

Benzyl Iodide.—Benzyl iodide exchanges with iodine both thermally and photochemically.¹³ The rate is less than that of allyl iodide but is greater than that of any other organic iodides that have been investigated. The carbon-iodine bond in this compound is very weak, and benzyl iodide reacts with sodium at a rate comparable with that of allyl iodide.⁶ We believe that the observed rate of exchange with iodine is not inconsistent with a carbon radical mechanism, but a definite decision must await more detailed studies which are now being undertaken.¹⁴

Conclusion

Even the meager kinetic data available at the present time permit us to make some rather definite generalizations as to the mechanisms of reactions in which halogen atoms replace other halogens in organic compounds.

(A).—If the compound contains π electrons either in a double bond or in an aromatic ring, the transition state of lowest free energy for exchange of a neighboring halogen atom will usually involve a

(13) S. I. Miller, unpublished observations.

(14) NOTE ADDED IN PROOF.—Studies by Mr. Moshe Gazith indicate that benzyl iodide exchanges by the carbon radical mechanism. The details will be published later.

direct substitution in which the entering atom reacts with these electrons. Thus, olefinic and allyl halides exchange by a direct substitution in which the electrons of the double bond are involved, and aryl halides also appear to react by a direct substitution mechanism.

(B).—If the carbon atoms are saturated in the neighborhood of the halogen that is replaced, the reaction path of lowest free energy involves a direct attack on halogen with the formation of a free carbon radical which subsequently reacts with a halogen molecule. This mechanism appears to be operative in the case of at least some saturated halides, but it is possible that halogen atoms are sometimes able to react with inversion as nucleophilic groups do. The rate of this carbon radical reaction is accelerated by decrease in the carbon-halogen bond strength, and in allyl iodide the reaction apparently goes at a rate which is considerably less than that of direct substitution but which is nevertheless measurable at room temperature. The observed rate of exchange of benzyl iodide could be accounted for by either mechanism, and a decision must await further experimental work.¹⁴

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Homogeneous Catalytic Hydrogenation. I. Activation of Molecular Hydrogen by Solutions of Cuprous Acetate

By SOL WELLER AND G. A. MILLS

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The catalytic activation of molecular hydrogen was studied in a homogeneous system in order to provide information more clearly interpretable than that obtained with usual more complex, solid catalyst surfaces. Detailed kinetic measurements were made at 100° for the reduction by hydrogen of two reductants, quinone or cupric ion, in quinoline catalyzed by cuprous acetate. The rate of hydrogenation can be expressed by: $-d H_2/dt = k p_{H_2} [Cu^I]_2$, independent of concentration of reductant, where $[Cu^I]_2$ represents a dimeric complex. The equilibrium constant for the formation of the complex was calculated to be equal to 11 mole⁻¹ l. The reduction reaction proceeds satisfactorily in solvents other than quinoline provided that, for those tried, the solvent is a nitrogen base, not necessarily heterocyclic, and free of complicating features such as chemical reactivity with the reductant, steric factors, or strong chelating tendency. When mixtures of hydrogen and deuterium are used, no appreciable exchange occurs during the homogeneous reduction period. However, HD was formed with solutions of reduced cupric acetate, which are relatively stable with regard to reduction to the metal. The rate of exchange is comparable to the rate of reduction of quinone or cupric ion. Hydrogen-deuterium exchange is believed to occur indirectly through the medium of a hydrogen donor which is probably aniline present as an impurity.

A mechanism of reduction of quinone or cupric ion by a stepwise alternate oxidation and reduction of cuprous ion catalyst, or the inverse, is not consistent with the data. Instead, the rate-determining step appears to be the reaction of a cuprous ion dimer with hydrogen to form a complex in which the hydrogen is *dissociated*. This complex is capable of reacting relatively rapidly with the reductant. The factors important to the effectiveness of the dimer appear to be: a structure possessing two sites capable of accommodating the two atoms of hydrogen simultaneously, an electronic structure permitting the formation of strong bonds with the hydrogen atoms, and also probably certain geometric features which make the two coordination positions available to hydrogen at the proper distance.

While in recent years the mechanism of acid catalysis has become understood in a fairly detailed manner, the exact nature of catalytic hydrogenation has remained largely unknown. The recognition of some general connection between hydrogenation catalysis and semi-conductivity of oxides and sulfides on the one hand, and of d band character of metals on the other, have been important advances. However, a generalized concept of the nature of the active complex has not been achieved in the same sense that the carbonium ion mechanism has been successful in acid systems. It was, therefore, the purpose of this study to inquire into the manner in which molecular hydro-

gen is activated, following a new approach. Almost all known hydrogenation catalysts are solids and their study is made difficult by the complexity of solid surfaces. It was proposed that investigation of a catalyst molecularly dispersed in solution could lead to more interpretable results than can be obtained with solid catalysts, since in solution the molecular species are better known. Moreover, ultimately by control of the environment in which the catalyst exists, it should be possible to employ complexing agents so as to adjust the catalyst properties to a precise degree. The nature of the complexing agent is known to alter the oxidation-reduction potential. The exact nature of the

complexing action is, of course, a feature believed influential in controlling the selectivity of biological catalysts such as enzymes.

Proceeding from this point of view it was found that Calvin^{1a} had already in 1938 described such a system: the reduction by hydrogen of quinone in quinoline solution, catalyzed by cuprous acetate. With the probable exception of the "oxo" reaction,² there appear to be no other examples in the literature of catalytic hydrogenation in which the catalyst is homogeneously dispersed. The reduction of aqueous solutions of cupric sulfate was accomplished under hydrogen pressure, but observations were made only when metallic copper had been produced.³ Certain Japanese workers⁴ have carried

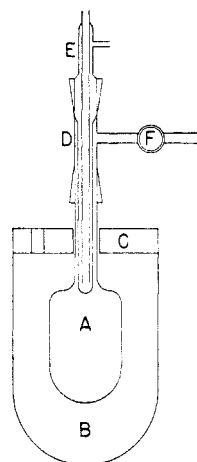


Fig. 1.

on extensive investigations using complex salts of the platinum group, but it appears likely that the first reaction was reduction to the metal. A number of bacteria contain the enzyme hydrogenase, which is able to activate molecular hydrogen⁵; however, there is some question whether enzymes should be classified as homogeneous catalysts. Wirtz and Bonhoeffer reported that KOH solutions catalyzed the exchange between H₂ and D₂O, but this was subsequently found by Abe to be caused probably by colloidal iron oxide impurities.⁶ It seemed logical, therefore, to start with a more extensive investigation of Calvin's system. A detailed kinetic study has been made of the hydrogen reduction of quinone in quinoline solution catalyzed by cuprous acetate; this has been extended to include the reduction of cupric acetate and oxyacetate to cuprous acetate in the same system as well as in the effect of solvent on these hydrogenations. The catalyzed hydrogen-deuterium exchange reaction also has been investigated. The mechanisms of the reactions are considered from the viewpoint of hydrogen activation and electron transfer in reduction.

