An analytical sample, m.p. 99–101°, was obtained as light gray prisms after several crystallizations from isopropyl ether.

Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.65; H, 6.38; N, 21.26.

The benzamide of 7-aminoindole was prepared from benzoyl chloride and was obtained as flat off-white needles, m.p. 217–218°, after three crystallizations from ethanol.

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.43; H, 5.30; N, 11.73.

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The Reduction of 2-Indanone Oxime to 2-Aminoindane. Methods and Mechanisms

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Several methods are described for the reduction, in high yield, of 2-indanone oxime (I) to 2-aminoindane (III), a conversion previously considered to be difficult. A study of the variables has been made of the nickel hydrogenation and the palladium hydrogenation. The data from various reductions, including the isolation of several by-products, have permitted speculation on the mechanism of reduction. A novel isomerization of 2-indanone oxime (I) to 2-amino-1-indanone (V) has been observed.

The conversion of 2-indanone oxime (I) to 2-aminoindane (III) has been considered to be a difficult reduction. Attempted reduction with sodium amalgam in acetic acid gave[1] only a small amount of III, and hydrogenation with palladium on charcoal in ethanolic hydrogen chloride reportedly failed completely.[2,3] Catalytic hydrogenation of I with platinum oxide in alcohol has been reported[4] to give diindanylamine (II), although no yield was specified. Until now, the only satisfactory method for conversion of I to III has required the use of specially prepared palladium catalysts.[2] Unfortunately, "these catalysts are extremely active, sensitive, and pyrophoric and care must be used in working with them."[2] In our studies of the preparation of 2-aminoindane hydrochloride, a nonnarcotic analgesic,[5] we investigated the reduction of the oxime (I) of 2-indanone[6] in detail in order to find a safer, more convenient, and less expensive method. Several such satisfactory reduction procedures are reported, together with a study of the variables in the palladium and in the nickel reductions. The results of the reduction studies permit speculation on the mechanisms involved in the reductions.

Attempts at chemical reduction, using methods which had been applied successfully to reductions of other oximes or of nitro compounds to their corresponding amines, were largely unsuccessful. Ferrous sulfate in aqueous ethanolic sodium hydroxide[7] (25°, 2 days) left I completely unchanged, whereas iron powder in aqueous ethanolic acetic acid[8] (reflux, 6 hours) gave a small amount of III. Zinc and acetic acid[9] (40–45°, 20 hours) gave 90–95% recovered oxime plus a trace of III. Clemmenson reduction conditions (zinc amalgam, concentrated hydrochloric acid, reflux, 22 hours) gave 2% III and 68% crude indane. Sodium borohydride in aqueous methanol, either with or without added 10% palladium on charcoal,[10] gave back starting I. Reduction of I with a two molar quantity of lithium aluminum hydride[11] in ethyl ether (reflux, 2 hours) gave a 45% yield of crude III hydrochloride. Stannous chloride and hydrochloric acid[12] (reflux, 6 hours) gave recovered I plus *ca.* 9% 2-amino-1-indanone (V), isolated as the hydrochloride salt. The conversion of I to V, which caused skin, wood, and fabric to turn "shocking pink," is discussed in connection with palladium–methanolic hydrogen chloride reduction. Addition of a solution of I in aqueous potassium hydroxide to a suspension of nickel–aluminum alloy in aqueous methanol[13] gave a 75% yield of III, when isolated as the hydrochloride salt.

Oximes are known to react with hydrogen in the presence of nickel catalysts, but the proportions of primary and secondary amine products can vary widely.[14] The general usefulness of Raney nickel for *low pressure* hydrogenation of aliphatic oximes has been reported,[15] but the method has not been applied widely. Experiments using active nickel catalyst for low pressure hydrogenation of I are listed in Table I. Yields from the reduction of I in neutral or acidic solution were poor even at elevated temperatures and pressures. When the residue from the mother liquor of III hydrochloride from reduction of I with nickel in acetic acid was slurried with a small amount of methylene chloride, some diindanylamine (II) hydrochloride was isolated directly as an insoluble white solid, m.p. 299–302°.

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(1) H. Benedickt, *Ann.*, **275**, 351 (1893).

(2) N. Levin, B. E. Graham, and H. G. Kolloff, *J. Org. Chem.*, **9**, 380 (1944).

(3) Levin, *et al.*,[2] attributed to Hückel and co-workers[4] a chemical reduction of I with sodium and alcohol to a mixture of isomeric amines and a catalytic hydrogenation of I using platinum oxide to approximately 30% yield of III. In fact, these reductions were carried out not on I, but on a hexahydro derivative of I.

(4) W. Hückel, M. Sachs, J. Yantschulewitsch, and F. Nerdel, *Ann.*, **518**, 155 (1935).

(5) L. B. Witkin, C. F. Huebner, F. Galdi, E. O'Keefe, P. Spitaletta, and A. J. Plummer, *J. Pharmacol. Exptl. Therap.*, **133**, 400 (1961).

(6) J. E. Horan and R. W. Schiessler, *Org. Syn.*, **41**, 53 (1961).

(7) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N.Y., 1956, p. 113.

(8) A. R. Surrey and R. A. Cutler, *J. Am. Chem. Soc.*, **73**, 2413 (1951).

(9) E. Testa and F. Fava, *Chimia*, **11**, 310 (1957).

(10) T. Neilson, H. C. S. Wood, and A. G. Wylie, *J. Chem. Soc.*, 371 (1962).

(11) A. Burger and W. B. Bennet, *J. Am. Chem. Soc.*, **72**, 5414 (1950).

(12) F. Ebel and W. Deuschel, *Chem. Ber.*, **89**, 2799 (1956).

(13) D. Papa, E. Schwenk, and B. Whitman, *J. Org. Chem.*, **7**, 587 (1942); N. Roy and N. Kundu, *Nature*, **188**, 581 (1960).

(14) See, for example, the discussion by V. I. Komarewsky, C. H. Riesz, and F. L. Morritz in A. Weissberger, "Technique of Organic Chemistry," Volume II, 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1956, pp. 137–140.

(15) H. Adkins and H. R. Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948); D. C. Iffland and Teh-Fu Yen, *ibid.*, **76**, 4180 (1954).

In basic solution (ammonia,[16] potassium carbonate), especially in methanolic sodium methoxide or in methanolic sodium hydroxide, the yield of 2-aminoindane hydrochloride rose as high as 92–94%.[17] Slightly elevated temperatures resulted in a more rapid uptake of hydrogen, more effective use of the nickel catalyst, and higher yields of product. For example, hydrogenating with a half weight (catalyst to oxime) of nickel instead of with an equal weight led to a drop in yield of almost 20% when the reductions were carried out at room temperature, but resulted in no change in yield when the reductions were carried out at 30–60° (see Table I). When less than an equimolar ratio of sodium methoxide to oxime I was used, the yield of III dropped. It may be that one molecule of sodium methoxide is needed to activate properly each site on the nickel where a molecule of oxime is to be reduced. The use of lesser amounts of nickel catalyst than one-half weight (which is approximately equimolar with oxime), even at slightly elevated temperatures and in the presence of sodium methoxide, resulted in lower yields. Although reductions in methanolic sodium methoxide or in methanolic sodium hydroxide were not affected by small amounts of water, the reduction yields in methanolic ammonia dropped when water was present. Adding small amounts of 5% palladium on charcoal or 5% platinum on charcoal to a methanolic ammonia–nickel reduction resulted in a lowering of the yield.

Hydrogenation of I using Raney cobalt catalyst under conditions similar to those which were successful with sponge nickel catalyst also gave satisfactory results (85% yield of III hydrochloride). A slightly lower yield was obtained using a greater amount of cobalt catalyst, consistent with the known lesser activty of cobalt compared with that of nickel.

Catalytic hydrogenation of I using palladium on charcoal in anhydrous ethanol containing hydrogen chloride reportedly[2] failed unless a specially prepared, highly active catalyst was used. We have found that commercially available, nonpyrophoric 5% palladium on charcoal in glacial acetic acid–sulfuric acid[18] reduces 2-indanone oxime (I) to 2-aminoindane (III) rapidly and in high yield (90–95%). The use of 100% palladium black was less efficient in its use of the expensive palladium than the charcoal-supported catalyst, and resulted in more color in the reaction solution.

