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

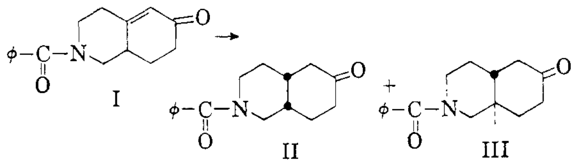
Stereochemistry of the Catalytic Hydrogenation of Some Bicyclic α, β-Unsaturated Ketones

ROBERT L. AUGUSTINE

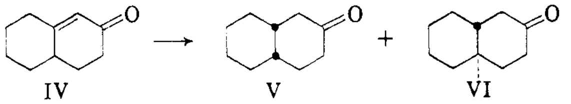
Received July 21, 1958

Catalytic hydrogenation of $\Delta^{1,9}$-octalone-2 and $\Delta^{4,5}$-hexahydroisoquinolone-6 under a variety of conditions was studied. The *cis* isomer was obtained as the predominant product under acidic conditions.

In the course of other work in this laboratory it became necessary to prepare *cis* 2-benzoyl-1,2,3,4,4a,7,8,8a-octahydro-6(5)-isoquinolone(II). Since preparation of 2-benzoyl-1,2,3,4,8,8a-hexahydro-6(7)-isoquinolone (I) could be accomplished by the reaction of 1-benzoyl-3-carbethoxy-4-piperidone[1] with the Mannich base of methyl vinyl ketone by Robinson's method[2] or by addition of methyl vinyl ketone to the pyrrolidine enamine of 1-benzoyl-4-piperidone using the procedure described by Stork,[3] this material was considered as a likely intermediate in the preparation of II. It was hoped that none of the *trans* isomer (III) would be obtained on catalytic hydrogenation of I.



However, examination of the literature showed that $\Delta^{1,9}$ octalone-2 (IV) was reported to give on catalytic hydrogenation either the *cis* β-decalone[2,4] (V), the trans decalone[5] (VI), or mixtures of these two isomers.[6] The nature of the product reported depended primarily on the method of analysis used even though somewhat different conditions were used by the various workers.



It was considered necessary, therefore, to reexamine the hydrogenation of the octalone (IV) to find conditions necessary for obtaining a reaction product consisting of essentially the *cis* isomer only. The method of analysis chosen was vapor phase chromatography through a ten foot 30% Reoplex-400 column. The octalone (IV) was prepared readily from the cyclohexanonepyrrolidine enamine and methyl vinyl ketone.[3] The pure *trans* β-decalone-(VI) was prepared from IV by reduction with lithium in liquid ammonia.[7] Its absorption time on the chromatography column was noted; thus, in the chromatography of the hydrogenation product, the *trans* isomer came off the column first followed shortly by the *cis* isomer.

When IV was hydrogenated in ethanol using 10% palladium-on-charcoal as the catalyst under one atmosphere of hydrogen at room temperature, the product consisted of equal amounts of both the *cis* and the *trans* isomers. Using methanol as the solvent gave a mixture with slightly more of the *cis* isomer. The same ratio was obtained when the reduction was carried out at three atmospheres. The use of platinum oxide, 2% palladium on strontium carbonate, or 30% palladium on charcoal gave a mixture which was somewhat richer in the *cis* isomer (see Table I). Since the addition of base to the hydrogenation mixture is known to give *cis* compounds in the hydrogenation of some steroid derivatives,[8] this procedure was tried, but the in-

TABLE I

PRODUCT RATIO OBTAINED FROM THE HYDROGENATION OF IV

Solvent	Catalyst	% Cis	% Trans
Ethanol	10% Pd/C	53	47
Methanol	10% Pd/C	59	41
Methanol	10% Pd/C[a]	63	37
Dioxane	10% Pd/C	50	50
Ethanol	2% Pd/$SrCO_3$	64	36
Ethanol	PtO_2	72	28
Acetic acid	PtO_2	70	30
Ethanol	30% Pd/C	82	18
Ethanol/aq. NaOH	10% Pd/C	62	38
Ethanol/aq. HCl	10% Pd/C	93	7
Lithium/liquid ammonia reduction			100

[a] The hydrogen pressure in this run was three atmospheres—in all others it was one atmosphere.