Further work, which will be reported later, included measurements with other quinones, effect of addition of chelating agents, and use of other metals.

Apparatus and Materials

Catalyst, solvent and reducible substrate were weighed

into reaction flask A (Fig. 1), which was connected to a high-vacuum manifold via a flexible glass coil. The reaction system was equipped with a mercury manometer and a gas buret for measuring volumes of gas absorbed. Storage bulbs for nitrogen and hydrogen were attached to the manifold; these were filled, after evacuation, with cylinder gas which had been passed through hot copper and then through dehydrated silica-alumina of high surface area at -195°. The manifold was also equipped with an outlet for transferring gas samples from the reaction system into a previously evacuated sample bulb.

The reaction vessel employed in most of this work is shown in greater detail in Fig. 1. The cell, A, was fitted with a condenser head to prevent loss of solvent during evacuation. Capacity of the cell was about 100 ml. and normally 40 ml. of solvent was employed. Thermostating was accomplished by surrounding the cell with a bath, B, partially filled with a liquid (usually water) held at its boiling point by external heating. The bath was equipped with a reflux condenser, not shown, to prevent loss of the thermostating liquid. The entire assembly was mounted on a plywood shaking board, which was oscillated by a motor driven eccentric at a speed sufficient to provide vigorous agitation in the solution in A.

The quinoline used was Eastman Kodak Co. synthetic material. It was fractionated under reduced pressure and stored in a refrigerator. Cuprous acetate, with which most of this work was carried out, is sensitive toward hydrolysis and oxidation. It was prepared under a dry, reducing atmosphere in the special apparatus shown in Fig. 2. Cuprous oxide (5-10 g.), glacial acetic acid (500 ml.) and acetic anhydride (50 ml.) were placed in a digestion flask, A, which was equipped with a water condenser, C, and gas inlet tube, B. The reaction mixture was refluxed for several hours in a slow stream of hydrogen. The hot solution was then siphoned through a detachable, sintered glass filter, E, into flask D, which had been previously evacuated; the solution was then permitted to cool in D under vacuum. The cuprous acetate, which crystallized when the solution was cooled, was collected on the removable, sintered glass filter, F, by filtration as shown at the right of Fig. 2. The solid was washed with several portions of anhydrous ether, in the absence of air, freed of ether by evacuation, and transferred to a storage container in a "dry-box" filled with nitrogen.

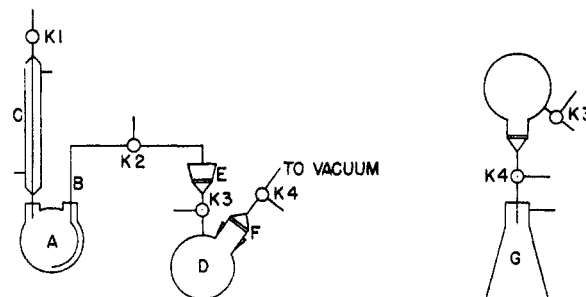


Fig. 2.

X-Ray diffraction patterns of cuprous acetate and of anhydrous cupric oxyacetate, prepared by oxidation of cuprous acetate at 100° with O₂, have been published previously.⁷

Attempts were made to prepare anhydrous cupric acetate by treatment of the monohydrate, Cu(OOCCCH₃)₂·H₂O, with acetic anhydride. Analysis of the products for copper, however, indicated that the material was still the monohydrate. In the experiments described below with "cupric acetate," it is to be understood, therefore, that the monohydrate was used.

Normal operation during a hydrogenation experiment was as follows: flask A, containing the reaction mixture, was heated to temperature (usually 100°) under vacuum. The "dead space" in the flask was determined with nitrogen, the flask was re-evacuated, and hydrogen was admitted at a predetermined pressure. The course of the reaction was followed volumetrically, pressure being held constant by adjustment of the mercury in the gas buret. It is noteworthy that the initial apparent hydrogen uptake

(1) (a) M. Calvin, *Trans. Faraday Soc.*, **34**, 1181 (1938); *THIS JOURNAL*, **61**, 2230 (1939). (b) Subsequent to the preparation of this paper, the authors learned from Dr. Calvin that further work on this problem was carried out by himself and Dr. W. K. Wilmarth in 1939-1940. This work, which led to conclusions similar, in part, to those presented here, is being prepared for publication.

(2) I. Wender, M. Orchin and H. H. Storch, *ibid.*, **72**, 4842 (1950).

(3) V. N. Ipatieff, B. B. Corson and J. D. Kurbatov, *J. Phys. Chem.*, **43**, 589 (1939).

(4) Y. Sibata and E. Matumoto, *J. Chem. Soc. Japan*, **60**, 1173 (1939); M. Iguti, *ibid.*, **60**, 1287 (1939).

(5) M. Stephenson and L. H. Stickland, *Biochem. J.*, **25**, 205, 215 (1931); **26**, 712 (1932); **27**, 1517 (1933); H. D. Hoberman and D. Rittenberg, *J. Biol. Chem.*, **147**, 211 (1943).

(6) K. Wirtz and K. F. Bonhoeffer, *Z. physik. Chem.*, **A177**, 1 (1936); S. Abe, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **38**, 287 (1941).

(7) H. Shimizu and S. Weller, *THIS JOURNAL*, **74**, 4469 (1952).

("zero" time) usually coincided closely with the "dead space," determined with nitrogen; this indicates that the solubility of hydrogen in the systems studied was very small. In cases where it was desirable to sample the gas phase in the reaction flask, the flask stopcock, F (Fig. 1), was closed, the manifold was evacuated, and the gas was permitted to expand into a previously evacuated, 300-ml. gas sample bulb.

Forty ml. of solvent was used in each experiment and the pressure of hydrogen (or deuterium) was usually 515 mm. Unless the effect of concentration was being studied, 2 millimoles of quinone and about 3 millimoles of cuprous acetate were normally used.

Experimental Results

Quinone Hydrogenation.—The course of a typical hydrogenation of quinone (*p*-benzoquinone), catalyzed by cuprous acetate in quinoline solution, is shown in Fig. 3. The quantity of hydrogen absorbed increases linearly with time until a point is reached (hereafter called break point) where a change in slope occurs. (Note: 1 millimole $H_2 = 36.3$ ml. H_2 (515 mm., 27°)). The solution is optically clear up to the break point, but past the break point metallic copper is precipitated. The color of the solution is deep red throughout the hydrogenation. In most cases, at the end of each run, the solutions were filtered through a fine, sintered glass filter; if any precipitate was present, it was washed with alcohol, dried and analyzed for copper. The amount of copper found was usually stoichiometrically equivalent to the amount of hydrogen absorbed past the break point. If the run was terminated prior to the break point, no copper was found on filtration. The amount of hydrogen absorbed up to the break point was approximately that necessary for reduction of quinone to the semiquinone (or quinhydrone) stage, in agreement with Calvin's findings.^{1a} The exact position of the break point was not well duplicable; molar ratios of (hydrogen absorbed):(quinone) at the break point usually varied from 0.4 to 0.6, although occasionally even wider deviations from 0.5 occurred. The rates of quinone hydrogenation, however, as measured by the slopes of the hydrogen uptake curves up to the break point, were usually quite reproducible. It appears that the hydrogen absorption up to the break point is to be associated with a reduction of quinone catalyzed by dissolved cuprous acetate; hydrogen absorption past the break point corresponds to reduction of cuprous acetate to metallic copper.

