under nitrogen for 42 hr. The dioxane was removed by evaporation at reduced pressure. The residue was taken up in ether, which was washed with sufficient dilute hydrochloric acid to remove the excess tryptamine, washed with saturated salt solution, dried over magnesium sulfate and evaporated. The crude residue was chromatographed on Florisil (eluted with ether and ether–chloroform) to give 264 mg. of crystalline material. Two recrystallizations from ethyl acetate–petroleum ether mixture gave 159 mg. (48%) of the piperidone, m.p. 124.5–125.0°.

Anal. Calcd. for $C_{19}H_{26}ON_2$: C, 76.47; H, 8.78. Found: C, 76.53; H, 8.72.

***dl*-Dihydrocorynantheane.**—The piperidone (159 mg.) and 0.4 ml. of freshly distilled phosphorus oxychloride were heated under reflux protected from moisture in 15–20 ml. of dry benzene for 3 hr. on the steam-bath. The flask was allowed to cool, and the crystals were filtered off and washed with benzene. The intermediate cyclization product was not characterized but hydrogenated directly. It rapidly took up 90% of the theoretical amount of hydrogen over platinum (14 mg. of platinum oxide) in ethanol at atmospheric pressure. The catalyst was filtered off, the solvent evaporated and the residue crystallized from ethanol to give 102 mg. of colorless, crystalline ***dl*-dihydrocorynantheane hydrochloride**, dec. 270°. The free base was prepared by pouring the crystals into a saturated solution of potassium carbonate containing a little potassium hydroxide, covering the mixture with ether, and allowing to stand several hours, *i.e.*, until the crystals had dissolved. From the ether phase was isolated 96 mg. (64% from the piperidone) of *dl*-dihydrocorynantheane, m.p. 147–152°. Recrystallization from ethyl acetate–petroleum ether to constant melting point gave m.p. 154–156°.

Anal. Calcd. for $C_{19}H_{26}N_2$: C, 80.80: H, 9.28. Found: C, 81.00; H, 9.02.

The infrared spectrum of the synthetic product was identical with that of naturally derived dihydrocorynantheane but differed from that of naturally derived corynantheidane. The spectra were all run in chloroform solution on a Perkin–Elmer double-beam spectrophotometer.[16]

Stability of Reserpine in Hydrochloric Acid.—Reserpine (504 mg., m.p. 267–269°, $[\alpha]^{25}D$ −119°) was dissolved in a mixture of 15 ml. in hydrochloric acid and 30 ml. of dioxane with warming. After dissolution was complete, the temperature was held at 70–80° for 2 hr. The solution was cooled and made basic with dilute ammonium hydroxide to give 490 mg. of crude product. Crystallization from methanol gave 286 mg. of reserpine, m.p. 265.5–267°, $[\alpha]^{25}D$ −119°. Chromatography of the mother liquors furnished 42 mg. more of reserpine, m.p. 262.5–266°, $[\alpha]^{25}D$ −118°. The remaining material was an intractable tar. Total recovery of reserpine was 328 mg. (65%).

(16) The authors are indebted to Prof. Prelog for the infrared spectra.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Azo Compounds.[1] Oxidation of 1,1-Disubstituted Hydrazines. The Synthesis and Oxidation of *cis*- and *trans*-1-Amino-2,6-diphenylpiperidine. A New Stereospecific Ring Closure

BY C. G. OVERBERGER, JOSEPH G. LOMBARDINO[2] AND RICHARD G. HISKEY

RECEIVED JUNE 18, 1957

The synthesis, identification and oxidation of the *cis* and *trans* isomers of 1-amino-2,6-diphenylpiperidine is described. Oxidation of these 1,1-disubstituted hydrazines with mercuric oxide gave a theoretical evolution of nitrogen with high yields of 1,2-diphenylcyclopentane. The *trans*-hydrazine yields mostly *trans*-1,2-diphenylcyclopentane, while the *cis*-hydrazine yields only *cis*-1,2-diphenylcyclopentane; a smaller amount of 1,5-diphenyl-1-pentene was obtained from both hydrazines. A stereospecific ring closure is indicated by retention of configuration of the benzyl carbon atoms; the small amount of inversion accompanying oxidation of the *trans*-hydrazine is best explained by the facile isomerization of this hydrazine to the corresponding *cis* isomer before or during oxidation.

The results of many oxidations of 1,1-disubstituted hydrazines as reported in the early literature are summarized in a book on the hydrazines by Wieland.[3] In almost every case a tetrazene was the principal product, and we shall refer to tetrazene formation hereafter as the "normal" oxidation product.

There are, in addition, three examples of abnormal oxidations of 1,1-disubstituted hydrazines where nitrogen gas is eliminated with resultant carbon–carbon bond formation. Busch and Weiss[4] were the first to observe nitrogen evolution and the formation of bibenzyl, when 1,1-dibenzylhydrazine was oxidized in ethanol solution with mercuric oxide. More recently, Hinman and Hamm[5] reported oxidation of *p*-substituted 1,1-dibenzylhydrazines with mercuric oxide in ethanolic solution to give only 4-substituted bibenzyls in varying yields depending on the *p*-substituent.

$$p\text{-}x\text{-}C_6H_4CH_2\text{—}N(NH_2)\text{—}CH_2C_6H_5 \xrightarrow{[O]} p\text{-}x\text{-}C_6H_4CH_2CH_2C_6H_5 + N_2$$

These authors also report the formation of 2-(β-phenylethyl)-furan in 35% yield on oxidation of 1-benzyl-1-furfurylhydrazine.

