and DeTar to give δ-phenylvaleramide in 29% yield.[19] In an 8-inch Pyrex ignition tube were sealed 3.0 g. of sulfur, 1.0 g. of phenyl *n*-butyl ketone-β-d_2, 3.0 ml. of pyridine, 2.0 ml. of ammonium polysulfide and 5 ml. of 15 *M* ammonium hydroxide. The tube was heated five hours at 165–170°, cooled, and the contents washed into a beaker using concentrated ammonia. The mixture was evaporated to dryness on the steam-bath, the residue was ground and leached with 20 ml. of boiling water. Evaporation and subsequent recrystallization from hot water yielded 55 mg. of δ-phenylvaleramide, m.p. 104–105°.

Combustion of the Compounds.—The technique involved is fully described in a paper by Anderson, Delabarre and Bothner-By.[20]

Samples of the organic compounds, weighing between 5 and 10 milligrams, were combusted in oxygen at one atmosphere. The resultant gases were bled into a vacuum system where the water was condensed in a Dry Ice–acetone trap and the carbon dioxide in a liquid nitrogen trap, the oxygen carrier being pumped away. The water trap was designed to give a small internal surface area. The amount of carbon dioxide was determined manometrically, to ensure that complete combustion had taken place. To eliminate troublesome exchange of deuterated water with adsorbed water, three consecutive combustions were run, and the third water sample used in the conversion to ethane.

Conversion of Heavy Water to Ethane.—A detailed description of the apparatus and technique involved in the conversion of deuterated water to ethane is given by Friedman and Irsa.[21]

The synthesis of diethylzinc followed a method described in "Organic Syntheses" in which ethyl iodide and a copper-zinc couple were the starting materials.[22] The product was fractionated at ordinary pressure in a nitrogen atmosphere. It was transferred to a reservoir bulb on the vacuum manifold described by Friedman and Irsa[21] which permitted removal of the nitrogen and storage of the reagent *in vacuo*.

The procedure afforded quantitative conversion of a sample of deuterated water to pure ethane which was removed from the vacuum line in a gas sample bulb. The joint of this bulb fitted the mass spectrometer by means of which the deuterium assay was obtainable.

Mass Spectrometric Assay of Ethane.—The ethane was analyzed in a Consolidated–Nier model 21-201 mass spectrometer using the superposition method of analysis. The atom per cent. deuterium was calculated by this method from the relative ion intensities of the mass 30 and mass 31 peaks in the observed spectra. By multiplying the atom per cent. deuterium by the number of hydrogen atoms in the molecule one obtains the number of atoms of deuterium per molecule of organic compound.

Samples of the alcohol, ketone and amide, were combusted in duplicate. The deuterated water from each combustion was then converted to ethane. To aid in the calibration of the spectrometer a sample of "light" or distilled water, as well as a sample of "heavy" water (99.8% D_2O) was converted to ethane. From the atom per cent. deuterium in each sample the data presented in the table were obtained.

Acknowledgments.—We are indebted to several members of the Chemistry Department of Brookhaven National Laboratory: Dr. R. W. Dodson for making available the laboratory facilities, Dr. Aksel A. Bothner-By for valuable suggestions in the work, especially for the method of synthesis of the deuterated ketone, Miss Yvette Delabarre for the microcombustions of the deuterated compounds, and to Dr. Lewis Friedman and Mr. A. P. Irsa for the mass spectrometric assays.

UPTON, L. I., N. Y.
NEW YORK 58, N. Y.

---

[19] D. F. DeTar and M. Carmack, THIS JOURNAL, **68**, 2025 (1946).

[20] R. C. Anderson, Y. Delabarre and A. A. Bothner-By, *Anal. Chem.*, **24**, 1298 (1952).

[21] L. Friedman and A. P. Irsa, *ibid.*, **24**, 876 (1952).

[22] Reference 17, pp. 184–187.

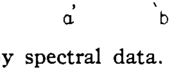
[CONTRIBUTION FROM THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

The Problem of the Unsaturated Three-membered Ring Containing Nitrogen

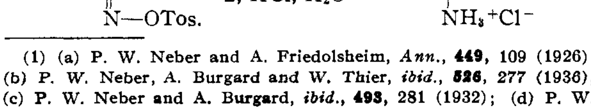
BY DONALD J. CRAM AND MELVIN J. HATCH

RECEIVED MARCH 26, 1952

The structure of the unstable intermediate isolated in the application of the Neber rearrangement to the 2,4-dinitrophenylacetoneoxime system has been further investigated. The structural evidence, both old and new, is most simply rationalized on the basis of formula (A). The ring has been opened at "a" by catalytic hydrogenation to give in the presence of acetic anhydride an acylated vinylamine, and in the absence of acylating reagent and in the presence of water, 2,4-dinitrophenylacetone. The double bond at "b" was reduced with lithium aluminum hydride to give an ethylenimine. These results coupled with the observation of Neber that the double bond at "b" undergoes solvolytic cleavage to give aminoketals or aminoketones suggest that the intermediate is an unsaturated three-membered heterocyclic ring. The position assigned to the double bond in the ring is supported by spectral data.