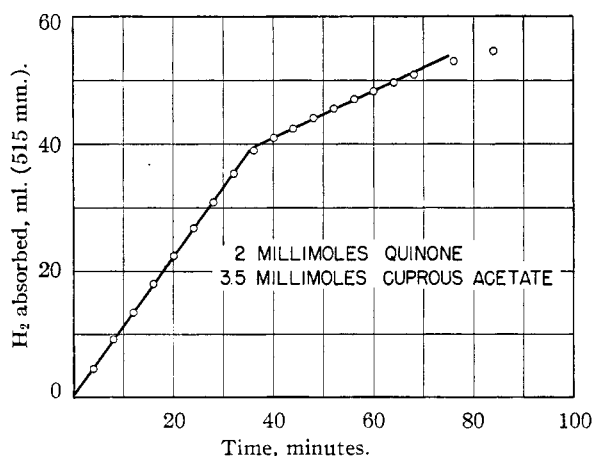


Fig. 3.—Hydrogenation of quinone.

A study was made of the effect of hydrogen pressure, quinone concentration and cuprous acetate concentration on the rate of quinone reduction. Within the limits of experimental error, the rate of reduction, expressed as ml. (S.T.P.) H_2 absorbed per unit time, was linearly dependent on hydrogen pressure over the range 250–770 mm. Quinone concentration appeared to have very little effect on the rate; under the fixed conditions of 515 mm. hydrogen pressure and 3 millimoles of cuprous acetate per 40 ml. of quinoline, essentially the same rates of hydrogenation were observed with amounts of quinone varying from 1 to 3 millimoles. The precision of the data was not sufficient

to establish the slight inhibitory effect of high quinone concentrations claimed by Calvin.

The rate of quinone hydrogenation depends in a non-linear way on the concentration of cuprous acetate. This is shown by the individual points in Fig. 4, each of which represents a separate experiment, carried out at a hydrogen pressure of 515 mm. and a quinone concentration of 0.05 mole l.⁻¹. Calvin had suggested^{1a} that the active catalyst was a dimeric complex of cuprous acetate and the data shown in Fig. 4 are consistent with such a hypothesis. If the rate were proportional to the concentration of a cuprous acetate dimer, the following equations would obtain

$$\text{Rate} = k[(Cu^I)_2] \quad (1)$$

and

$$K = [(Cu^I)_2]/[Cu^I]^2 \quad (2)$$

where k is a specific rate constant including the effect of hydrogen pressure, $[(Cu^I)_2]$ represents the concentration of dimer, $[Cu^I]$ is the concentration of monomer and K is the dimerization constant. If the total concentration of cuprous acetate is expressed as C , where

$$C = [Cu^I] + 2[(Cu^I)_2] \quad (3)$$

then the rate of hydrogenation is given by

$$\text{Rate} = k \frac{4KC + 1 - \sqrt{8KC + 1}}{8K} \quad (4)$$

In the low concentration range, where dissociation of the dimer is almost complete, the rate expression becomes

$$\text{Rate} = kKC^2 \quad (5)$$

In the high concentration range, where dimerization is almost complete, it becomes

$$\text{Rate} = \frac{1}{2}kC \quad (6)$$

The variation of rate with concentration should thus change from a square dependence at very low concentrations to a linear dependence at high concentrations.

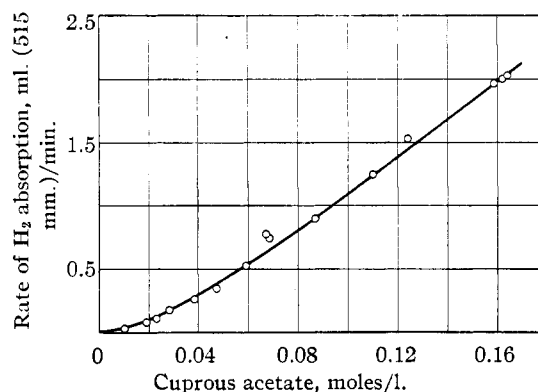


Fig. 4.—Rate of quinone hydrogenation vs. cuprous acetate concentration.

The continuous curve shown in Fig. 4 has been calculated from eq. (4) with the use of the following values for the two parameters: $K = 11.2$ mole⁻¹ l., $k = 41.9$ ml. (at 515 mm.) min.⁻¹ mole⁻¹ l. It is clear that, essentially within experimental error, the experimental data can be fit by an expression of the form of eq. (4); i.e., the data are consistent with the hypothesis that the active catalyst is a dimer of cuprous acetate.

A direct, though approximate, determination of the dimerization constant, K , has been made by the method of boiling point elevation. The precision of the measurements was poor because of the low vapor pressure of quinoline at 100° . Values of K in the range 7 to 10 mole⁻¹ l. were computed, which, in view of the experimental uncertainties, may be considered to be a reasonable check of the value deduced from the kinetic data.

It may be mentioned that the value of 0.53 g./50 ml. given by Calvin for the solubility of cuprous acetate in quinoline at 100° is low.^{1a} The solubility is in the range 0.8 to 0.9 g./50 ml., or 0.16 to 0.18 mole/l.; this is consistent with the fact that the rate of quinone hydrogenation con-

tinuously increases with increasing concentration of cuprous acetate at least up to a concentration of 0.16 mole/l. (Fig. 4).

The apparent activation energy for quinone hydrogenation was determined to be 15.3 kcal./mole in the temperature range 78–100°. This is a good check of the value 14.3 kcal./mole reported by Calvin.¹⁸

Hydrogenation of Cupric Acetate.—When work on this problem was begun, it was believed that the over-all catalyzed hydrogenation of quinone might occur by a series of "partial reactions" involving alternate oxidation and reduction of the cuprous acetate. This possibility is considered in detail in the section entitled "Discussion." In order to evaluate such a hypothesis, it was necessary to study the hydrogenation of cupric acetate as a separate step.