Overberger and co-workers[6] reported a 9% yield of bibenzyl and the normal tetrazene acid decomposition products when 1,1-dibenzylhydrazine was oxidized with bromine in aqueous ethanol. Oxidation of 1,1-dibenzylhydrazine with *t*-butyl hypochlorite gave a 12% yield of bibenzyl.[6] These workers also have examined the oxidation behavior of 1-amino-2,6-dicyano-2,6-dimethylpiper-

(1) This is the 19th in a series of papers concerned with the preparation and decomposition of azo compounds. For the previous paper in this series, see C. G. Overberger, N. R. Byrd and R. B. Mesrobian, THIS JOURNAL, **78**, 1961 (1956). For a preliminary report of this work see C. G. Overberger, J. G. Lombardino and R. G. Hiskey, *ibid.*, **79**, 1510 (1957).

(2) This paper comprises a portion of a thesis presented by Joseph G. Lombardino in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

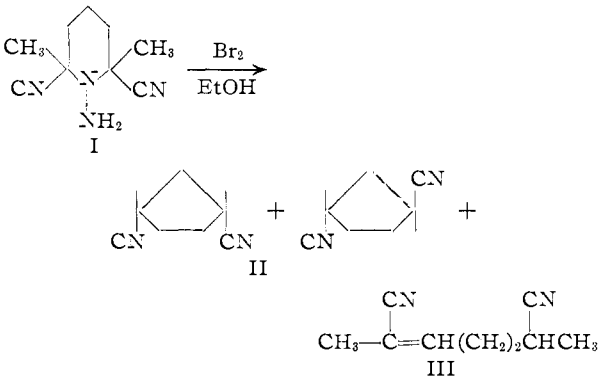
(3) H. Wieland, "Die Hydrazine," Verlag von Ferdinand Enke, Stuttgart, 1913, pp. 38, 39.

(4) M. Busch and B. Weiss, *Ber.*, **33**, 2701 (1900).

(5) R. L. Hinman and K. L. Hamm, Abs. of Papers, 130th Meeting, Am. Chem. Soc., 1956, p. 17-O.

(6) C. G. Overberger and B. S. Marks, THIS JOURNAL, **77**, 4104 (1955).

idine (I).[7-9] Bromine oxidation[8] yielded three products, *cis*- and *trans*-1,2-dicyano-1,2-dimethylcyclopentane (II) and 2,6-dicyano-2-heptene (III).



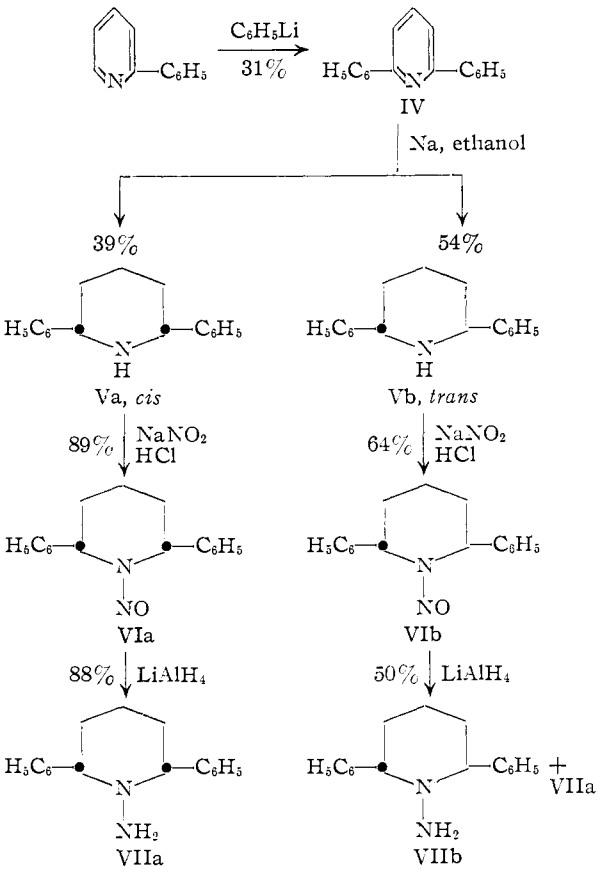
Oxidation of I with potassium permanganate[6] yielded 32.4% of II and 26.3% of the tetrazene. Although the stereoisomeric nature of I was not established, it can be assumed to be a pure isomer, since it is reported as a sharp melting solid (m.p. 104.8–105.4°).

It should be noted that in all cases to date of an abnormal oxidation of a 1,1-disubstituted hydrazine, the hydrazine contains groups which can contribute to the resonance energy of the elimination process. This resonance stabilization of an intermediate or transition state as nitrogen is lost could account for some of the driving force required to eliminate nitrogen in preference to forming tetrazene. If the loss of nitrogen is concomitant with product formation, resonance effects may play a lesser role but may still be pronounced. With this in mind and with the added object of following the stereochemical course of the abnormal oxidation, the synthesis of the *cis* and *trans* isomers of 1-amino-2,6-diphenylpiperidine (VIIa and VIIb) was carried out and their oxidation behavior studied.

Preparation of the Hydrazines.—The sequence of reactions to prepare VIIa and VIIb is summarized in Table I.

The starting material for the synthesis of VIIa and VIIb was prepared by the addition of phenyllithium to 2-phenylpyridine, affording a 31% yield of 2,6-diphenylpyridine (IV). The catalytic reduction of IV has been reported,[10-12] although the results are not consistent. However, Scholtz[13] has reported the reduction of IV with sodium in ethanol gave, on fractional crystallization of the hydrochloric acid salts, a solid, m.p. 71°, and a liquid isomer ("iso"), b.p. 205° (15 mm.). The *cis–trans* relationship of the liquid and solid was suggested, but attempts to resolve the *trans* isomer were unsuccessful. In our hands, reduction of IV with sodium in alcohol afforded 39% of a solid,

TABLE I



m.p. 73.3–74.3°, and 54% of a liquid 2,6-diphenylpiperidine, b.p. 154° (1.0 mm.) (Va and Vb). Conformation of the assigned piperidine structure for each of the isomers was established by elemental analysis of the compounds and their picrate salts. Infrared spectra of the two compounds were similar and showed N–H stretching frequencies, phenyl absorption, but no aliphatic unsaturation. The absence of unsaturation was further demonstrated by unsuccessful attempts to catalytically hydrogenate either of the isomers.

