazene, **21**, as a tan powder: mp 141–182°; ir spectrum (Nujol), NH at 3285, C=O at 1658, C=N at 1650 cm^{-1}; uv spectrum, λ_{max} 273 mμ (ϵ 8200).

A mixture of 20 mg of **21** and 690 mg of polyphosphoric acid was stirred under nitrogen and heated to 135–140° for 30 min. The mixture was cooled and 10 g of ice was added. Filtration gave a gray powder which was recrystallized from ethanol with hot filtration through a pad of Norit to give 15 mg (80%) of **21**: mp 311–315° dec (lit.[4a] mp 313–315°); the ir spectrum of this material was identical with that of an authentic sample;[14] infrared spectrum, NH at 3180, C=O at 1645 cm^{-1} (Nujol); uv spectrum, λ_{max} 225 mμ (ϵ 31,100), 275 (6610, sh), 283 (7320), 291 (6370) [lit.[4a] λ_{max} 225 mμ (ϵ 31,600), 283 (6460), 291 (6030)]. Ibogamine lactam[20] had λ_{max} 223 mμ (ϵ 34,500), 283 (7600), and 291 (6650).

9-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepine-7-carboxylic Acid (23).—A solution of 2.13 g of **12** in 600 ml of *t*-butyl alcohol in a quartz reaction vessel was photolyzed under nitrogen with 2537-Å light for 66 hr at 50°. After evaporation of the alcohol, the residual yellow froth was dissolved in ether and filtered to remove 240 mg of high melting point powder. Evaporation of the ether gave a froth which was dissolved in 5 ml of acetonitrile and allowed to stand in the cold. Filtration gave 340 mg of crude **23**, mp 198–206°. Successive crops of the crude product were obtained from acetonitrile and from acetone to give a total of 710 mg (33%). Recrystallization from acetone gave pure **23** as yellow crystals: mp 224–225.5°; ir spectrum (Nujol), NH at 3270, acid OH at 2600, acid C=O at 1670, ketone C=O at 1632 cm^{-1}; uv spectrum, λ_{max} 230 mμ (ϵ 15,500, sh), 245 (21,150), 302 (15,130), 373 (4900); nmr spectrum, CH$_3$ at δ 2.63 (singlet, 3), aromatic CH at 7.75 (doublet, 1, J = 2 Hz) and at 8.43 (doublet, 1, J = 2 Hz), COOH at 9.43 (singlet, 1), NH at 2.95 (multiplet, 1). The last two protons were exchangeable with deuterium oxide.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.78; H, 6.77; N, 6.09.

Registry No.—**1b,** 19034-53-8; **4,** 19029-01-7; **5,** 19029-02-8; **7,** 19029-03-9; **8,** 19029-04-0; **9,** 19029-05-1; **10,** 19029-06-2; **11,** 19029-07-3; **12,** 19029-08-4; **13,** 19029-09-5; **14,** 19034-54-9; **16,** 19029-10-8; **17,** 19029-11-9; **18,** 19029-12-0; **21,** 19034-55-0; **22,** 19034-56-1; **23,** 19029-13-1.

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[20] M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Amer. Chem. Soc.*, **80**, 126 (1958).

Catalytic Hydrogenation of α,β-Unsaturated Ketones. IV.[1,2] The Effect of the Medium on Product Stereochemistry

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Received January 10, 1968

The hydrogenation of $\Delta^{1,9}$-octalone-2 has been run in a number of different solvents and under a variety of conditions. In neutral medium it has been found that the product stereochemistry was dependent not only on the polarity but also on the type of solvent used. In aprotic media it is proposed that a nonpolar solvent promotes a 1,2-adsorption process and a polar solvent favors one occurring through 1,4 adsorption. In hydroxylic media hydrogen bonding to the carbonyl group or hemiketal formation is thought to occur in solvents of high polarity thus forcing the reaction to take place by way of 1,2 adsorption while in less polar hydroxylic solvents such solvation is not important and the reaction proceeds through a 1,4-adsorption process. The product stereochemistry not only depends on the nature of the adsorption process but also on the "hydrogen availability" to the catalyst. In acidic media product stereochemistry is dependent on the strength of the acid, the mode of adsorption of the substrate and the "hydrogen availability" to the catalyst. These data are shown to be compatible with a protonation–hydride ion transfer mechanism or with a process involving hydrogenation of the enol but not with one in which the acid serves only to increase the polarity of the solvent. In basic solutions the product stereochemistry obtained was markedly dependent on the amount of base present, particularly in the very dilute region. These results are interpreted as indicating that the reaction proceeds by way of kinetically and thermodynamically controlled enolate ion formation. It is proposed that these enolates are very strongly adsorbed on the catalyst surface and that the product stereochemistry can best be explained by way of a hydride ion transfer from the catalyst followed by protonation of the adsorbed species from the solution.

While the mechanistic aspects of the hydrogenation of simple olefins has been the subject of extensive investigation for the past 30 years,[4] little work has been done on the mechanism of the hydrogenation of polarized double bonds such as carbonyl groups and the double bonds of α,β-unsaturated ketones. Those mechanistic proposals which have been made concerning these latter hydrogenations have been essentially attempts to rationalize the marked effect which the reaction medium has on the stereochemistry of the products obtained.

For instance, Brewster[5] has proposed a mechanism for the hydrogenation of substituted cyclohexanones to account for the influence which the reaction medium has on the product stereochemistry. In acid, initial protonation of the carbonyl oxygen to give a carbonium ion was proposed. This ion was then adsorbed on the

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[1] Paper III in this series: R. L. Augustine, *J. Org. Chem.*, **28**, 152 (1963).

[2] (a) Supported by Grant GM-09696 from the National Institutes of Health and Grant 2474 from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgement is made of this support. (b) Presented in part at the 152nd National Meeting of the American Chemical Society, Sept 1966, Abstracts, U-012; *Div. Pet. Chem. Preprints*, **11**, A-53 (1966).

[3] Taken in part from the Doctoral Dissertations submitted by D.C.M. and R.E.F. (1966) and the Master's Thesis submitted by C.S.S. (1963) to Seton Hall University in partial fulfillment of the requirements for the respective degrees.

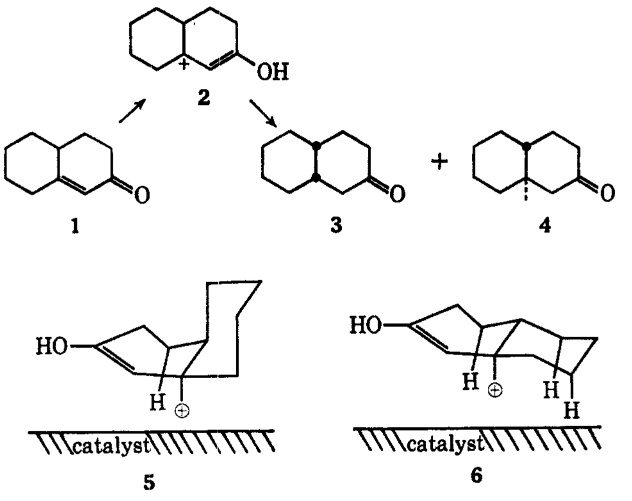
[4] (a) G. C. Bond, *Quart. Rev.* (London), **8**, 279 (1954); (b) B.M.W. Trapnell, *ibid.*, **8**, 404 (1954); (c) R. L. Burwell, Jr., *Chem. Rev.*, **57**, 895 (1957); (d) G. C. Bond and P. B. Wells, *Advan. Catal.*, **15**, 91 (1964); (e) S. Siegel, *ibid.*, **16**, 123 (1966).

[5] J. H. Brewster, *J. Amer. Chem. Soc.*, **76**, 6361 (1954).

catalyst surface in such a way as to have the bulky metal substituent in the equatorial conformation. Hydride ion transfer from the metal gave the axial alcohol. In neutral media it was suggested that the reaction proceeded by way of an initial adsorption of the carbonyl oxygen on the catalyst surface with subsequent transfer of a hydride ion from the catalyst to the oxygen. The adsorbed oxygen moiety, being bulky, assumed the equatorial configuration.

A mechanistic hypothesis similar to this acid rationale was put forth later to explain the predominant formation of the *cis*-β-decalone (**3**) on hydrogenation of $\Delta^{1,9}$-octalone-2 (**1**) in acid (Scheme I).[6] This proposal also involved a protonation of the carbonyl oxygen to give a carbonium ion, **2**. Adsorption of this species followed by hydride ion transfer completed the reaction which involved, in effect, a 1,4 addition of hydrogen to the conjugated system. According to this proposal the formation of **3** predominated since adsorption of **2** on the catalyst would be expected to be less hindered in the *cis* (**5**) rather than the *trans* form (**6**).

