Anal. Calcd. for $C_{16}H_{12}Br_2O$: C, 50.56; H, 3.18. Found: C, 50.82; H, 3.24.

Absorption: λ_{max} 268 mμ, ϵ 18,900; λ_{min} 243 mμ, ϵ 12,000. Infrared μ, 3.30m, 6.00s, 6.20m, 6.30s, 6.71m, 6.95w, 7.17m, 8.02s, 8.34w, 8.51w, 9.23m, 9.33s, 9.90s, 10.20w.

Acid-catalyzed inversion to the trans isomer of a 5 × $10^{-5}M$ solution of the *cis* isomer in 1–10 by volume mixture of concentrated hydrochloric acid and 95% ethanol was followed spectrophotometrically. The λ_{max} changed rapidly, in 30 min. approaching and in 2 hr. coming to a steady state at 307 mμ, ϵ 22,400.

trans-p,p'-Di(dimethylamino)dypnone was prepared like *trans*-dypnone (above), but the product crystallized upon removal of solvent; recrystallized from 95% ethanol (16%), m.p. 156–158°.

Anal. Calcd. for $C_{20}H_{24}N_2O$: C, 77.88; H, 7.87. Found: C, 78.13; H, 7.74.

Absorption: λ_{max}, 250, 362.5 mμ, ϵ 18,210, 24.880; infrared, μ, 3.41w, 6.75s, 6.38s, 6.59s, 6.98m, 7.30s, 7.76w, 8.11m, 8.30w, 8.60s (bifurcation), 8.87bm, 9.51m, 10.60w, 11.11w, 12.21s.

After irradiation of a 5 × $10^{-5}M$ solution in 95% ethanol for three 0.5-hr. periods, spectrophotometric analysis indicated decomposition; no *cis* isomer could be obtained when operating on a larger scale.

trans-p,p'-Di(dimethylamino)dypnone oxime was prepared in the usual way[21] and was recrystallized from absolute ethanol; yield 34%, m.p. 149–150°.

Anal. Calcd. for $C_{20}H_{26}N_3O$: C, 74.27; H, 7.79. Found: C, 73.98; H, 7.66.

Acknowledgment is gratefully made to Phillip Zoretic for checking some of the data.

CHARLOTTESVILLE, VA.

[COMMUNICATION NO. 2208 FROM THE KODAK RESEARCH LABORATORIES, EASTMAN KODAK CO.]

cis and *trans* Isomers of 2-Styrylpyridine

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Further work on the photodimerization of 2-styrylpyridine, its methiodide, and hydrochloride has revealed that the normally isolated forms of such 2-styrylpyridines are in the *trans* configuration. Ultraviolet irradiation in the solid state of the methiodide or the hydrochloride causes dimerization while analogous irradiation in solution gives both isomerization to the *cis* configuration and dimerization. Irradiation of the free base under nitrogen in benzene solution produces only *cis*-2-styrylpyridine.

It was previously reported[1] that solid-state irradiation of 2-styrylpyridine methiodide (Ia) gave a dimeric salt (II) which was pyrolytically converted into the isomeric dimers (IIIa and IIIb), with the elimination of methyl iodide. An irradiation time of eighty hours with a 450-watt ultraviolet source at a distance of ten inches was required to convert 25 g. of Ia to II.[1] Recently, this reaction has been carried out more efficiently. 2-Styrylpyridine methiodide (Ia) was ball-milled in benzene to provide a suspension in which 50 g. of Ia was converted quantitatively to the dimer II by six hours of irradiation time, using a 550-watt source. In contrast, when Ia was irradiated in water with sunlight, a rapid shift occurred in λ_{max} from 340 mμ (ϵ 28,000) to 325 mμ (ϵ 14,600). This shift represented the photoisomerization of *trans*-2-styrylpyridine methiodide (Ia) to the corresponding *cis* configuration (Ib). Subsequently, dimer II was formed at a slower rate. Fractional crystallization of the photoproducts showed the reaction mixture to contain dimer II, 64.5%, and *cis*-2-styrylpyridine methiodide (Ib), 28%. Upon rapid heating, Ib melted at 180–183°, but resolidified when held at 195–200° for several minutes. The solid (Ia) then remelted at 225–230°. During storage for several months, the melting point of Ib changed from 180–183° to 193–196°, indicating a gradual conversion to the *trans* form.