The *trans* nature of the liquid isomer was established by resolution. Although other resolving agents gave rise to amorphous salts, as reported by Scholtz,[13] dibenzoyl-*d*-tartaric acid monohydrate yielded a crystalline salt which on treatment with bicarbonate gave an optically active base, $[\alpha]^{26}D$ 80.7°. Similar results on other racemic bases have been reported[14] previously using dibenzoyl-*d*-tartaric acid monohydrate as the resolving agent. Repeated attempts to resolve the solid isomer using several resolving agents failed. The solid isomer can then be assigned a *meso* and hence *cis* configuration.

Both piperidine isomers could be nitrosated by published procedures to give the N-nitroso derivatives VIa and VIb in good yield. Treatment of the *cis*-nitrosamine (VIa) with lithium aluminum hydride in ether proceeded smoothly, affording an 88% yield of the *cis*-1-amino 2,6-diphenylpiperidine

(7) C. G. Overberger, T. B. Gibbs, Jr., S. Chibnik, P. Huang and J. J. Monagle, THIS JOURNAL, **74**, 3290 (1952).

(8) C. G. Overberger, P. Huang and T. B. Gibbs, Jr., *ibid.*, **75**, 2082 (1953).

(9) C. G. Overberger and B. S. Marks, *ibid.*, **77**, 4097 (1955).

(10) H. Adkins, L. Kuick, M. Farlow and B. Wojcik, *ibid.*, **56**, 2425 (1934).

(11) A. W. Singer and S. M. McElvain, *ibid.*, **57**, 1135 (1935).

(12) J. Overhoff and J. P. Wibaut, *Rec. trav. chim.*, **50**, 957 (1931).

(13) M. Scholtz, *Ber.*, **34**, 1616 (1901).

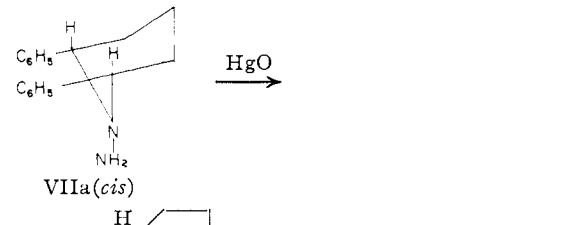
(14) W. von E. Doering and V. Z. Pasternak, THIS JOURNAL, **72**, 143 (1950).

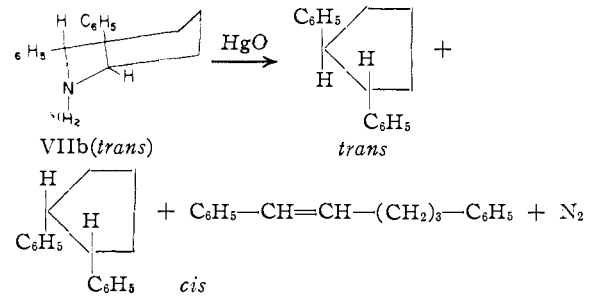
(VIIa). The 1,1-disubstituted hydrazine structure of VIIa was confirmed by elemental analysis, infrared spectrum and the formation of a benzal derivative. In view of the ease of reduction of the *cis*-nitrosamine, similar results using lithium aluminum hydride were expected with the *trans*-1-nitroso-2,6-diphenylpiperidine (VIb). However, under the same conditions VIb remained unaffected while under more strenuous reaction conditions, a mixture of the isomeric hydrazines, VIIa and b, was obtained. Fractional crystallization from *n*-hexane afforded 50% of *trans*-1-amino-2,6-diphenylpiperidine (VIIb) and 15% of the *cis*-hydrazine VIIa. An independent experiment on pure *trans*-hydrazine VIIb confirmed the interesting observation of isomerization of the *trans* series to the *cis* by lithium aluminum hydride in refluxing ether. The greater stability of the *cis* isomer over the *trans* isomer has previously been reported for the 1,3-dimethylcyclohexanes.[15]

A wide variety of reducing agents were employed in an attempt to effect the conversion of VIb to pure VIIb. Thus, lithium aluminum hydride at room temperature by direct[16,17] and inverse addition,[18] catalytic hydrogenation with Adams catalyst and sodium borohydride–aluminum chloride reagent[19] yielded only starting material. In contrast, denitrosation occurred when reduction was attempted with zinc dust in acetic acid, Raney nickel–hydrazine in ethanol and sodium in liquid ammonia. In these cases, the reaction product was identified as Vb by infrared analysis and the picrate derivative. Unexpected results were obtained when the nitrosamine VIb was treated with sodium hydrosulfite in alkaline solution. A quantitative evolution of nitrogen was observed, and a 30% yield of *trans*-1,2-diphenylcyclopentane was isolated. Under similar conditions the *cis*-nitrosamine VIa yielded 33% of *cis*-1,2-diphenylcyclopentane, and N-nitrosodibenzylamine yielded 77% of bibenzyl. Further work on the nature of the other reaction products and the scope of this unusual transformation will be reported at a later date.

Oxidation of the Hydrazines.—The *cis*- and *trans*-hydrazines VIIa and VIIb were oxidized using mercuric oxide. Oxidation of the *cis* isomer at 58° yielded 65% of *cis*-1,2-diphenylcyclopentane and 25% of 1,5-diphenyl-1-pentene.

Oxidation of the *trans*-hydrazine VIIb at 58° yielded 59% of *trans*-1,2-diphenylcyclopentane, 12% *cis*-1,2-diphenylcyclopentane and 14% 1,5-diphenyl-1-pentene.