TABLE I

REDUCTION OF 5.00 g. OF 2-INDANONE OXIME WITH NICKEL CATALYST

Ni, g. (solvent cover)	Volume of methanol, ml.	Added acid or base	Reaction temp., °C.	Yield of III.HCl, %
20 (EtOH)	75[a]	. . .	20–25	47.8
20 (EtOH)	75[a]	. . .	70–80[b]	58.4
20 (EtOH)	75[a]	1.4 g. NH_3[c, d]	20–25	86.1
20 (EtOH)	75[a]	1.4 g. NH_3[c, d]	70–80[b]	85.8
10 (MeOH)	50	1.4 g. NH_3[c, d]	20–25	90.3
10 (H_2O)	50	1.4 g. NH_3[c, d]	20–25	86.9
10 (H_2O)	50	5.5 ml. 28% NH_3[d]	20–25	76.5
10 (H_2O)	50	. . .	20–25	59.0
10 (H_2O)	. . .	50 ml. EtOAc	20–25	48.7
10 (H_2O)	. . .	50 ml. HOAc	20–25	10.3
10 (MeOH)	50	11.6 g. $BF_3 \cdot Et_2O$[d]	20–25	8.9
10 (MeOH)	50	11.3 g. K_2CO_3[d]	20–25	83.0
10 (MeOH)	50	4.4 g. $NaOCH_3$[d]	20–25	91.6
5 (MeOH)	50	4.4 g. $NaOCH_3$[d]	20–25	90.8
5 (MeOH)	50	4.4 g. $NaOCH_3$[d]	30–60	93.8
5 (MeOH)	50	1.4 g. NH_3[c, d]	20–25	85.9
5 (MeOH)	50	1.4 g. NH_3[c, d]	30–60	86.4
5 (H_2O)	50	1.4 g. NH_3[c, d]	20–25	82.2
5 (H_2O)	50[e]	1.4 g. NH_3[c, d]	20–25	7.7
5[f] (MeOH)	50	1.4 g. NH_3[c, d]	20–25	78.1
5[g] (MeOH)	50	1.4 g. NH_3[c, d]	20–25	76.7
2.5 (MeOH)	50	4.4 g. $NaOCH_3$[d]	20–25	72.2
2.5 (MeOH)	50	4.4 g. $NaOCH_3$[d]	30–60	93.0
2.5 (MeOH)	50	2.2 g. $NaOCH_3$[h]	30–60	90.0
2.5 (MeOH)	50	1.1 g. $NaOCH_3$	30–60	86.2
2.5 (MeOH)	50	0.55 g. $NaOCH_3$	30–60	84.7
2.5 (MeOH)	50	0.27 g. $NaOCH_3$	30–60	76.5
2.5 (MeOH)	50	. . .	30–60	53.4
2.5 (MeOH)	25	2.2 g. $NaOCH_3$[h]	20–25	70.4
2.5 (MeOH)	25	2.2 g. $NaOCH_3$[h]	30–60	92.4
2.5 (H_2O)	25	2.2 g. $NaOCH_3$[h]	30–60	92.0
2.5 (MeOH)	25	1.63 g. NaOH[h]	30–60	91.3
2.5 (H_2O)	25	1.63 g. NaOH[h]	30–60	92.5
1.25 (MeOH)	25	2.2 g. $NaOCH_3$	30–60	86.4
0.63 (MeOH)	25	2.2 g. $NaOCH_3$	30–60	81.0
0.31 (MeOH)	25	2.2 g. $NaOCH_3$	30–60	71.0

[a] Anhydrous ethanol was used instead of methanol. [b] The pressure of hydrogen gas was raised to 700 p.s.i.g. [c] Anhydrous ammonia. [d] Equivalent to 2.4 moles per mole of oxime. [e] Methanol–water (1:1) was used instead of methanol. [f] In addition to the nickel catalyst, 0.5 g. of 5% palladium on charcoal was added. [g] In addition to the nickel catalyst, 0.5 g. of 5% platinum on charcoal was added. [h] Equivalent to 1.2 moles per mole of oxime.

Experiments using palladium catalysts are listed in Table II. The reduction of I was complete in 1–2 hours when 50% (weight per weight of oxime) or more of 5% palladium on charcoal was used, but required 5–7 hours when 30% of catalyst was used and took 20–24 hours (with some loss in yield) when only 20% of catalyst was used. With 10% of catalyst, a poor yield of III was isolated even after 96 hours. Pre-treatment of the glacial acetic acid with 5% palladium on charcoal (stirred overnight, filtered, catalyst discarded) permitted faster (5–7 hours) and more complete reduction with the 20% catalyst quantity. When using only a 10% weight of catalyst, the yield of III hydrochloride was only 59% with untreated acetic acid but 81% with pre-treated acetic acid. Reducing the amount of sulfuric acid in the acetic acid from 2.2 moles to 1.1 moles per mole of oxime resulted in a lowering of the yield from 93 to 86%. When the amount of sulfuric was reduced further to 0.55 mole per mole of oxime, or when it was omitted completely, the yield of III hydrochloride was negligible. In the absence of sulfuric acid, 42% of

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(16) The reduction of oximes with nickel catalyst in the presence of ammonia, added primarily to suppress the formation of secondary amines,[14] is well known [G. Mignonac, British Patent 282,083 (1928)], but such reductions are usually carried out at hydrogen pressures of 700 p.s.i.g. or higher. In our hands, the use of elevated temperature (70–80°) and pressure (700 p.s.i.g.) did not improve the yield of the reduction of I in the presence of ammonia (see Table I).

(17) The activation of nickel catalysts by alkali has been discussed by R. Schröter in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 83. Alkali-activated nickel catalysts have been used at low temperatures and pressures by M. Schenk and H. Richter [U. S. Patent 2,982,783 (1961)] to convert 2-oximino-1-indanone to 2-amino-1-indanol derivatives, but the oximes they described also were reducible in high yield by palladium on charcoal in methanol containing hydrogen chloride, conditions we have found to be inferior for 2-indanone oxime itself. Apparently the presence of a 1-keto group makes reduction of the 2-oxime easier.

(18) This reduction medium was used by K. W. Rosenmund and E. Karg, *Ber.*, **75**, 1850 (1942), for the reduction of 2-oximino-1-indanone to III. These authors found that the sulfuric acid could be replaced by perchloric acid, or boron trifluoride–acetic acid, or zinc chloride–hydrogen chloride. We found that no hydrogen was absorbed by I when the sulfuric acid was replaced by phosphoric acid or by anhydrous hydrogen chloride.

TABLE II

REDUCTION OF 5.00 g. OF 2-INDANONE OXIME WITH PALLADIUM CATALYST

Catalyst, g.	Solvent[a]	Added acid[a] or base (moles per mole of oxime)	Yield of III HCl, %
1.5 100% Pd	HOAc	H_2SO_4 (2.2)	90.4
0.25 100% Pd	HOAc	H_2SO_4 (2.2)	*ca.* 13
5.0 5% Pd–C	HOAc	H_2SO_4 (2.2)	90.5
2.5 5% Pd–C	HOAc	H_2SO_4 (2.2)	92.9
2.5 5% Pd–C	HOAc	H_2SO_4 (1.1)	86.1
2.5 5% Pd–C	HOAc	H_2SO_4 (0.55)	*ca.* 2
2.5 5% Pd–C	HOAc	. . .	1.2
2.5 5% Pd–C	EtOAc	H_2SO_4 (2.2)	87.7
2.5 5% Pd–C	MeOH	H_2SO_4 (2.2)	27.2
2.5 5% Pd–C	MeOH	NH_3 (2.2)	. . .[b]
2.5 5% Pd–C	MeOH	. . .	. . .[b,c]
2.5 5% Pd–C	HOAc	H_3PO_4 (2.2)	. . .[b]
2.5 5% Pd–C	HOAc	HCl (4.4)	<1[b]
1.5 5% Pd–C	HOAc	H_2SO_4 (2.2)	92.3
1.0 5% Pd–C	HOAc	H_2SO_4 (2.2)	86.5
1.0 5% Pd–C	HOAc[d]	H_2SO_4 (2.2)	95.2
1.0 5% Pd–C	HOAc[e]	H_2SO_4 (2.2)	75.5
0.5 5% Pd–C	HOAc	H_2SO_4 (2.2)	59.3
0.5 5% Pd–C	HOAc[d]	H_2SO_4 (2.2)	81.1

