[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Catalytic Hydrogenation of α,β-Unsaturated Ketones. II. The Mechanism of Hydrogenation in Acidic Medium.[1,2]

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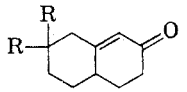
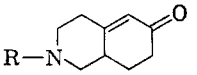
The catalytic hydrogenation of several α,β-unsaturated ketones under acidic conditions has been studied. The results of these experiments are discussed in the light of a mechanism postulated earlier.

In a previous communication,[3] the effect of acidic and basic media on the hydrogenation of $\Delta^{1,9}$-2-octalone (I. R=H) and *N*-benzoyl-$\Delta^{4,5}$-hexahydro-6-isoquinolone (II. R=C_6H_5CO) was noted. As hydrogenation in acidic medium gave primarily

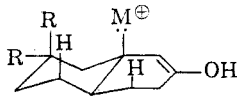


I

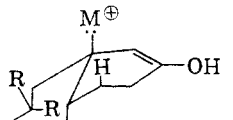


II

the *cis* isomer, a mechanism which involved a 1,4-addition of hydrogen was proposed. The intermediates for both the *cis* and *trans* cases can be represented as I-*cis* and I-*trans*, in which M is the catalyst surface on which the enolic portion of the molecules is also adsorbed. As there is less steric



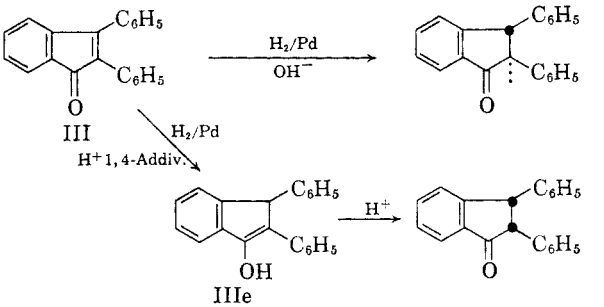
I *trans*



I *cis*

hindrance in the *cis* transition state, it follows that the *cis* isomer might predominate. Further evidence for this mechanism is found in that the *N*-methylisoquinolone (II. R=CH_3) was reported to give the *trans* isomer on hydrogenation in neutral medium[4] and the *cis* isomer in acid medium.[5]

This mechanism, however, is at variance with that of Weidlich, who proposed a 1,2-addition under acid conditions and a 1,4-addition under basic conditions.[6a] He made this proposal after finding that 2,3-diphenylindanone (III) gave the *cis* isomer on hydrogenation under acid conditions and the *trans* isomer under basic conditions.[6b] These results can be explained using the present mechanism as well. Under acidic conditions the hydrogenated product would be desorbed from the catalyst as the enol (IIIe) which would then ketonize. Zimmerman[7] has shown that rapid ketonization of enols takes place by attack of the acid from the least hindered side. Thus, ketoniza-



IIIe

tion of IIIe would result in the formation of the *cis* isomer. As the *trans* isomer is the more stable of the two, it would be expected to predominate under basic conditions in which equilibration is possible.

It was thought, however, that further evidence was needed to support the idea that hydrogenation under acidic conditions did proceed *via* 1,4-addition. Introduction of more steric hindrance at a position 1–3 to the primary attachment of the catalyst surface would be one way of testing this hypothesis. Toward this end, 7,7-dimethyl-$\Delta^{1,9}$-2-octalone (I. R=CH_3) was synthesized by the reaction of 3,3-dimethyl-6-carbethoxycyclohexanone[8] with methyl vinyl ketone. It was predicted that hydrogenation of this unsaturated ketone in acidic medium should give almost entirely the *cis* isomer, as in the *trans* intermediate state (I *trans* R=CH_3) there is considerable steric hindrance. This prediction was borne out as the product contained over 95% of the *cis* isomer as shown by vapor phase chromatographic analysis.

It was then considered necessary to extend the study to nonoctalone type systems. Toward this end, 5,6,7,8-tetrahydroindanone-5 (IV),[9] 4,5,6,7-tetrahydroindanone-2 (V),[10] and 3,5-dimethyl-

(1) This work was supported by a grant from the University of Texas Research Institute.

(2) Presented in part at the 136th National American Chemical Society Meeting in Atlantic City, August, 1959.

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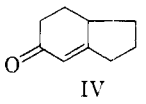
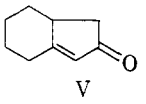
cyclohex-2-eneone (VI)[11] were synthesized and hydrogenated under neutral, acidic, and basic conditions. The ratio of products obtained was determined by vapor phase chromatographic analysis and the results are listed in Table I along with the results from the hydrogenation of I (R = CH_3). In each of these latter cases only one product was obtained regardless of the nature of the medium. However, because it is known that acid has an effect on the nature of the reaction, the same mechanism used to explain the results in the octalone series should also hold here.