---

[1] S. M. McElvain and R. E. McMahon, *J. Am. Chem. Soc.*, **71**, 901 (1949).

[2] C. DuFeu, R. J. McQuillan, and R. Robinson, *J. Chem. Soc.*, 53 (1937).

[3] G. Stork and H. Landesman, *J. Am. Chem. Soc.*, **78**, 5128 (1956).

[4] E. E. van Tamelin and W. C. Proost, Jr., *J. Am. Chem. Soc.*, **76**, 3632 (1954).

[5] C. Mannich, W. Koch, and F. Borkowsky, *Ber.*, **70**, 355 (1937).

[6] H. H. Zeiss and W. B. Martin, Jr., *J. Am. Chem. Soc.*, **75**, 5935 (1953).

[7] F. Sondheimer, O. Mancera, G. Rosenkranz, and C Djerassi, *J. Am. Chem. Soc.*, **75**, 1282 (1953).

[8] A. L. Wilds, J. A. Johnson, Jr., and R. E. Sutton, *J. Am. Chem. Soc.*, **72**, 5524 (1950).

crease in *cis* isomer obtained was only 10% over that obtained using a neutral medium. However, the addition of a small amount of dilute hydrochloric acid to the hydrogenation mixture gave a product which was essentially the pure *cis* isomer. The physical constants for both the *cis* and *trans* β-decalones obtained agree with those found in the literature (see experimental).

After these results were obtained, I was subjected to catalytic hydrogenation under a variety of conditions. Since the products, II and III, are both solids, vapor phase chromatography could not be used to determine the isomer ratio of the products. It was thought that the use of the infrared spectra of the hydrogenation products would give this information. For this to be feasible, however, samples of the pure isomers were necessary to prepare known mixtures for comparison. The *cis* isomer (II) was obtained by fractional crystallization of the reaction mixture obtained from the hydrogenation of I using 10% palladium on charcoal in the presence of dilute hydrochloric acid. Preparation of III was attempted through a lithium–liquid ammonia reduction of I. Since no proton source was present during the reduction, it was hoped that the amide grouping would survive.[9] However, the product obtained consisted of a small amount of brown oil that smelled strongly of benzaldehyde. Attempts to isolate an amine from the acidic aqueous solution from which the benzaldehyde was isolated gave only a thick oil, which, after treatment with benzoyl chloride gave nothing which resembled III. A report by Marchant and Pinder[10] that the 2-methyl analog of I gave the *trans* isomer on catalytic hydrogenation prompted the hydrogenation of I in ethanol using 10% palladium on charcoal in an attempt to prepare III. The reaction mixture yielded III after several recrystallizations.

A tentative configurational assignment for these isomers is based on their mode of formation by analogy to the β-decalone series and by application of the von Auwers–Skita rule.[11]

Examination of the infrared spectra of these isomers showed that the *trans* spectrum had a strong peak at 9.1 microns and one of medium intensity at 7.6 microns which were both absent in the *cis* spectrum, while the *cis* spectrum had a medium intensity peak at 7.7 microns which was absent in that of the *trans* isomer. Thus isomer ratios could be determined through the infrared spectra of the reaction products.

Preparation of a series of known isomer mixtures and comparing their spectra with those of the various reaction mixtures readily gave the isomer ratio obtained in these reactions. However, using this method of analysis the ratio could be determined only within ±5% (see Table II). In all cases the amount of *trans* isomer was greater than that obtained from the corresponding β-decalone case. In neutral medium 70% of the *trans* isomer was obtained, while in acidic medium, this amount was reduced to 15%.