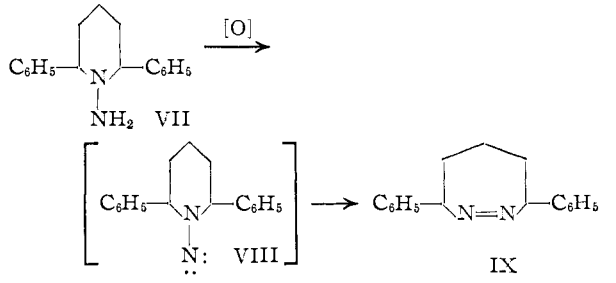




The ready conversion of the *trans*-hydrazine VIIb to the *cis*-hydrazine VIIa suggests that some *trans* hydrazine may be isomerizing under the conditions of the oxidation, prior to nitrogen elimination. The stereospecificity in the oxidation of the *cis*-hydrazine VIIa lends further support to this argument.

A plot of nitrogen evolution with time for the oxidation of both VIIa and VIIb gave first-order kinetics. However, in both cases the rate constants showed a marked dependence on the concentration of the insoluble mercuric oxidation.

The mechanism for the abnormal oxidation of 1,1-disubstituted hydrazine has been previously mentioned,[6] and two possible reaction paths have been proposed. One path involves the simultaneous elimination of nitrogen with formation of products, while another path postulates initial rearrangement to an azo intermediate which then decomposes in the usual manner. If the latter path were followed in the oxidation of VIIa or VIIb, the cyclic seven-membered azo compound (IX) should be the intermediate. However, an



isomer of IX has been prepared[20] and shown to have a half-life of 305 minutes at 61°. Furthermore, nearly equal amounts of *cis*- and *trans*-1,2-diphenylcyclopentanes were obtained in the decomposition of IX with no indication of stereospecificity. Support for an intermediate such as VIII has been given by McBride and Kruse[21] who

(15) M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 20.

(16) H. Zimmer, L. Andrieth, M. Zimmer and R. Rowe, THIS JOURNAL, **77**, 790 (1955).

(17) C. G. Overberger, B. S. Marks, L. Palmer and N. Byrd, *ibid.*, **77**, 4100 (1955).

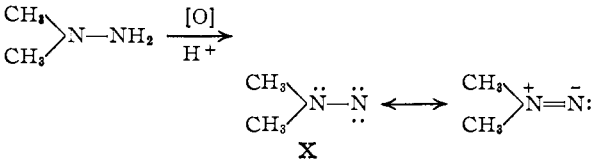
(18) R. H. Poirier and F. Benington, *ibid.*, **74**, 3192 (1952).

(19) H. C. Brown and B. C. SubbaRao, *ibid.*, **78**, 2582 (1956).

(20) C. G. Overberger, Joseph G. Lombardino, I. Tashlick and Richard G. Hiskey, *ibid.*, **79**, 2662 (1957).

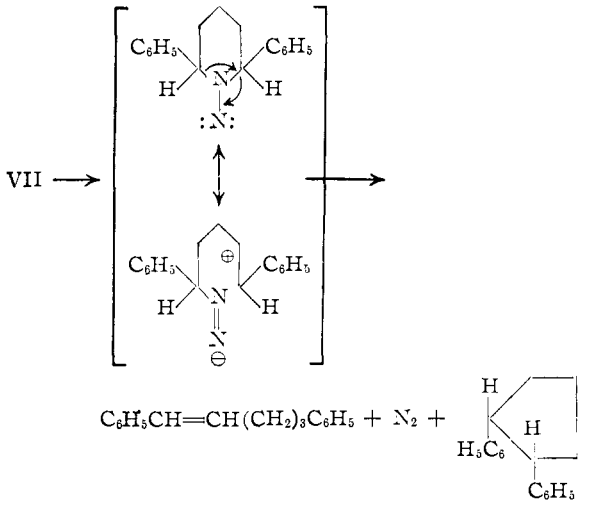
(21) W. R. McBride and H. W. Kruse, *ibid.*, **79**, 572 (1957); J. Kenner and E. C. Knight, *Ber.*, **69**, 341 (1936), have also suggested a similar intermediate for the oxidation of 1,1-dibenzylhydrazine with mercuric oxide; see also J. Kenner and J. Wilson, *J. Chem Soc.*, 1108 (1927).

obtained spectral evidence for the existence of the conjugate acid of X in strong acid solution. Accordingly, we suggest that the elimination reaction



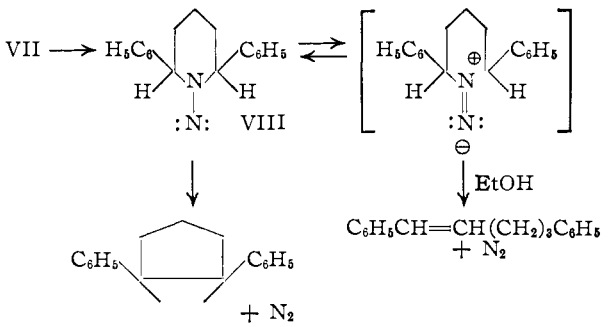
X

proceeds as indicated.



The elimination mechanism accounts for the retention of configuration in the formation of the cyclopentanes and also satisfactorily explains olefin formation. This mechanism also accounts for the results of Hinman and Hamm[5] who reported that the oxidation of 1,1-dibenzylhydrazines substituted in the *p*-position did not give mixed bibenzyls.

An alternate way of writing the mechanism is indicated. Here the ionization of VIII is treated as a distinct step in the mechanism of formation of the olefin.



Although a biradical mechanism cannot be discounted at the present time, using the rationalization that the radicals do not have time to dissociate and isomerize before recombining, the evidence favors the above mechanism particularly so because of the non-stereospecificity of IX on decomposition to give the same products.