[a] See Experimental section for standard amounts. [b] Little or no hydrogen uptake. [c] Although little or no hydrogen uptake could be observed on the pressure gage, work-up of the reaction mixture gave a 10–15% yield of diindanylamine (II) hydrochloride, m.p. 291–301°, in addition to the recovered oxime (I). [d] Acetic acid was pretreated with 5% palladium on charcoal (using 10% weight per volume of acetic acid). [e] Reaction temperature was raised to 50–60°.

the oxime (I) was recovered unchanged, and only a 1.2% yield of III hydrochloride was isolated; the methylene chloride mother liquors of the III hydrochloride were composed largely of diindanylamine (II) hydrochloride, according to the paper chromatograms, and the concentrated solution gave a 10% yield of crystalline II hydrochloride, m.p. 298–300°. Increased reaction temperature in the acetic acid–sulfuric acid reduction caused a lowering of both the yield and the quality of the product (III hydrochloride), evidently because of increased side reactions. Increased hydrogen pressure (from 45 to 700 p.s.i.g.) resulted in no change. Acetic acid could be replaced by ethyl acetate, with only a slight drop in yield (from 93 to 88%), but it could not be replaced by methanol (only 27% yield of III hydrochloride was isolated). When methanolic hydrogen chloride was used as reaction medium, the yield of III hydrochloride under conditions which gave high yields using acetic acid–sulfuric acid (50% catalyst quantity) was only *ca.* 10%, although increased reaction time or additional palladium-on-charcoal catalyst raised the yield to *ca.* 50%. In this reducing system, however, significant amounts of either 2-amino-1-indanone (V) or *trans*-2-amino-1-indanol (VI) (depending on the amount of palladium-on-charcoal catalyst used) was formed as by-product.

The use of 5% rhodium on charcoal[19] (20% of the weight of oxime) in acetic acid containing 2.2 moles of sulfuric acid resulted in no hydrogen uptake.

Hydrogenation of 2-indanone oxime (I) with 5% platinum on charcoal (20% of the oxime weight) in anhydrous ethanol gave 68% recovered I and a 16% isolated yield of diindanylamine (II). When the amount of 5% platinum on charcoal was increased to a weight equal to that of starting I, the yield of diindanylamine (II) increased to over 33%. In contrast to the formation of II in neutral ethanol solvent, reduction of I with an equal weight of 5% platinum on charcoal in methanolic hydrogen chloride gave no II at all, but instead gave a 30–35% yield of 2-(hydroxylamino)indane (IV).[20] Hydrogenation of I with 5% platinum on charcoal (20% of the oxime weight) in glacial acetic acid (no sulfuric acid) gave 78% recovered I and approximately 5% each of II hydrochloride and III hydrochloride. In contrast, hydrogenation with 5% platinum-on-charcoal (20% of the oxime weight) in acetic acid–sulfuric acid (2.2 moles per mole of oxime), solvent conditions which gave high yields of III with 5% palladium-on-charcoal catalyst, gave a 54% yield of 2-(hydroxylamino)indane (IV).

Although the data are consistent with several different reduction schemes, all of the observations can be accommodated by assuming one reaction sequence for neutral (including acetic acid) or basic reductions and a second reaction sequence for the acidic (mineral acid-catalyzed) reductions. In the absence of mineral acid, catalytic reductions presumably proceed by hydrogenolysis of the N–O bond of I to give an intermediate imine.[14] The imine may either be reduced further to 2-aminoindane (III) or react further with a molecule of III followed by hydrogenolysis of the amino group (or elimination and hydrogenation) to give diindanylamine (II), depending on the reaction conditions.[14] Thus, reductions with nickel in methanol containing base gave high yields of III, whereas nickel reduction in acetic acid gave low yields of III and some II. Diindanylamine (II) has also been isolated from platinum-catalyzed hydrogenation in ethanol, palladium-catalyzed hydrogenation in methanol, and from platinum- or palladium-catalyzed hydrogenations in acetic acid, but it has never been isolated from hydrogenations in solvent containing mineral acid.

In the presence of mineral acid, the oxime (I) is protonated. The hydrochloride of I has been isolated, but hydrogen chloride is lost readily, even on vacuum drying at room temperature. Elimination of the C-1 proton instead of the nitrogen proton would give 2-(hydroxylamino)indene, an isomer of the oxime (I) and presumably the key intermediate in the mineral acid-catalyzed reductions.[21] With platinum catalyst, the indene double bond is apparently reduced rapidly, giving 2-(hydroxylamino)indane (IV).[23] Hydrogenolysis of the N–O bond of IV is slow with either platinum- or palladium-catalyzed hydrogenation. Since IV is the major product and III is only a minor product with platinum-catalyzed hydrogenation of I in acetic acid–sulfuric acid, platinum-catalyzed hydrogenolysis of IV to III is

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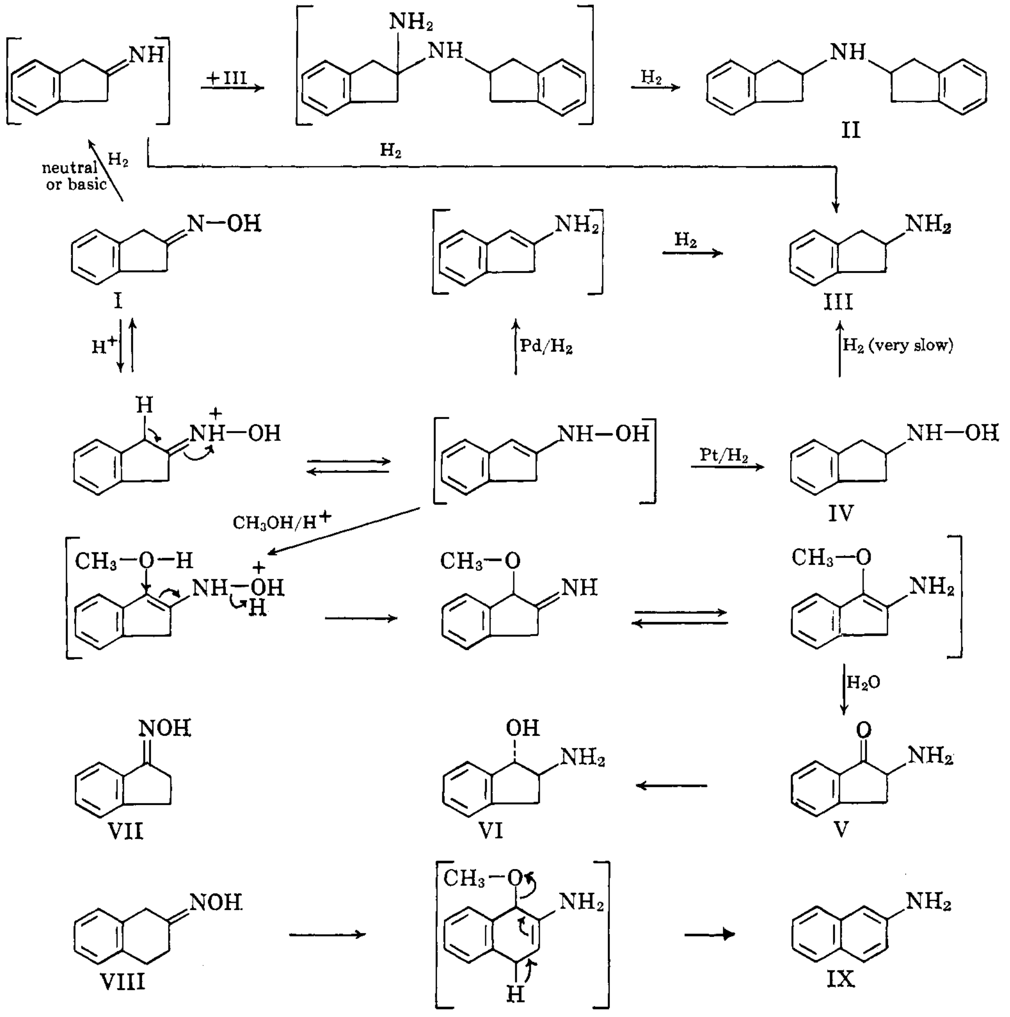
(19) M. Freifelder, *J. Org. Chem.*, **26**, 1835 (1961).