In the previous paper,[1] powdered 2-styrylpyridine (IVa) (λ_{max} 309) was irradiated in air to produce only a 2.6% yield of dimer IIIa; the remaining materials were products of photooxidation. Since that time, it has been found that irradiation of *trans*-2-styrylpyridine (IVa) (λ_{max} 309) in a nitrogen atmosphere gave 58.3% conversion to *cis*-2-styrylpyridine, λ_{max} 290. No dimer IIIa was obtained. If, however, *trans*-2-styrylpyridine hydrochloride (V) was irradiated as a benzene dispersion, dimer IIIa was obtained in 85% yield. Alternatively, when V was irradiated in aqueous solution, approximately equal quantities of dimer IIIa hydrochloride and *cis*-2-styrylpyridine (IVb) hydrochloride were produced. The *cis* configuration (IVb) is assigned to this other modification of IVa, since IVb possesses absorption characteristics at a shorter wave length than *trans*-IVa. *trans*-IVa has λ_{max} 309 mμ (ϵ 28,000), while *cis*-IVb has λ_{max} 290 mμ (ϵ 11,400). *cis*-IVb can be converted quantitatively to *trans*-IVa by heating in *p*-cymene with a trace of 15% palladium on charcoal catalyst. Under the same conditions, in the absence of catalyst, no conversion occurs. Both IVa and IVb hydrogenate under the same conditions, absorbing one mole equivalent of hydrogen. Quaternization of IVb with methyl *p*-toluenesulfonate, followed by treatment of the re-

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(1) J. L. R. Williams, *J. Org. Chem.*, **25**, 1839 (1960).

sulting salt with aqueous sodium iodide, gave the methiodide, m.p. 178°, spectrally identical with Ia.

When dimer IIIa produced from II, IVa, or V was quaternized with methyl *p*-toluenesulfonate and the anion was replaced by sodium iodide exchange, the dimer salt obtained was identical with II. However, when dimer IIIb is treated in a like manner, only partial quaternization occurs. The resulting salt melts over a wide range. Dimer IIIb is therefore produced as a result of thermal rearrangement occurring during the pyrolysis of II to IIIa.

The physical properties of the 2-styrylpyridines and their methiodides studied in this work are summarized in Table I.

TABLE I
PHYSICAL PROPERTIES OF 2-STYRYLPYRIDINE AND DERIVATIVES

Compound	M.P.	λ_{max}, mμ	ϵ
cis-2-Styrylpyridine (IVb)	b.p. 145–155 (10 mm.)	290	11,400
trans-2-Styrylpyridine (IVa)	91.5–93	309	28,800
cis-2-Styrylpyridine methiodide (Ib)	180–183	325	14,600
trans-2-Styrylpyridine methiodide (Ia)	229–230	340	28,000

EXPERIMENTAL

Irradiations. All irradiations except where noted were conducted using a water-cooled, 550-watt Hanovia high pressure quartz lamp. The integrated output of the lamp in the region of 250–400 mμ was 83 watts. All irradiation mixtures were stirred by means of Teflon-covered magnet bars. The system was not protected from the air except where noted.

Ultraviolet spectra. All spectra were determined in methanol solution (5×10^{-5} *M*), using a 1-cm. quartz cell in a Cary Model 14 instrument.

trans-2-Styrylpyridine (IVa). One hundred fifty grams (0.46 mole) of *trans*-2-styrylpyridine methiodide (Ia)[2,3] was placed in a distillation flask equipped with a water-cooled, sidearm receiver, dry ice trap, and mechanical vacuum pump. The pressure was reduced to 0.1–0.5 mm. Careful heating by means of a direct flame caused the smooth pyrolysis of Ia to IVa and methyl iodide. By this procedure an average of 75 g. of crude IVa was produced. Recrystallization of the solid from 600 ml. of petroleum ether (b.p. 30–60°) after treatment with decolorizing carbon gave 60 g. (71.5%) of IVa, melting at 91.5–93°. A sample prepared by the method of Shaw and Wagstaff[4] melted at 91–93° (λ_{max} 309 mμ, ϵ 28,800).