Although the synthesis of α-aminoketones from oximetosylates through the use of the Neber rearrangement was discovered over 25 years ago,[1a] this novel reaction has received little more than passing attention since the discoverer completed his original series of investigations.[1d] While attempting to determine the course of the rearrangement, in two cases Neber[1c,1d] succeeded in isolating unstable intermediates whose assigned structures (IIIA and IIIB) he considered to provide a satisfactory justification for the gross mechanism of the general reaction. The presumed substance, 2-(2,4-dinitrophenyl)-3-methyl-2-azirine (IIIA) was well characterized through analyses and molecular weight determinations. However, the suggestion that the unstable intermediates contain an azacyclopropene ring (azirine ring system)[2] warrants critical examination.[3]



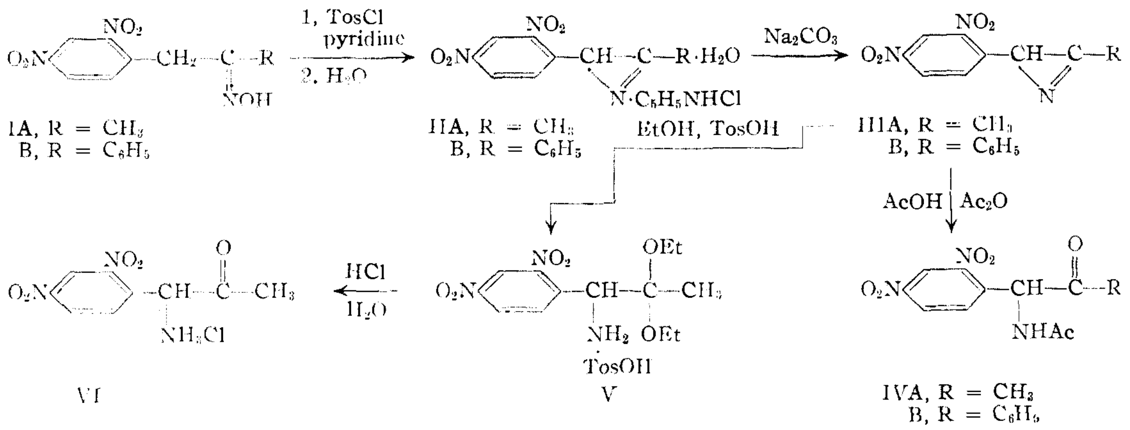
$$—CH_2—\underset{\underset{N—OTos.}{\|}}{C}— \xrightarrow[2,\ HCl,\ H_2O]{1,\ NaOEt,\ EtOH} —\underset{\underset{NH_3{}^+Cl^-}{|}}{CH}—\overset{\overset{O}{\|}}{C}—$$

---

[1] (a) P. W. Neber and A. Friedolsheim, *Ann.*, **449**, 109 (1926); (b) P. W. Neber, A. Burgard and W. Thier, *ibid.*, **526**, 277 (1936); (c) P. W. Neber and A. Burgard, *ibid.*, **493**, 281 (1932); (d) P. W. Neber and G. Huh, *ibid.*, **515**, 283 (1935).

[2] A. M. Patterson and L. T. Capell, "Ring Index," Reinhold Publishing Corp., New York, N. Y., 1940, p. 3.

[3] The widely recognized instability of ethylenimines [for references, see Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 61] coupled with the strain associated with three-membered rings containing double bonds [see M. J. Schlatter, THIS JOURNAL, **63**, 1734 (1941)] indicate that structures IIIA and IIIB should be accepted with reserve.



The present investigation was undertaken with two objectives: to substantiate or disprove the azirine structure for these intermediates; to elaborate in more detail the mechanism and scope of the over-all Neber rearrangement. This paper reports the results directed toward the first of these objectives.

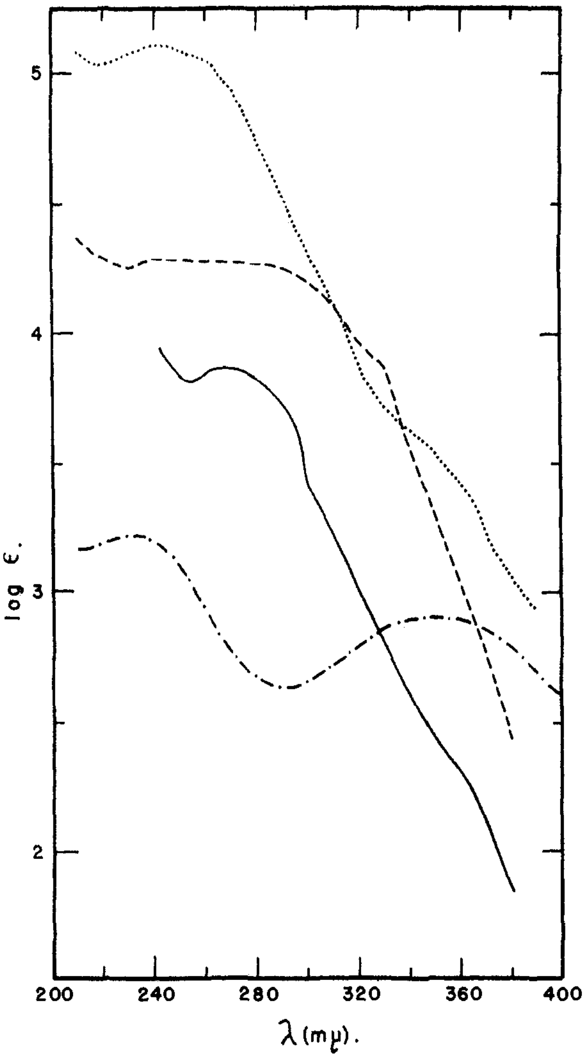
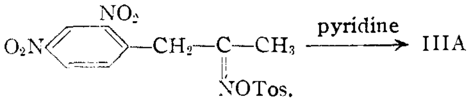


Fig. 1.—Ultraviolet absorption spectra (Cary spectrophotometer, model 11PMS) in 95% ethanol: ....., 2,4-dinitrophenylacetoneoxime (I); ----, 2-(2,4-dinitrophenyl)-3-methyl-2-azurine (IIIA); —, 2-(2,4-dinitrophenyl)-3-methylethylenimine (X); -.-., 1-(2,4-dinitrophenyl)-2-acetamido-1-propene (IXB).