(20) The reduction of oximes to hydroxylamines with platinum black in methanolic hydrogen chloride was previously shown by G. Vavon and A. L. Berton, *Bull. soc. chim. France*, **37**, 296 (1926); G. Vavon and Krajcinovic, *ibid.*, **43**, 231 (1928).

(21) Although these reaction sequences are suggested specifically for the hydrogenation of 2-indanone oxime, it is obvious that other oximes might be reduced in a similar way. However, mineral acid catalysis for platinum-catalyzed hydrogenation of oximes has also been observed for oximes which do not have a hydrogen on the α-carbon atom.[22] The mechanism of acid-catalyzed reduction of such oximes cannot be the same.[23]

(22) W. H. Hartung, *J. Am. Chem. Soc.*, **50**, 3370 (1928).

(23) Alternatively, the mechanism involving prior shift of the carbon–nitrogen double bond into the five-membered ring may apply only to palladium reductions. The platinum reductions in acid may involve direct hydrogenation of the carbon–nitrogen double bond of I, to give IV directly.



obviously slow. Attempted hydrogenation of IV itself with platinum catalyst under the same reaction conditions gave only traces of III; the recovered material was a mixture of starting IV and a new compound which has not been identified. Attempted hydrogenation of IV with palladium catalyst under conditions which afford 90–95% III from I (50% catalyst quantity, acetic acid, sulfuric acid, room temperature, 4 hours) gave 70–80% recovered IV and only 10–20% III. Even increasing the reaction time for this hydrogenolysis reaction to 40 hours did not completely convert IV to III. The palladium-catalyzed reduction of I to III, therefore, does not proceed *via* IV in the liquid phase. To test this conclusion, a palladium-catalyzed reduction was interrupted after half of the theoretical amount of hydrogen had been absorbed. The product mixture contained no IV; it was composed only of starting I, the product III, and trace impurities.[24] In the palladium-catalyzed hydrogenation in acetic acid–sulfuric acid, the activated N–O bond of 2-(hydroxylamino)-indene is apparently attacked more quickly than the indene double bond; the resulting intermediate 2-aminoindene would be expected to reduce rapidly to III. When palladium catalyst was used with methanol instead of acetic acid, either with added sulfuric acid or with added hydrochloric acid, the yield of III from I dropped and the major by-products were IV, which presumably resulted from hydrogenation of the double bond of the 2-(hydroxylamino)indene, and 2-amino-1-indanone (V), which is an isomer of 2-indanone oxime.

The formation of V from palladium–methanolic hydrogen chloride and from stannous chloride–hydrochloric acid reductions offers support for the existence in acid solution of the 2-(hydroxylamino)indene intermediate. The presence of a double bond extending to C-1 would permit attack of a hydroxyl oxygen at C-1, whereas oxidative attack on a C-1 methylene group is unlikely in a reducing environment. When I was treated with methanolic hydrogen chloride alone (*i.e.*, no metal catalyst or hydrogen atmosphere), yields of approximately 50% of V were isolated. A rearrangement of oxime *tosylates* by *base* to α-amino ketones was discovered by Neber,[25] and a mechanism involving a three-membered nitrogen ring intermediate has been discussed.[26] A reasonable mechanism for this interesting *acid*-isomerization is shown in the flow diagram. In one palladium-catalyzed reduction in methanolic hydrogen chloride, where twice the usual amount of palladium was used (*i.e.*, using equal weights of 5% palladium on charcoal and oxime), *trans*-2-amino-1-indanol (VI) was a major product. A sample identical with VI, prepared by catalytic hydro-

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[24] It is possible, but not likely, that oxime is adsorbed on the palladium catalyst and reduced first to IV and then rapidly to III without ever leaving and without ever releasing IV to the reaction solution. In such a case, if IV itself were only slowly adsorbed on the palladium catalyst, reduction of IV might be slow even though it was an intermediate.

[25] P. W. Neber and A. Friedolsheim, *Ann.*, **449**, 109 (1926).

[26] D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953); M. J. Hatch and D. J. Cram, *ibid.*, 38 (1953); H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 307 (1963).

genation of 2-oximino-1-indanone,[27] was shown to be the *trans* isomer[29a] by nuclear magnetic resonance spectroscopy.

Although V formed readily from I in methanolic hydrogen chloride, it was found to be formed in only *ca.* 2% yield in acetic acid–sulfuric acid (no catalyst or hydrogen) and in *ca.* 7% yield in acetic acid–sulfuric acid–5% palladium on charcoal (no hydrogen). The high yield reduction of I to III with 5% palladium on charcoal in acetic acid–sulfuric acid, therefore, does not proceed through V as intermediate, even though V could be reduced to III under these reduction conditions (70% yield).

As a test of the scope of the isomerization reaction (I → V), 1-indanone oxime (VII) and 2-tetralone oxime (VIII) were subjected to methanolic hydrogen chloride isomerizing conditions. With VII, the only identified products were recovered VII (81%) and 1-indanone (6–7%). With VIII, which has an active benzyl hydrogen adjacent to the oximino group, a reaction did occur, but the product was 2-naphthylamine (IX, 58% yield), not 2-amino-1-tetralone. The isomerization of VIII presumably proceeded to the 1-methoxy-2-imino stage, analogous to the isomerization of I to V, but the driving force for aromatization resulted in elimination of methanol (probably *via* the enamine intermediate shown). This aromatization reaction was observed previously with 1-phenyl-2-tetralone oxime and dilute (1.4% weight/volume) ethanolic hydrogen chloride,[29b] although the previous workers claimed that 2-tetralone oxime itself was not converted to 2-naphthylamine under their reaction conditions (55°, 36 hours).

Experimental[30]

All low pressure reductions were carried out in a standard Parr hydrogenation apparatus, using a 4-l. reserve tank. For a normal 5.00-g. oxime run, the pressure dropped from 45 to 40 p.s.i.g. over 0.5–2.0 hr., representing an uptake of 2 moles of hydrogen per mole of oxime. The high pressure reductions were carried out in a rocking autoclave using a Pyrex glass liner.

Starting Materials.—The sponge nickel catalyst was purchased as a water suspension from the Davison Chemical Co., Division of W. R. Grace and Co., Baltimore, Maryland. It reportedly is produced by controlled caustic leaching of 140-mesh nickel-aluminum alloy and is composed of 90% nickel and 10% aluminum. (Equivalent results were obtained, using the optimum conditions, with active Raney nickel catalyst purchased from the Raney Catalyst Co.) The wet nickel catalyst was measured out in "measuring spoons," and consisted of 5.0 g. of nickel plus 3.6 g. of water for one measured teaspoon (4 ml.). So-called "methanol-covered" catalyst resulted from four 50-ml. washes of this catalyst with methanol. The Raney active cobalt catalyst in water and the nickel–aluminum alloy (Raney catalyst powder no. 2813) were purchased from the Raney Catalyst Co., Inc., Chattanooga, Tenn. The 5% palladium on charcoal and 5% platinum on charcoal were purchased from Engelhard Industries, Inc., Newark, N. J. All solvents were analytical grade and were used without further purification.

Paper Chromatography.—The routine use of paper chromatography was invaluable in carrying out these studies, especially for analyzing mixtures. The system employed was butanol–formic acid–water (10:2:15), the upper layer being used as the mobile phase and the lower layer being used to saturate the chamber. The descending technique, with Whatman no. 1 filter paper, was used. Spots were detected by ultraviolet absorption and fluorescence, and with Dragendorff reagent. The found R_f values were: I (0.95), II (0.85), III (0.60), IV (0.80), V (0.40), VI (0.45).

Preparation of 2-Indanone Oxime (I).—A solution of 3.17 g. (20% excess) of hydroxylamine hydrochloride in a mixture of 5.0 ml. of ethanol and 5.0 ml. of water was added to a stirred solution of 5.00 g. of 2-indanone[6] in 12.5 ml. of pyridine. After 10 min., the suspension was diluted with 100 ml. of water, giving 5.36 g. (96.4%) of white solid oxime, m.p. 153–154.5° (lit. m.p. 152–153° dec.,[2] 155°[1]).

A 1.00-g. sample of I was dissolved in 75 ml. of methylene chloride and treated with gaseous hydrogen chloride, giving 1.13 g. (91%) of I hydrochloride, m.p. 126° dec. Recrystallization from methanol–benzene (removing methanol at room temperature and reduced pressure) gave pure I hydrochloride.

