

UNITED STATES PATENT OFFICE

2,233,823

PROCESS FOR THE REDUCTION OF
ARYLNITROALKENES

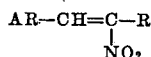
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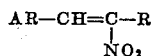
Our invention relates to a process for the re-
duction of arylnitroalkenes, and more specifi-
cally, to a method for the production of arylalka-
nones, arylalkanone oximes, and arylalkyla-
mines.

The arylnitroalkenes may be produced by the
condensation of aromatic aldehydes and nitro-
paraffins (Knoevenagel and Walter, Ber. vol. 37,
p. 4502 (1904); Worrall, Jour. Am. Chem. Soc.
vol. 56, p. 1556 (1934); Alles, Jour. Am. Chem.
Soc. vol. 54, p. 271 (1932)). Compounds of this
type are desirably reduced to form amino com-
pounds, and more or less successful reductions
have been obtained in the case of compounds
such as omega-nitrostyrene, obtained by the
condensation of nitromethane with an aromatic
aldehyde. However, in the case of nitroalkenes
of the type



it has been found to be extremely difficult to
effect satisfactory reduction. For example,
"Benzedrine" (1-phenyl-2-aminopropane) may
theoretically be obtained by the reduction of 1-
phenyl-2-nitropropene, but in practice it has
been found to be almost impossible to effect the
desired reaction. Relatively low yields of
"Benzedrine" have been secured by electrolytic
reduction of the nitropropene but catalytic hy-
drogenation appears to yield only high molecu-
lar weight polymerization products.

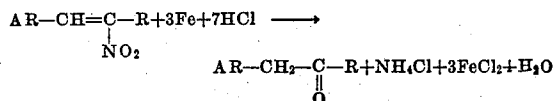
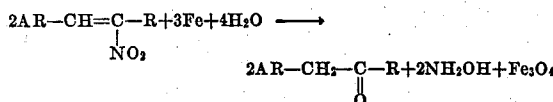
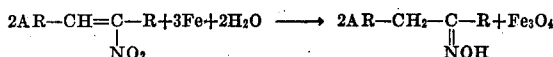
We have now discovered that arylnitroalkenes
of the type



may be successfully reduced to arylalkanones
or arylalkanone oximes by a single stage reduc-
tion by means of iron, and can be reduced to
amino compounds of the "Benzedrine" type in
a two-stage reduction in which the initially ob-
tained oxime is further reduced. One advan-
tage of our process is the fact that the initial
reduction may be controlled to yield either pre-
dominantly the ketone compound or predomi-
nantly the oxime, depending upon the reduction
conditions. Other advantages of our process

will be evident from the following description.

The initial reduction of our process is effected
in aqueous solution in the presence of sufficient
finely divided iron to effect the reduction of all
of the nitroalkene. An acid need not be em-
ployed in conjunction with the iron, but if em-
ployed, the concentration of the acid will affect
the nature of the reduction process. With no
acid or only low concentrations of acid, the re-
action product is predominantly the oxime, whereas
in the presence of relatively high concen-
trations of acid the reaction product is pre-
dominantly the ketone. The mechanism of the
reactions is not definitely known, but the follow-
ing type reactions are probably involved:



As may be seen from the above reactions, an
amount of iron equal to at least 1.5 mol per mol
of nitroalkene is required, and the amount re-
quired by one of the equations is 3 mols per
mol of nitroalkene. At least the lower limit of
1.5 mol of iron should be employed to effect sat-
isfactory reduction, and we prefer, in general,
to use more than 3 mols of iron per mol of nitro-
alkene. An excess of iron is not harmful and
it serves to insure as complete reduction as pos-
sible.

It may also be seen from the above equations
that at least 1 mol of water is required per mol
of nitroalkene in order to secure reduction to
the oxime. We prefer, however, to utilize a con-
siderable excess of water in order to obtain a
mixture which can be satisfactorily handled,
and agitated during the reaction. Other sol-
vents can be employed in conjunction with wa-
ter if desired, but these should preferably be
miscible with water in order to maintain a single

liquid phase and thus facilitate the reduction. The use of an organic solvent in conjunction with water may be an advantage in controlling the type of reduction product secured. Thus, if it is desired to obtain the oxime rather than the ketone, the use of an aliphatic alcohol in conjunction with water will tend to increase the ratio of oxime to ketone in the products.