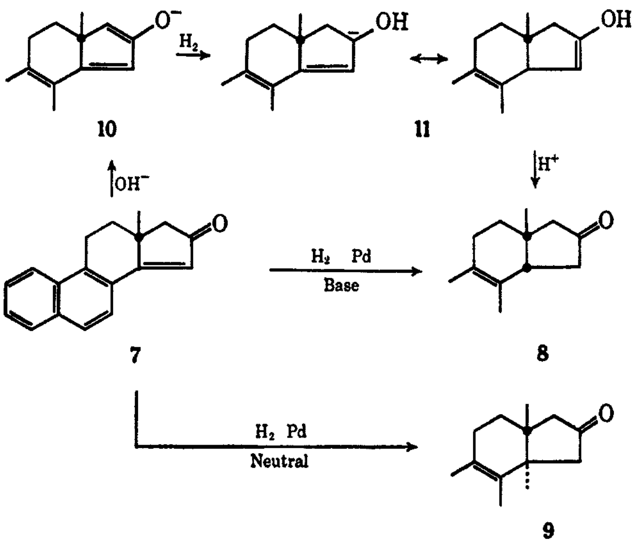
SCHEME I



On the other hand, Weidlich[7] proposed a 1,2 hydrogen addition to a double bond in acid and a 1,4 addition in base to account for the products observed on hydrogenation of 2,3-diphenylindenone. More recently, McQuillin[8] proposed that the reaction medium served to influence the extent of carbonyl participation in the adsorption step through polarization of the double bond with product stereochemistry determined by the extent of this polarization.

The hydrogenation of Δ^4-3-keto steroids and related materials in basic media leads to the almost exclusive formation of the *cis* A/B ring-fused product.[9] However, the effect of base on the hydrogenation of simpler α,β-unsaturated ketones is not as predictable with a wide range of *cis*/*trans* ratios observed on hydrogenation of a number of substituted β-octalones and similar compounds.[6] In about the only attempt to rationalize the effect of base in these reactions, Wilds[10] proposed an enolization sequence to account for the formation of the *cis* C/D ring-fused product, **8**, from the hydrogenation of the equilenone, **7**, in base. In contrast to this, the *trans* isomer, **9**, is obtained in neutral media. According to this proposal **7** was enolized to **10** which was then hydrogenated to **11** (Scheme II). Since isomerization of the double bond from the 14–15 to the 15–16 position in 17-keto steroids has been shown to give the *cis* C/D ring-fused product,[11] it was felt reasonable that protonation of **11** should also give the *cis* product.

SCHEME II



Each of these mechanistic proposals was based only on a limited amount of data; usually the products are obtained in two or three solvents. Therefore it was felt necessary to investigate more fully the hydrogenation of unsaturated ketones and to study the effect of variables such as pressure, temperature, and solvent on the reaction. In this way a more firm basis could be provided for the future development of a general mechanism for the reaction. This approach would also lend itself to a correlation with the data obtained on hydrogenation of unconjugated olefins and would, therefore, facilitate the extrapolation of the results so obtained to other systems thus increasing the synthetic utility of the reaction. It was, therefore, decided to use product stereochemistry data as a probe for the mechanistic study and to correlate these results with the hydrogen availability to the catalyst as has been done for the hydrogenation of unconjugated olefins.[4e]

Since the stereochemistry of the hydrogenation of octalone (**1**) has been shown to be greatly influenced by reaction conditions,[1,6] this material was chosen as the substrate to be used in this study. The reaction conditions were chosen so that a single variable could be changed systematically to determine what effect, if any, it would have on the reaction rate and product distribution.

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(6) (a) R. L. Augustine, *J. Org. Chem.*, **23**, 1853 (1958); (b) R. L. Augustine and A. D. Broom, *ibid.*, **25**, 802 (1960).

(7) H. A. Weidlich and M. Meyer-Delius, *Ber.*, **74**, 1195 (1941); H. A Weidlich, *Chem.*, **58**, 30 (1945).

(8) F. J. McQuillin, W. O. Ord, and P. L. Simpson, *J. Chem. Soc.*, 5996 (1963).

(9) H. J. E. Lowenthal, *Tetrahedron*, **6**, 269 (1959).

(10) A. L. Wilds, J. A. Johnson, Jr., and R. E. Sutton, *J. Amer. Chem. Soc.*, **72**, 5524 (1950).

(11) W. S. Johnson, J. W. Peterson, and C. D. Gutsche, *ibid.*, **69**, 2942 (1947).

Experimental Section

Materials.—The $\Delta^{1,9}$-octalone-2 was prepared as previously described.[12] All metal on charcoal catalysts were obtained from Engelhard Industries, Newark, N. J. The 5% palladium on barium sulfate was prepared using the procedure described by Mozingo.[13]

The acidic aqueous ethanol solutions were prepared by bubbling hydrogen chloride gas through the alcohol at 0° for 4 hr. The resulting solution was diluted with water; aliquots were diluted with additional aqueous alcohol. Water was added to each of these aliquots to bring all of the solutions to an equal water content. The acid concentrations were varied from 0.03 to 0.9 *N*. The water content was determined by the Karl Fisher procedure.[14] Each solution contained 109.5 ± 0.7 mg of water per ml of solution. The very weakly acidic solutions were prepared by diluting reagent grade acid with aqueous ethyl alcohol to give solutions with approximately equal water content. A similar procedure was used to prepare the perchloric acid solutions used.

The ethanolic potassium hydroxide solutions were prepared as follows. Aqueous base solutions were prepared in advance at approximately 20 times the desired final concentration. The same water volume was used in making up all concentrations. Immediately before each hydrogenation 1 ml of standardized base was titrated from a 10-ml microburet into 19 ml of absolute ethanol also measured by titration from a 50-ml buret.

The methanol, acetone, N,N-dimethylformamide, ethyl acetate, *t*-butyl alcohol, and isopropyl alcohol were purified by distillation. The dioxane was purified by distillation from lithium aluminum hydride. Eastman spectrograde cyclohexane was used without purification, as were reagent grade ethanol, *n*-hexane, carbon tetrachloride, acetonitrile, *n*-propyl alcohol, *n*-butyl alcohol, and *s*-butyl alcohol.

Apparatus.—The hydrogenation apparatus used was essentially that described previously[1] with a modification; a stopcock was added to the bottom of the gas buret which was used to titrate mercury from a raised leveling bulb into the buret to maintain a constant atmospheric pressure as indicated by the equalization of the two arms of the water manometer. The low hydrogen availability runs were stirred with a magnetic stirrer at a constant setting while the high hydrogen availability runs utilized a "Vibro-mix"[15] stirrer to agitate the mixture. For higher pressures a Parr low pressure hydrogenator reservoir was filled with hydrogen to the desired pressure and connected through a Wallace and Tiernan Model No. FA145 pressure gauge to the hydrogenation flask. A magnetic stirrer was used for agitation in these cases. The hydrogenation vessel[16] was a 50-ml round-bottomed flask surrounded by a jacket through which water at constant temperature could be pumped. The flask also had a thermometer well and a septum adapter. For those reactions utilizing the Vibro-mix stirrer a wide-mouth (40/50 joint) 50-ml round-bottomed flask was used.

Hydrogenation Procedures.—The standard reaction conditions used in this work were 20 ml of solvent, 100 mg of 5% palladium on charcoal presaturated with hydrogen, 250 μl of $\Delta^{1,9}$-octalone-2 (1.7 mmol), temperature 20 ± 0.5° under an atmosphere of hydrogen with the reaction mixture stirred with a magnetic stirrer placed at a constant setting. Changes of these variables were made systematically.

The magnetic stirring bar, catalyst and solvent were placed in the reaction flask and water from a constant-temperature water bath was circulated through the water jacket of the hydrogenation vessel. After the temperature of the solvent had reached a constant value, the apparatus, with the water manometer isolated from the system, was alternately evacuated and filled with hydrogen three times. The pressure of hydrogen was adjusted to atmospheric and the catalyst allowed to become completely saturated with hydrogen. The octalone was then injected into the reaction mixture through the septum using a syringe equipped with a Chaney adapter. During the entire reaction the pressure was kept constant by titrating mercury from a raised levelling bulb into the gas buret by manipulation of the stopcock at the bottom of the buret. The reaction was allowed to proceed until hydrogen uptake ceased after which time the catalyst was removed by filtration. Acidic or basic reaction mixtures were neutralized and the majority of the solvent was removed by distillation. The residue was poured into water and extracted thoroughly with ether. The extracts were washed with water, dried over magnesium sulfate, filtered and evaporated.

