Tetrahedron Letters No.24, pp. 2329-2332, 1967. Pergamon Press Ltd. Printed in Great Britain.

# CATALYTIC HYDROGENOLYSIS AS AN ALTERNATIVE TO THE WOLFF-KISHNER OR CLEMMENSEN REDUCTION METHODS FOR AZABICYCLIC KETONES

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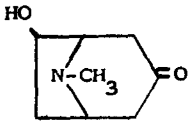
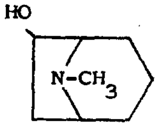
(Received 28 March 1967)

Although hydrogenolysis of conjugated (*i.e.*, allylic or benzylic) alcohols or ketones is a well known reaction (1), the hydrogenolysis of the *unconjugated* carbonyl group (*e.g.*, I → II) is not a recognized synthetic procedure (2). We wish to report some results, summarized in the Table, which suggest that hydrogenolysis over platinum in acid may be a useful general procedure for azacyclic ketones.



I



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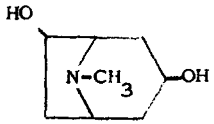

III

We find that, in general, the hydrogenolysis reaction is favored, relative to reduction to the carbinol (*e.g.*, III) by increased acid and catalyst concentrations, although the sensitivity of the reaction to these parameters varied from system to system. For example, the percent hydrogenolysis product (II) obtained from I increased from 68 to 80 to 100%, when the substrate-to-catalyst ratio was changed from 5:1 to 2:1 to 1:1. For this system, little or no change in the ratio of products was obtained by increasing the acid concentration, provided the amino ketone was neutralized with at least one equivalent of hydrochloric acid, hence reduced entirely in the form of its hydrochloride salt. On the other hand, a marked effect of the acidity was noted in hydrogenations of the hydrochloride of IV. Here, without excess acid, a 4/96% ratio of hydrogenolysis/reduction product was obtained. Addition of increasing amounts of excess hydrochloric acid correspondingly favored the hydrogenolysis reaction; in 6 *N* acid, a 95/5%

## TABLE

### Results of Hydrogenolysis of Azacyclic Ketones

| Compound Hydrogenated[a] | Specificity for Hydrogenolysis Product (%)[b] |
|---|---|
| 3-Quinuclidinone | 100 |
| 1-Azabicyclo[2.2.1]heptan-3-one | 100[c] |
| 1-Azabicyclo[3.2.1]octan-3-one | 100[d] |
| 1-Azabicyclo[3.2.1]octan-4-one | 100[d] |
| 1-Azabicyclo[3.2.1]octan-6-one | 75[e] |
| Tropan-3-one (tropinone) | 100[f] |
| 6-β-Hydroxytropan-3-one (I) | 100 |
| Tropan-6-one | 65[e] |
| 3-Oxo-9,10-dimethoxy-1,2,3,4,6,7-hexahydro-11bH-benzo[a]quinolizine (IV) | 95 |
| 2-Oxo analog of IV | 65[e,g] |
| Pseudopelletierine (V) | 65[e,h] |
| 2-Oxoindolizidine (VI) | 97[e] |

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[a] General conditions: Equal amounts (10 mg.) of amino ketone and platinum dioxide (Englehard Industries, Newark, N.J., or J. Bishop & Co., Malvern, Pa.) in 1 to 3 ml. of 1 to 6 N hydrochloric acid at 50 psig hydrogen pressure for 1 to 3 hrs. in a Parr hydrogenator.

[b] Product composition (glpc), not isolated yields. Isolated products characterized by IR (in comparison to authentic material, if available).

[c] Data of D.O. Spry.

[d] Data of B.P. Thill.

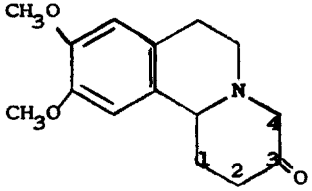
[e] Obtained from ratio of glpc areas, and may differ slightly from a true molar percentage; balance equals the reduction product.

[f] Data of C.P. Rader and R.L. Young.

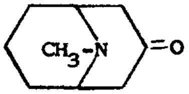
[g] Data of C.P. Ferguson.

[h] Only 50% hydrogenated in 24 hr.

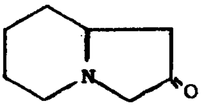
ratio was obtained. For this system, only a negligible increase in the hydrogenolysis product could be obtained by increasing the catalyst concentration at any given acidity.



IV



V



VI

The reaction apparently proceeds by the direct hydrogenolysis of the carbonyl group to a hydrocarbon at the catalyst surface, since the amino alcohols (the reduction products) are not hydrogenolyzed when subjected to the same conditions. In this sense, the mechanism seems related to that which has been formulated for the Clemmensen reduction (3), except, β-oxo amines appear not to undergo rearrangement during the hydrogenolysis reaction (4), and the proximity of the ammonium function appears to be important.

The method is suggested as a more attractive experimental alternative to either the Wolff-Kishner or Clemmensen methods, or lengthier indirect procedures, such as Raney-nickel cleavage of the dithio ketal or hydride reduction of the carbinol tosylate. As indicated in the Table, the hydrogenolysis product is often the exclusive product. However, carbinol contaminant, if formed, generally may be easily separated. The applicability of the reaction to other than azacyclic tertiary ketones and with other than platinum catalyst has not been investigated.

## REFERENCES

1. (a) H.O. House, *Modern Synthetic Reactions*, p. 10, W.A. Benjamin, Inc. New York, N.Y. (1965).

   (b) R.L. Augustine, *Catalytic Hydrogenation*, p. 135 *ff*, Marcel Dekker, Inc., New York, N.Y. (1965).

2. We find that similar results have been reported for hydrogenations of both 2- and 3-tropanone [W.A.M. Davies, A.R. Pinder and I.G. Morris, *Tetrahedron* **18**, 405 (1962)] and for 2-methyl-2-azabicyclo [2.2.2] octan-5-one [W.A.M. Davies, J.B. Jones, and A.R. Pinder, *J. Chem. Soc*. 3504 (1960)]. [The latter compound is incorrectly identified here as 2-tropanone, see I.G. Morris and A.R. Pinder, *J. Chem. Soc*. 1841 (1963)]. These hydrogenations were reported without comment as to their unusual course, however, and the method has remained buried in the literature.

3. J.H. Brewster, *J. Am. Chem. Soc.* **76**, 6364 (1954).

4. In β-oxo amines, the Clemmensen method is generally precluded by virtue of the rearrangements that occur. See for example, N.J. Leonard, J.W. Curry and J.J. Sagura, *J. Am. Chem. Soc*. **75**, 6249 (1953), and preceeding papers.