Although the reduction to the oxime may be effected in the absence of any acid, we prefer to employ an acid in conjunction with the iron for reduction either to the oxime or to the ketone. Any acid may be utilized for this purpose, and the term acid in this connection is to be construed as a material yielding hydrogen ions. In general, however, we prefer to employ a mineral acid such as hydrochloric acid or a relatively strong organic acid such as acetic acid. The concentration of acid employed will depend upon the nature of the product desired. If it is desired to produce predominantly the oxime, an acid concentration not substantially higher than 0.06 mol of hydrochloric acid per mol of nitroolefin should be employed, or the equivalent amount of another acid, as for example, 0.03 mol of sulfuric acid. Increasing concentration of acid will produce an increase in the ratio of ketone to oxime in the reduction product. Approximately 2 mols of hydrochloric acid per mol of nitroolefin will produce almost entirely the ketone with only a trace of the oxime or none at all. Intermediate concentrations of acid can of course be employed if it is desired to produce intermediate ratios of the two products.

When employing no acid in conjunction with the iron it is desirable to employ a small amount of an iron salt as a catalyst, for example, ferric chloride. When acid is used in conjunction with the iron, on the other hand, no such catalyst is required since the initial reaction of acid with the iron in the process will produce some of the necessary catalytic material. The use of a catalyst in conjunction with acid will, however, eliminate the short induction period required for the formation of a salt by the action of acid on the iron, and for this reason it may be advantageous to employ a catalyst in addition to acid, especially for large scale operations. The amount of catalyst to be employed is not critical, amounts ranging from 0.01 mol to 0.10 mol per mol of nitroalkene being generally satisfactory.

The reduction of nitroalkenes to ketones and oximes may be further illustrated by the following specific example:

Example I

1-phenyl-2-nitropropene was dissolved in water, organic solvent or aqueous organic solvent. Forty mesh iron filings were added and in some cases acid and/or ferric chloride was incorporated into the mixture. The molar quantities of solvent, iron, acid, and catalyst, per mol of 1-phenyl-2-nitropropene, for the various reductions are shown in the table below. In each case the mixture was agitated for a period of approximately 5½ hours in a vessel equipped with a reflux condenser. At the conclusion of this period, the mixture was made alkaline with sodium hydroxide solution and steam distilled. The products were recovered from the steam distillate, dried, and carefully fractionated in a rectifying column to determine the yield of phenylpropanone and of the oxime of phenylpropanone. The conversions to these products,

based on original 1-phenyl-2-nitropropene, are shown in the table below:

Table

Mols H ₂ O	Mols organic solvent	Mols FeCl ₃	Mols Fe	Mols acid	Percent conversion based on phenyl- nitropropene	
					Oxime of phenyl- propa- none	Phenyl- propa- none
28	0	0	2	0	0.0	0.0
28	0	0.06	2	0	20.1	0.0
28	0	0	2	0.06	49.0	5.2
28	0	0.06	2	0.06	45.0	3.7
28	0	0	2	0.23	27.4	24.6
28	0	0	2	0.46	23.1	36.5
28	0	0.06	2	1.39	20.2	41.1
28	0	0.06	2	1.74	13.4	56.0
28	0	0.06	7.15	1.74	0.0	75.0
28	0	0.06	7.15	1.97	0.0	77.0
28	0	0	2	0.10	32.5	11.3
28	0	0	2	0.52	37.5	10.5
0	4 12.4	0.06	2	0.06	0.0	0.0
14	4 12.4	0.06	2	0.06	62.6	10.5
14	4 4.4	0.06	2	0.06	64.2	9.9
14	4 8.9	0.06	2	0.06	63.0	9.7

¹ Hydrochloric acid.

² Sulfuric acid.

³ Acetic acid.

⁴ Methyl alcohol.

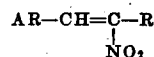
⁵ Ethyl alcohol.