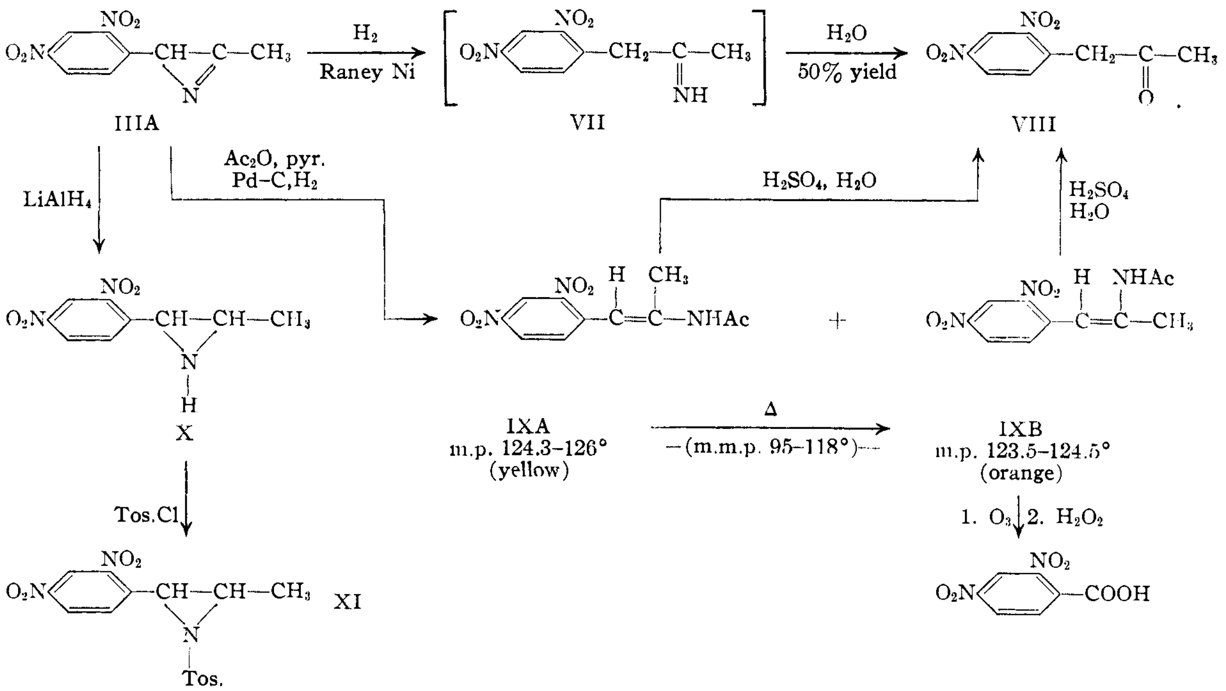
Reactions of the Azirine Ring System.—In Neber's original preparation of IIIA,[4] the pyridine–azirine salt (IIA) resulted from an attempt to prepare the oxime tosylate by the usual method.[1c] To remove potential ambiguities from the reaction course, the tosylate of the starting oxime was prepared in the present investigation, and was shown to rearrange in pyridine to give material identical with IIIA prepared by the method of Neber.[1c]



Compound IIIA when submitted to hydrogenation (one mole of hydrogen and a Raney nickel catalyst) produced a dark semi-solid which when chromatographed on alumina produced 2,4-dinitrophenylacetone (VIII). The reduction probably took place to give the imino compound, VII, which hydrolyzed, probably during the chromatographic stage. When the hydrogenation of IIIA was carried out in pyridine and acetic anhydride with a palladium–carbon catalyst, the two isomeric vinylacetamide compounds IXA and IXB were obtained. The structures of these compounds were demonstrated as follows (the configurational assignments given to the two isomers are completely arbitrary). Upon melting, IXA isomerized to IXB, and admixture of the two compounds produced a substantial depression in melting point. Upon acid hydrolysis, both isomers produced ketone VIII. The more stable substance (IXB) when submitted to ozonolysis and subsequent oxidation (hydrogen peroxide) gave 2,4-dinitrobenzoic acid. The ultraviolet absorption spectrum of IXB is recorded in Fig. 1, and this spectrum and the color of the compound are compatible with the assigned structure. The oxime (I) serves as an unconjugated model (Fig. 1). The ultraviolet absorption spectra of the two isomers were identical. The great susceptibility of the carbon–nitrogen single bond of the three-membered ring to hydrogenolysis is explained as a consequence of the strain associated with the azirine ring and with the stabilizing effect of the nitro

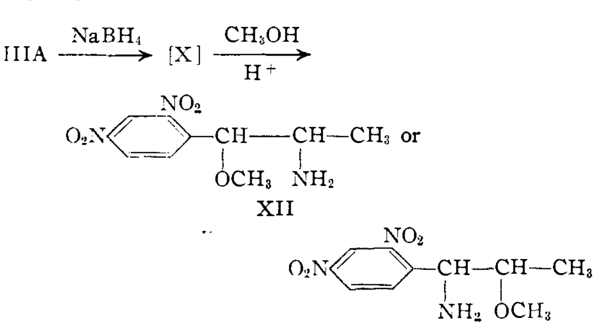
---

[4] Structure IIIA is assumed for the unstable intermediate for purposes of discussion.