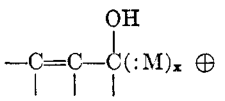
TABLE II

Product Ratio Obtained from the Hydrogenation of I

Solvent	Catalyst	% Cis	% Trans
Ethanol	10% Pd/C	30	70
Ethanol	10% Pd/C[a]	25	75
Ethanol	2% Pd/SrCO$_3$	40	60
Ethanol	PtO$_2$	65	35
Ethanol	30% Pd/C	55	45
Ethanol/aq. NaOH	10% Pd/C	50	50
Ethanol/aq. HCl	10% Pd/C	85	15
Ethanol/aq. HCl	30% Pd/C	85	15

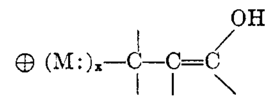
[a] The hydrogen pressure in this run was three atmospheres—in all others it was one atmosphere.

This is another example of the effect of an acid on the stereochemistry of the products obtained by reduction on metal surfaces. In acidic medium the metal surface and the α,β-unsaturated carbonyl system form isomers of the type VIIa and VIIb.[12] If VIIb is assumed to be the species present, the



$-\underset{|}{C}=\underset{|}{C}-\underset{|}{\overset{OH}{C}}(:M)_x \oplus$

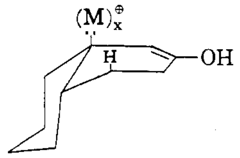
VIIa



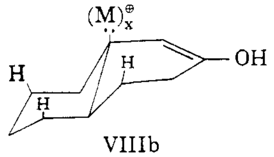
$\oplus\ (M:)_x-\underset{|}{\overset{|}{C}}-\underset{|}{C}=C{<}^{OH}$

VIIb

corresponding structures leading to the *cis* and *trans* isomer in bicyclic ring systems can be pictured as VIIIa and VIIIb, respectively.



VIIIa



VIIIb

In VIIIa there is only one 1–3 interaction between an axial hydrogen and the metal surface while in VIIIb there are three such interactions. Thus, VIIIa is more favored sterically. This accounts for the high percentage of *cis* isomer formed in acidic medium.

---

(9) A. J. Birch, J. Cymerman-Craig, and M. Slaytor, *Australian J. Chem.*, **8**, 512 (1955), report the reduction of amides to aldehydes using sodium in liquid ammonia in the presence of a proton source. Reduction of the amide was unexpected here since no proton source was present. Under the same conditions, the ketone in IV was not reduced.

(10) A. Marchant and A. R. Pinder, *J. Chem. Soc.*, 327 (1956).

(11) D. von Auwers, *Ann.*, **420**, 91 (1920); A. Skita, *Ber.*, **53**, 1792 (1920).

(12) J. H. Brewster, *J. Am. Chem. Soc.*, **76**, 6361 (1954).

EXPERIMENTAL[13]

Catalysts were obtained from Baker Catalyst Co. Inc., Newark, N. J.

Hydrogenation of $\Delta^{1,9}$*-octalone-2* (IV). (*a*) Neutral medium: A mixture of 500 mg. of IV,[3] 10 ml. of the solvent, and 50 mg. of the catalyst was hydrogenated at room temperature under one atmosphere of hydrogen. After one mole of hydrogen was absorbed the reaction ceased. The catalyst was filtered and the solvent removed under reduced pressure. The residue was subjected directly to vapor phase chromatography through a 10-foot column of 30% Reoplex-400 on 30–60 mesh John's Manville C-22 fire brick in 1/4 inch o.d. copper tubing. The temperature was maintained at 215–220° and helium was used as the eluent gas at an 80 ml. per minute flow rate.

(*b*) Acidic or neutral medium: A mixture of 500 mg. of IV, 9 ml. of ethanol, 50 mg. of 10% palladium-on-charcoal, and 1 ml. of either 3*N* hydrochloric acid or 10% aqueous sodium hydroxide was subjected to hydrogenation at room temperature under one atmosphere of hydrogen. After one 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.

(*c*) At three atmospheres: A mixture of 500 mg. of IV, 10 ml. of methanol, and 50 mg. of 10% palladium on charcoal was shaken in a Parr hydrogenation apparatus for two hours under 40 p.s.i. of hydrogen. The catalyst was removed by filtration and the solvent evaporated under reduced pressure. The residue showed no unsaturation nor hydroxyl peaks in the infrared. It was subjected to vapor phase chromatography as described above.