In the second stage of our reduction process the oxime obtained in the first stage is further reduced to the amine. Any suitable means for reducing the oxime without undue hydrolysis may be employed for this purpose. Among these methods may be mentioned reduction with sodium amalgam and acetic acid, reduction with metallic sodium in alcoholic solution, and hydrogenation with a platinum, palladium or nickel catalyst. We prefer to employ hydrogenation with a nickel catalyst, and this process is illustrated in the example below:

Example II

Approximately 9 parts by weight of the oxime of phenylpropanone was dissolved in approximately 60 parts by weight of 95% ethanol, containing 5 parts by weight of a nickel catalyst, prepared by dissolving aluminum from a nickel-aluminum alloy by means of caustic alkali. The resulting mixture was sealed in a bomb under a hydrogen pressure of 1880 lbs. per sq. in. and reduction was effected for a period of 3½ hrs. at a temperature of 25° C., at the conclusion of which period the pressure was found to have dropped to approximately 1680 lbs. per sq. in. The pressure was then released and the catalyst removed by filtration. The filtrate was acidified with concentrated hydrochloric acid and the product was recovered by crystallization as the hydrochloride of 1-phenyl-2-amino-propane (melting point 144-146° C.). A conversion of 78%, based on the original oxime was obtained.

It is to be understood, of course, that the above examples are merely illustrative and do not limit the scope of our invention. Although our invention is particularly adapted to the production of 1-phenyl-2-aminopropane ("Benzedrine"), any of the aryl nitroalkenes of the type

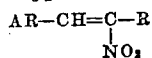


may be reduced in accordance with our process. In this formula AR may represent any aryl group, but preferably phenyl or substituted phenyl, and R may represent any alkyl group. It will be ap-

parent to those skilled in the art that the procedures employed in the above examples could be modified in numerous respects, and the use of any such modifications or any equivalents which would naturally occur to those skilled in the art is to be considered within the scope of our invention.

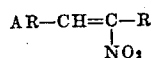
Our invention now having been described, what we claim is:

- 10 1. In a process for the reduction of an aryl-nitroalkene of the type



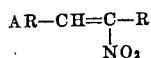
- 15 in which AR represents an aryl group and R represents an alkyl group, the step which comprises subjecting said nitroalkene, in the presence of water, to the reducing action of iron.

- 20 2. In a process for the reduction of an aryl-nitroalkene of the type



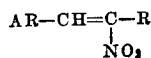
- 25 in which AR represents an aryl group and R represents an alkyl group, the step which comprises subjecting said nitroalkene, in the presence of water and an iron salt, to the reducing action of iron.

- 30 3. In a process for the reduction of an aryl-nitroalkene of the type



- 35 in which AR represents an aryl group and R represents an alkyl group, the step which comprises subjecting said nitroalkene, in the presence of water and a water-miscible organic solvent, to the reducing action of iron.

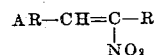
- 40 4. In a process for the reduction of an aryl-nitroalkene of the type



in which AR represents an aryl group and R represents an alkyl group, the step which comprises

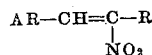
subjecting said nitroalkene, in the presence of water, to the reducing action of iron and an acid.

- 5 5. In a process for the reduction of an aryl-nitroalkene of the type.



in which AR represents an aryl group and R represents an alkyl group, the step which comprises 10 subjecting said nitroalkene, in the presence of water, to the reducing action of iron and a mineral acid.

- 15 6. In a process for the reduction of an aryl-nitroalkene of the type



in which AR represents an aryl group and R represents an alkyl group, to form primarily the 20 oxime of the corresponding ketone, the step which comprises subjecting the said nitroalkene to the reducing action of iron in an aqueous medium having an acid content not substantially greater than 0.06 equivalent of acid per mole of 25 nitroalkene.

7. In a process for the reduction of 1-phenyl-2-nitropropene, the step which comprises 30 subjecting said 1-phenyl-2-nitropropene, in the presence of water, to the reducing action of iron and an acid.

8. In a process for the reduction of 1-phenyl-2-nitropropene to form primarily the oxime of 35 phenylpropanone, the step which comprises subjecting said 1-phenyl-2-nitropropene to the reducing action of iron in an aqueous organic solvent medium having an acid content not substantially greater than 0.06 equivalent of acid per 40 mole of 1-phenyl-2-nitropropene.

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