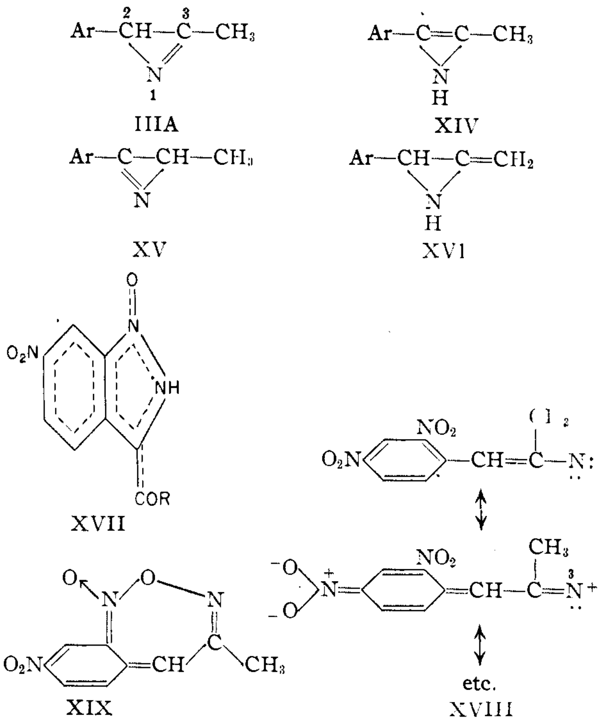
groups upon the transition state of the reduction reaction. The shift of the double bond into conjugation with the aromatic nucleus during the reductive–acetylation reaction can be attributed to the enhanced resonance of stabilization associated with structures IXA and IXB.

Treatment of azirine IIIA with lithium aluminum hydride produced a small yield of 2-(2,4-dinitrophenyl)-3-methylethylenimine (X) which was characterized through its tosyl derivative (XI). This reaction again demonstrates the ability of the azirine ring to compete with the nitro groups for the action of reducing agents. The ultraviolet absorption spectrum of the ethylenimine is recorded in Fig. 1. Reduction of IIIA with sodium borohydride in methanol (slightly acidic) probably first gave the imine (X) which underwent ring opening to produce either XII or XIII.



Attempts to produce optically active azirine (IIIA) both through resolution and by asymmetric synthesis failed. In the synthesis attempt, brucine was used as a catalyst to convert 2,4-dinitrophenylacetoneoxime tosylate to IIIA. Although good yields of IIIA were obtained, the material was optically inactive.

The Structure of the Intermediate in the Neber Rearrangement.—Seven structures can be reconciled with the results of Neber's investigations of the intermediate to which he attributed structure IIIA: these structures are IIIA, XIV, XV, XVI, XVII[5] (or one of its tautomers), XVIII[6] and XIX.[6]



Of the four tautomerically related structures (IIIA, XIV, XV and XVI), XV is inconsistent with both the hydrolytic behavior of the intermediate (noted by Neber[1c]), as well as with the reduction reactions reported here. Although tautomeric shifts during these reactions are possible, the movement of a

---

(5) This structure was suggested by R. B. Woodward (private communication) as consistent with the data of Neber, *et al.* (ref. 1).

(6) These structures were suggested and justified by one of the Referees.

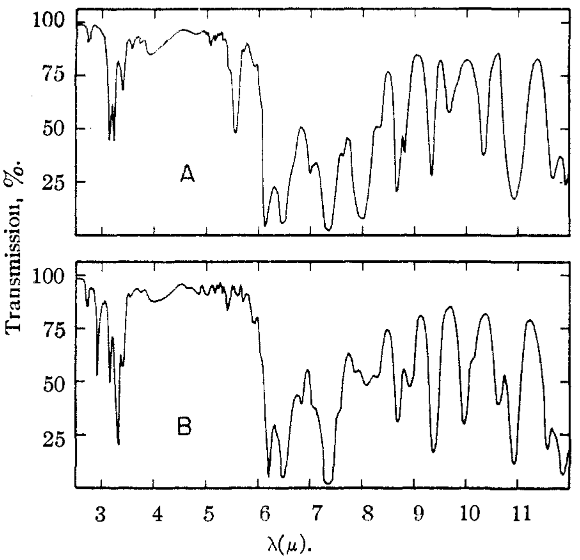
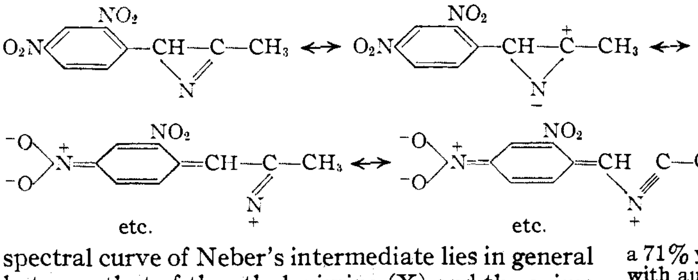