In Fig. 5 are shown typical curves for the course of the reduction of cupric acetate in quinoline solution, in the absence (I) and in the presence (II) of added cuprous acetate. In both cases the hydrogen pressure was 515 mm. and the temperature 100°. The shape of curve I suggests that the reaction is autocatalytic, a conclusion which is confirmed by the almost complete disappearance of the induction period when cuprous acetate is added. In both cases the quantity of hydrogen absorbed is close to the theoretical value for the reduction of Cu^{II} to Cu^{I} .⁸ It is noteworthy that, after reduction to the cuprous state was complete, further reduction to metallic copper seemed to occur very slowly, if at all; this is shown by the flatness of the final portions of the hydrogen absorption curves and by the absence of metallic copper on filtration of the solution at the end of an experiment. The reason for the exceptionally slow precipitation of copper from these solutions is not known and is the subject of further investigation. It is of interest in this connection that the reduction of a quinoline solution of cuprous acetate, in the absence of quinone or reduced quinone, is also very slow. As will be seen later, this property furnished a convenient means for the preparation of relatively stable solutions of cuprous acetate for use in deuterium exchange experiments.

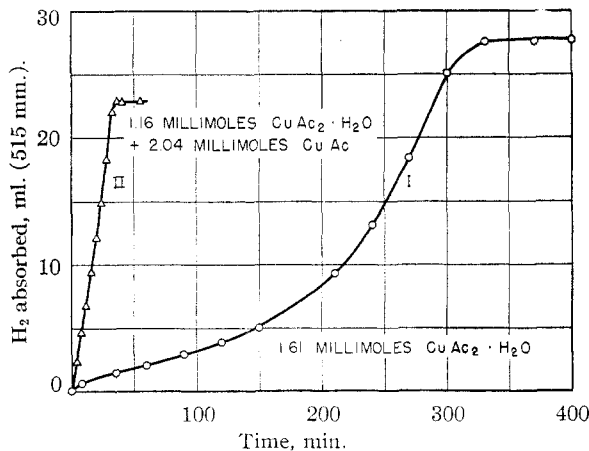


Fig. 5.—Hydrogenation of cupric acetate: effect of cuprous acetate.

Similar experiments were carried out on the hydrogenation of cupric oxyacetate, prepared by oxidation of cuprous acetate. The course of the hydrogenation is very similar to that shown in Fig. 5 for cupric acetate, with one exception: in the case of the cupric oxyacetate, a slow reduction to metallic copper occurs when the hydrogenation is carried beyond the point of complete reduction to cuprous acetate.

As the curves in Fig. 5 show, the instantaneous rate of hydrogenation, which depends on the instantaneous concentration of cuprous acetate, increases with increasing

(8) G. N. Tyson and R. E. Vivian (THIS JOURNAL, 63, 1403 (1941)) reported that the magnetic susceptibility of cupric disalicylaldehyde was unchanged on reduction with hydrogen; this would imply that reduction of the organic moiety, and not of Cu^{II} , occurred. These results are apparently in error, possibly because of exposure of the reduced solutions to air, and repetition of the experiments has shown the reduced material to be diamagnetic (M. Calvin, personal communication).

time almost up to the point of complete reduction of Cu^{II} to Cu^{I} . The individual points in Fig. 6 represent instantaneous rates, picked off the curves for nine separate experiments in which cupric acetate or oxyacetate was reduced, as a function of the total amount of cuprous acetate present at the corresponding time. The total cuprous acetate was taken as the sum of the cuprous acetate initially added (if any) and that produced by reduction of the cupric salt. The solid curve in Fig. 6 is a curve drawn through the individual points of Fig. 4; it represents the observed variation of the rate of quinone hydrogenation with concentration of cuprous acetate. It is a striking fact that, within a range of 10–20%, the rates of quinone hydrogenation and Cu^{II} hydrogenation are identical for a given cuprous acetate concentration. This result strongly suggests that the same step is rate-determining for both reactions.

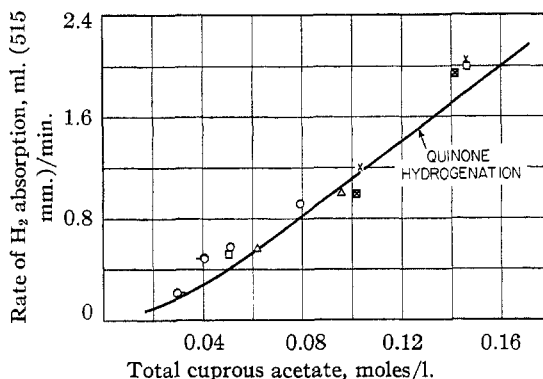


Fig. 6.—Reduction of Cu^{II} -quinoline solution.

On this basis one can deduce the course of cupric acetate hydrogenation during any single experiment. The rate is again assumed to be proportional to the concentration of cuprous acetate dimer

$$\text{Rate} = k[(\text{Cu}^{\text{I}})_2] \quad (7)$$

The rate increases with time, since cuprous acetate is a product of the reaction. The integrated form of eq. (7) is

$$\log \frac{1 - \sqrt{1 + 8Ky}}{1 - \sqrt{1 + 8K(\text{Cu}^{\text{I}}_0)}} + \frac{1}{1 - \sqrt{1 + 8Ky}} - \frac{1}{1 - \sqrt{1 + 8K(\text{Cu}^{\text{I}}_0)}} = \frac{k}{4}t \quad (8)$$

where t = time, k = specific rate constant (including the effect of hydrogen pressure), K = dimerization constant, (Cu^{I}_0) = initial total concentration of cuprous acetate, and $y = (\text{Cu}^{\text{I}}_0) + (\text{Cu}^{\text{I}}_x)$ where (Cu^{I}_x) is the cuprous ion concentration calculated to have been formed from cupric ion by the particular amount of hydrogen absorbed. Figure 7 shows the agreement obtained between the theoretical curve (solid curve) and the observed data (circles) for an experi-

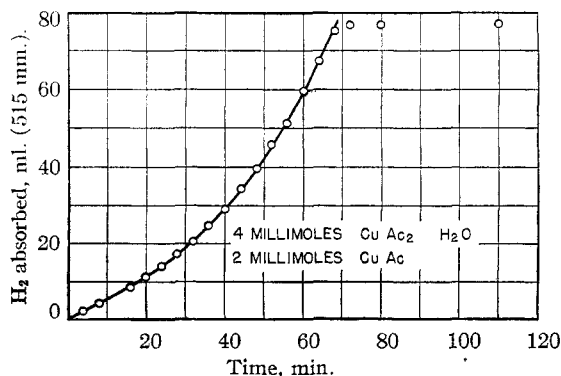


Fig. 7.—Hydrogenation of cupric acetate: comparison of theory with experiment.