Trans-β-decalone (VI). To two liters of liquid ammonia was added 55 g. (0.37 mole) of IV in 500 ml. of anhydrous ether. To the milky solution lithium metal was added in small pieces until the blue color persisted (3 g., 0.43 mole). After 15 min. the blue color faded but was regenerated by the addition of another 150 mg. of lithium. The blue solution was stirred for 1 hr. and the reaction mixture decomposed by the addition of 80 g. of ammonium chloride. The ammonia was allowed to evaporate slowly overnight. The residue was taken up in water and extracted with ether. The ether solution was washed with 3*N* hydrochloric acid, water, and saturated sodium chloride solution, dried, and evaporated. The residue was distilled giving 35 g. of VI (70%), b.p. 127–128° (28 mm.), n_D^{23} 1.4820. Reported, n_D^{25} 1.4814.[4]

The semicarbazone had a m.p. 191–192°. Reported m.p. 192–193°.[14]

The 2,4-dinitrophenylhydrazone had a m.p. 165–166°. Reported m.p. 164.7–165.2°.[15]

Cis-β-decalone (V). A mixture of 50 g. (0.33 mole) of IV, 5.0 g. of 10% palladium on charcoal, 250 ml. of absolute ethanol, and 25 ml. of 3*N* hydrochloric acid was hydrogenated at 27° under one atmosphere of hydrogen. After one mole of hydrogen was absorbed the uptake ceased. The catalyst was filtered off and washed with acetone. The combined solvents were evaporated under reduced pressure to a small volume and the residue was taken up in ether. The ether was washed with saturated sodium chloride solution, dried, and evaporated. The residue was distilled giving 35 g. (70%) of V, b.p. 120–121° (23 mm.), n_D^{25} 1.4904. Reported n_D^{25} 1.4915.[4]

The semicarbazone had a m.p. 185–186°. Reported m.p. 182–183°.[14]

The 2,4-dinitrophenylhydrazone had a m.p. 154–155°. Reported m.p. 155–156°.[2]

2-Benzoyl-1,2,3,4,8,8a-hexahydro-6(7)-isoquinolone (I).[16] A solution of 89 g. (0.45 mole) of 1-benzoyl-4-piperidone[1] and 36 g. (0.50 mole) of pyrrolidine in 400 ml. of benzene was refluxed under nitrogen for 12 hr. with the water formed in the reaction being collected in a Dean-Stark water separator. The benzene was removed and the yellow residue was taken up in 400 ml. of purified dioxane. To this solution was added 31 g. (0.45 mole) of methyl vinyl ketone with a noticeable heat evolution. The red solution was allowed to stand at room temperature for 45 min. and refluxed for 3 hr. The mixture was hydrolyzed by refluxing for 1 hr. with a mixture of 90 ml. of acetic acid, 45 g. of sodium acetate and 90 ml. of water.[17] After refluxing, the solution was poured into 2 l. of water and extracted with chloroform. The chloroform was washed with 10% sodium hydroxide and saturated sodium chloride until neutral, dried, and evaporated, yielding a dark oily residue. Crystals formed on standing. I was isolated by trituration with carbon tetrachloride and removing the crystals by filtration. Recrystallization from benzene gave 32 g. of I, m.p. 140–143°. Evaporation of the benzene gave a dark residue from which another 4 g. of I could be obtained by decolorizing with Norit and further recrystallization from benzene. Total yield, 36 g. (32%). A sample was recrystallized from benzene-cyclohexane for analysis, m.p. 144–145°. Ultraviolet: $\lambda_{max} = 242$ mμ (ϵ = 12,000).

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.48; H, 6.81.

The 2,4-dinitrophenylhydrazone was recrystallized from chloroform-ethanol, m.p. 226–227°.

Anal. Calcd. for $C_{22}H_{21}N_5O_5$: C, 60.68; H, 4.86. Found: C, 60.73; H, 5.08.