Fig. 2.—Infrared absorption spectra (Beckman IR2T spectrophotometer, NaCl prism): A, 22 wt. % of 2-(2,4-dinitrophenyl)-3-methyl-2-azurine (IIIA) in chloroform; B, 21 wt. % of 2-(2,4-dinitrophenyl)-3-methylethylenimine in chloroform (X).

double bond out of conjugation with an aromatic system is improbable. The infrared spectral data (Fig. 2) provide a means of distinguishing between the other three tautomers. Thus in the spectrum of the ethylenimine (X), a band appears at 2.92 μ which is characteristic of an N-H stretching vibration of an imine.[7] Since structures XIV and XVI contain an N-H linkage, and yet the band at 2.9 μ is missing in the spectrum of Neber's intermediate, these two structures become unlikely.

In contrast, structure IIIA (that suggested by Neber) is consistent with both the chemical and spectral data. On the basis of this structure, the band occurring at 5.55 μ in the infrared spectrum of the intermediate and absent in that of the derived ethylenimine X can be attributed to the >C=N— stretching vibration present in the intermediate and absent in the imine. The fact that this band occurs at a wave length shorter than the normal >C=N— absorption (λ ~ 5.9 μ) is consistent with the rigidity of azirine ring system. The ultraviolet absorption spectral curve of Neber's intermediate lies in general between that of the ethylenimine (X) and the oxime of 2,4-dinitrophenylacetone (see Fig. 1), these two substances serving as models for the azirine structure, IIIA. The resonance of stabilization associated with structure IIIA provides a possible reason why such a strained substance might be isolatable, and why the two nitro groups on the aromatic system appear to be necessary for its stability.[8]



Structure XVII is completely eliminated for Neber's intermediate on the basis of the reduction reactions. Structures XVIII and XIX, although improbable in the light of the reduction reactions, cannot be completely dismissed. Structure XVIII is isoelectronic with diazomethane and, although unusual, is relatively strainless. Structure XIX provides an explanation of why Neber's intermediate is isolated only in those cases in which an o-nitro group is present. Thus an unequivocal structural assignment to this intermediate must await the results of electron diffraction studies that are currently being conducted by Dr. K. N. Trueblood of this Laboratory.

Experimental Part

Preparation of the *p*-Toluenesulfonate of 2,4-Dinitrophenylacetoneoxime.—The oxime was prepared in 83% yield, m.p. 137–139°, by the method of Borsche.[9] A mixture of 11.9 g. (0.050 mole) of powdered oxime, 16.5 g. (0.0865 mole) of powdered *p*-toluenesulfonyl chloride, 11.0 g. (0.131 mole) of dry powdered sodium bicarbonate, 100 ml. of pure dioxane and 300 ml. of water was stirred vigorously. After four hours the solution became slightly acidic, and after a total of six hours of stirring, the mixture was filtered. The solid was stirred with 100 ml. of pure benzene, the mixture was filtered, and the undissolved solid was washed with 25 ml. of benzene to give 6.0 g. of recovered oxime, m.p. 136–138°.

The benzene solution was overlaid with 300 ml. of low-boiling petroleum ether, and the very light yellow material that separated was collected (2.4 g.), m.p. 114–122°. The addition of 500 ml. of petroleum ether to the filtrate gave an additional 0.3 g. of like material. The combined solids were recrystallized from hot methanol to give 1.66 g. of small white chunky crystals of oxime tosylate, m.p. 128–129° (another 0.19 g. of like material was recovered from the mother liquor, total yield 18%). A second recrystallization from methanol gave pure product, m.p. 129–130°.

Anal. Calcd. for $C_{16}H_{15}N_3SO_7$: C, 48.85; H, 3.84. Found: C, 48.85; H, 4.00.

Reaction of 2,4-Dinitrophenylacetoneoxime Tosylate with Pyridine.—The oxime ester (0.580 g. or 0.00150 mole) was added in one portion (as fine crystals) to 2.00 ml. of dry, pure, cold (0°) pyridine, and the suspension was allowed to stand at 0° for two hours. The resulting solution was poured into *ca.* 75 ml. of ice-water, and the mixture was extracted with 50-ml. portions of pure ether. Air was bubbled through the aqueous solution to remove dissolved ether, and 3 ml. of a 2 *N* aqueous sodium carbonate solution was added. The precipitate which formed was collected, wt. 0.196 g. (59%), m.p. 75–77°, m.m.p. with authentic azirine[10] (IIIA), 76–78°. The product in ethanol gave a characteristic green color test for the azirine with aqueous sodium bicarbonate solution.

When brucine was substituted for pyridine and the reaction was conducted in chloroform, a 71% yield of impure azirine resulted, m.p. 72–75° (m.m.p. with authentic material, 73–76°). Fractional recrystallization of this substance from benzene gave light yellow needles, m.p. 75–77°. This material in benzene ($c \cong 10\%$) showed no detectable optical activity.

Attempts to resolve the azirine with *d*-camphor-10-sulfonic acid failed.

Catalytic Reduction of the Azirine (IIIA) with Hydrogen on a Raney Nickel Catalyst.—A mixture of azirine (5.0 g.