IV


V

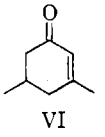

VI

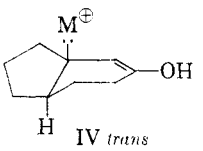
TABLE I

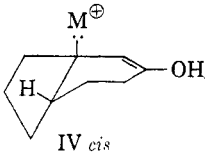
PERCENT *cis* ISOMER OBTAINED[a]

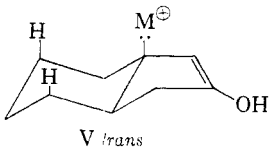
Compound	Medium		
	Neutral	Acid	Base
I(R = CH_3)	70	95	30
IV	100	100	100
V	100	100	100
VI	100	100	100

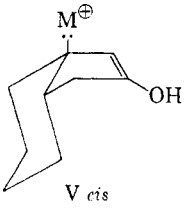
[a] As determined by vapor phase chromatography. In all cases an isomer of known configuration was chromatographed to note absorption time on the column, thus enabling the distinction of isomers, where necessary.

Thus in the acidic hydrogenation of each of the two indanones, two intermediates are possible, IV and V *trans* and IV and V *cis*. It is clear from an examination of these intermediates that the *cis* in each case has less steric hindrance than the *trans* and should, therefore, be favored.

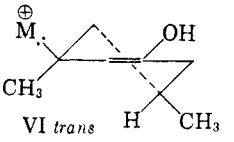

IV *trans*

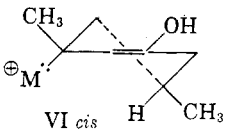

IV *cis*


V *trans*


V *cis*

In the case of VI, inspection of models shows that when the ring is in the half-chair conformation the *cis* intermediate has less steric hindrance. The *trans* is favored, however, when the molecule is in the half-boat conformation; but, as the half-chair is more stable than the half-boat,[12] there is no need to consider the half-boat case here.


VI *trans*


VI *cis*

Thus it seems quite probable that the mechanism for acidic hydrogenation is the one postulated. The effect of base, however, has not been defined. It has been proposed that in the hydrogenation of ring D unsaturated equilenin derivatives, the material hydrogenated in basic medium is not the unsaturated ketone, but instead the enol of the ketone.[13] If models of the enols of the various unsaturated ketones used in this work are examined they show that in all cases the isomer obtained is that which would be predicted on the basis of hydrogenation of these enols. Further clarification of this concept is, however, necessary before any general statement can be made.

EXPERIMENTAL[14]

7,7-Dimethyl $\Delta^{1,9}$*-octalone-2* (I. R = CH_3). To a solution of 1.6 g. of sodium in 100 ml. of absolute ethanol and 100 ml. of dry benzene was added slowly 13 g. of 3,3-dimethyl-6-carbethoxycyclohexanone.[8] The resulting solution was refluxed for 3 hr. and then cooled in an ice bath. To this cold solution was added dropwise a solution of 5.2 g. of methyl vinyl ketone in 50 ml. of dry benzene. The reaction mixture was stirred at room temperature overnight and refluxed for 1 hr. The mixture was cooled, poured into water, and extracted with benzene. The benzene was removed and the residue was refluxed overnight with a mixture of 40 ml. of 50% aqueous potassium hydroxide and 250 ml. of methanol under nitrogen. This reaction mixture was poured into water and the mixture extracted with ether. The ether solution was washed with dilute hydrochloric acid and water, dried over magnesium sulfate, filtered, and the ether removed. The residue was distilled, giving 4.6 g. of I (R = CH_3), b.p. 153°–154° (19 mm.). λ_{max} 240 mμ (ε = 13,000). The *2,4-dinitrophenylhydrazone* was recrystallized from ethyl acetate, m.p. 196°–197°.

Anal. Calcd. for $C_{18}H_{22}N_4O_4$; C, 60.33; H, 6.19. Found: C, 60.37; H, 6.22.

Hydrogenation reactions. (*a*) *Neutral Medium.* A mixture of 500 mg. of the unsaturated ketone, 10 ml. of ethanol, and 50 mg. of 10% palladium-on-charcoal was hydrogenated at room temperature under 1 atmosphere of hydrogen. After 1 mole of hydrogen was absorbed the reaction ceased. The catalyst was filtered and the solvent was removed under reduced pressure. The residue was subjected directly to vapor phase chromatography through a Perkin-Elmer Vapor-Fractometer, Model 154B, using a column composed of 1 m. of didecyl phthalate and 1 m. of 2-ethylhexyl sebacate. The temperature was maintained at 175° for all materials except those obtained by hydrogenation of I (R = CH_3) for which a temperature of 210° was used. Helium was used as the eluent gas at a 40 ml. per minute flow rate.