The product was analyzed by gas chromotography using an 8 ft stainless steel column containing 20% water soluble UCON on Chromosorb W. At a temperature of 195° with helium as the eluent gas at a flow rate of 65 cc/min the retention times for the *cis*- and *trans*-β-decalone were 13.6 and 10.9 min, respectively. Analysis for the β-naphthol was accomplished using a column of 10% SE-30 on Chromosorb P at 200°. β-Naphthol was identified by isolation and comparison with an authentic sample. Peak areas were measured using the peak height times peak width at half-height method.

Mixtures of known quantities of the *cis*- and *trans*-β-decalones were placed in the reaction flask with the catalyst and various acidic, basic, and neutral solvents and stirred under hydrogen for 3–24 hr. The decalones were isolated as described above. The resulting mixtures were analyzed and shown to be unchanged with respect to the proportion of the isomers.[17]

Subatmospheric pressures were obtained by drawing a vacuum on the system and filling the apparatus only partially with hydrogen. Reactions run under pressures greater than atmospheric were allowed to proceed for 30 min.

Determination of Hydrogen Solubility.—The amount of hydrogen required to presaturate the catalyst prior to the addition of the substrate to the reaction medium was taken as a measure of the hydrogen solubility in the reaction medium. In all cases the volume of solvent and the quantity of catalyst were kept constant.

Rate of Hydrogenation.—The rates of hydrogenation were determined as the volume of hydrogen adsorbed per minute at constant temperature as indicated by the amount of mercury titrated into the gas buret in order to maintain a constant atmospheric pressure inside the hydrogenator. The rate of hydrogen uptake was essentially constant throughout the reaction.

Error Analysis of Data.—The values reported for the product stereochemistry were accurate to at least ±1.4% based on a 95% confidence level. This was determined by duplicating both the hydrogenations and the vapor phase chromatographic analysis for a number of the runs. The error was calculated by basing the confidence interval on the range, the difference between the largest and smallest values in the sample.[18]

The values given for the rate of the hydrogen uptake in milliliters per minute for the hydrogenations performed under low hydrogen availability conditions were accurate to an average value of ±0.06 ml/min based on a 95% confidence level. This was determined by duplicating a number of the hydrogenations and calculating the confidence interval by basing it on the range.

Results

The hydrogenation of octalone was investigated in a large number of neutral solvents. At first there appeared to be no correlation between the dielectric constant of the solvent, the rate of reaction, or the amount of *cis*-decalone (**3**) obtained. However, when these solvents were separated into hydroxylic and nonhydroxylic categories, correlations were evident. The data obtained using these two groups of solvents are given in Tables I and II. With the aprotic solvents the more polar the solvent the greater the per cent *cis* isomer in the product. The rate of hydrogen uptake,

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(12) R. L. Augustine and J. A. Caputo, *Org. Syn.*, **45**, 80 (1965).

(13) R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p 685.

(14) J. Mitchell, Jr., and D. M. Smith, "Aquametry," Interscience Publishers, New York, N. Y., 1948.

(15) Vibromixer Model El, Chematec, Inc., Hoboken, N. J.

(16) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1965, p 20.

(17) The possible presence of other species such as desoxy compounds, alcohols and condensation products was investigated but no evidence for their presence was found by spectroscopic and gas chromatographic techniques.

(18) H. A. Laitenen, "Chemical Analysis," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 547.

TABLE I

RATE OF HYDROGENATION AND PRODUCT STEREOCHEMISTRY OF HYDROGENATIONS IN NEUTRAL APROTIC SOLVENTS

Solvent	Rate, ml/min	ε	% *cis*-β-decalone
n-Hexane	2.19	1.89	48
Cyclohexane	0.43	2.07	51
Dioxane	0.20	2.2	52
Diethyl ether	0.73	4.34	58
Ethyl acetate	0.71	6.0	57
Acetone	0.88	21.0	63
N,N-Dimethylformamide	0.25	38.0	79
Acetonitrile	0.87	37.5	30
Carbon tetrachloride	0.16	2.2	97

TABLE II

RATE OF HYDROGEN UPTAKE, PRODUCT STEREOCHEMISTRY, AND SOLUBILITY OF HYDROGEN IN NEUTRAL PROTIC SOLVENTS

Solvent	ε	% *cis*	Rate, ml/min	H_2 Solubility[a]
Methanol	33.6	41	2.30	10.2
Isopropyl alcohol	26.0	49	0.98	7.3
Ethanol	25.1	55	1.10	3.7
Propanol	21.8	68	0.33	1.7
s-butyl alcohol	18.7	70	0.48	2.3
Butanol	17.8	71	0.30	1.2
t-Butyl alcohol	10.9	91	0.75	3.5

[a] The total amount of hydrogen soluble in a mixture of 20 ml of solvent and 100 mg of catalyst.

however, was not associated with either solvent polarity or hydrogen solubility in the reaction medium.[19-21] Since it is possible for carbon tetrachloride to be at least slightly hydrogenolyzed to give hydrogen chloride[22] and acetonitrile hydrogenated to an amine[23] under the conditions used here, these solvents should not properly be considered neutral. As will be discussed later, when even a small amount of acid is present in anhydrous media, over 95% of the *cis* product is obtained. The presence of amines in the reaction mixture, however, leads to the formation of approximately 30% of the *cis*-decalone.

The data observed in protic solvents also showed a product stereochemistry dependence on solvent polarity. In these solvents, however, as the dielectric constant of the medium increased the per cent *cis* isomer obtained decreased as shown in Table II.[24] In these solvents it was found that the rate of hydrogen uptake was generally related to the hydrogen solubility in the reaction medium. In an extension of this hydroxylic solvent effect it was observed that as the quantity of water present in the reaction medium increased the amount of *cis* product formed decreased (Table III).

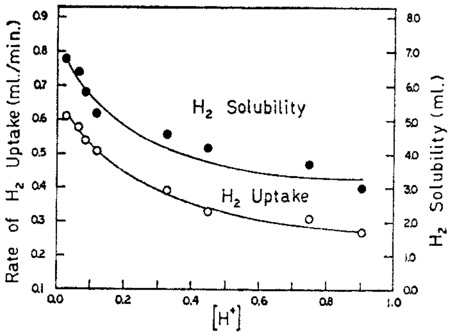

Figure 1.—Effect of acid concentration on the rate of hydrogen uptake (○) and hydrogen solubility in the reaction mixture (90% ethanol, ●).

TABLE III

EFFECT OF WATER ON THE RATE OF HYDROGEN UPTAKE AND STEREOCHEMISTRY OF THE PRODUCTS OBSERVED IN THE HYDROGENATION OF $\Delta^{1,9}$-OCTALONE-2

Solvent	% *cis*-β-decalone	Rate, ml/min
Absolute ethanol	55	1.10
90% ethanol	50	0.86
Water	43	0.25

The data concerning the effect of acid on both the rate of hydrogen uptake and hydrogen solubility in the reaction mixture is given in Figure 1. Since the rate of hydrogen uptake parallels the hydrogen solubility, it seems likely that under the standard reaction conditions (see Experimental Section) diffusion of hydrogen to the catalyst is rate determining and, thus, these reactions are run with a low availability of hydrogen at the catalyst surface. This conclusion was borne out by the fact that the apparent energies of activation for reactions run under these conditions ranged from 0.1 to 1.0 kcal/mol, considerably lower than what might be expected if diffusion of hydrogen were not limiting.[25] When the reactions were run using a Vibro-Mix[15] as a more efficient means of catalyst agitation the activation energies ranged from 5 to 7 kcal/mol, showing that a higher hydrogen concentration was available to the catalyst under these conditions. These higher hydrogen availability conditions were also obtained using hydrogen pressures of up to 4 atm. The activation energies were calculated from rate data obtained at several temperatures using the Arrhenius equation. Representative rate data for both low and high hydrogen availability reactions are listed in Table IV.

TABLE IV

EFFECT OF TEMPERATURE ON RATE OF HYDROGEN UPTAKE

	Hydrogen uptake, ml/min	
Temp, °C	Standard conditions	Vibro-Mix stirring[c]
0	0.46[a] (0.40)[b]	10.5
20	0.54[a] (0.47)[b]	44
40	0.62[a] (0.56)[b]	185

[a] $[H^+] = 0.0831\ N$. [b] $[H^+] = 0.5050\ N$. [c] $[H^+] = 0.0914\ N$.