TABLE I

SOLVENT EFFECT IN REDUCTION OF QUINONE OR CUPRIC ACETATE

Reaction conditions: 2.5–3.0 millimoles CuAc, 2.0 millimoles quinone or CuAc₂, 515 mm. H₂ pressure, 100°

Solvent	Quinone reduction		Cupric acetate reduction			Remarks
	Rate ^a	Completion, % ^b	Initial ^a rate	Final ^a rate	Completion, %	
Quinoline	0.60	100	0.66	1.25	100	
2-Methylquinoline	.0	0	0.47	0.50	50	Not autocatalytic
4-Methylquinoline	.0	0	1.25	.60	70	Not autocatalytic
6-Methylquinoline	.75	110	
8-Methylquinoline	0.15–.32 ^f	115	0.10	.26	230	
8-Hydroxyquinoline	0.0	0	
Isoquinoline	.80	50	1.24	2.0	120	
Pyridine ^c	0.20	0.36	105	
4-Methylpyridine77	1.25	100	
2,4,6-Trimethylpyridine	.46	70	.30	0.50	45	
5-Ethyl-2-methylpyridine50	1.25	130	
2-Hexylpyridine ^d	.75	90	.20	..	Low	Precipitate present
α,α' -Dipyridyl ^e12	0.19	95	
Indole	.0	0	
Formamide	.0	0	.0	..	0	
Dibutyl phthalate	.0	0	
Dimethylaniline0	..	0	Precipitate present
Diamylamine0	..	0	Precipitate present
Diethanolamine0	
Dodecylamine	.0	0	.60	0.86	95	

^a Rate expressed as ml. H₂ (at 515 mm. pressure) per min. ^b Computed on basis of reduction to semiquinone stage. ^c Run at 80°. ^d 25 ml. of solvent, 2 millimoles of quinone, 1.7 millimoles of CuAc. ^e 5 g. of dipyridyl in 40 ml. of diphenylmethane used as solvent. ^f Autocatalytic.

ment in which the hydrogenation of 4 millimoles of cupric acetate was carried out in the presence of 2 millimoles of cuprous acetate. The theoretical curve was obtained from eq. (8) with the use of the values of 31.9 ml. min.⁻¹ mole⁻¹ and 11.2 mole⁻¹ for the two parameters, k and K , respectively. It is noteworthy that this is the same value for the dimerization constant as that used for fitting the data on quinone hydrogenation (Fig. 4), though the value for the specific rate constant is somewhat smaller. The fit shown in Fig. 7 is excellent up to the point of exhaustion of the cupric acetate (break point). It is clear that, as far as the kinetics are concerned, the catalyzed hydrogenations of both quinone and cupric acetate are consistent with the same mechanism.

Solvent Effect in Hydrogenation.—It is reasonable to assume that, in quinoline solution, one or more quinoline molecules is coordinated with the cuprous acetate catalyst and that the presence of quinoline in the "coordination sphere" influences the behavior of the catalyst. In order to achieve a better understanding of the role of the solvent in this reaction, a study was made of a variety of solvents. The results are shown in Table I.

In the quinoline series, quinoline itself is a satisfactory solvent for the reductions of quinone and cupric acetate. Introduction of a methyl group in the 2- or 4-position prevents quinone reduction and strongly changes the character of cupric acetate reduction. These effects are presumably due to the known reactivity of groups ortho and para to the nitrogen atom in quinoline. This is substantiated by the normal behavior of 6-methylquinoline for quinone reduction. 8-Methylquinoline exhibits an unusual autocatalytic reaction for quinone reduction and an enormous hydrogen absorption during cupric acetate reduction; in both cases the rate of reduction is very low, presumably because of steric factors.

Isoquinoline gave a faster rate than quinoline for both quinone and cupric acetate reduction, but the quinone reduction was only about 50% complete.

In the pyridine series, normal behavior seems to be the rule, 2-hexyl- and 4-methylpyridine showing rates of quinone and cupric acetate reduction comparable to those obtained in quinoline. Reduction of cupric acetate in 2,4,6-trimethyl- and 5-ethyl-2-methylpyridine was somewhat slower. Since the total pressure was kept constant at 515 mm. in these experiments, the hydrogen partial pressure was significantly less with the lower molecular weight solvents than with quinoline, and the observed rates should be corrected for this effect if quantitative comparisons are

made. Because of its high vapor pressure, pyridine was tested only at 80°. It is of interest that the color of cuprous acetate solutions in pyridine and its 4-methyl derivative are amber in color, rather than deep red and the dodecylamine solution (see below) is colorless. α,α' -Dipyridyl in diphenylmethane also supported the reduction of cupric acetate.

Several miscellaneous solvents were tested for activity. Poor dissolving power and steric factors probably account for the inertness of dimethylaniline and diamylamine. Diethanolamine and 8-hydroxyquinoline are chelating agents which apparently form too stable a chelate complex to allow activation of hydrogen by cuprous acetate. Indole, formamide and dibutyl phthalate are all neutral or weakly basic solvents, which fact may be responsible for their inertness. Dodecylamine did not sustain quinone reduction, but it gave an autocatalytic rate for cupric acetate reduction similar to that with quinoline.

Within the range of solvents studied, it seems to be a sufficient condition for the activation of hydrogen that the solvent be a nitrogen base, not necessarily heterocyclic, and free of complicating features such as unusual chemical reactivity, steric factors, or exceptionally strong chelating tendency. There are some indications (4-methylquinoline, isoquinoline, 4-methylpyridine) that an increase in base strength of the solvent results in increased catalytic activity, but the data are insufficient to permit a definitive conclusion.

Hydrogen-Deuterium Exchange.—Calvin had reported that if parahydrogen was used for the reduction of quinone or of cupric acetate, no para- to orthohydrogen conversion occurred up to the break point in the hydrogen uptake curve; if, however, the reduced solution was allowed to cool to room temperature and the shaking with parahydrogen continued, the conversion was complete in less than 10 hours.^{1a} Because experiments of this sort furnish an opportunity to achieve a more detailed understanding of the fate of the hydrogen during reaction, exchange reactions were investigated in this system. The hydrogen-deuterium exchange, rather than the para-orthohydrogen conversion has been studied, because of both greater convenience and less ambiguity in interpretation. The results are summarized in Table II. The exchange reaction was studied at 100° in all cases except run 321, which was at 30°.

In the first experiment (run 305) an equimolar mixture of hydrogen and deuterium was used for the reduction of cupric acetate in the presence of cuprous acetate. A gas