Cis-2-benzoyl-1,2,3,4,4a,7,8,8a-octahydro-6(5)-isoquinolone (II). A mixture of 5.0 g. (0.02 mole) of I, 100 ml. of ethanol, 10 ml. of 3*N* hydrochloric acid, and 500 mg. of 10% palladium-on-charcoal was hydrogenated at room temperature under one atmosphere of hydrogen. After one mole was absorbed the hydrogen uptake ceased. The reaction mixture was filtered, the residue was washed with chloroform and filtered again. The combined solutions were evaporated to a small volume under reduced pressure. The residue was taken up in chloroform. The chloroform was washed with 3*N* hydrochloric acid, saturated sodium bicarbonate solution, and saturated sodium chloride solution, dried, and evaporated. The solid residue was recrystallized from benzene and benzene-cyclohexane giving 2.7 g. (54%) of II, m.p. 148–149°.

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44. Found: C, 74.68; H, 7.35.

The 2,4-dinitrophenylhydrazone was recrystallized from benzene, m.p. 200–201°.

Anal. Calcd. for $C_{22}H_{23}N_5O_5$: C, 60.40; H, 5.30. Found: C, 60.58; H, 5.43.

Trans-2-benzoyl-1,2,3,4,4a,7,8,8a-octahydro-6(5)-isoquinolone (III). A mixture of 5.0 g. (0.02 mole) of I, 100 ml. of ethanol, and 500 mg. of 10% palladium-on-charcoal was hydrogenated under one atmosphere of hydrogen at room temperature. After one mole of hydrogen was absorbed the reaction stopped. The solution was filtered and the residue washed with chloroform. The solution was evaporated. The solid residue was recrystallized several times from 95% ethanol giving 1.3 g. of III (26%), m.p. 159–160°.

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44. Found: C, 74.97; H, 7.35.

The 2,4-dinitrophenylhydrazone was recrystallized from benzene-cyclohexane, m.p. 205–206°.

---

(13) Melting points are uncorrected.

(14) W. Huckel, *Ann.*, **441**, 12 (1925).

(15) W. G. Daubin and R. C. Tweit, *J. Am. Chem. Soc.*, **76**, 3197 (1954).

(16) Prepared while working at Columbia University under Prof. Gilbert Stork.

(17) F. W. Heyl and M. E. Herr, *J. Am. Chem. Soc.*, **75**, 1918 (1953).

Anal. Calcd. for $C_{22}H_{23}N_5O_5$: C, 60.40; H, 5.30. Found: C, 60.53; H, 5.45.

Hydrogenation of I. (*a*) In neutral medium: A mixture of 500 mg. of I, 20 ml. of ethanol, and 50 mg. of the catalyst was hydrogenated at room temperature under one atmosphere of hydrogen. After one mole of hydrogen was absorbed the uptake stopped. The catalyst was removed by filtration and washed thoroughly with chloroform. The combined solution and washings were evaporated to dryness. The residue was taken up in 10 ml. of chloroform and the infrared spectrum taken. The isomer ratio was determined by comparing the length of the bands at 7.6, 7.7, and 9.1 microns with those of known mixtures.

(*b*) Acid or basic medium: A mixture of 500 mg. of I, 18 ml. of ethanol, 50 mg. of the catalyst, and 2 ml. of 3*N* hydrochloric acid or 10% aqueous sodium hydroxide was hydrogenated as above; the solution was filtered. The residue was washed with chloroform and the solution evaporated to a small volume. The residue was taken up in chloroform, washed with 3*N* hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride, dried, and evaporated. The residue was taken up in chloroform at a volume of 1 ml. of chloroform to 50 mg. of the residue. The isomer ratio was determined as above.

(*c*) At three atmospheres: A mixture of 500 mg. of I, 20 ml. of ethanol, and 50 mg. of 10% palladium on charcoal was shaken on a Parr hydrogenation apparatus under 41 p.s.i. of hydrogen at room temperature for one hour and worked up as in (*a*). The infrared spectra showed no unsaturation nor hydroxyl peaks. The isomer ratio was determined as described above.