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(19) It has been reported that there is no simple correlation between the solvent viscosity, its dielectric constant, or the solubility of hydrogen in the solvent on the rate of hydrogenation of crotonic acid[20a] or allyl alcohl[20b] over platinum. From the viscosity data available[21] there is no correlation in the present work between this parameter and either the product stereochemistry or rate of hydrogenation of octalone.

(20) (a) E. B. Maxted and V. Stone, *J. Chem. Soc.*, 454 (1938); (b) L. I. Antropov and T. I. Pochekaeva, *Zh. Fiz. Khim.*, **27**, 1710 (1953); *Chem. Abstr.*, **49**, 5943 (1955).

(21) "International Critical Tables," Vol. V, p 10; Vol. VII, p 211; McGraw-Hill Book Co., Inc., New York, N. Y., 1929.

(22) K. Isogai, *Nippon Kagaku Zasshi*, **80**, 1082 (1959); *Chem. Abstr.*, **55**, 4423 (1961).

(23) P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York, N. Y., 1967, p 209–211. See also ref 16, p 96.

(24) In a previous paper[6a] it was reported that in methanol more of the *cis* isomer was obtained than in ethanol. These apparently contradictory data are probably in error and are due to a relatively inefficient glpc separation of the isomers in this earlier work. A similar deviation from these original results was also found in paper III of this series.[1] In order to check these results the present hydrogenations were repeated a number of times by various workers with the results reported herein obtained each time.

(25) H. C. Yao and P. H. Emmett, *J. Amer. Chem. Soc.*, **81**, 4125 (1959).

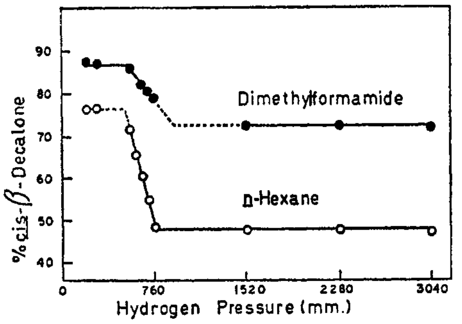

Figure 2.—Effect of pressure on product stereochemistry in aprotic solvents: ○, *n*-hexane; ●, dimethylformamide.

Figures 2 and 3 show the effect of hydrogen availability on product stereochemistry in aprotic and protic solvents, respectively.

The influence of acid concentration and hydrogen availability in acidic media on product distribution is shown in Figures 4 and 5. These data were obtained using aqueous ethanolic solutions of hydrochloric acid. However, the same results were found with perchloric acid solutions of the same concentrations. Since it was found that product stereochemistry was strongly dependent on the quantity of water in the reaction medium, the acid solutions all contained the same quantity of water.

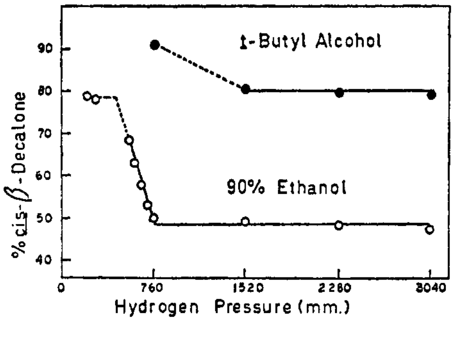

Figure 3.—Effect of pressure on product stereochemistry in protic solvents: ○, 90% ethanol; ●, *t*-butyl alcohol.

To ascertain briefly the effect of the type of catalyst and catalyst support on the stereochemistry of this hydrogenation, the series of reactions was repeated using palladium on barium sulfate instead of palladium on charcoal. The results obtained were essentially the same as those reported above. However, when platinum on charcoal was used the results shown in Figure 6 were obtained. The break points observed using a platinum catalyst correspond with those found using a palladium catalyst but the product distribution spread is much narrower indicating that less equilibration of the adsorbed species occurs over platinum than over palladium as is the case in olefin hydrogenation over these catalysts.[4e,26] The hydrogenation of $\Delta^{1,9}$-octalone-2 (**1**) was also investigated in a number of solutions containing varying concentrations of potassium hydroxide in aqueous ethanol. In agreement with previous work[27] little variation in the rate of hydrogen uptake was observed as the hydroxide ion concentration in the medium was changed over a wide range. It was also noted that, in contrast to the results found in acidic and neutral media, the presence of different quantities of water in the reaction medium had no effect on product stereochemistry. With the exception of hydrogenations run in extremely dilute base, diffusion of hydrogen through the medium, while influencing the reaction rate, had no effect on the *cis/trans* ratio of the products obtained. The product stereochemistry dependence on hydroxide ion concentration is shown in Figure 7.[28] It can be seen that there

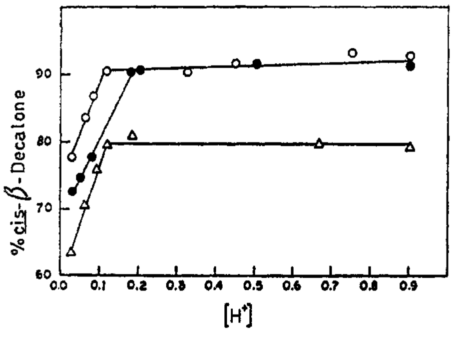

Figure 4.—Effect of acid concentration on product stereochemistry: ○, standard conditions; ●, double octalone concentration; △, Vibro-Mix stirring.

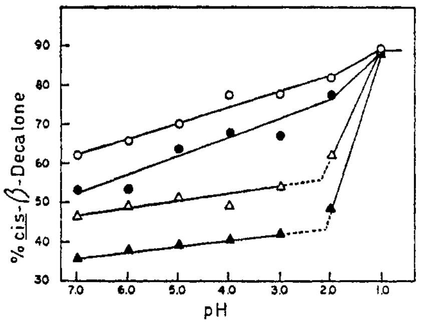

Figure 5.—Effect of weak acid and weight of catalyst on product stereochemistry: ○, 500 mg of 5% Pd/C; ●, 250 mg; △, 50 mg; ▲, 25 mg.

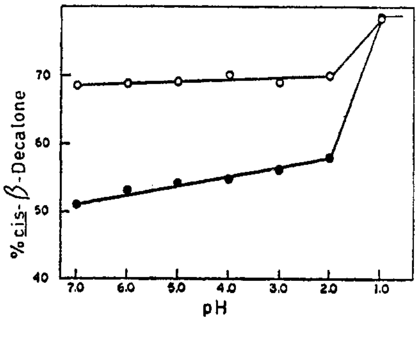

Figure 6.—Effect of weak acid on product stereochemistry using a platinum catalyst: ○, 250 mg of 5% Pt/C; ●, 50 mg.

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(26) S. Siegel and G. V. Smith, *J. Amer. Chem. Soc.*, **82**, 6082, 6087 (1960).

(27) F. J. McQuillin and W. O. Ord, *J. Chem. Soc.*, 2902 (1959).

(28) The product distribution at the neutral point is somewhat different from that shown in Figures 4 and 5. This difference is due to the fact that 10% Pd/C was used with the basic study but 5% Pd/C was used in the other work. The increase in the amount of *cis* isomer obtained is as expected from an increase in the quantity of catalyst used in a neutral medium. There are also some deviations from results reported earlier[6] which are due to the use of more efficient glpc analysis conditions in the present case.

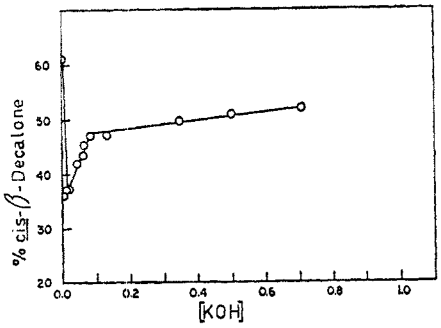


Figure 7.—Effect of base on product stereochemistry in the hydrogenation of $\Delta^{1,9}$-octalone-2.

are three distinct portions to this curve. Figure 8 shows an expansion of the very weakly basic portions of this curve.

It was found that the position of the minimum break point in these curves could be varied by changing the quantity of catalyst used in the reaction. Figure 9 illustrates the relationship found between the hydroxide ion concentration at the minimum point and the quantity of palladium metal present in the catalyst. These data were obtained by the use of varying percentages of palladium on charcoal as well as different weights of 10% palladium on charcoal or 5% barium sulfate. Each point on the graph represents several runs each involving different catalyst composition but in which the weight of palladium present was kept constant from run to run.[29]

The position of the second break point in Figure 7 was shown to be directly proportional to the amount of octalone present in the reaction mixture. Halving the octalone concentration caused a shift in this break point to a hydroxide ion concentration of one-half of that found originally as illustrated in Figure 8.