Anal. Calcd. for $C_9H_{10}NOCl$ (183.64): C, 58.86; H, 5.49; N, 7.63. Found: C, 58.63; H, 5.78; N, 7.60.

A sample of I hydrochloride was dried at 75° at 0.5 mm. for 2 hr., giving regenerated I, m.p. 151–153°.

Anal. Calcd. for C_9H_9NO (147.17): C, 73.45; H, 6.16; N, 9.52. Found: C, 73.19; H, 6.29; N, 9.53.

Reduction of I with 5% Palladium-on-Charcoal Catalyst.—A mixture of 5.00 g. of 2-indanone oxime and 2.50 g. of 5% palladium on charcoal in 76.6 ml. of glacial acetic acid and 4.0 ml. of concentrated sulfuric acid was shaken in a hydrogen atmosphere at room temperature and 40–45 p.s.i.g. Within 2 hr., the theoretical uptake for two molar equivalents of hydrogen was complete and the reduction stopped. After catalyst had been removed by filtration, the clear colorless filtrate was treated with 24 ml. of 6 *N* sodium hydroxide, with cooling, and the precipitated sodium sulfate was removed by filtration. Acetic acid was removed at reduced pressure, and the residue was dissolved in 25 ml. of water and basified with 20 ml. of 50% aqueous potassium hydroxide (cooling). Five 25-ml. extracts with methylene chloride were combined, backwashed twice with 25-ml. portions of water, and dried over anhydrous sodium sulfate. The filtered methylene chloride solution was concentrated to 50 ml. at reduced pressure and saturated with gaseous hydrogen chloride (stirring and cooling). The white solid was collected, washed with methylene chloride, and dried in vacuum at 60° giving 5.35 g. (92.9%) of white 2-aminoindane hydrochloride, m.p. 246–249° (lit. m.p. 232°,[2] 240–241°[31]), homogeneous by paper chromatography; λ_{max} 258 mμ (ε 630), 265 (980), 272 (1040); λ_{min} 228 mμ (ε 30), 261 (610), 269 (430); $pK_a^{25^\circ}$ 9.7 (H_2O).[32]

Anal. Calcd. for $C_9H_{12}NCl$ (169.66): C, 63.71; H, 7.13; N, 8.26. Found: C, 63.88; H, 7.21; N, 8.42.

Reduction of I with Sponge Nickel Catalyst. (A). With Anhydrous Methanolic Sodium Methoxide.—A mixture of 5.00 g. (34.0 mmoles) of 2-indanone oxime, 2.5 g. of methanol-covered sponge nickel, and 2.20 g. (40.8 mmoles) of sodium methoxide in 25 ml. of methanol was shaken in a Parr hydrogenation machine and heated to 55–60°. After 30 min., hydrogen uptake stopped and the reaction was allowed to cool to room temperature; the uptake after cooling corresponded to 2 moles of hydrogen per mole of oxime. After 3.14 ml. (38.5 mmoles) of concentrated hydrochloric acid was added, the catalyst was removed by filtration and washed thoroughly with methanol. The combined filtrate plus wash was acidified by treatment with 3.14 ml. of concentrated hydrochloric acid and was concentrated at reduced pressure to the original volume (28 ml.). The cloudy green suspension was diluted with 50 ml. of water, washed with three 15-ml. portions of methylene chloride to remove color, basified with 3.2 ml. of 50% aqueous sodium hydroxide, and extracted

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(27) Levin, *et al.*,[2] reduced 2-oximino-1-indanone to 2-amino-1-indanone (V) with palladium on charcoal in absolute ethanol, and then converted V hydrochloride to VI hydrochloride with palladium on charcoal plus palladium chloride in ethanol. Their product, m.p. 171–172°, represented one of the two 2-amino-1-indanol hydrochlorides previously reported[28] as m.p. 178° and m.p. 206°. Our purest sample of VI hydrochloride had m.p. 181–182°.

(28) German Patent 598,142 (June 1934).

(29)(a) Unpublished work (in collaboration with L. Dorfman). Evidently the amine nitrogen of 2-amino-1-indanone (V), which is the intermediate in the hydrogenation of 2-oximino-1-indanone,[2] is adsorbed on the catalyst surface, and hydrogen is delivered *cis* to the amine to give the *trans* isomer VI; (b) H. E. Zaugg, M. Freifelder, and B. W. Horrom, *J. Org. Chem.*, **15**, 1197 (1950).

(30) Melting points were determined on an electrically heated aluminum block and are uncorrected. All ultraviolet absorption spectra were taken in 95% ethanol. Infrared spectra were taken routinely and were consistent with all assigned structures. Analytical samples were dried over Drierite at 75° at 0.5 mm. for 3–5 hr.

(31) J. Kenner and A. M. Mathews, *J. Chem. Soc.*, **105**, 745 (1914).

(32) 2-Aminoindane (III) itself was reported to have $pK_H^{25^\circ}$ 9.52 (H_2O), $pK_H^{21.5^\circ}$ 9.60 (H_2O) by F. Kieffer, *Compt. rend.*, **238**, 1043 (1954).

with three 15-ml. portions of methylene chloride. The three extracts were combined, washed once with 15 ml. of water, dried over anhydrous sodium sulfate, filtered, and saturated with anhydrous hydrogen chloride (stirring and cooling). After standing overnight, the solid was collected, washed thoroughly with cold methylene chloride, and dried in vacuum at 60°, giving 5.31 g. (92.4%) of white 2-aminoindane hydrochloride, m.p. 246–249°, homogeneous by paper chromatography.

B. With Wet Methanolic Sodium Hydroxide.—A mixture of 5.00 g. of 2-indanone oxime, 2.5 g. of water-covered (one-half measured teaspoon, composed of 2.5 g. of catalyst covered by 1.8 g. of water) sponge nickel, and 1.63 g. (40.8 mmoles) of sodium hydroxide in 25 ml. of methanol was shaken at 45 p.s.i.g. of hydrogen pressure and heated to 55–60°. The theoretical hydrogen uptake was completed in 30 min., and the reaction was allowed to cool to room temperature. Work-up as described in method A afforded 5.32 g. (92.5%) of white 2-aminoindane hydrochloride, m.p. 244–246° (in an evacuated capillary it had m.p. 249–251°).

Crystallization from methanol–isopropyl alcohol, the methanol being removed in large part by concentrating at reduced pressure, gave a 93.0% recovery of white prisms having m.p. 249.5–252.5°.

Reduction of I with Raney Cobalt Catalyst.—A mixture of 5.00 g. of 2-indanone oxime, 7.2 g. of methanol-covered Raney cobalt catalyst, and 4.41 g. of sodium methoxide in 50 ml. of methanol was shaken under 45 p.s.i.g. of hydrogen pressure and heated to 55–60°. Hydrogen uptake was completed in 2 hr., and the reaction mixture was allowed to cool to room temperature. The reaction was worked up as described for reduction with sponge nickel catalyst, and gave 4.89 g. (85.1%) of off-white 2-aminoindane hydrochloride, m.p. 244–247°, homogeneous by paper chromatography.

Reduction of I with Nickel-Aluminum Alloy.[33]—A solution of 5.00 g. of 2-indanone oxime and 25 g. of potassium hydroxide in 100 ml. of water was added over 2 hr. to a well stirred suspension of 40 g. of nickel–aluminum alloy in 50 ml. of water plus 50 ml. of methanol, the temperature being maintained at 55–60°. After 16 hr. at 55–60°, the reaction mixture was treated with a solution of 16.9 g. of potassium hydroxide in 68 ml. of water over 1 hr. and stirred an additional 4 hr. at 55–60°. Steam distillation removed the 2-aminoindane, which was extracted from the distillate with methylene chloride and treated with gaseous hydrogen chloride, giving 4.32 g. (75.0%) of 2-aminoindane hydrochloride, m.p. 246–248°, homogeneous by paper chromatography.

2-Aminoindane (III).[33]—A solution of 36.7 g. of 2-aminoindane hydrochloride in water was made basic with aqueous sodium hydroxide, extracted with methylene chloride, and fractionally distilled, giving 18.0 g. (62.7%) of clear colorless III, b.p. 85–86° (4 mm.), n^{25}_{D} 1.5587. A sample was redistilled [b.p. 79° (3 mm.), n^{24}_{D} 1.5596] for elemental analysis [lit.[31] b.p. 229.5° (753 mm.)].