TABLE II
 DEUTERIUM EXCHANGE EXPERIMENTS AT 100°

Run no.	System ^a	Treatment	Time, min.	Product gas analyses, %		
				D ₂	HD	H ₂
382	CuAc + Q + quinoline	D ₂ ^b	40 ^d	97.8	2.2	0
313	CuAc + Q + quinoline	D ₂	20 ^{*c}	78.2	19.9	1.9
317	CuAc + CuAc ₂ + quinoline	D ₂	35 [*]	36.9	40.4	22.7
315	CuAc + quinoline	D ₂	48	77.3	20.3	2.4
316	CuAc + quinoline	D ₂	45	64.4	28.2	6.0
319	Quinoline only	D ₂	60	98.2	1.8	0
321	CuAc + quinoline ^e	D ₂	120	96.5	2.0	1.5
328	CuAc, dry	D ₂	60	98.0	2.0	0
338	CuAc + CuAc ₂ , dry	D ₂	60	98.0	1.9	0.1
336	CuAc ₂ + quinoline	D ₂	120	96.9	2.8	0.3
386	Acetic acid + quinoline	D ₂	60	98.1	1.9	0
388	Cu powder + quinoline	D ₂	60	98.6	1.3	0.1
394	Cu powder + quinoline	H ₂ -D ₂	45	49.9	0.8	49.3
332	CuAc + CuAc ₂ + quinoline	H ₂	60			
		Vacuum	5			
		D ₂	60	33.3	42.6	24.1
381	CuAc + CuAc ₂ + quinoline	Same as 332		34.1	34.3	31.6
346	CuAc + CuAc ₂ + quinoline	Same as 332		36.2	41.9	21.9
346a	346, filtered at 25°	D ₂	60	42.3	40.0	17.7
333	CuAc + CuAc ₂ + quinoline	H ₂	60			
		Vacuum	960			
		D ₂	60	42.6	50.0	7.4
341	CuAc + CuAc ₂ + quinoline	Same as 333		45.8	39.7	14.5

^a CuAc = cuprous acetate; CuAc₂ = cupric acetate. ^b D₂ used in all experiments except 388 and 394 contained 98.2% D₂, 1.8% HD; D₂ in 388 and 394 contained 99.5% D₂, 0.5% HD. ^c Asterisk indicates time after the break point in the H₂ uptake curve. ^d Time required to reach break point, 52 minutes. ^e Exchange run at 30°.

sample taken 13 minutes after the break point in the hydrogen (deuterium) uptake curve was found to contain 52.0% H₂, 31.3% D₂ and 16.7% HD (by volume). Aside from the very appreciable amount of HD formed, the most striking aspect of this result was the decrease in deuterium content. Since it is unlikely that deuterium reacts more rapidly than hydrogen, this suggested that the deuterium might be exchanging with some hydrogen donor in solution as well as with gaseous hydrogen. Subsequent experiments which are summarized in Table II, were carried out with pure D₂, rather than a H₂-D₂ mixture, in the gas phase. As will be seen, the production of HD and even H₂ demonstrates that this exchange with a donor in solution does indeed occur.

Runs 382, 313 and 317 (Table II) confirm Calvin's results: very little exchange is observed prior to the time of complete reduction of reducible substrate, but extensive exchange occurs after this time. Occurrence of the exchange does not depend on the initial presence of either quinone or cupric acetate, since quinoline solutions of cuprous acetate alone can produce this result (duplicate runs 315 and 316). Quinoline alone does not catalyze the exchange (run 319), nor does dry cuprous acetate (run 328), dry cuprous acetate-cupric acetate mixture (run 338), or 2.5% acetic acid in quinoline (run 386). Freshly reduced copper powder in quinoline does not result in any HD production when either D₂ (run 388) or H₂-D₂ (run 394) is used. Exchange proceeds very slowly with a solution of cuprous acetate at 30° (run 321) and with a solution of cupric acetate alone (run 336); the result in the latter case is probably due to the production of a small amount of cuprous acetate during the course of the experiment.

It is of interest that the rate of quinone reduction with deuterium (runs 382, 313) was as great, within 5-10%, as the rate observed with hydrogen. This is unusual, since deuterium normally reacts at an appreciably lower rate, and it may be due to a greater solubility of deuterium than of hydrogen in quinoline.

The last six experiments listed in Table II were concerned with the problem of establishing that the exchange is truly a homogeneous catalysis. The system used in most of the exchange experiments is obtained by reducing cupric acetate in quinoline to the cuprous stage. It will be recalled that under these circumstances no further reduction to metallic copper seems to occur. If the solution, after

reduction of the cupric acetate, contained a very finely dispersed solid which was the active catalyst, one would expect that (1) "aging" the solution prior to the exchange experiment would change the particle size distribution and, therefore, the catalytic activity, and (2) filtering the solution after reduction, prior to exposure to D₂, would remove the solid and change the activity. In duplicate runs 333 and 341, the solutions were held overnight under vacuum after the reduction of Cu^{II} to Cu^I had been completed; D₂ was then admitted. In triplicate runs 332, 381 and 346, D₂ was admitted immediately after the initial reduction had been completed and the excess H₂ evacuated. Immediately after run 346, the system was evacuated, and the solution was cooled to room temperature, filtered through a fine, sintered glass disc in the absence of air and retested with D₂ at 100° (run 346a). Inspection of the data shows that, within the limits of experimental duplicability, the exchange occurred in all cases to about the same extent. The product gas analysis for run 333 appears to be faulty, since the value of the ratio $p_{HD}^2/p_{H_2}p_{D_2}$ in this case exceeds the equilibrium constant, K , which is 3.4 at 100°. As far as can be ascertained, therefore, the exchange is catalyzed by a homogeneous solution of cuprous acetate in quinoline.

Preliminary results indicate that the rate of the deuterium-hydrogen donor exchange is comparable with the rate of quinone reduction at the same cuprous acetate concentration. The significance of this is discussed below.

Evidence has been obtained that the hydrogen donor is probably aniline, which is known to be present as an impurity in the quinoline solvent even after fractionation. A number of experiments were performed in which the exchange between gaseous D₂ and the hydrogen donor in quinoline solutions of cuprous acetate was allowed to proceed to equilibrium; a reaction period of 4-6 hours at 100° was sufficient for this purpose. The assumption was made that, at equilibrium, the H/D atom ratio in solution was identical with that in the gas phase. From the equilibrium gas composition and the amount of D₂ initially introduced, it was then possible to calculate the amount of hydrogen donor present. Results of these experiments are summarized in Table III.

Forty ml. of the quinoline normally used was found to contain an amount of hydrogen donor equivalent to 1.5-2.0 millimoles of H₂. Repetition of the same experiment with

a sample of quinoline specially purified by diazotization, steam distillation and fractionation gave a value of only 0.5 millimole of hydrogen donor. Addition of water resulted in a small, but much less than stoichiometric, increase in amount of hydrogen donor. Addition of aniline, on the other hand, caused an exactly equivalent increase in hydrogen donor. It is also significant that, if the hydrogen donor is identified with aniline, the amount of aniline computed to be present in the quinoline normally used (sample "A," Table III) is about 0.4%, which is approximately the amount believed to be present.

TABLE III

NATURE OF THE HYDROGEN DONOR IN CUPROUS ACETATE-QUINOLINE SOLUTIONS

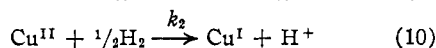
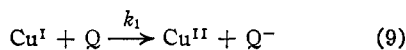
Quinoline sample ^a	Aniline added, millimoles	H ₂ O added, millimoles	Hydrogen donor, ^b millimoles (basis H ₂)
A	0	0	1.5-2.0
B	0	0	0.5
B	0	11	2.0
B	5.5	0	6.0

^a A, Eastman Kodak Co. synthetic quinoline, fractionated; B, Eastman synthetic quinoline, diazotized, steam distilled, fractionated. ^b Computed from extent of exchange at equilibrium.