Infrared Spectra.—A Perkin–Elmer model 21 double beam recording infrared spectrometer was employed with a NaCl prism to study the 2–15 μ range. Solid samples were run as potassium bromide pellets. The authors are grateful to Mr. H. Talts for carrying out the infrared determinations.

Experimental[22]

Preparation of 2-Phenylpyridine.—The procedure of Evans and Allen[23] was followed with some modifications to give increased yields. The phenyllithium was made one molar in ether in order to decrease the formation of biphenyl which complicates the purification of the product. A 50% excess of dry, redistilled pyridine was found to give maximum yield. A large excess of water (500 ml.) for hydrolysis followed by a 0.5 hr. reflux of the hydrolyzed mixture facilitated work-up of the reaction by dissolving most of the lithium bromide which otherwise adsorbs much of the product. From 302 g. (3.75 moles) of pyridine and 2.5 moles of phenyllithium after two distillations was obtained 236.5 g. (61%) of a light yellow liquid, b.p. 146° (15 mm.), $n^{24.5}$D 1.6170 (b.p. 140° (12 mm.), yield 40–49%).[23]

A picrate was prepared in ethanol, m.p. 174–175° dec. (m.p. 174–175°).[24]

2,6-Diphenylpyridine (IV).—To a stirred suspension of 26.9 g. (3.88 g. atoms) of lithium ribbon and 1100 ml. of anhydrous ether under dry nitrogen was added dropwise 305 g. (1.94 moles) of redistilled bromobenzene dissolved in 900 ml. of anhydrous ether. After complete addition, the mixture was stirred at room temperature for 30 minutes. The reaction was then cooled to 0°, and a solution containing 240 g. (1.55 moles) of 2-phenylpyridine in 600 ml. of dry xylene was added in 10 minutes. The mixture was refluxed for 30 minutes after which all material boiling below 94° was removed by distillation and replaced by 750 ml. of xylene. The reaction mixture was refluxed overnight at 125°, and then 260 ml. of water was added slowly with cooling. The hydrolyzed mixture was heated at reflux for 30 minutes, cooled, the lithium bromide removed by filtration and washed with 500 ml. of hot xylene and the combined xylene layers dried over potassium hydroxide pellets. The xylene solution was removed by flash distillation and the residual oil vacuum distilled through a modified Claisen head to yield a liquid, b.p. 190° (2.5 mm.), which readily crystallized. Two recrystallizations from ethanol afforded 112.5 g. (31%) of 2,6-diphenylpyridine, m.p. 80–81° (m.p. 81°)[25] (14% yield).[26]

A picrate was prepared in ether, m.p. 169–170.5° dec. (m.p. 169°).[25]

Preparation of *cis*- and *trans*-2,6-Diphenylpiperidine (Va, Vb).[27,28] A solution of 500 ml. of absolute ethanol (dried by treating commercial absolute ethanol with 1/20th its weight of sodium and distilling) and 80 g. (0.35 mole) of 2,6-diphenylpyridine was prepared under dry nitrogen and after solution, 113 g. (4.90 g. atoms) of sodium metal in large pieces was added as rapidly as possible. An additional 200 ml. of dry ethanol was added to prevent the reaction mixture from solidifying. The reaction was refluxed for 3 hr. with three 100-ml. portions of ethanol added at intervals to prevent solidification. After all the sodium metal had reacted, 500 ml. of water was added slowly as the ethanol was removed by distillation. The addition of each drop of water is accompanied by a vigorous exothermic reaction and foaming. The reaction solidified after the addition of approximately 100 ml. of water, but continued addition of water again gave a solution. After hydrolysis was complete, all material boiling below 90° was removed by distillation, the residual liquid extracted with methylene chloride and the extracts dried over magnesium sulfate.

Removal of the solvent yielded a yellow oil which was dissolved in 150 ml. of ethanol and 5 ml. of water, cooled and seeded. The seeds were obtained from a previous preparation of 2,6-diphenylpiperidine which had crystallized after being doubly distilled. Filtration of the white needles, followed by two more seedings and filtrations, yielded 32.1 g. (39%) of 2,6-diphenylpiperidine (Va), m.p. 73.3–74.3° (m.p. 71°, no yield given).[13]

(22) All melting points are uncorrected. Elemental analyses by Schwarzkopf Microanalytical Laboratories, New York, N. Y.

(23) J. C. Evans and C. F. H. Allen, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 517.

(24) K. Ziegler and H. Zeiser, *Ber.*, **63**, 1847 (1930).

(25) M. Scholtz, *ibid.*, **28**, 1730 (1895).

(26) H. Gilman and J. T. Edwards, *Can. J. Chem.*, **31**, 457 (1953).

(27) H. Adkins, S. Kuick, M. Farlow and B. Wojcik[10] have reported a b.p. of 193–194° (10 mm.) for the material obtained on catalytic hydrogenation of 2,6-diphenylpyridine using Raney nickel.

(28) A. W. Singer and S. M. McElvain[11] report that Raney nickel hydrogenation of 2,6-diphenylpyridine yielded an oil, b.p. 193–194° (10 mm.), n^{25}D 1.5168, d^{25}_4 0.9507.

Anal. Calcd. for $C_{17}H_{19}N$: C, 86.02; H, 8.07; N, 5.90 Found: C, 86.09; H, 7.79; N, 6.15.

A picrate of this solid was prepared in ether, m.p. 211.5–212° dec. (m.p. 212°).[13]

Anal. Calcd. for $C_{23}H_{22}O_7N_4$: C, 59.22; H, 4.76; N, 12.01. Found: C, 59.09; H, 4.98; N, 11.90.