Irradiation of trans-2-styrylpyridine hydrochloride (V). *Method A: In aqueous solution. cis-2-Styrylpyridine* (IVb) *and dimer* IIIa. A stirred solution of 30 g. (0.165 mole) of V in 2700 ml. of water and 18 ml. of concd. hydrochloric acid was irradiated for 13 hr. The reaction mixture was made alkaline with sodium carbonate and the solid-liquid mixture extracted with three 200-ml. portions of benzene. The combined extracts were dried over anhydrous potassium carbonate, and the benzene was distilled at the water pump using a steam cone. The residue was extracted with 200 ml. of petroleum ether. The solid residue (IIIa), after drying, weighed 12 g. (40%) and melted at 189–190°. The petroleum ether extract was distilled; the fraction boiling at 145–155° (10 mm.) and weighing 14 g. (46.5%) was collected. It was *cis*-2-styrylpyridine (IVb), (λ_{max} 290 mμ, ϵ 11,400), n_D^{25} 1.6272.

Anal. Calcd. for $C_{13}H_{11}N$: C, 86.5; H, 6.1; N, 7.8. Found: C, 86.5; H, 6.3; N, 7.8.

A second, higher boiling fraction (IVa), b.p. 185–190° (10 mm.), m.p. 90–93°, wt., 1 g. (λ_{max} 309 mμ) was identified as IVa.

Method B: In benzene suspension. Dimer IIIa. A solution of 20 g. (0.11 mole) of IVa in 2700 ml. of benzene was saturated with dry hydrogen chloride. The hydrochloride (V) separated as a fine suspension which was irradiated for 15 hr. using a 550-watt, water-cooled, immersion-type ultraviolet source. The solid was collected, dried, and dissolved in 800 ml. of water. The products were isolated in the manner of Method A. The crude residue was extracted with 300 ml. of petroleum ether. The residue (IIIa) weighed 17 g. (85%) and was characterized by its melting point 189–190°. Concentration of the mother liquors to 50 ml. yielded an additional 1.0 g. of IIIa, m.p. 189–190°. The mother liquors were further concentrated to 15 ml. to give 0.5 g. of IVa, m.p. 90–92°.

Irradiation of trans-2-styrylpyridine (IVa). *Method A: In benzene solution. cis-2-Styrylpyridine* (IVb). A solution of 30 g. (0.165 mole) of *trans*-2-styrylpyridine (IVa) in 2700 ml. of benzene was irradiated under a nitrogen atmosphere for 15 hr. The benzene was distilled at the water pump, and the residue extracted with 250 ml. of petroleum ether. The residual solid, 4.6 g., melted at 90–92°. By distillation of the extract, there was obtained 17.5 g. (58.3%) of IVb, b.p. 120–125° (0.5 mm.). Its spectrum was identical with that of IVb obtained from V by irradiation in aqueous solution.

The following derivatives of IVb were prepared.

cis-2-Styrylpyridine methyl p-toluenesulfonate. A mixture of 5 g. of IVb and 5 ml. of methyl *p*-toluenesulfonate was heated for 18 hr. on the steam bath. Acetone (50 ml.) was added, and the white crystals were filtered and washed with acetone to give 6.1 g. of product, m.p. 98–100°.

Anal. Calcd. for $C_{21}H_{21}O_3NS$: C, 68.2; H, 5.7. Found: C, 68.4; H, 5.6.

cis-2-Styrylpyridine methiodide (Ib). A solution of 4 g. of this salt in 20 ml. of water was treated with 3 g. of sodium iodide in 5 ml. of water at 40–50°. The reaction mixture was chilled, and the well formed crystals were collected by filtration and crystallized from acetonitrile; yield, very pale yellow needle-like crystals, 4.1 g., m.p. 178°; ultraviolet spectrum: λ_{max} 325 mμ; ϵ 14,600.

Anal. Calcd. for $C_{14}H_{14}NI$: C, 51.9; H, 4.3. Found: C, 51.8; H, 4.2.