---

[7] H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl ["Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 6] place the N-H stretching vibration in different functions from 2.88–3.28 μ. The exact position of this band in ethylenimines must be about 2.9 μ as shown by the correspondence of the bands in this region in the spectra of X, of 2,3-diphenylethylenimine, and of 2,3-(bis-*p*-chlorophenyl)-ethylenimine (see ref. 9).

[8] M. J. Hatch and D. J. Cram, THIS JOURNAL, **75**, 38 (1953).

[9] W. Borsche, *Ber.*, **42**, 602 (1909), and *Ann.*, **390**, 25 (1912).

or 0.23 mole of IIIA), 25 ml. of purified dioxane and *ca.* 3 g. of Raney nickel catalyst (washed free of ethanol with dioxane) was hydrogenated at atmospheric pressure and room temperature until 0.20 mole of hydrogen was absorbed. The reaction required five minutes, and the mixture warmed to 40°. The resulting mixture was filtered, the filtrate was evaporated under reduced pressure, and the residue (dark semi-solid oil) was stirred with 150 ml. of benzene. This solution was chromatographed on a 3 × 20 cm. column of alumina with pure benzene as eluant.[10] The column filtrate (1500 ml. of benzene from the point at which the filtrates became colored) was evaporated, and the concentrate was stirred with ligroin to give small yellow crystals, m.p. 66–70°. Recrystallization of these crystals from ethanol and water (charcoal treatment) gave 2.50 g. (49% yield) of 2,4-dinitrophenylacetone, m.p. 69–71.5°, m.m.p. with authentic material, 70–71.5°.

Catalytic Reduction of Azirine (IIIA) with Hydrogen on a Palladium-Carbon Catalyst.—A mixture of 4.44 g. (0.0200 mole) of azirine, 35 ml. of pure dry pyridine, 6.0 ml. of 90–95% C.P. acetic anhydride and 1.0 g. of 5% Pd-on-Norit was hydrogenated at atmospheric pressure and room temperature. The mixture absorbed 450 ml. of hydrogen (*ca.* 0.02 mole) in four minutes. After the mixture stood under hydrogen for 3.5 hours, it was filtered and 150 ml. of chloroform was added to the filtrate. The resulting solution was washed with several portions of ice-water, dried and evaporated under reduced pressure to a red brown sirup. This sirup was dissolved in 30 ml. of a one-to-one mixture of pure benzene and chloroform, and this solution was chromatographed on a 3 cm. × 25 cm. alumina column made up in benzene. Benzene was used as an eluant. After passing 2250 ml. of benzene through the column (a series of colored bands were eluted), a fraction was eluted (3250 ml. of benzene) which upon concentration to a low volume produced 0.99 g. of golden needles, m.p. 122–124°. Recrystallization of this material (twice) from pure chloroform and benzene gave pure IXB, m.p. 123–124° (heated 3° min.).

Anal. Calcd. for $C_{11}H_{11}N_3O_5$:[11] C, 49.82; H, 4.18; N, 15.84; mol. wt., 265. Found: C, 49.65; H, 4.25; N, 15.92; mol. wt., 259 (Rast).

The original filtrate was cooled to give 156 mg. of dark orange crystals, m.p. 90–110°. The filtrate was overlaid with pentane, and the mother liquor was decanted from the small amount of oil and crystals that separated. This liquor was concentrated under aspirator pressure until chunky yellow crystals separated, wt. 165 mg., m.p. 118–120°. This material was recrystallized from chloroform and pentane to give 115 mg. of flat yellow needles of IXA, m.p. 124.5–126°. Admixture of this material with IXB gave a melting point of 95–118°.

Anal. Calcd. for $C_{11}H_{11}N_3O_5$: C, 49.82; H, 4.18; N, 15.84; mol. wt., 265. Found: C, 49.25, 44.63, 53.60, 44.29; H, 5.50, 4.72, 6.08, 4.14; N, 15.42; mol. wt., 249 (Rast).

Although this nitro-compound was burned mixed with copper oxide, the carbon–hydrogen analyses were erratic.

Characterization of Isomers IXA and IXB.—The orange isomer (IXB) in absolute ethanol produced an immediate red-orange coloration when a drop of 1.5 *N* potassium hydroxide solution was added. The compound was hydrolyzed to 2,4-dinitrophenylacetone by the following procedure. Compound IXB (26 mg.) was dissolved in 1.0 ml. of C.P. concentrated sulfuric acid, and the solution was warmed for one minute on the steam-bath. Water (2.5 ml.) was then added and the resulting mixture was diluted with water and extracted with ether. The ether layer was dried and evaporated to give 15 mg. of a soft brown solid. This material was recrystallized (with a charcoal treatment) from a benzene–pentane mixture to give 8.0 mg. of 2,4-dinitrophenylacetone, m.p. 70–71°; undepressed by admixture with an authentic sample.

Ozonolysis of isomer IXB was accomplished as follows. Ozone was passed into a solution of 180 mg. of IXB in 12 ml. of pure ethyl acetate for 30 minutes. The light yellow solution was poured into 200 ml. of ice-water, and 50 ml. of a 10% solution of aqueous hydrogen peroxide was added. After standing at room temperature for three hours, and then for five hours on the steam-bath the solution was concentrated to 100 ml., cooled and extracted with ether. Evaporation of the solvent under reduced pressure gave a residue which was dissolved in a sodium bicarbonate solution. This solution was washed with ether, acidified with excess 2 *N* hydrochloric acid solution, and extracted with ether. The ether layer was dried, and evaporation of the solvent gave a residue which smelled strongly of acetic acid. This material was triturated with 2 ml. of water, the solid was collected and dried to give 12 mg. of crystals. Evaporation of the filtrate produced 12 mg. of like material. The combined solids were recrystallized from ethyl acetate and pentane to give light yellow crystals, m.p. 176–178°, undepressed by admixture with an authentic sample of 2,4-dinitrobenzoic acid.