Lithium-liquid ammonia reduction of I. Four and one-half grams (0.015 mole) of I in 250 ml. of dioxane was added to 500 ml. of liquid ammonia. Seven tenths of a gram (0.1 mole) of lithium was added and the solution was stirred for 0.5 hr. The solution turned a dirty brown color. Another 0.7 g. of lithium was added and the solution turned blue. The blue solution was stirred for 3 hr. and the reaction mixture decomposed by the addition of 50 g. of ammonium chloride. The ammonia was allowed to evaporate overnight. The residue was taken up in 500 ml. of water, the aqueous solution was made acidic with concentrated hydrochloric acid, saturated with sodium chloride, and extracted with chloroform. The chloroform solution was washed with saturated sodium bicarbonate and saturated sodium chloride solutions, dried, and evaporated giving one gram of a brown oil which smelled strongly of benzaldehyde.

The aqueous solution from the extraction was evaporated to a small volume. Five hundred milliliters of chloroform was added and enough sodium carbonate to neutralize the solution plus 10 g. excess was then added. This was followed by 10 g. of benzoyl chloride. The mixture was stirred and refluxed for 2 hr., 10 ml. of ethanol was added, and the solution refluxed an additional 0.5 hr. The mixture was cooled, water was added to dissolve the salts, and the chloroform was separated. The chloroform was washed with 10% sodium hydroxide solution, 3*N* hydrochloric acid, and saturated sodium chloride solution, dried, and evaporated, giving a dark brown oily residue. Treatment of the residue with carbon tetrachloride resulted in the precipitation of 200 mg. of water soluble crystals not identical with III. Since III is insoluble in carbon tetrachloride, none of this material was present. The nature of the crystals isolated was not determined.

Acknowledgments. The author wishes to thank the Research Corp. for the Frederick Gardner Cottrell grant which made this work possible and Dr. H. L. Lochte of this department for the use of his vapor phase chromatography apparatus. He also wishes to thank Professor Gilbert Stork for his discussions concerning the enamine reactions.

AUSTIN, TEX.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE AEROJET-GENERAL CORPORATION AND THE GENERAL TIRE & RUBBER CO.]

Reaction of Methyl Isopropenyl Ketone with Formaldehyde

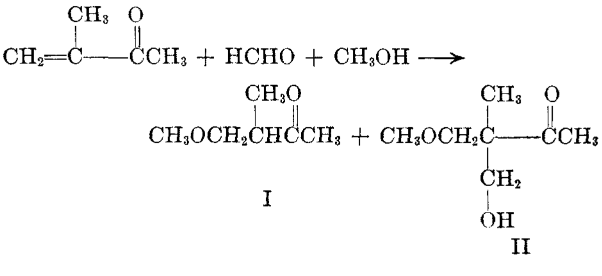
CHARLES H. TIEMAN* AND MARVIN H. GOLD

Received July 24, 1958

Formaldehyde and methyl isopropenyl ketone in the presence of base were found to react with participation of the solvent methanol to give 3-methoxymethyl-2-butanone and 3-hydroxymethyl-3-methoxymethyl-2-butanone. When excess methyl isopropenyl ketone was used as solvent, a thermally unstable product, believed to be 1-hydroxy-4-methyl-4-penten-3-one, was obtained.

The aldol condensation of aldehydes with α,β-unsaturated ketones was recently investigated by Powell and Wasserman.[1] The products isolated included the olefins formed by dehydration of the intermediate β-ketols, but not the ketols themselves. Butyraldehyde and mesityl oxide, for example, were found to give 2-methyl-2,5-nonadien-4-one. In the present work the condensation of methyl isopropenyl ketone with formaldehyde was studied.

In methanol solution, methyl isopropenyl ketone and paraformaldehyde with potassium carbonate as catalyst were found to produce 3-methoxymethyl-2-butanone (I) and 3-hydroxymethyl-3-methoxymethyl-2-butanone (II) in yields of about 20 and 50%, respectively.



$$CH_2{=}C(CH_3){-}C(=O)CH_3 + HCHO + CH_3OH \longrightarrow CH_3OCH_2CH(CH_3)C(=O)CH_3 + CH_3OCH_2C(CH_3)(CH_2OH){-}C(=O)CH_3$$

I

II

---

(1) S. G. Powell and W. L. Wasserman, *J. Am. Chem. Soc.*, **79**, 1934 (1957).

* Present address: Shell Development Co., Modesto, Calif.