Anal. Calcd. for $C_9H_{11}N$ (133.20): C, 81.16; H, 8.32; N, 10.52. Found: C, 80.65; H, 8.40; N, 11.17.

When III contacted the air, it immediately formed a white solid carbonate salt, m.p. 118–120°.

Derivatives of 2-Aminoindane Other than Hydrochloride. A.—The acetyl derivative had m.p. 125–127° (lit.[31] m.p. 126–127°).

B.—The phthaloyl derivative, prepared in 95.2% yield by refluxing 2.00 g. of 2-aminoindane hydrochloride, 1.74 g. (equivalent amount) of phthalic anhydride, and 2.3 ml. (excess) triethylamine in 85 ml. of toluene for 4 hr. with continuous water take-off (Barrett trap), stripping at reduced pressure, and slurrying with cold 1% aqueous hydrochloric acid, had m.p. 197–200°. Crystallization from benzene gave white crystals of the same melting point.

Anal. Calcd. for $C_{17}H_{13}NO_2$ (263.28): C, 77.55; H, 4.98; N, 5.32. Found: C, 77.72; H, 5.14; N, 5.24.

C.—The maleic acid salt had m.p. 154–154.5°.

Anal. Calcd. for $C_{13}H_{15}NO_4$ (249.27): C, 62.64; H, 6.07; N, 5.62. Found: C, 62.57; H, 6.11; N, 5.69.

D.—The picric acid salt after one recrystallization from methanol had m.p. 252–253°.

Anal. Calcd. for $C_{15}H_{14}N_4O_7$ (362.31): C, 49.73; H, 3.90; N, 15.47. Found: C, 49.89; H, 4.04; N, 15.56.

Reduction of I with 5% Platinum on Charcoal. A. In Anhydrous Ethanol (Formation of II).—A mixture of 5.00 g. of I and 1.00 g. of 5% platinum on charcoal in 76.6 ml. of anhydrous ethanol was hydrogenated at room temperature for 6 hr.; very little hydrogen was taken up. The reaction mixture was heated on the steam bath to dissolve any insoluble organic material and filtered hot to remove catalyst. The filtrate was acidified by addition of 1.3 ml. of concentrated hydrochloric acid and cooled. The off-white solid which separated was collected and dried, giving 0.77 g. (15.9%) of diindanylamine (II) hydrochloride, m.p. 299–303°. [Another run using 5.00 g. of 5% platinum-on-charcoal gave 1.60 g. (33.0%) of II hydrochloride, m.p. 296–299°, and its filtrate was composed largely of II hydrochloride according to paper chromatography.] Two recrystallizations from methanol gave white crystals (yellow cast), m.p. 300–303°; $\lambda_{\max}$ 251 mμ (ϵ 672 sh), 259 (1350), 265 (2140), 271 (2360); $\lambda_{\min}$ 261 mμ (ϵ 1310), 269 (870).

Anal. Calcd. for $C_{18}H_{20}NCl$ (285.82): C, 75.64; H, 7.05; N, 4.90. Found: C, 76.01; H, 7.31; N, 5.00.

The ethanolic hydrochloric acid mother liquors were stripped to dryness at reduced pressure and the light yellow residue was slurried with water. The insoluble solid was collected and dried, giving 3.40 g. (68%) starting I, m.p. 148–151°. The aqueous mother liquors were composed largely of II hydrochloride, according to paper chromatography.

When a solution of 0.35 g. of II hydrochloride in 15 ml. of methanol–water (1:5) was made basic with aqueous sodium hydroxide, 0.21 g. (66%) of white solid II separated, m.p. 99–100°; concentration of the mother liquors at reduced pressure gave 0.05 g. (16%) of white solid, m.p. 91–96°, as a second crop. Recrystallization of the first crop from methanol–water (4:1) gave 0.16 g. of long white prisms of II, m.p. 99–100° (lit.[4] m.p. 102°); $\lambda_{\max}$ 251 mμ (ϵ 750 sh), 259 (1560), 266 (2510), 273 (2740); $\lambda_{\min}$ 261 mμ (ϵ 1540) 269 (1080).

Anal. Calcd. for $C_{18}H_{19}N$ (249.36): C, 86.72; H, 7.68; N, 5.62. Found: C, 86.61; H, 7.71; N, 5.49.

A sample of II was converted to its picric acid salt and then recrystallized from 95% ethanol, giving long yellow prisms of II picrate, m.p. 189.5–190°; $\lambda_{\max}$ 239 mμ (ϵ 12,030 sh), 265 (5700 sh), 271 (4570), 358–360 (16,860); $\lambda_{\min}$ 269 mμ (ϵ 3510), 282 (1540). A spectrophotometric determination of molecular weight[34] gave a value of 468.

Anal. Calcd. for $C_{24}H_{22}N_4O_7$ (476.47): C, 60.25; H, 4.63; N, 11.71. Found: C, 60.17; H, 4.65; N, 11.74.

B. In Acetic Acid–Sulfuric Acid (Formation of IV).—A mixture of 5.00 g. of I and 1.00 g. of 5% platinum on charcoal in 76.6 ml. of glacial acetic acid and 4.0 ml. of concentrated sulfuric acid was shaken under hydrogen in a Parr hydrogenation apparatus for 6 hr. at room temperature; approximately 2 moles of hydrogen per mole of oxime was absorbed. The catalyst was removed by filtration, and the light pink filtrate was worked up as described for a similar reduction using palladium catalyst. The white solid was collected, washed with methylene chloride, and dried *in vacuo* at 60°, giving 3.41 g. (54.0%) of 2-hydroxylaminoindane (IV) hydrochloride (contaminated with some III hydrochloride, according to paper chromatography), m.p. 184–186°. The hydrochloride salt was dissolved in water, and made basic with aqueous sodium hydroxide; precipitated IV was collected, dried, and recrystallized once from ethyl acetate and once from isopropyl alcohol to give white solid IV, m.p. 115–116°; $\lambda_{\max}$ 251 mμ (ϵ 380 sh), 259 (780), 266 (1220), 273 (1360); $\lambda_{\min}$ 261 mμ (ϵ 750), 270 (500).

Anal. Calcd. for $C_9H_{11}NO$ (149.20): C, 72.45; H, 7.43; N, 9.39. Found: C, 72.74; H, 7.46; N, 9.27.

A 0.42-g. sample of IV was dissolved in 5 ml. of isopropyl alcohol and treated with gaseous hydrogen chloride. Chilling at −15° overnight precipitated 0.41 g. (79%) of IV hydrochloride as a pale greenish white crystalline solid, m.p. 195°. One crystallization from methanol–ethyl acetate gave white (green cast) crystalline IV hydrochloride, m.p. 198–200°; $\lambda_{\max}$ 236–248 mμ (ϵ 469 plateau), 259 (822), 265 (1220), 272 (1360), 289 (229 sh); $\lambda_{\min}$ 225 mμ (ϵ 284), 261 (821), 269 (628).

Anal. Calcd for $C_9H_{12}NOCl$ (185.66): C, 58.23; H, 6.52; N, 7.54; Cl, 19.10. Found: C, 58.54; H, 6.89; N, 7.40; Cl, 19.21.

Molecular weight determination by single crystal technique (X-ray diffraction) gave a found value of 184. The orthorhombic unit cell dimensions are $a = 6.05$, $b = 7.35$, $c = 20.56$ Å., $Z = 4$, d 1.339, and space group $P\,2_12_12$.

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[33] Experiment carried out by M. P. Linfield.

[34] K. G. Cunningham, W. Dawson, and F. S. Spring, *J. Chem. Soc.*, 2305 (1951).

A 0.22-g. sample of IV in hot 95% ethanol was treated with 4 ml. of saturated ethanolic picric acid, and the solution heated on the steam bath for 10–15 min. The clear yellow solution was allowed to stand at room temperature overnight, and the crystalline yellow-orange precipitate was collected, washed, and dried, giving 0.39 g. (88.5%), m.p. 153–160°. One crystallization from methanol–benzene raised the melting point to 161.5–162°; λ_{max} 237 mμ (ϵ 11,560 sh), 265 (3950 sh), 272 (2830), 358–360 (15,060); λ_{min} 270 mμ (ϵ 2540), 280–285 (1190). A spectrophotometric determination of molecular weight[34] gave a found value of 371.