A hydrochloric acid salt was prepared in ether solution, m.p. 315.5–317° (m.p. 316°).[13]

The filtrate of the three seeding operations were combined and distilled to yield 44.4 g. (54%) of 2,6-diphenylpiperidine (Vb), b.p. 154° (1.0 mm.), $n^{25}D$ 1.5830, d^{25}_4 1.0576 (b.p. 204° (15 mm.), d^{20}_4 1.0657, no yield given).[13]

Anal. Calcd. for $C_{17}H_{19}N$: C, 86.02; H, 8.07; N, 5.90; *MR*, 74.90. Found: C, 86.22; H, 7.99; N, 6.17; *MR*, 75.20.

A picrate of this liquid formed slowly in ether, m.p. 180–182° dec. (liquid picrate salt).[13]

Anal. Calcd. for $C_{23}H_{22}O_7N_4$: C, 59.22; H, 4.76; N, 12.01. Found: C, 59.49; H, 4.77; N, 12.12.

A hydrochloric acid salt prepared in ether melted at 305° dec. (m.p. 218°).[13]

The liquid Vb could not be hydrogenated with Adams catalyst in ethanol at room temperature and atmospheric pressure indicating that the compound is a piperidine derivative and not a partially reduced pyridine.

The combined yields of the isomeric 2,6-diphenylpiperidines (Va and Vb) was 93%.

Resolution of *trans*-2,6-Diphenylpiperidine (Vb).—A solution of 2.05 g. (0.0087 mole) of the liquid isomer of 2,6-diphenylpiperidine (Vb) in 25 ml. of ethanol was mixed with a solution of 3.3 g. (0.0088 mole) of dibenzoyl-*d*-tartaric acid monohydrate,[29] 87.5–89°, in 25 ml. of ethanol. The solvent was removed and the residual oil taken up in chloroform. Prolonged cooling at Dry Ice temperature yielded a salt which was recrystallized from 80 ml. of a 1:1 ethanol–water mixture, m.p. 153–153.8°. After four recrystallizations from ethanol–water, the salt melted at 156.5–157°. The amine was regenerated with 5% sodium bicarbonate, extracted with ether and the ether extracts washed successively with 5% sodium bicarbonate and water. The ether layer was then dried over magnesium sulfate to yield after removal of the ether an oil, $[\alpha]^{26}D$ +80.7° (*c* 5.1, ethanol).

Several attempts to resolve the solid 2,6-diphenylpiperidine (Va) using various resolving agents under a variety of conditions failed.

Both *d*-10-camphorsulfonic acid and *d*-tartaric acid gave amorphous salts with the liquid isomer Vb, as reported by Scholtz.[13]

***cis*-1-Nitroso-2,6-diphenylpiperidine (VIa).**—The nitrosation of *cis*-2,6-diphenylpiperidine (Va) was carried out according to Hatt,[30] except that a 1:1 ethanol–water solution was used as solvent. The product, an orange-red liquid, was extracted with ether and the extracts dried over magnesium sulfate. Evaporation of the solvent yielded an oil which was taken up in 100 ml. of ethanol, allowed to cool slowly and the precipitated solid filtered. From 0.10 mole of amine, in the form of the hydrochloric acid salt in 300 ml. of 1:1 ethanol–water, was obtained 22.4 g. (89%) of *cis*-1-nitroso-2,6-diphenylpiperidine (VIa), m.p. 66.5–67.5°.

The solid gave a positive Liebermann nitroso test,[31] and an infrared spectrum indicated the presence of a nitroso group by strong absorption peaks at 7.00, 7.42 and 8.58 μ.[32]

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.65; H, 6.77; N, 10.31.

***cis*-1-Amino-2,6-diphenylpiperidine (VIIa).**—The procedure of Schueler and Hanna[33a,b] was used with some modifications to give increased yields and safer working conditions. A suspension of 2.85 g. (0.075 mole) of lithium aluminum hydride and 100 ml. of anhydrous ether was prepared while passing dry nitrogen into the system, and the suspension was stirred under reflux for 1 hr. After cooling to 0°, a solution of 15 g. (0.056 mole) of *cis*-1-nitroso-2,6-diphenylpiperidine (VIa) in 135 ml. of anhydrous ether was added dropwise over a 1.5-hr. period. After complete addition, the suspension was stirred at 0° for 1 hr. and at room temperature for an additional 1.5 hr. The yellow suspension was hydrolyzed by the dropwise addition of 10 ml. of ethanol followed by the dropwise addition of 35 ml. of water. The ether layer was decanted and the precipitated aluminates washed with two portions of ether. Throughout this entire reaction, no frothing or violent reaction of any kind was observed.

The combined ether layers were dried over magnesium sulfate and after removal of solvent gave a solid which, after one recrystallization from ethanol, yielded 12.4 g. (88%) of white plates, m.p. 133–134°.

Anal. Calcd. for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.74; H, 8.09; N, 11.37.

Benzal Derivative of *cis*-1-Amino-2,6-diphenylpiperidine.—To 0.50 g. (0.0020 mole) of *cis*-1-amino-2,6-diphenylpiperidine (VIIa) in 20 ml. of hot ethanol was added 0.27 g. (0.0025 mole) of benzaldehyde and the solution warmed on a steam-bath for five minutes. After the addition of two drops of acetic anhydride, the solution was refluxed on a steam-bath for 15 minutes. At the end of this time, 25 ml. of water was added and the resulting emulsion extracted with ether. The ether extracts were dried over magnesium sulfate and removed to yield a white solid which, after recrystallization from ethanol, melted at 119.5–120.6°. An infrared spectrum of this solid showed a medium absorption peak at 6.13 μ which can be assigned as C=N.[34] The ultraviolet spectrum showed, λ^{EtOH}_{max} 253 mμ, ϵ 6,250; λ_{max} 292, ϵ 2500.