In all of this work the ratio of *cis* and *trans* isomers was determined by measuring the relative areas under the peaks of the gas chromatogram of the reaction mixture. The quantity reported is the per cent of *cis* isomer present in the decalone mixture. In almost all cases only the two decalones were present in the product mixture but occasionally the presence of a small amount (<5%) of the starting material was detected. By interrupting hydrogenations run in several representative solvent systems at various stages of completion it was established that the *cis*/*trans* ratio remained constant throughout the course of the reaction. It was also shown that prolonged exposure of a decalone mixture to hydrogenation conditions in acidic, neutral and basic media had no effect on the composition of this mixture.

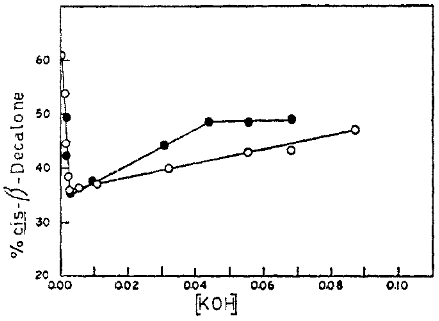


Figure 8.—Effect of dilute base on product stereochemistry: ○, standard conditions; ●, 0.5 standard octalone concentrations.

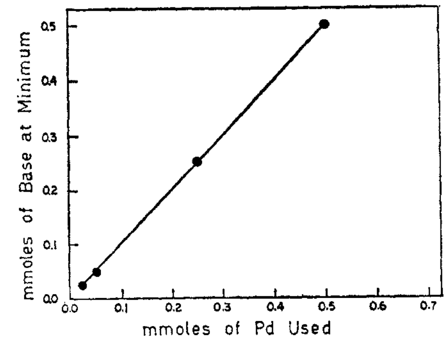


Figure 9.—Relationship between base concentration at the minimum point and the quantity of palladium used.

The presence of other reaction products was also considered but no evidence of any saturated or unsaturated alcohols or deoxygenated species could be detected either by gas chromatography or infrared spectroscopy. The only time a product other than the decalones was obtained was in the subatmospheric pressure hydrogenations run in acidic media. These data are shown in Table V.

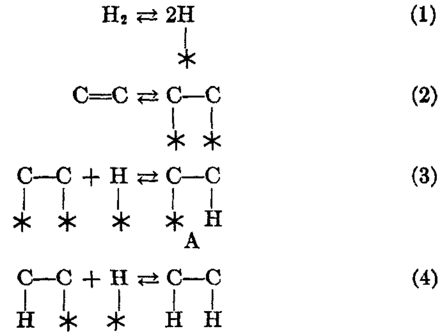
Table V

Formation of β-Naphthol at Various Pressures of Hydrogen

Acid strength, *N*	Pressure, mm	% β-naphthol
0.0231	760	
0.0231	710	
0.0231	660	Trace
0.0231	610	2.7
0.0231	560	8.4
0.0231	210	16.2

Discussion

Neutral Media.—It is generally concluded[4] that the hydrogenation of simple olefins takes place by way of the Horiuti–Polanyi mechanism[30] as shown in eq 1–4. When conditions promoting a high hydrogen availability to the catalyst are present the product stereochemistry is determined by the direction of initial olefin adsorption (eq 2). This species is assumed to have a geometry resembling that of the free olefin.[4e] Under low hydrogen availability conditions steps 2 and



$$\mathrm{H_2} \rightleftarrows \begin{array}{c}\mathrm{2H}\\ |\\ \ast\end{array} \qquad (1)$$

$$\mathrm{C{=}C} \rightleftarrows \begin{array}{ccc}\mathrm{C}&-&\mathrm{C}\\ |&&|\\ \ast&&\ast\end{array} \qquad (2)$$

$$\begin{array}{ccc}\mathrm{C}&-&\mathrm{C}\\ |&&|\\ \ast&&\ast\end{array} + \begin{array}{c}\mathrm{H}\\ |\\ \ast\end{array} \rightleftarrows \begin{array}{ccc}\mathrm{C}&-&\mathrm{C}\\ |&&|\\ \ast&&\mathrm{H}\\ &\mathrm{A}&\end{array} \qquad (3)$$

$$\begin{array}{ccc}\mathrm{C}&-&\mathrm{C}\\ |&&|\\ \mathrm{H}&&\ast\end{array} + \begin{array}{c}\mathrm{H}\\ |\\ \ast\end{array} \rightleftarrows \begin{array}{ccc}\mathrm{C}&-&\mathrm{C}\\ |&&|\\ \mathrm{H}&&\mathrm{H}\end{array} \qquad (4)$$

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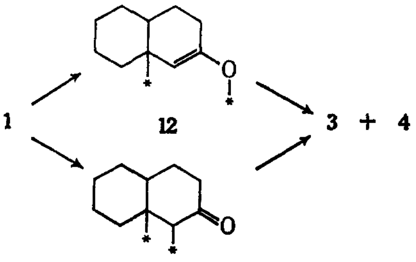
[29] It was considered possible that the reaction of this initial quantity of base was the neutralization of some acid present on the catalyst. This reasoning was dismissed when it was found that there was no change in pH of these weakly basic solutions even when a very large amount of catalyst was added.

[30] I. Horiuti and M. Polanyi, *Trans. Faraday Soc.*, **30**, 1164 (1934).

3 can equilibrate and product composition is determined by the factors influencing the formation of the various half-hydrogenated states (A) available to the system. The geometry of the transition state leading to the half-hydrogenated state is considered to be essentially that of an eclipsed 1,2-diadsorbed alkane.[4e]

One might anticipate a similar process to be occurring on hydrogenation of α,β-unsaturated ketones and, indeed, the data shown in Figure 2 establish a relationship between hydrogen availability and product stereochemistry in the hydrogenation of **1**. However, as seen from both Table I and Figure 2 the polarity of the solvent is also important in determining product composition from this reaction. Since it has been shown that increasing the polarity of the solvent promotes an increase in the polarization of α,β-unsaturated ketones[31] the hydrogenation of these compounds might be expected to take place by way of the Horiuti–Polanyi mechanism involving a 1,4-adsorbed species (**12**)[32] in solvents of high dielectric constant and 1,2 adsorption (**13**) in nonpolar solvents (Scheme III).



In Figures 10 and 11 are shown drawings of the *cis*- and *trans*-1,2- and -1,4-adsorbed octalone with the geometry each of these species would be expected[4e] to have on initial adsorption and on formation of the half-hydrogenated state. From these diagrams it can be seen that with the 1,2-adsorbed olefin the steric differences between *cis* and *trans* adsorption are very slight but in the respective half-hydrogenated states *cis* adsorption is preferred. With both the 1,4-initially adsorbed species and the half-hydrogenated state *cis* adsorption is more favored than it is in the corresponding 1,2-adsorbed series.

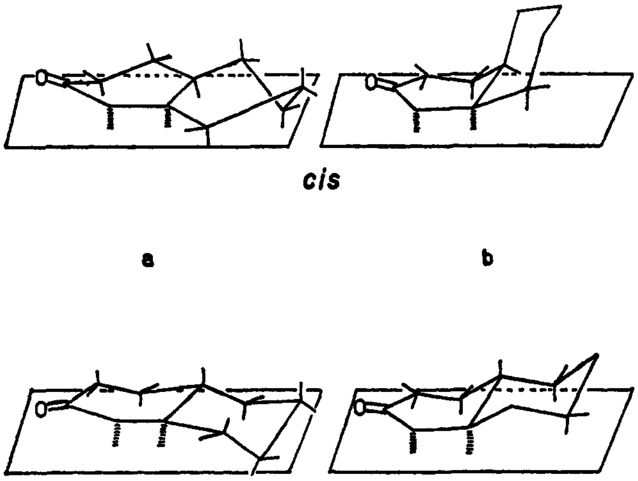


Figure 10.—*cis*- and *trans*-1,2-adsorbed octalone in geometry for (a) initial adsorption and (b) the formation of the half-hydrogenated state.