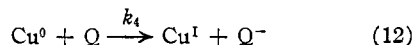
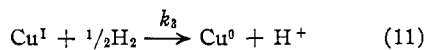
Discussion

It was mentioned earlier that when this problem was begun, it was believed that the over-all hydrogenation of quinone might proceed by consecutive oxidation and reduction of the Cu^I catalyst. Two such schemes may be considered as

Scheme I



Scheme II



where Cu^I represents the catalyst in the cuprous state, Cu^{II} in the cupric state, Cu⁰ metallic (or atomic) copper, Q quinone and Q⁻ semiquinone (or quinhydrone) ion. Since it is known that the over-all rate depends linearly on hydrogen pressure and is almost independent of quinone concentration, if scheme I occurs, it is necessary that $k_1 \gg k_2$; if scheme II is obeyed, $k_4 \gg k_3$.

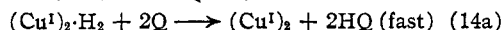
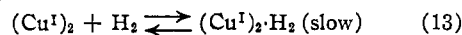
Scheme I may be considered first. The requirement that $k_1 \gg k_2$ means that reaction (9) would proceed to equilibrium rapidly compared with reaction (10), and (10) becomes the rate-determining step. The rate of reaction (10) should depend on the concentration of Cu^{II}, which, in turn, should be influenced by the relative amounts of Q and Q⁻ according to the equilibrium indicated by reaction (9); *i.e.*, the rate should change as the reaction proceeds. This is contrary, however, to the known zero-order behavior of the reaction over the entire period of quinone reduction (Fig. 3). Perhaps an even greater difficulty with scheme I is the fact that, when reaction (10) is studied by itself, the rate of reduction of Cu^{II} is found to be much slower than is the rate of quinone reduction (curve I, Fig. 5). This is, of course, not permissible if reaction (10) is to be a step in the over-all reduction of quinone. Moreover, scheme I can scarcely account for the hydrogenation of cupric acetate,

which apparently involves the same mechanism as the hydrogenation of quinone.

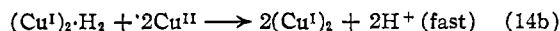
A similar difficulty arises in connection with scheme II. The rate of reaction (11), studied by itself, is much lower than that of the over-all quinone hydrogenation; this is illustrated by the decreased slope of the hydrogen uptake curve after the break point in Fig. 3 and by the even slower reduction of cuprous acetate which is observed in the absence of quinone. Reaction (11), therefore, cannot be a significant step in the hydrogenation of quinone.

It appears that neither scheme I nor II is compatible with the facts of the kinetics. Presumably one has to assume that the hydrogenation proceeds *via* a mechanism similar to scheme III, originally suggested by Calvin without a rigorous experimental basis^{1a}

Scheme III



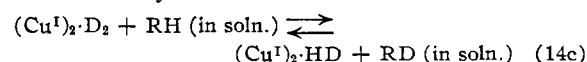
or



Reaction (13) is assumed to be the rate-determining step. It involves the reaction of a dimeric Cu^I compound with hydrogen to form a material, written in (13) as (Cu^I)₂H₂, in which the hydrogen has been "activated," and with which reducible substrates are able to react rapidly. The low solubility of hydrogen in a solution of cuprous acetate means that the equilibrium represented by (13) (in the absence of reducible substrate) is far to the left; *i.e.*, at any time, only a small fraction of the Cu^I is combined with hydrogen in the form of the "activated complex." This provides that the rate of quinone or cupric acetate reduction, which is the rate at which reaction (13) proceeds in the forward direction, may be taken as proportional to the pressure of hydrogen and to the concentration of cuprous dimer. The rate of quinone hydrogenation in any single experiment will be constant, in agreement with experiment, since the concentration of cuprous dimer remains essentially constant throughout.

The H₂-D₂ exchange occurs to an appreciable extent only under conditions when H₂ (or D₂) is not being absorbed rapidly in a chemical reaction such as the reduction of quinone or cupric acetate. This is consistent with the idea that the rate-determining step in the reduction is the activation of hydrogen by cuprous acetate (reaction (13)), the activated hydrogen being rapidly removed by reaction with quinone or Cu^{II} before it can return to the gas phase.

The fact that the exchange rate is comparable with that of the reduction means that the exchange is not a slow, secondary reaction. Here, also, reaction (13) is presumably the rate-determining step, while the exchange step proper may be schematically written as

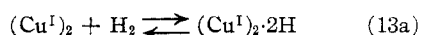


The exchange and hydrogenation reactions are competitive, in the case that a reducible substrate

is present. It is not possible to determine, from these data, the relative rates of (14a), (14b) and (14c); all that can be said is that these reactions are fast compared with (13).

It should be noted that the formation of HD from a mixture of H_2 and D_2 does not require a direct interchange. Collisions between activated D_2 and H_2 are not likely. Instead it would appear likely that D_2 is activated and exchanges with a hydrogen donor according to equation 14c and that subsequently H_2 is activated and exchanges with the deuterated donor.

The occurrence of the exchange reaction is of great importance. Since it is to be expected that the difficult step in the over-all reaction is the dissociation of the stable hydrogen molecule, it is probable that the hydrogen is dissociated on activation, and reaction (13) is more properly to be written in the form



the symbol on the right signifying that the hydrogen is dissociated on reaction with cuprous acetate. No information is available to determine whether the dissociation is symmetrical or whether it results in the formation of a positive and negative ion. The former seems to be the simpler and more reasonable assumption.

It appears to be no coincidence that a cuprous dimer, rather than monomer, is necessary for catalytic action. Breaking a hydrogen-hydrogen bond requires the expenditure of a large amount of energy, and it is probable that in order to achieve the dissociation, two strong copper-hydrogen bonds must be formed; in other words, the dimer is necessary to provide simultaneous acceptors for the two hydrogen atoms. This may be seen more clearly by reference to Fig. 8, which is a schematic representation of the relative energy states in the cuprous acetate-hydrogen system.

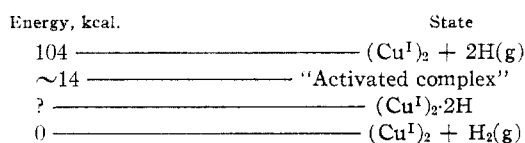
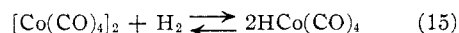


Fig. 8.—Energy relations in the cuprous acetate-hydrogen system (schematic).