(*b*) *Acidic or Basic Medium.* A mixture of 500 mg. of the

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(14) All melting points are uncorrected.

unsaturated ketone, 9 ml. of ethanol, 50 mg. of 10% palladium-on-charcoal, and 1 ml. of 3*N* hydrochloric acid or 1 ml. of 10% aqueous potassium hydroxide was subjected to hydrogenation at room temperature under 1 atmosphere of hydrogen. After 1 mole of hydrogen was taken up the reaction stopped. The catalyst was removed by filtration, the solvent evaporated under reduced pressure, and the residue taken up in ether. The ether solution was washed neutral with saturated sodium chloride solution, dried, and evaporated. The residue was subjected to vapor phase chromatography as described above.

trans-7,7-Dimethyl-2-decalone. One gram of I (R=CH_3) in 20 ml. of anhydrous ether was added to 150 ml. of liquid ammonia. To this milky solution was added 100 mg. of lithium metal giving a persistant blue solution. The solution was stirred for 2 hr. and the reaction mixture decomposed by the addition of 5 g. of ammonium chloride. The ammonia was evaporated and the residue taken up in water. The aqueous solution was extracted with ether and the extracts dried and evaporated. Yield, 0.7 g.

The *2,4-dinitrophenylhydrazone* was recrystallized from ethanol, m.p. 164°–165°.

Anal. Calcd. for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71. Found: C, 59.98; H, 6.66.

cis-7,7-Dimethyl-2-decalone. A mixture of 1 g. of I (R=CH_3), 20 ml. of ethanol, 2 ml. of 3*N* hydrochloric acid, and 100 mg. of 10% palladium-on-charcoal was subjected to hydrogenation at room temperature under 1 atmosphere of hydrogen. After hydrogen uptake ceased the catalyst was removed by filtration and the solvent evaporated under reduced pressure. The residue was taken up in ether and washed with saturated sodium chloride solution. The ether solution was dried and evaporated giving 0.8 g. of product.

The *2,4-dinitrophenylhydrazone* was recrystallized from 95% ethanol, m.p. 129°–130°.

Anal. Calcd. for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71. Found: C, 59.90; H, 6.79.

cis *2-Hydrindanone* was obtained from hydrogenation of IV[9] in acidic, basic, or neutral medium.

The semicarbazone was recrystallized from aqueous ethanol, m.p. 212°–213°. Reported m.p. 215°216°.[15]

cis *5-Hydrindanone* was obtained from hydrogenation of V[10] in acidic, basic, or neutral medium.

The *2,4-dinitrophenylhydrazone* was recrystallized from ethanol, m.p. 166°–167°. Reported m.p.'s 163°,[16] 163°–164°,[17] 168°–169°.[18]

The *semicarbazone* was recrystallized from aqueous ethanol, m.p. 195°–196°; reported melting points 203°,[16] 193°–195°,[17] 196°–197°,[18] 193°–195.5°.[19]

cis *3,5-Dimethylcyclohexanone* was obtained from hydrogenation of VI[11] in acidic, basic or neutral medium.

The *2,4-dinitrophenylhydrazone* was recrystallized from ethanol, m.p. 164°–165°; reported m.p. 166°–167°.[20]

The *semicarbazone* was recrystallized from aqueous ethanol, m.p. 200°–201°; reported melting points 206°–207°,[20] 200°,[21] 202°–203°.[22]

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Methioninemethylsulfonium Salts

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Methioninemethylsulfonium fluoborate was prepared. Its reaction with potassium salts of various acids afforded the corresponding sulfonium salts. Methioninemethylsulfonium perchlorate and fluosilicate were also prepared.

Only two existing methods are available for preparing DL-methioninesulfonium salts. One of the methods which affords sulfonium bromides and iodides as well as sulfates involves the interaction of alkyl halides[1-3] or sulfates[2,4,5] with methionine; while the other method which gives sulfonium chlorides[2] and acetates[2,4] employs anion exchange of sulfonium salts with the appropriate salts or acids.

Although the latter method has an advantage in that acetates and chlorides are obtainable which can never be prepared by the former method, an anion exchange method still has the limitations that intermediate sulfonium salts are prepared and purified with difficulty, and the desired sulfonium salts cannot easily be separated from the inorganic salts formed as a by-product.

During our investigation of sulfonium com-

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