A higher boiling fraction, at 130–145° (0.5 mm.), weighed 3 g. and was identified by its spectra as IVa. Dimer IIIa was not found to be present.

Isomerization of cis-2-styrylpyridine (IVb) *to trans-2-styrylpyridine* (IVa). A solution of 0.5 g. of IVb (λ_{max} 290 mμ, ϵ 11,250) in 2 ml. of *p*-cymene was heated under reflux with 0.02 g. of a 15% palladium on charcoal catalyst for 1.5 hr. The reaction mixture was cooled to 70°, and the catalyst was filtered after dilution with 5 ml. of petroleum ether. After chilling, there was obtained 0.45 g. of crystals melting at 88–91° (λ_{max} 309 mμ; ϵ 26,000). A mixed melting point of this crude IVa with pure IVa was 90–92°.

Irradiation of trans-2-styrylpyridine methiodide (Ia). *Method A: In aqueous solution. cis-2-Styrylpyridine methiodide and dimer* II. A solution of 19 g. (0.058 mole) of Ia in 6 l. of water was allowed to stand exposed to daylight in six 1-l., Vycor flasks during 18 days of June 1960. Room-temperature evaporation of the solution to 200 ml. caused crystallization of a crude solid. The crude solid was extracted with 75 ml. of boiling water. Upon cooling, the extract gave 2.5 g. of

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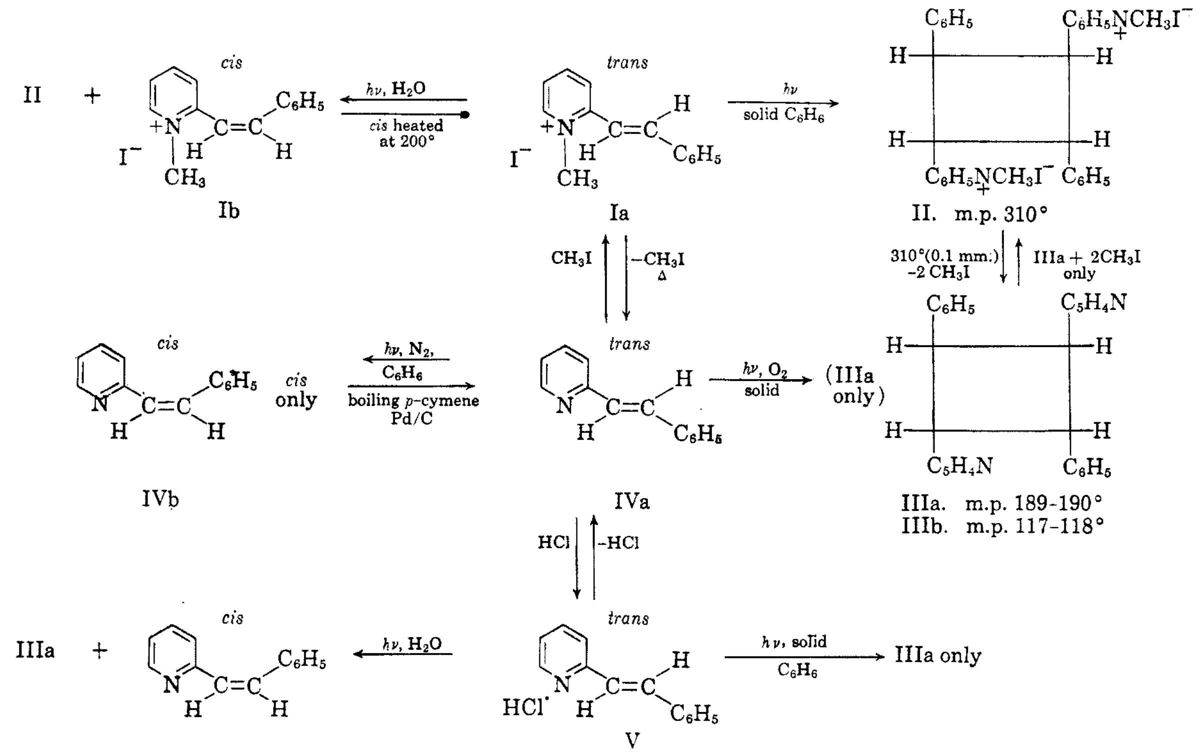
(2) A. P. Phillips, *J. Org. Chem.*, **12**, 333 (1947).