Isomer IXA was hydrolyzed to 2,4-dinitrophenylacetone by a procedure similar to that reported for IXB. Isomer IXA was converted to IXB by the following procedure. The substance (4 mg.) was brought slowly (in a melting point tube) to 125° and held at that temperature for one minute. The resulting melt was crystallized and recrystallized twice from chloroform and pentane (a benzene wash was used) to give IXB (Orange flakes) m.p. 123–124.5°, undepressed by admixture with authentic IXB.

Reduction of Azirine (IIIA) to Ethylenimine (X) with Lithium Aluminum Hydride.—To a mechanically stirred solution of 11.1 g. (0.050 mole) of azirine in 5 liters of dry ether cooled to −55° was added slowly (35 minutes) a 0.57 *N* ethereal solution of lithium aluminum hydride (200 ml. or 0.0143 mole). The mixture was then stirred for five more minutes and 3 liters of water was added. After standing for five hours, the ether layer was separated and the water layer was washed with ether. The ether solutions were combined, dried and the solvent was evaporated at reduced pressure. The residual dark brown semi-solid was mixed with *ca.* 100 ml. of pure benzene and applied to a column (2.5 cm. × 35 cm.) of activated alumina. After the material was adsorbed, the column was allowed to stand for two hours in order to polymerize any unreacted azirine, and then was developed with benzene. The column eluate was cut into twelve fractions (125–200 ml. each) each of which was evaporated under reduced pressure to a small volume. Fraction 6 gave after crystallization and recrystallization from a benzene–pentane mixture 31 mg. of very light yellow prisms, m.p. 70–105°. After drying at 2 mm. for 36 hours (room temperature) the material was analyzed.

Anal. Calcd. for $C_{12}H_{12}N_3O_4$: C, 54.96; H, 4.58. Found: C, 54.86; H, 4.50.

This material appears to be the ethylenimine (X) which has crystallized with one-half a mole of benzene. When the sample was pulverized and heated *in vacuo* at 54° for 36 hours, the benzene was lost and the compound melted at 115.5–117°.

Anal. Calcd. for $C_9H_9N_3O_4$: C, 48.46; H, 4.07. Found: C, 48.29; H, 3.84.

From fractions 7 and 8 was obtained 0.32 g. of X ($+ {}^1/_2$ mole C_6H_6), m.p. 85–100°, and by rechromatographing the residues from fractions 3–9 and recrystallizing the product from hot benzene, another 0.3 g. of less pure product was obtained.

Although the sample of imine containing half a mole of benzene appeared to be relatively light-stable, the benzene-free imine darkened rapidly in the presence of light. Attempts to obtain a molecular weight using camphor or borneol failed due to extensive decomposition of the imine. The compound in benzene solution appeared to polymerize to a red-orange solid when treated with dry HCl gas. The substance dissolved in aqueous acid to form brownish solutions.

An attempt to make a *p*-toluenesulfonate derivative of the imine (X) which had not been freed of benzene gave back only starting material. Benzene-free imine went readily to the derivative. Impure imine (*ca.* 0.1 g.) was mixed with *ca.* 65 mg. of pure, powdered *p*-toluenesulfonyl chloride and 10 ml. of 1.4 *N* aqueous potassium hydroxide. The mixture was warmed with shaking for five minutes and extracted with ether (three portions of 20 ml. each). The extracts were combined and dried; the solvent was evaporated under reduced pressure, and the residue was stirred with a mixture of 2 ml. of benzene and 10 ml. of pentane. A tan solid separated, wt. 130 mg. Several recrystallizations of this

---

[10] When an equal volume of the same batch of alumina was heated to 300°, over a gram of water was liberated.

[11] The carbon and hydrogen analyses were carried out by burning a mixture of sample and copper oxide.

material (charcoal) from chloroform–pentane mixtures gave 20 mg. of small shiny platelets (very slightly yellow), m.p. 144.5–146°.

Anal. Calcd. for $C_{16}H_{15}N_3SO_6$: C, 50.92; H, 4.01; mol. wt., 377. Found: C, 50.71; H, 4.12; mol. wt., 362 (Rast).

Reduction of Azirine (IIIA) with Sodium Borohydride in Acid Solution.—A solution of 1.5 g. of sodium borohydride (0.042 mole) in 80 ml. of pure methanol, and 50 ml. of 2 *N* aqueous hydrochloric acid solution (0.1 mole) were added *alternately* in small portions over a period of three minutes at room temperature to a stirred solution of 5.0 g. (0.0044 mole) of azirine (IIIA) in 325 ml. of pure methanol. The yellow solution warmed slightly and became orange. The acidity was reduced to a *p*H of 2–3 with aqueous 3% sodium bicarbonate solution. After stirring for ten minutes, the solution was made alkaline with more sodium bicarbonate, and the excess hydride was destroyed by adding 30 ml. of acetone. When concentrated under reduced pressure (temperature, 45–60°) the solution deposited brown crystals, wt. 4.1 g. After recrystallizing the crude product from hot methanol (carbon-treatment) a total of 3.0 g. (including mother liquor workup) of light yellow-tan needles was obtained, m.p. 156–158° (dec.). Several more recrystallizations from methanol gave very light yellow prisms, m.p. 158–159° (dec.) (compound XII or XIII).