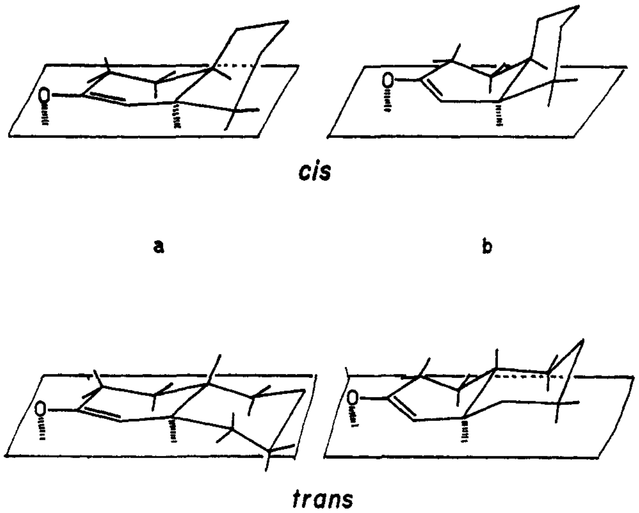


Figure 11.—*cis*- and *trans*-1,4-adsorbed octalone in geometry for (a) initial adsorption and (b) the formation of the half-hydrogenated state.

Thus, with nonpolar solvents such as *n*-hexane, in which little polarization would be expected,[31] hydrogenation of octalone under conditions of high hydrogen availability (pressures greater than atmospheric) gives nearly equal amounts of the *cis*- and *trans*-β-decalone as shown by the data in Figure 2. At subatmospheric pressures (low hydrogen availability conditions) considerably more of the *cis* product is obtained. With dimethylformamide as the solvent extensive polarization[31] and, hence, 1,4 adsorption would be expected thus giving more of the *cis* isomer than is found with hexane under both high and low hydrogen availability conditions. In solvents of intermediate polarity a combination of the 1,2- and 1,4-adsorption processes would be operating.

The results shown in Table II for the hydrogenation of **1** in hydroxylic solvents are also in agreement with these concepts provided one makes the additional proposal that in hydroxylic solvents hydrogen bonding to the carbonyl oxygen[33] or, possibly, hemiketal formation will inhibit 1,4 adsorption.[8] Therefore, the more polar the hydroxylic solvent, the more hydrogen bonding, and the more 1,2 adsorption is favored leading to a decrease in the amount of *cis*-β-decalone obtained. The hypsochromic shift observed in the n → π* transition of carbonyl compounds in hydroxylic solvents of increasing polarity has also been ascribed to increasing hydrogen bonding to the carbonyl oxygen.[34] The hydrogen availability data shown in Figure 3 also indicate that in comparison with the aprotic solvent results, a 1,2-adsorption process is occurring in 90% ethanol and 1,4 adsorption taking place in *t*-butyl alcohol. It has also been found that as the quantity of water in the

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[31] E. M. Kosower, *J. Amer. Chem. Soc.*, **80**, 3253 (1958); E. M. Kosower and D. C. Remy, *Tetrahedron*, **5**, 281 (1959).

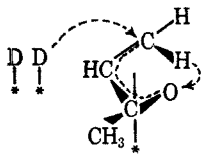
[32] The operation of a 1,4-addition process can be inferred from the isolation of the enol on hydrogenation of certain α,β-unsaturated ketones: K. Heusler, P. Wieland, and A. Wettstein, *Helv. Chim. Acta*, **42**, 1586 (1959); J. Attenburrow, J. E. Connett, W. Graham, J. F. Oughton, A. C. Ritchie, and P. A. Wilkinson, *J. Chem. Soc.*, 4547 (1961).

[33] V. G. Krishna and L. Goodman, *J. Amer. Chem. Soc.*, **83**, 2042 (1961).

[34] A. Balasubramanian and C. N. R. Rao, *Spectrochim. Acta*, **18**, 1337 (1962); S. Singh, A. S. N. Murthy, and C. N. R. Rao, *Trans. Faraday Soc.*, **62**, 1056 (1966).

reaction medium increases the amount of *cis* product formed decreases (Table III). This is an extension of the hydroxylic solvent effect resulting in increasing hydration or hydrogen bonding and, therefore, 1,2 adsorption.

These results all tend to substantiate the premise that the mechanism of the hydrogenation of unsaturated ketones in neutral medium is dependent on the polarity and hydrogen-bonding capabilities of the solvent. However, another mechanism for this hydrogenation has been proposed which must be considered. It has been suggested[35] that a 1,4-intramolecular hydrogen abstraction process similar to that proposed for the hydrogenation of α,β-unsaturated esters[36] is taking place with unsaturated ketones. In this procedure, the cyclic transition state, **14**, is invoked to rationalize the predominant incorporation of deuterium into the β position on deuteration of methyl vinyl ketone. It must be pointed out that such a transition state is only possible for acyclic compounds. Since this same deuterium distribution pattern has been observed in the deuteration of Δ^4-3-keto steroids,[37] it must be concluded that a more generalized mechanism is applicable to this reaction. These results do not conflict with the polarization mechanism proposed here, but it is apparent that a study of the effect of solvent on deuterium substitution patterns observed on deuteration of α,β-unsaturated ketones is clearly indicated.



14

Acidic Media.—It has been found that in acid the hydrogenation of the double bond of α,β-unsaturated ketones occurs in preference to the saturation of other olefins but the reverse is true in neutral solvents.[38] These results indicate that in acid a species is formed which is more strongly adsorbed on the catalyst than is the original unsaturated ketone. The sharp break points shown in the product composition data given in Figure 5 not only lend support to this concept but also preclude the possibility that in acid the product stereochemistry is determined merely by an increase in solvent polarity as previously proposed.[8] If this latter concept were true one would expect a gradual change in product composition with increasing acidity. The sharp change which is observed is much more consistent with the initial formation of a strongly adsorbed species at hydrogen ion concentrations near 10^{-2} *N*.

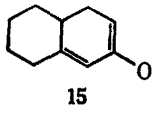
In acid concentrations lower than pH 2, no interaction would be expected to take place with the very weakly basic carbonyl oxygen[39] and hence under these conditions only 1,2 adsorption should take place as noted previously. The product composition obtained from these reactions is essentially that expected for hydrogenations run in neutral medium as discussed above. With an increase in the quantity of catalyst present the amount of hydrogen available in the reaction mixture is distributed over a larger number of active sites, thereby decreasing the hydrogen availability per site and permitting more substrate equilibration. The formation of more of the *cis*-decalone is expected from the preceding discussions.

The rapid increase in the amount of *cis*-decalone obtained between acid concentrations of 10^{-2} and 10^{-1} *N* is also reasonable and expected on the basis of the strong adsorption of an "acidified" species since between these break points all of these species present in the reaction mixture would be hydrogenated with 1,2 addition occurring on some unprotonated molecules. As the acidity increases the relative amount of the "acidified" molecules present would also increase, thus resulting in the diminishing of the contribution which the 1,2-addition process would make to the product distribution. At a hydrogen ion concentration of 10^{-1} *N* the relative amounts of the "acidified" and neutral molecules present in the reaction mixture would be such that, when considered in conjunction with the strong adsorption of the former, only it reacts regardless of the quantity of catalyst present. This premise was verified by the fact that when the ratio of "acidified" to neutral molecules was changed by increasing the octalone concentration for a given acid strength, the position of the break point also changed as shown by the data in Figure 4.

In an acidic solution of an α,β-unsaturated ketone a number of species such as hydrates, hemiacetals, enols and protonated molecules must be considered as being present. Of all of these only the enols and protonated species might be expected to have stronger adsorption characteristics than the unsaturated ketone.

In order to account for the increase in the amount of *cis*-β-decalone obtained on hydrogenation of octalone in acid it was previously proposed[6] that initial protonation occurred to give carbonium ion **2**. Adsorption of this species followed by hydride ion transfer[40] from the catalyst completed the reaction. The factors influencing the direction of adsorption of the carbonium ion (*cf.* **5** and **6**) are very similar to those of the 1,4-adsorbed species shown in Figure 11. In fact, the protonation–hydride ion transfer mechanism can be considered as an extreme sample of 1,4 addition. If this similarity holds true then the amount of *cis* product formed should decrease as hydrogen availability to the catalyst increases. The data given in Figure 4 show that this is the case.

However, the protonated species is not the only moiety possibly present in acidic solutions which can account for the observed product composition data. Hydrogenation of homoannular enol **15** can also lead to



15

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[35] G. V. Smith and J. F. Deany, *J. Catal.*, **6**, 14 (1966).

[36] G. V. Smith and J. A. Roth, *ibid.*, **4**, 406 (1965).

[37] J. W. Chamberlin, Ph.D. Dissertation, Stanford University, 1963.