Anal. Calcd. for $C_{24}H_{24}N_2$: C, 84.37; H, 7.11; N, 8.23. Found: C, 84.58; H, 7.13; N, 8.37.

Oxidation of *cis*-1-Amino-2,6-diphenylpiperidine (VIIa).—A 250-ml., three-necked flask equipped with a mercury-sealed stirrer, solids addition tube[35] and water condenser was immersed in a constant temperature water-bath maintained at 58°. A ground glass gas delivery tube was placed at the top of the condenser leading evolved gases into a 1-liter graduated cylinder filled with water and inverted into a 2-liter beaker of water. A solution of 3.9 g. (0.015 mole) of *cis*-1-amino-2,6-diphenylpiperidine (VIIa) in 100 ml. of commercial absolute ethanol was placed in the reaction flask and stirred for 30 minutes under a stream of nitrogen in the open system. In the solids addition tube was placed 6.7 g. (0.031 mole) of yellow mercuric oxide and the system sealed. The mercuric oxide was added to the solution over 10 minutes, accompanied by a smooth evolution of nitrogen. After 90 minutes, 380 ml. (100 ± 2%) of nitrogen had been evolved, and further stirring gave no additional nitrogen evolution.

The green reaction mixture was filtered through Super-Cel and the filtrate concentrated *in vacuo*. Cooling the residue yielded 2.21 g. (64.5%) of white needles, m.p. 45.8–47°. This solid was identical in infrared spectrum and melting point to a sample of *cis*-1,2-diphenylcyclopentane[36] prepared according to Japp and Lander[37]; m.p. 45.8–47°. A mixture melting point of the two samples was not depressed, m.p. 45.8–47°.

The filtrate obtained from the reaction products after isolation of the *cis*-1,2-diphenylcyclopentane was concentrated to yield a liquid which was dissolved in 2 ml. of glacial acetic acid. To this was added a solution of 0.53 g. (0.0023 mole) of 2,4-dinitrobenzenesulfenyl chloride. After standing for 3 days, with alternate cooling and warming, a crop of yellow crystals separated, m.p. 114–115.5°. A mixture m.p. with the 2,4-dinitrobenzenesulfenyl chloride derivative prepared from an authentic sample of 1,5-diphenyl-1-pentene, m.p. 113.5–115°, melted at 113–115°.

In another experiment, the crude mixture of reaction products was reduced quantitatively with platinum oxide in ethanol at atmospheric pressure and room temperature. The amount of hydrogen absorbed indicated the presence of 24.5% of the theoretical amount of 1,5-diphenyl-1-pentene.

Quantitative infrared spectra of mixtures of authentic samples of *cis*-1,2-diphenylcyclopentane and 1,5-diphenyl-1-pentene were prepared. These spectra were qualita-

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(34) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 226.

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(36) H. A. Weidlich, *Ber.*, **71**, 1601 (1938).

(37) F. Japp and G. Lander, *J. Chem. Soc.*, **71**, 131 (1897).

tively identical with a spectrum of the crude mixture of reaction products. Using a peak at 10.37 μ as a quantitative estimate of the olefin present indicated 25.5% of the reaction product was 1,5-diphenyl-1-pentene.

In another experiment, the reaction products were fractionally distilled to give a liquid fraction, b.p. 139° (2 mm.), which on redistillation gave an infrared spectrum identical with that of 1,5-diphenyl-1-pentene.

Oxidation of *cis*-1-amino-2,6-diphenylpiperidine (VIIa) using potassium permanganate in acetone solution under conditions described above afforded a 35% yield of *cis*-1,2-diphenylcyclopentane accompanied by 88% of the theoretical evolution of nitrogen.

trans-1-Nitroso-2,6-diphenylpiperidine (VIb).—This nitrosation was carried out in a manner similar to that used for the *cis* isomer, VIa. From 53.2 g. (0.22 mole) of the liquid *trans*-2,6-diphenylpiperidine (Vb) run as the hydrochloric acid salt in 400 ml. of 1:1 ethanol–water was obtained 38.4 g. (63.5%) of a solid which after two recrystallizations from ethanol melted at 87–88°.

This solid gave a positive Liebermann nitroso test[31] only after standing with the reagents for 1 hr. The infrared spectrum exhibited strong absorption peaks at 7.03, 8.53 and 8.68 μ, indicative of a nitrosamine.[32]

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.44; H, 6.86; N, 10.30.

Preparation of *trans*-1-Amino-2,6-diphenylpiperidine (VIIb).—A suspension of 0.93 g. (0.024 mole) of lithium aluminum hydride and 100 ml. of anhydrous ether was stirred under nitrogen at reflux temperatures for 1 hr. After cooling to 0°, a solution of 3.18 g. (0.012 mole) of *trans*-1-nitroso-2,6-diphenylpiperidine (VIb) in 75 ml. of anhydrous ether was added dropwise over 45 minutes. After complete addition, the reaction was heated under reflux for 12 hr. At the end of this time the reaction was hydrolyzed immediately by the dropwise addition of 20 ml. of ethanol followed by 15 ml. of water. The ether layer was filtered and the residual aluminates washed with ether. The combined ether layers were evaporated to give a residual ethanol–water solution of products. On cooling, the solution deposited 2.3 g. (76%) of a white solid, m.p. 65–105°. This mixture of products was fractionated by dissolving in 20 ml. of hot *n*-hexane and cooling slowly. After 1 hr., 0.54 g. (18%) of crystals were removed by filtration, m.p. 125–129°. On further purification this crop proved to be identical in infrared spectrum with *cis*-1-amino-2,6-diphenylpiperidine (VIIa).