Anal. Calcd. for $C_{10}H_{13}N_3O_5$: C, 47.06; H, 5.13. Found: C, 47.00; H, 5.48.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

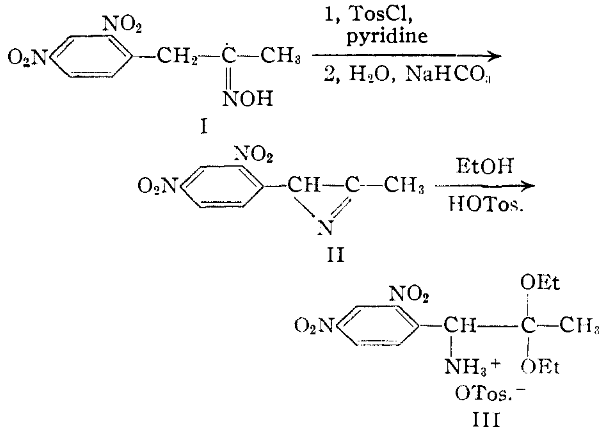
Observations on the Mechanism and Scope of the Neber Rearrangement

BY MELVIN J. HATCH[1] AND DONALD J. CRAM[2]

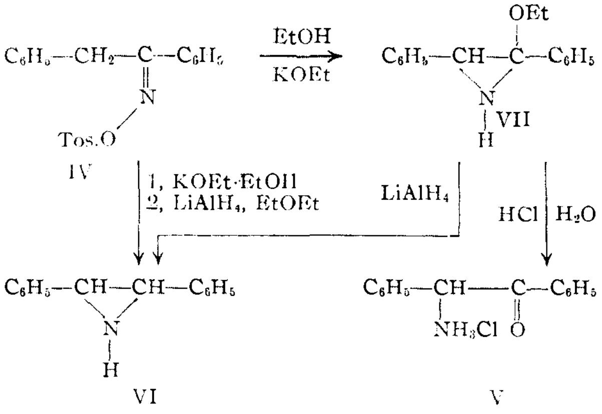
RECEIVED MARCH 26, 1952

In a further study of the Neber rearrangement, the *p*-toluenesulfonate of desoxybenzoinoxime (*syn*-benzyl) was treated with potassium ethoxide in ethanol to produce a new class of compound, the unstable 2,3-diphenyl-2-ethoxyethylenimine (VII), which when treated with lithium aluminum hydride gave *cis*-diphenylethylenimine. When hydrolyzed in aqueous acid, VII gave desylamine. Analogous reactions were demonstrated to occur in the *p,p'*-dichlorodesoxybenzoinoxime *p*-toluenesulfonate (*anti-p*-chlorobenzyl) system. These reactions constitute a new and simple means of synthesis of ethylenimines. The mechanism and scope of the Neber rearrangement are discussed.

The Neber[3] rearrangement can be classified as one of several "abnormal" rearrangements of ketoximes or their derivatives. When applied to the 2,4-dinitrophenylacetone system, the Neber rearrangement has been formulated[3c] as giving an azirine–pyridine hydrochloride complex which can be converted to azirine (II) and ultimately through hydrolysis to the amino ketal salt III. This reaction system represents a structural extreme, being atypical in two respects. (1) Due to the strong electron withdrawing ability of the nitro groups the hydrogen atoms on the benzyl carbon are acidic enough to allow the reaction to be initiated by pyridine instead of the usual sodium ethylate. (2) Again due to the nitro groups, the azirine itself (II)[4] would be expected to be far more resonance stabilized than in the usual systems submitted to the Neber reaction.[4] Therefore, the object of the present study has been to determine the nature of the reaction intermediates in more typical systems, and thereby to establish a more general framework for the over-all reaction mechanism.



The Neber Rearrangement in the Desoxybenzoin and *p,p'*-Dichlorodesoxybenzoin Systems.—Although the *p*-toluenesulfonate of desoxybenzoinoxime (IV) had previously been submitted to the Neber rearrangement to give desylamine hydrochloride[3d] (V), no intermediates were isolated. In the present investigation this ester (IV) was treated with potassium ethylate in ethanol, but aqueous acid was not added as usual to the filtered reaction mixture. Instead, ice-water was added to the solution, and the unstable solid that separated was dissolved in ether and reduced with lithium aluminum hydride to give *cis*-2,3-diphenylethylenimine (VI).



---

[1] Parke, Davis Predoctoral Research Fellow, 1951–1952.

[2] Requests for reprints should be addressed to this author.

[3] (a) P. W. Neber and A. Friedolsheim, *Ann.*, **449**, 109 (1926); (b) P. W. Neber and A. Uber, *ibid.*, **467**, 52 (1928); (c) P. W. Neber and A. Burgard, *ibid.*, **493**, 281 (1932); (d) P. W. Neber and G. Huh, *ibid.*, **515**, 283 (1935); (e) P. W. Neber, A. Burgard and W. Thier, *ibid.*, **526**, 277 (1936).

[4] The structure of this intermediate has been discussed elsewhere [D. J. Cram and M. J. Hatch, THIS JOURNAL, **75**, 33 (1953)].