[38] A. L. Markman, *Zh. Obshch. Khim.*, **24**, 2184 (1954); *Chem. Abstr.*, **50**, 5426 (1956).

[39] V. A. Palm, U. L. Haldna, and A. J. Talvik in "Chemistry of the Carbonyl Group," S. Patai, Ed., Interscience Publishers, New York, N. Y., 1966, pp 421 ff.

[40] Hydride ion transfer from the catalyst has been proposed in a number of other instances as well. See, for instance, the previously cited ref 5 and 7 as well as L. Hernandez and F. F. Nord, *J. Colloid Sci.*, **3**, 363 (1948); F. J. McQuillin, *Chem. Ind.* (London), 251 (1957); and E. F. Ullman, *J. Amer. Chem. Soc.*, **81**, 5386 (1959).

the observed product stereochemistry. This species would be expected as the predominant enol present if data on the enolization of Δ^4-3-keto steroids[41] can be extrapolated to octalone. The *cis*- and *trans*-adsorbed enols and their respective half-hydrogenated states are depicted in Figure 12. The steric requirements which regulate the direction of adsorption of these species are very similar to those involved in 1,4 adsorption (Figure 11). Thus one would expect similar stereochemical results from either the carbonium ion or the enol.

At pressures less than atmospheric where an increase in the extent of equilibration might be expected, there was virtually no change in the amount of *cis* product obtained. This leveling effect could be attributed to a complete equilibrium control of the reaction at pressures below atmospheric and that under these conditions the product composition represents the thermodynamic mixture of *cis*- and *trans*-adsorbed carbonium ions **5** and **6** or enol half-hydrogenated states. This conclusion, however, is made somewhat suspect by the fact that increasing amounts of β-naphthol were isolated from the reaction mixture as the pressure was decreased from atmospheric as indicated in Table V.

An influence of water on product stereochemistry was observed in acidic media as it was in neutral solvents with the amount of *cis* product obtained decreasing with increasing water concentration. The use of nonhydroxylic solvents containing either gaseous hydrogen chloride or a small amount of concentrated hydrochloric acid lead to the formation of 95–98% *cis*-β-decalone.

The data presented here cannot be used to distinguish between the two reaction intermediates proposed above or even to establish conclusively that the processes described are actually involved in the acidic hydrogenation of octalone.[42] These concepts, although they are probably considerably oversimplified, do serve well as working hypotheses and they can be used to rationalize and predict the product stereochemistry obtained on hydrogenation of unsaturated ketones in acidic media.[6,43,44]

Basic Media.—In base, as in acid, α,β-unsaturated ketones are hydrogenated in preference to the saturation of isolated double bonds but the reverse is usually true in neutral solvents.[9,45] The fact that there is no change in product distribution on changing hydrogen availability to the catalyst in the present instance supports the presence in the reaction medium of a reactive intermediate which is not only strongly adsorbed but adsorbed so strongly as to prevent equilibration before hydrogenation. One species which not only would be present in basic solutions of carbonyl compounds but which might also be expected to have strong adsorption characteristics would be an enolate ion.

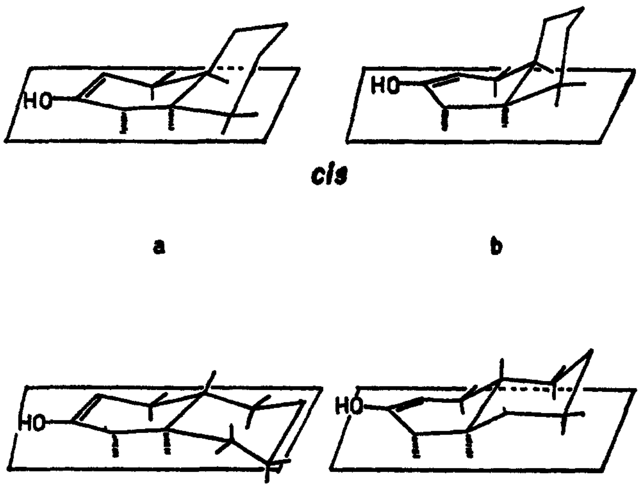

Figure 12.—*cis*- and *trans*-adsorbed homoannular enol, **15**, in geometry for (a) initial adsorption and (b) the formation of the half-hydrogenated state.

The mechanistic hypotheses presented below are based on the premise that not only is the enolate anion the species involved in the basic hydrogenation of unsaturated ketones but also that the initial adsorption of this moiety is the product determining step in the reaction.

The various possible enolate ions which can be formed from octalone (**1**) are shown in Figure 13. Malhotra and Ringold[41] have established that the homoannular enolate corresponding to **16** is the initial product formed on reaction of Δ^4-3-keto steroids with strong base and the sole product formed in the reaction with weak base. This enolate isomerizes the heteroannular enolate, *cf.* **17**, on treatment with strong base. House[46] has recently found similar results in the reaction of

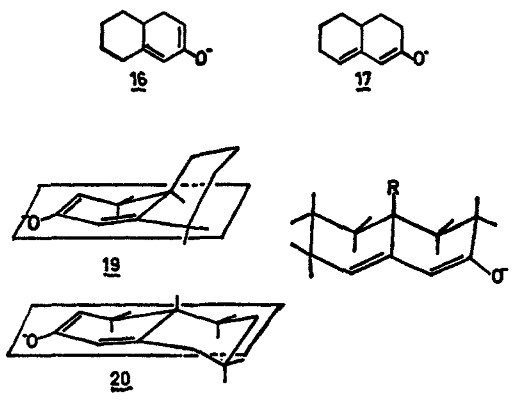

Figure 13.—Modes of adsorption for the enolate anions **16**, **17**, and **18**.

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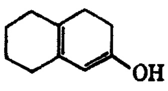
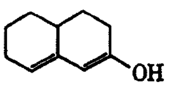
[41] S. K. Malhotra and H. J. Ringold, *J. Amer. Chem. Soc.*, **86**, 1997 (1964).

[42] For instance considerable amounts of enols i and ii could be present in the reaction mixture. However, neither of these species by itself would be expected to give the observed product distribution since if hydrogenation of i occurred without further double bond isomerization the *cis* isomer would be the sole product formed under all conditions. With ii nearly equal amounts of the *cis* and *trans* products would be expected as discussed later under basic hydrogenations. The presence of either or both of these enols in small to moderate amounts along with **15**, though, would be compatible with the stereochemistry data observed.



i



ii

[43] (a) S. Durand-Henchoz and R. C. Moreau, *Bull. Soc. Chim. Fr.*, 3416 (1966); (b) S. Nishimura, M. Shimabara, and M. Shiota, *J. Org. Chem.*, **31**, 2394 (1966).

[44] The introduction of an angular methyl group on either **2** or **15** inhibits *cis* adsorption more than it does *trans*. Thus, in the acidic hydrogenation of Δ^4-3-keto steroids the formation of nearly equal amounts of the *cis* and *trans* A/B ring-fused products would be expected.[8, 43b]

[45] R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 1194 (1958).

[46] H. O. House, B. M. Trost, R. W. Magin, R. G. Carlson, R. W. Franck, and G. H. Rasmusson, *J. Org. Chem.*, **30**, 2513 (1965).

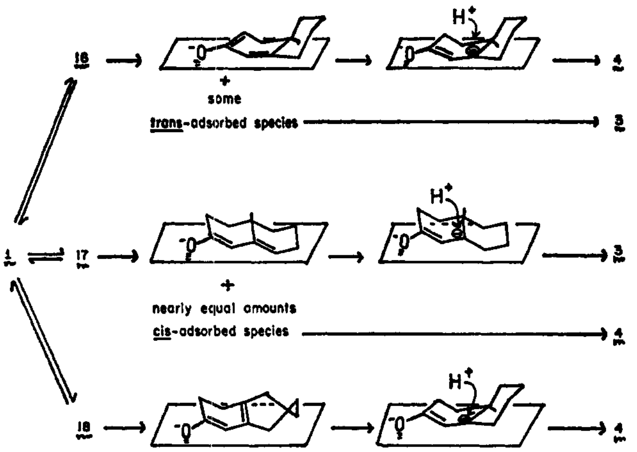


Figure 14.—Proposed mechanism for the hydrogenation of **1** in basic media.

octalone with strong base. Under these conditions the heteroannular enolate, **17**, is the major species formed but the two homoannular enolates, **16** and **18**, are also present in the reaction mixture in considerable quantity. While initial enolate ion formation was not studied with **1**, it can be assumed that, by analogy with the steroids, enolate **16** would be formed preferentially, but the extent to which enolate **18** would be formed cannot be predicted.