Anal. Calcd. for $C_{15}H_{14}N_4O_8$ (378.31): C, 47.62; H, 3.73; N, 14.81. Found: C, 47.87; H, 3.92; N, 15.07.

A clear, colorless solution of 0.50 g. of IV in 10 ml. of pyridine and 5 ml. of acetic anhydride was allowed to stand overnight at room temperature. The solution was diluted with water and extracted with methylene chloride. The combined extract was washed free of pyridine with dilute hydrochloric acid, dried, and stripped to dryness at reduced pressure. The yellow-orange liquid residue was taken up in 3 ml. of acetone and chilled at −15°. The 0.16 g. of white solid precipitate was recrystallized from acetone to give 0.09 g. of 2-(hydroxylamino)indane N,O-diacetate, m.p. 58–60°. The infrared spectrum showed ν_{max}^{Nujol} 1793, 1682 cm.$^{-1}$, similar to peaks reported for the infrared spectrum of hydroxylamine N,O-diacetate itself (ν_{max}^{Nujol} 1802, 1664 cm.$^{-1}$).[35]

Anal. Calcd. for $C_{13}H_{15}NO_3$ (233.27): C, 66.94; H, 6.48; N, 6.01. Found: C, 67.20; H, 6.95; N, 5.92.

Preparation of *trans*-2-Amino-1-indanol (VI).—A mixture of 7.50 g. of 2-oximino-1-indanone,[36] 1.13 g. of 100% palladium black, 29 ml. of glacial acetic acid, and 1.5 ml. of concentrated sulfuric acid[18] was shaken in a Parr hydrogenation apparatus at room temperature and 30–45-p.s.i.g. hydrogen pressure for 7 hr. The reaction mixture was worked up as previously described,[36] giving 5.43 g. of crude solid amine (compared with the previously isolated 3.9 g. of oily base III[36]). A sample of this crude solid was crystallized once from isopropyl alcohol and twice from benzene, giving white crystals of VI, m.p. 105–109°, homogeneous by paper chromatography; λ_{max} 251 mμ (ϵ 290 sh), 258 (540), 265 (810), 271 (870); λ_{min} 232–233 mμ (ϵ 40), 260 (530), 269 (370).

Anal. Calcd. for $C_9H_{11}NO$ (149.19): C, 72.45; H, 7.43; N, 9.39. Found: C, 72.35; H, 7.42; N, 9.30.

Another sample of crude amine was dissolved in isopropyl alcohol, treated with gaseous hydrogen chloride, and chilled at −5°. The crystalline VI hydrochloride was recrystallized twice from methanol–benzene, to give white crystals, m.p. 181–182° dec., homogeneous by paper chromatography (lit. m.p. 171–172°,[2] 178°[28]).

Anal. Calcd. for $C_9H_{12}NOCl$ (185.66): C, 58.22; H, 6.52; N, 7.54. Found: C, 58.17; H, 6.49; N, 7.34.

Reduction of I with Stannous Chloride (Formation of V).—A suspension of 5.00 g. of I and 17.0 g. of stannous chloride dihydrate in 110 ml. of concentrated (37%) hydrochloric acid was refluxed with stirring for 6 hr. The yellow suspension was filtered, basified, and extracted with methylene chloride. The washed and dried solution was saturated with gaseous hydrogen chloride, giving 0.60 g. (*ca.* 9%) of V hydrochloride, m.p. 208–212° dec., slightly contaminated according to paper chromatography. A similar run was carried out with 16 hr. of refluxing. The acid-insoluble material (m.p. 151–154°) accounted for 84% of the starting I, and addition of hydrogen chloride to the concentrated methylene chloride extract precipitated 0.15 g. (*ca.* 2.3%) of tan solid V hydrochloride, m.p. 214–218° dec. Recrystallization from methanol–isopropyl alcohol (addition of a drop of concentrated hydrochloric acid reduced the sensitivity to warming) gave a pale pink-white solid, decomposing *ca.* 210–220°; λ_{max} 247 mμ (ϵ 13,200), 292 (2540); λ_{min} 221 mμ (ϵ 1390), 271 (1150). The ultraviolet absorption spectrum was typical of 2-substituted 1-indanone derivatives, and the decomposition behavior agreed with reports in the literature for V hydrochloride: "darkening at 200°,"[2] "turning brown at *ca.* 200° and decomposing by 240°,"[37,38] "darkens at 220°."[39] The product had the same staining properties as authentic V (see next section).

Anal. Calcd. for $C_9H_{10}NOCl.0.25H_2O$ (188.14): C, 57.46; H, 5.63; N, 7.46; Cl, 18.84. Found: C, 57.58; H, 5.62; N, 7.53; Cl, 18.95.

A 0.20-g. sample of V hydrochloride was treated with excess picric acid in 95% ethanol (heated 10 min., chilled at −15°), and the 0.27 g. of V picrate which separated was recrystallized from methanol, giving yellow crystals, 145° dec. (previously reported: 154–156°,[37] 152°,[38] 148° dec.[39]); λ_{max} 244 mμ (ϵ 23,430), 289 (4310 sh), 297–300 (4860), 356–360 (16,530); λ_{min} 222 mμ (ϵ 15,220), 275 (3200), 306 (4560). A spectrophotometric determination of molecular weight[34] gave a found value of 386.

Anal. Calcd. for $C_{15}H_{12}N_4O_8$ (376.29): C, 47.88; H, 3.21; N, 14.89. Found: C, 47.95; H, 3.46; N, 14.78.

Preparation of 2-Amino-1-indanone (V) Hydrochloride from 2-Indanone Oxime (I).—A solution of 5.00 g. of I in 200 ml. of methanol, previously saturated with gaseous hydrogen chloride, was stirred and refluxed for 8 hr. under a drying tube. The black solution was stripped to dryness at reduced pressure, and the residue was stirred 30 min. with 200 ml. of 3.7% hydrochloric acid and filtered. The yellow solution was basified with 17 ml. of 50% aqueous sodium hydroxide and was extracted with five 25-ml. portions of methylene chloride. The combined purple-black methylene chloride extract was washed twice with water and dried over anhydrous sodium sulfate. The fitered solution was saturated with gaseous hydrogen chloride and chilled at −5° for 4 hr. The yellow-tan precipitate was collected, washed with cold methylene chloride, and dried, giving 2.85 g. (45.7%) of V hydrochloride, m.p. 215° dec. Based on ultraviolet absorption intensities, this material was 90–95% pure; λ_{max} 246 mμ (ϵ 12,000), 292 (2380). One recrystallization from methanol–isopropyl alcohol (containing 2 drops of concentrated hydrochloric acid; most methanol removed by distilling at reduced pressure) gave white solid, shrinking *ca.* 200°, m.p. 213–215° dec. (turned black, gaseous evolution); λ_{max} 247 mμ (ϵ 13,170), 292 (2470), λ_{min} 221 mμ (ϵ 1750), 271 (1160); the infrared spectrum in Nujol showed typical NH peaks in the 2000–2800 cm.$^{-1}$ region, a N-H deformation peak at 1605 cm.$^{-1}$, and a conjugated five-membered ring ketone peak at 1715 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{10}NOCl$ (183.64): C, 58.86; H, 5.49, N, 7.63; Cl, 19.31. Found: C, 58.70; H, 5.37; N, 7.88, Cl, 19.35.

When the reflux time was reduced from 8 hr. to 1 hr., the yield of crude product, λ_{max} 248 mμ (ϵ 11,700), 292 (2480), rose to 52.0%. When the reaction was carried out at room temperature for 17 hr., the yield of crude product, λ_{max} 248 mμ (ϵ 9500), 274 (1420), 292 (1960), was 46.4%.

Aqueous solutions of the free base V caused skin, wood, and fabric to turn "shocking pink." Aqueous sodium hydroxide changed the color to purple, whereas hydrochloric acid eliminated the color. The color and staining properties of V have been reported previously.[36]

The ultraviolet absorption spectrum of a solution of V hydrochloride in 0.1 *N* ethanolic potassium hydroxide, compared with the spectrum in neutral ethanol, had maxima at higher wave lengths; λ_{max} 255 mμ (ϵ 26,880), 303 (2760 sh), λ_{min} 235 mμ (ϵ 12,900). After standing at room temperature, or more rapidly if heated, the peak at 255 mμ gradually decreased, while the shoulder at 303 mμ increased in intensity to a distinct peak and then gradually decreased; λ_{max} (20 min.) 253–255 mμ (ϵ 21,870), 300 (4040); λ_{max} (1 hr.) 252 mμ (ϵ 13,750), 302 (5900); λ_{max} (2 hr.) 245 mμ (10,420 sh), 253 (10,020 sh), 303 (5010); λ_{max} (24 hr.) 240 mμ (sh area, ϵ 8760), 302 (3910). The final ultraviolet absorption spectrum in 0.1 *N* ethanolic potassium hydroxide showed strong end absorption plus a broad shoulder area (ϵ *ca.* 2000) centered at *ca.* 290 mμ.