On evaporation of the hexane filtrate to one-half volume and cooling overnight, 0.97 g. (32%) of *trans*-1-amino-2,6-diphenylpiperidine (VIIb) was collected, m.p. 79–81°. A third crop of crystals from the hexane solution, wt. 0.55 g. (18%), m.p. 78–81°, also proved to be the *trans*-hydrazine (VIIb). An analytical sample was prepared by recrystallization from hexane, m.p. 80–81°.

Anal. Calcd. for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.71; H, 7.89; N, 10.93.

Isomerization of the *trans*-Hydrazine (VIIb) to the *cis*-Hydrazine (VIIa).—To 0.20 g. (0.00079 mole) of *trans*-1-amino-2,6-diphenylpiperidine (VIIb), m.p. 79–81°, in 40 ml. of anhydrous ether was added approximately 10 g. of lithium aluminum hydride. The reaction was heated under reflux and protected from moisture for 24 hr. After hydrolysis with ethanol–water, the reaction was filtered and any residual solids washed with ether. Evaporation of the ether followed by cooling of the residual ethanol–water solution yielded a solid, m.p. 40–90°. Fractional crystallization from hexane yielded 0.03 g. (15% of *cis*-1-amino-2,6-diphenylpiperidine (VIIa), m.p. 130–132°. A mixture melting point with an authentic sample melted at 130–133°. The remainder of the solid proved to be the starting material, *trans*-1-amino-2,6-diphenylpiperidine (VIIb).

An identical experiment using *cis*-1-amino-2,6-diphenylpiperidine (VIIa) as starting material gave a 100% recovery of starting material.

Benzal Derivative of *trans*-1-Amino-2,6-diphenylpiperidine.—To 0.25 g. (0.0010 mole) of *trans*-1-amino-2,6-diphenylpiperidine (VIIb) dissolved in 15 ml. of ethanol was added 0.14 g. (0.0017 mole) of benzaldehyde. After the addition of two drops of acetic anhydride, the reaction was refluxed for 1 hr. At the end of this time the reaction was poured onto 50 ml. of ice-water. The curdy, white solid was filtered and after recrystallization from 15 ml. of hexane, melted at 147–148°.

Anal. Calcd. for $C_{24}H_{24}N_2$: C, 84.37; H, 7.11; N, 8.23. Found: C, 84.53; H, 7.39; N, 8.07.

An infrared spectrum of this solid showed a medium absorption peak at 6.27 μ which can be assigned as C=N.[34] The ultraviolet spectrum showed λ_{max}^{EtOH} 306 mμ, ϵ 18,900 with a shoulder at 260 mμ, ϵ 4450.

Oxidation of *trans*-1-Amino-2,6-diphenylpiperidine (VIIb).—In the system previously described for the oxidation of the *cis*-hydrazine VIIa was placed 1.50 g. (0.0059 mole) of *trans*-1-amino-2,6-diphenylpiperidine (VIIb) and 50 ml. of commercial absolute ethanol. The solution was stirred under a nitrogen atmosphere in a water-bath maintained at 58°. In the solids addition tube was placed 3.90 g. (0.018 mole) of yellow mercuric oxide and the system sealed. The mercuric oxide was added in one portion, causing immediate gas evolution. In 8 minutes, a 102 ± 3% yield of nitrogen was obtained.

The green reaction was filtered through Super-Cel and the filtrate evaporated. To the residual ethanolic solution was added 10 drops of water and the solution cooled to yield 0.78 g. (59%) of *trans*-1,2-diphenylcyclopentane, m.p. 62.5–64° (m.p. 65°).[36] An analytical sample was prepared by recrystallizing from ethanol–water, m.p. 65.8–66°.

Anal. Calcd. for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.90; H, 8.01.

The filtrate was concentrated and taken up in 2 ml. of glacial acetic acid. To this was added a solution of 0.25 g. (0.0011 mole) of 2,4-dinitrobenzenesulfenyl chloride in 4 ml. of acetic acid. Prolonged cooling yielded a yellow solid, m.p. 112–114°. A mixture melting point with the 2,4-dinitrobenzenesulfenyl chloride prepared from authentic 1,5-diphenyl-1-pentene, m.p. 113.5–115°, melted at 112.5–114.5°. The filtrate of the dinitrobenzenesulfenyl chloride derivative was chromatographed on neutral alumina using hexane as the eluent. The first two colorless fractions yielded 0.16 g. (12%) of *cis*-1,2-diphenylcyclopentane, m.p. 44–46°. An independent experiment indicated that *trans*-1,2-diphenylcyclopentane does not isomerize to *cis*-1,2-diphenylcyclopentane on an alumina column.

In another experiment, the crude mixture of reaction products was quantitatively reduced with platinum oxide in ethanol at room temperature and atmospheric pressure. The amount of hydrogen absorbed indicated the presence of 14% of the theoretical yield of 1,5-diphenyl-1-pentene.

Preparation of 1,5-Diphenyl-1-pentene.—This material was prepared by the procedure of Overberger and Monagle[38]; b.p. 146° (1.0 mm.), $n^{24.5}D$ 1.5828 (b.p. 128–130° (0.7 mm.), $n^{25.5}D$ 1.5832).[38]

A 2,4-dinitrobenzenesulfenyl chloride derivative of the olefin was prepared by dissolving 1.0 g. (0.0045 mole) of 1,5-diphenyl-1-pentene in 5 ml. of glacial acetic acid. To this was added a solution of 1.05 g. (0.0045 mole) of 2,4-dinitrobenzenesulfenyl chloride in 12 ml. of acetic acid. After a prolonged period of alternate cooling and warming, a yellow solid separated, 0.95 g. (46%), m.p. 113.5–115°. An analytical sample was prepared by recrystallization from hexane–benzene, m.p. 113.5–115°.

Anal. Calcd. for $C_{23}H_{21}O_4N_2SCl$: C, 60.46; H, 4.63; N, 6.13. Found: C, 60.52; H, 4.46; N, 6.32.

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