Adsorption of homoannular enolate **16** on the catalyst can occur in either a *cis*, **19**, or *trans*, **20**, orientation. *cis*-Adsorbed species **19** is the more favored. The steric differences between *cis* and *trans* adsorption of heteroannular enolate **17**, however, are very slight. *trans* adsorption, though, is probably slightly favored. The transfer of hydrogen from the catalyst to the enolate can occur in a number of ways. However, the procedure which is followed must account for the marked dependence of product stereochemistry on the hydroxide ion concentration (Figures 7 and 8) and for the formation of a large predominance of the *trans*-decalone at the minimum point shown in Figure 8. The mechanism depicted in Figure 14 explains all of this stereochemical data. It is proposed, then, that in the very weakly basic region (base strengths lower than that of the first break point) the formation of enolate **16** is operative. As soon as this enolate is formed it is selectively adsorbed on the catalyst surface. In this region between neutrality and the first break point, therefore, a competitive hydrogenation of the neutral molecules and the strongly adsorbed enolates is occurring. The fact that such competition is taking place is supported by the finding that only in this region is there any product dependency on hydrogen availability as would be expected from the hydrogenation of the neutral species. At the first break point the number of enolate ions formed is equal to the number of active sites on the catalyst[29] and therefore the product distribution at this point represents the product distribution which is obtained solely from the hydrogenation of homoannular enolate **16**. That this is indeed the case was established by showing that the use of a weak base, N-methylpiperidine, which would be expected[41] to form only **16**, gives a product composition corresponding to this minimum value at all base concentrations greater than $10^{-3}\ M$. It was shown before that the *cis*-adsorbed homoannular enolate, **19**, was more favored than the *trans*, **20**. However, at this minimum point about 70% of the *trans* product is obtained. If one proposes a hydride ion transfer[40] from the catalyst to give an adsorbed dianion which is then protonated *from the solution* to give the product the sterochemical results are consistent with the adsorption characteristics of the enolates. The *cis*-adsorbed species leads to the formation of the *trans* product and *vice versa*. It might be suspected that this dianion could desorb and be protonated to give the product. That this is not the case, however, can be seen from several lines of evidence. First, on desorption this dianion is identical with the intermediate proposed in the dissolving metal reductions of unsaturated ketones[47] which leads to the exclusive formation of the *trans*-β-decalone.[48] From hydrogenation, however, a product mixture containing only about 70% of the *trans* isomer is the best that can be obtained. Second, this same dianion would also be formed from the heteroannular enolate **17** and, therefore, it would be expected that product composition would be independent of base strength if protonation followed desorption. This is not observed. If, however, protonation of the adsorbed dianion occurs prior to or concurrent with the desorption process, the product stereochemistry is dependent on the mode of enolate adsorption.

At hydroxide ion concentrations greater than that at the minimum point homoannular enolate **16** is formed in amounts larger than the number of active sites on the catalyst and is, therefore, present in the solution along with the strong base. Under these conditions isomerization to the more stable enolate would be expected to occur[41] and the product distribution between the two break points is that resulting from a competition between the hydrogenation of the heteroannular, **17**, and the homoannular, **16**, enolates. Beyond the second break point hydrogenation of **17** predominates. As mentioned previously *cis* and *trans* adsorption of the heteroannular enolate should proceed with nearly equal facility with the *trans* adsorption being somewhat favored. Hydride ion transfer from the catalyst surface to this *cis,trans*-adsorbed mixture followed by protonation *from the solution* would lead to the formation of the nearly equal amounts of the isomeric products.

Throughout this entire sequence of reactions it is quite probable that varying amounts of homoannular enolate **18** are present in the reaction mixture.[46] Hydrogenation of this species by the proposed mechanism would lead to the exclusive formation of the *trans* product as shown. Since some of the *trans* decalone is obtained at all times it is difficult to determine the extent to which this enolate participates in the reaction and for simplicity it has been assumed in the preceding discussion that it was present to only a very slight extent. Actually, the stereochemical rationale will hold even when **18** is present, provided it is not the major enolate in the reaction mixture. In angularly substituted octalones the presence of this species presents no problem. Further work is under way to determine the extent to which this enolate ion is present in various basic media.

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(47) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **86**, 1761 (1964).

(48) It is possible that some of the *trans* product is formed by protonation after desorption.

While these concepts are merely mechanistic hypotheses they are quite useful in rationalizing the product stereochemistry data found on hydrogenating unsaturating ketones in basic media. For example, the hydrogenation of Δ^4-3-keto steroids and related materials in basic media gives almost exclusively the *cis* A/B ring-fused product.[9] The introduction of an angular methyl group onto heteroannular enolate **17** would result in greatly favored *trans* adsorption for this species. Hydride ion transfer from the catalyst followed by protonation from the solution would lead to the formation of the *cis*-ring-fused product. These concepts also account for the results reported by Wilds[10] for the hydrogenation of equilenone **7.** Since this substance and its enolate, **10,** are quite planar, adsorption on the catalyst should be controlled exclusively by the angular methyl group and would occur in a direction *trans* to that substituent. Therefore, in neutral medium *trans* product **9** is the expected and sole product obtained. In basic medium, adsorption of enolate ion **10** would again occur *trans* to the angular methyl group. Hydride ion transfer from the catalyst followed by protonation from the solution would give *cis* product **8.**

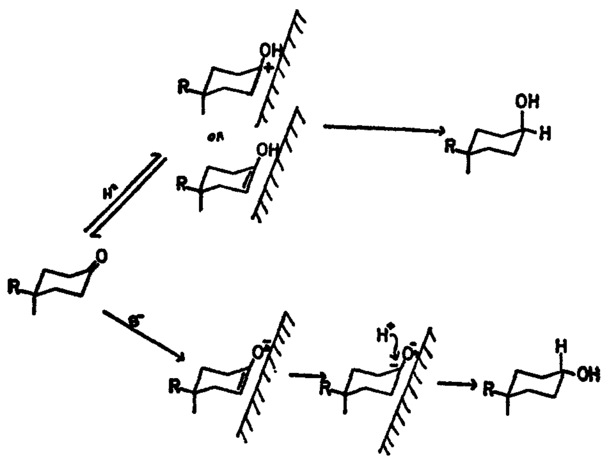
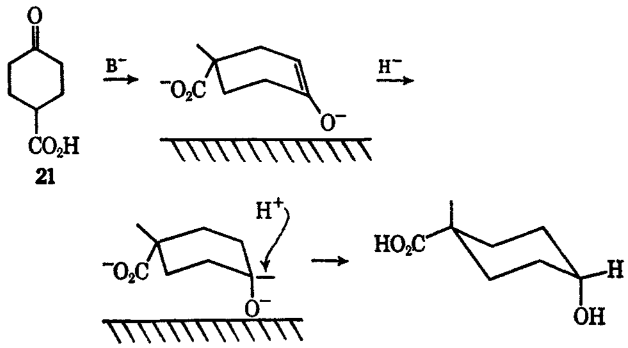


Figure 15.—Hydrogenation of cyclohexanones in acidic and basic media.

SCHEME IV



Hydrogenation of Carbonyl Groups.—The mechanistic postulates discussed above can also be utilized to explain the primary formation of the axial alcohol when cyclohexanones are hydrogenated in acid while the equatorial alcohol is obtained in basic media.[49] In acid the initially formed enol or the carbonium ion would be adsorbed on the catalyst from the least hindered side as shown in Figure 15. Transfer of hydrogen or a hydride ion would give the axial alcohol. In base enolate anion formation would take place first. Adsorption of the enolate from the least hindered side followed by hydride ion transfer from the catalyst and protonation from the solution leads to the formation of the equatorial alcohol. It has been reported, however, that hydrogenation of 4-carboxycyclohexanone (**21**) in basic media leads to the formation of the axial alcohol (Scheme IV).[50] Initial reaction of base with **21** would lead to carboxylate ion formation. The presence of this species would favor the adsorption of the substrate from the side *cis* to the carboxylate ion. Hydride ion transfer to the enolate from the catalyst and protonation from the solution would give the axial alcohol.

Registry No.—**1,** 1196-55-0.

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[49] M. Muhlstadt, R. Borsdorf, and F. J. Struber, *Tetrahedron Lett.*, 1879 (1966); L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed, Reinhold Publishing Corp., New York, N. Y., p 99.

[50] E. Hardegger, Pl. A. Plattner, and F. Blank, *Helv. Chim. Acta*, **27,** 793 (1944).