The state of lowest energy shown in Fig. 8 is that for gaseous hydrogen and a solution of cuprous dimer. The next higher level represents the compound of cuprous dimer and dissociated hydrogen. This level is shown lying above the base line because the low solubility of hydrogen in a solution of cuprous acetate implies that, at equilibrium, only a small fraction of the copper has combined with hydrogen; that is, formation of the compound involves a positive free energy change. The exact position of this level is not known, since formation of the compound may proceed through an "activated complex" lying at a somewhat higher level. It is possible, however, to establish the maximum height of this level. Formation of the copper-hydrogen compound has been taken to be the rate-determining step in quinone hydrogenation, which means that the

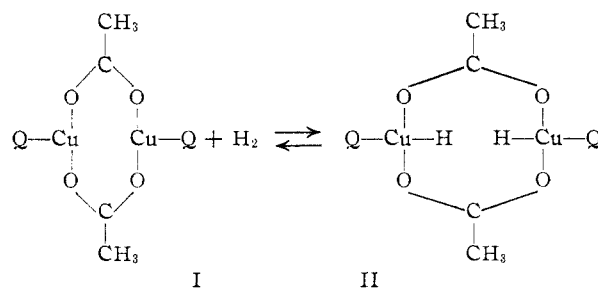
over-all activation energy for the hydrogenation is the activation energy for the formation of the compound. The activation energy for the hydrogenation is in the neighborhood of 14–15 kcal./mole. The energy level for the compound, relative to the ground level, either equals or is less than this value, depending on whether the activation energy does not or does exceed the "endothermicity" of the compound relative to the ground state. Now the dissociation of gaseous hydrogen molecules into gaseous atoms requires 104 kcal./mole. The formation of the compound from a solution of cuprous dimer and gaseous hydrogen atoms is, therefore, exothermic by at least $104 - 14 = 90$ kcal./mole; this may be interpreted as meaning that two copper-hydrogen bonds are formed, each having a bond energy of at least 45 kcal./mole. In this connection, it is of interest that the probable existence of the diatomic molecule $(CuH)^+$ has been reported by Mahanti,⁹ and the isoelectronic molecule NiH has a dissociation energy of about 60 kcal.¹⁰

There is a striking analogy between the activation of hydrogen by cuprous acetate, as indicated by eq. (13a), and that occurring under conditions of the "oxo" reaction. In the latter case, dissolved dicobaltoctacarbonyl, $[Co(CO)_4]_2$, is assumed to be the catalyst.² This compound is converted to cobalt hydrocarbonyl, $HCo(CO)_4$, under "oxo" conditions; the reaction may be written



Comparison of reactions (13a) and (15) shows the strong similarity: in both cases molecular hydrogen reacts with a dimeric metal complex to form a compound in which the hydrogen atoms have been separated. Detailed kinetic studies of the "oxo" reaction have not been published, but it is quite possible that the reaction is limited by the rate at which (15) proceeds in the forward direction. If this should be the case, the use of preformed cobalt hydrocarbonyl, which is relatively stable, would permit the reaction initially to proceed under milder conditions than are normally employed.

It is intriguing to speculate on the detailed structure of the dimer and the compound with hydrogen. Calvin suggested structure I, below, for the dimer; I may react with hydrogen to form II.



In these formulas, Q represents a quinoline molecule. For steric reasons, only threefold coordination may be possible around the copper ion in I. Noteworthy, the quinoline-cuprous chloride complex, which is readily isolable as a solid, has the empirical

(9) P. C. Mahanti, *Nature*, **127**, 557 (1931).

(10) A. G. Gaydon, "Dissociation Energies and Spectra of Diatomic Molecules," Chapman and Hall, London, 1947.

formula $\text{CuCl}\cdot\text{Q}$ (as reported by Calvin and verified in this Laboratory), only one quinoline molecule being coordinated to each copper ion. The tendency to achieve fourfold coordination may be satisfied by the formation of II.

Two possibilities for the outer electronic structure of copper in complex II are

	3d					4s 4p				
A:	2	2	2	2	1	2	2	2	2	sp^3
B:	2	2	2	2		2	2	2	2	dsp^2

Cuprous ion complexes with four ligands are normally tetrahedral, involving sp^3 hybrid orbitals (electronic distribution A). However, the cuprous-hydrogen complex II, which is of the form $[\text{Cu}^{\text{I}}\text{X}_3\text{H}]$, is isoelectronic with four coordinate complexes of cupric ion, of the form $[\text{Cu}^{\text{II}}\text{X}_4]$, which are known to be planar and to use dsp^2 orbitals (distribution B). It seemed possible, therefore, that because of its unusual electronic structure, complex II was also planar. Construction of scale (Fischer-Taylor-Hirschfelder) models indicates that this is probably not the case. A planar model of I can be constructed, but not of II; insufficient space exists to accommodate the hydrogen atoms between the copper ions in II. If, however, tetrahedral coordination is permitted about the copper ions, no steric difficulties occur in either case. In fact, the flexibility of the molecule is such that quite large variations can occur in the copper-copper distance and in the angle formed by the two copper-hydrogen bonds; this would be an advantage if some optimum geometric configuration were necessary for the activation of hydrogen. It is of interest that, with tetrahedral coordination, both *cis* and *trans* forms of I and II exist. Only in the *cis* form do the two unfilled orbitals of the cuprous ions in complex I approach sufficiently closely to react with a hydrogen molecule, and presumably only the *cis* form would be catalytically active.

The problem remains largely unsolved of determining in detail which properties of cuprous acetate permit it to act as a hydrogenation catalyst. The most difficult step in the hydrogenation is the activation of hydrogen, and this appears possible

through the circumstance that (a) the cuprous acetate is present in part as a dimer, and (b) the electronic and geometric structure of the dimer-solvent complex is such that two, strong, metal-hydrogen bonds can be simultaneously formed. Even less can be stated about the details of the subsequent fast reaction, which may involve transfer of either a hydrogen atom or an electron from the copper-hydrogen complex to the reducible substrate. Since this reaction is not rate-determining, kinetic studies furnish little information concerning its detailed mechanism.

A comparison of the homogeneous catalyst in the present system with the usual solid hydrogenation catalysts leads to two interesting conclusions. In the first place, the heterogeneous catalysts are normally metals or semi-conductive oxides. The fact that a molecularly dispersed material can act as a hydrogenation catalyst, however, means that the existence of wide electronic energy bands, which occur in solid catalysts as a result of the interaction of many atoms, is not a necessary condition for the activation of hydrogen. Secondly, it may be anticipated that homogeneous catalysts will be more selective than heterogeneous ones. Solid catalysts normally may possess a heterogeneity of activity, arising either from structural reasons or from cooperative forces between adsorbed molecules and the solid. A spectrum of energies is available, from which a particular reaction can select an optimum small range or band. A homogeneous catalyst, on the other hand, must be considered to be relatively homogeneous in activity. Except for possible variations in geometry, as illustrated in the discussion of the cuprous dimer, all of the "active centers" of a molecularly dispersed catalyst will have comparable energies; as a result, the catalyst should be able to promote only those reactions whose requirements happen to be fitted, more or less exactly, by the properties of the catalyst.

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MARCUS HOOK, PENNA.