(3) All preparations and isolations were carried out in a laboratory equipped with General Electric, F-40G0, gold fluorescent lights.

(4) B. D. Shaw and E. A. Wagstaff, *J. Chem. Soc.*, p. 26 (1933).



solid (Ib), melting at 181–184° (λ_{max} 325; ε 7000). The original mother liquors, when concentrated to 50 ml., gave an additional 2.8 g. of Ib, m.p. 180–183° (λ_{max} 325 mμ; ε 10,500).

Anal. Calcd. for $C_{14}H_{14}NI$: C, 52.0; H, 4.35; N, 4.35; I, 39.3. Found: C, 52; H, 4.5; N, 4.2; I, 39.2.

The total yield of Ib was 5.3 g. (28%). The crude solid was extracted again with 50 ml. of boiling water to yield on cooling 1.3 g. of dimer II, m.p. 292° (λ_{max} 272; ε 12,700).

Method B: In benzene dispersion. *Dimer* II. Fifty grams (1.54 moles) of Ia was ball-milled for 16 hr. with 400 ml. of benzene. The suspension was diluted to 4700 ml. and placed in an irradiation flask. After 6 hr. of irradiation, the solids were removed by filtration and dried *in vacuo* at room temperature. The crude solid was recrystallized from 500 ml. of water after a treatment with decolorizing carbon to yield 47 g. (97%) of pure dimer II, melting at 310°.

Isomerization of cis-2-styrylpyridine methiodide (Ib) *to trans-2-styrylpyridine methiodide* (Ia). On standing at room temperature, there was a slow conversion of the *cis* to the *trans* as evidenced by the change of m.p. from 178 to 227°. Pure Ib was first melted at 178°, and the temperature elevated to and held at 200° for 1 or 2 min; the melt resolidified. The temperature was then raised slowly, causing the solid to melt at 225–230° dec. (λ_{max} 340 mμ; ε 28,800).

ROCHESTER 4, N. Y.

[CONTRIBUTION FROM THE LABORATORIO DI CHIMICA TERAPEUTICA, ISTITUTO SUPERIORE DI SANITÀ]

Aryldiazaadamantanols. Alkylation of the 9-Position of 1,5-Diphenyl-3,7-diazaadamantan-9-ol

S. CHIAVARELLI AND L. V. FENNOY[1]

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From the reaction of the appropriate alkyllithium with 1,5-diphenyl-3,7-diazaadamantan-9-one a series of nine new 1,5-diphenyl-3,7-diazaadamantan-9-ols has been synthesized for investigation of strychnine-like activity. Attempts to triacetylate the 9-*n*-butyl derivative resulted in dehydration with the formation of an unsaturated bispidine. Reduction of 1,5-diphenyl-3,7-diazaadamantan-9-ol produced unexpectedly 1,5-dicyclohexyl-3,7-dimethylbispidin-9-ol.

The discovery[2] that 1,5-diphenyl-3,7-diazaadamantan-9-ol (III) (1757 I.S.) has strychnine-like activity has caused interest in other structures of this type. Chiavarelli and Settimj[3] prepared 1,5-diphenyl-3,7-diazaadamantan-9-one (I) by the Mannich reaction and reduced it with lithium aluminum hydride to the corresponding diazaadamantanol.

Since the keto group of I could be reduced with

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(1) This investigation was carried out during the tenure of a Postdoctoral Fellowship (L. V. F.) from the National Institute of Neurological Diseases and Blindness, United States Public Health Service.

(2) V. G. Longo, B. Silvestrini, and D. Bovet, *Boll. Soc. it. Biol. Sper.*, **39**, 1866 (1958); also see *J. Pharmacol. Exptl. Terap.*, **126**, 41 (1959).

(3) S. Chiavarelli and G. Settimj, *Gazz. chim. ital.*, **88**, 1239 (1958).