Preparation of 2-Tetralone Oxime (VIII).—The reaction conditions for conversion of 2-tetralone (Aldrich Chemical Co., Inc., Milwaukee, Wisconsin) to its oxime were the same as those for conversion of 2-indanone to I. Dilution with water precipitated an oil which was taken up in methylene chloride, washed free of pyridine with dilute hydrochloric acid, dried, freed of solvent by stripping at reduced pressure, and crystallized from ethanol–water (2:1). The white needles of oxime (50% yield), which

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[35] D. E. Ames and T. F. Grey, *J. Chem. Soc.*, 631 (1955).

[36] The reduction of 2-oximino-1-indanone to III hydrochloride in 52.7% yield by hydrogenation in acetic acid–sulfuric acid using 100% palladium black has recently been described by C. F. Huebner, E. M. Donoghue, P. L. Strachan, P. Beak, and E. Wenkert, *J. Org. Chem.*, **27**, 4465 (1962). The procedure described here uses only half the amount of palladium catalyst used by Huebner, *et al.*

[37] E. Pfaehler, *Ber.*, **46**, 1700 (1913).

[38] S. Gabriel and R. Stelzner, *ibid.*, **29**, 2603 (1896).

[39] F. S. Statham, *J. Chem. Soc.*, 213 (1951).

tended to sublime at high vacuum, had m.p. 89–90° (lit. m.p. 89°,[40] 86.5–87.5°[41]); λ_{max} 258 mμ (ϵ 315 sh), 264 (390), 271 (350); λ_{min} 241 mμ (ϵ 155); 269 (280).

Anal. Calcd. for $C_{10}H_{11}NO$ (161.21): C, 74.51; H, 6.88. Found: C, 74.32; H, 7.04.

Preparation of 2-Naphthylamine (IX) Hydrochloride from 2-Tetralone Oxime (VIII).—A solution of 0.20 g. of 2-tetralone oxime (VIII) in 8.0 ml. of saturated methanolic hydrogen chloride was refluxed for 1 hr. and then stripped to dryness at reduced pressure. The white solid residue was dissolved in dilute hydrochloric acid (2.0 ml. of concentrated hydrochloric acid diluted to 20 ml. with water), filtered, and made basic. The white solid separated, was collected, washed with water, dissolved in 4 ml. of methylene chloride, dried briefly over anhydrous sodium sulfate, and filtered. The solution was saturated with gaseous hydrogen chloride and chilled to 0°, giving 0.13 g. (58%) of white solid IX hydrochloride, m.p. 241–242.5°; λ_{max} 236 mμ (ϵ 53,420), 268 (4900 sh), 279 (5900), 290 (4270 sh), 338–340 (1260); λ_{min} 257 mμ (ϵ 3540), 305 (470) (the ultraviolet absorption spectrum is the same as that reported previously[42] for IX).

Anal. Calcd. for $C_{10}H_{10}NCl$ (179.65): C, 66.86; H, 5.61; N, 7.80; Cl, 19.73. Found: C, 66.87; H, 5.75; N, 7.69; Cl, 20.00.

Reduction of 2-Amino-1-indanone (V) Hydrochloride with 5% Palladium-on-Charcoal Catalyst.—A mixture of 1.50 g. of V-hydrochloride and 0.75 g. of 5% palladium on charcoal in 23 ml. of glacial acetic acid and 1.2 ml. of concentrated sulfuric acid was shaken in a hydrogen atmosphere at room temperature and 45 p.s.i.g. of pressure. The reaction mixture was worked up as described to give 0.97 g. (69.8%) of III hydrochloride, m.p. 234–238°, slightly contaminated according to paper chromatography.

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The Synthesis of 3-Ethyl-4-methylphenol and 3-Isopropyl-4-methylphenol from 3,4-Dimethylphenol *via* Trichloromethyl Intermediates[1]

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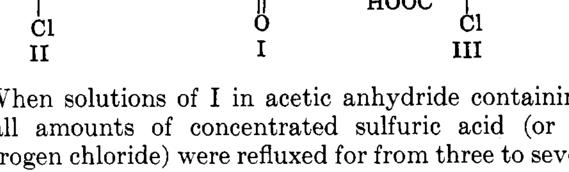
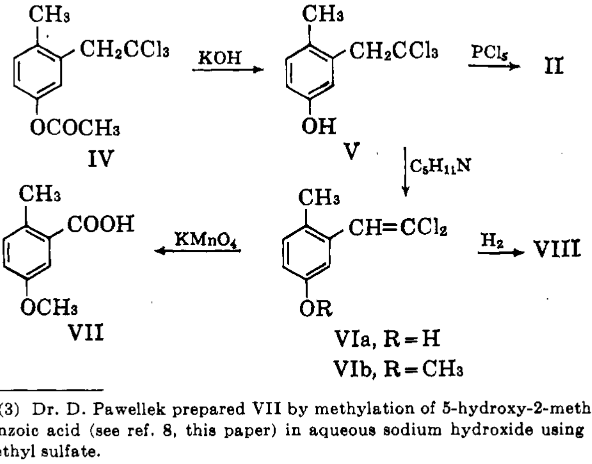
On refluxing solutions of 3,4-dimethyl-4-trichloromethyl-2,5-cyclohexadienone (I) in acetic anhydride containing an acid, rearrangement to the acetate of 4-methyl-3-(β,β,β-trichlorethyl)phenol (V) occurs in high yield. Treatment of V with piperidine yields 4-methyl-3-(β,β-dichlorovinyl)phenol (VIa) which on hydrogenation is converted into 3-ethyl-4-methylphenol (VIII). Condensation of VIII with carbon tetrachloride (aluminum chloride) affords 3-ethyl-4-methyl-4-trichloromethyl-2,5-cyclohexadienone (IX) which may be converted into 4-methyl-3-isopropylphenol (XIII) by a series of reactions analogous to those by which V is converted into VIII.

The rearrangements of 3,4-dimethyl-4-trichloromethyl-2,5-cyclohexadienone (I) to 4-methyl-3-(β,β,β-trichloroethyl)chlorobenzene (II) on treatment with phosphorus pentachloride and to 2-chloro-4,5-dimethylbenzoic acid (III) on treatment with polyphosphoric acid (PPA) have been described.[2] In these types of reaction the nuclear oxygen is replaced by chlorine. We now describe acid-catalyzed rearrangements of I, and of the corresponding 3-ethyl analog IX, in which the nuclear oxygen is retained. By means of these reactions and further reactions described later, the syntheses of 3-ethyl-4-methylphenol (VIII) from 3,4-dimethylphenol and of 3-isopropyl-4-methylphenol (XIII) from VIII have been accomplished.



When solutions of I in acetic anhydride containing small amounts of concentrated sulfuric acid (or of hydrogen chloride) were refluxed for from three to seven hours, yields of over 90% of 4-methyl-3-(β,β,β-trichloroethyl)phenyl acetate (IV) were obtained. The structure of IV was established by the following method: Brief alkaline hydrolysis of IV yielded 4-methyl-3-(β,β,β-trichloroethyl)phenol (V) which on heating with piperidine afforded 4-methyl-3-(β,β-dichlorovinyl)-phenol (VIa). Methylation of VIa yielded VIb which on oxidation yielded 5-methoxy-2-methylbenzoic acid (VII) identical with VII prepared by another route.[3] All yields were high. In addition, treatment of V with phosphorus pentachloride yielded a small amount of II.[2] Identity of the two samples of II was demonstrated by comparison of the infrared spectra.



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[3] Dr. D. Pawellek prepared VII by methylation of 5-hydroxy-2-methylbenzoic acid (see ref. 8, this paper) in aqueous sodium hydroxide using dimethyl sulfate.