TABLE IV

2-PHENYLIMINO-6-METHYLTETRAHYDRO-1,3-THIAZINE (IIF-1), 2-PHENYLIMINO-4-METHYLTETRAHYDRO-1,3-THIAZINE (IIF-2), 2-ANILINO-6-METHYL-4,5-DIHYDRO-6H-1,3-OXAZINE (IIG-1), AND 2-ANILINO-4-METHYL-4,5-DIHYDRO-6H-1,3-OXAZINE (IIG-2)

			Calcd, %				Found, %			
Compd	Mp, °C	Formula	C	H	N	S	C	H	N	S
IIf-1	103–104	$C_{11}H_{14}N_2S$	64.06	6.84		15.52	63.84	6.91		15.47
IIf-2	146–147	$C_{11}H_{14}N_2S$	64.06	6.84		15.52	64.09	6.93		15.08
IIg-1	109–110	$C_{11}H_{14}N_2O$	69.44	7.42	14.73		69.89	7.23	14.59	
IIg-2	111–113	$C_{11}H_{14}N_2O$	69.44	7.42	14.73		69.15	7.39	14.59	

TABLE V

THE PICRATES OF IIF-1, IIF-2, IIG-1, AND IIG-2

			Calcd, %				Found, %			
Compd	Mp, C°	Formula	C	H	N	S	C	H	N	S
IIf-1	165–166	$C_{17}H_{17}N_5O_7S$	46.90	3.94		7.37	46.52	3.97		7.97
IIf-2	187–188	$C_{17}H_{17}N_5O_7S$	46.90	3.94		7.37	46.88	4.05		7.56
IIg-1	176–178	$C_{17}H_{17}N_5O_8$	48.69	4.09	16.69		48.96	4.11	16.73	
IIg-2	180–182	$C_{17}H_{17}N_5O_8$	48.69	4.09	16.69		49.11	4.25	16.32	

after recrystallization from benzene and petroleum ether. It had bands at 3275 cm^{-1} (NH) and 1643 cm^{-1} (C=O) in its infrared spectrum.

Anal. Calcd for $C_{11}H_{14}N_2O$: N, 14.73. Found: N, 14.55.

2-Phenylimino-6-methyltetrahydro-1,3-thiazine (IIf-1) was prepared from 1-(3'-hydroxybutyl)-3-phenylthiourea by the cyclization reaction in concentrated hydrochloric acid. Other samples of II-1 and II-2 were prepared in a similar way. Analytical data are summarized in Table IV.

Analytical data of the picrates are summarized in Table V. The nmr signals of methyl hydrogens were located at τ 8.71, 8.82 (IIf-1), 8.89, 9.00 (IIf-2), 8.64, 8.75 (IIg-1), and 8.84, 8.95 (IIg-2), in chloroform with TMS as the internal standard.

Reaction of Ig with *p*-Toluenesulfonic Acid.—A mixture of 1.9 g (0.01 mole) of Ig and 1.7 g (0.01 mole) of *p*-toluenesulfonic acid in 10 ml of toluene was refluxed for 8 hr. The organic layer was extracted with 1 *N* sulfuric acid several times. After the aqueous solution was made alkaline, it was extracted with benzene. Evaporation of benzene gave 1.5 g (79%) of a mixture of IIg-1 and IIg-2 (by comparison of the infrared spectrum with those of IIg-1 and IIg-2). The mixture was dissolved in chloroform (in 10% concentration), and the solution was submitted to the nmr analysis. The errors in the determination of the ratio of II-1 and II-2 were about 5%.

Acknowledgment.—The authors wish to thank Nippon Soda Company, Ltd., for gifts of thiophosgene and 1-chloro-2-propanol which was the starting material of 4-amino-2-butanol.

The Reduction Products of a Dibenzo[*b,f*][1,5]diazocine[1]

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Reductions of 2,8-dichloro-6,12-diphenyldibenzo[*b,f*][1,5]diazocine gave both dihydro and tetrahydro derivatives. One of the dihydro products was found to be an indoloindole derivative (V) while the tetrahydro compounds were shown to be diastereomeric diphenyldibenzodiazocines (II and III). The interconversions of these products as well as those of their methyl derivatives are described. The condensation of the two diastereomeric tetrahydro derivatives II and III with formaldehyde led to the isolation of three methylene bridged isomers. The stereochemistry of these products was determined by nmr spectroscopy and in turn constitutes unequivocal proof for the stereochemical assignment for II and III.

The pharmacological interest[2] in 2,8-dichloro-6,12-diphenyldibenzo[*b,f*][1,5]diazocine[3] (I) prompts us to describe the products obtained by the reduction of this compound. Initial experiments gave mixtures which contained the products II, III, IV, and V in varying amounts. By changing the conditions used for these reductions we were able to separate, identify, and assign structures for these products.

Reduction of I with lithium aluminum hydride gave II, III, and IV. It was found that the ratio of these products was strongly influenced by the choice of solvent.

In pyridine, for example, a 78% yield of the dihydro derivative IV was obtained. The structure was proved by oxidation to I with chromic acid and, more conclusively, by further reduction to a mixture of the diastereomeric tetrahydro derivatives II and III.

The nmr spectra of IV and its monoacetyl derivative, as well as its monomethyl derivative XII, show pecularities which are worthy of discussion. Compound XII, for instance, shows unsymmetrical doublets for the aliphatic C*H* and also for the CH_3 groups. The ratio of the areas of the two peaks in each doublet is approximately 1:4.

An explanation for the spectral properties was suggested by an inspection of the Dreiding models for these compounds (see Figure 1). The C=N double bond in the eight-membered ring makes the model so rigid that the two preferred conformations are interconvertible only by the use of considerable force. It is, therefore, assumed that each of these compounds consists of a mixture of pairs of relatively stable conformational isomers. This was confirmed by nmr spectra

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[1] Some of this material was briefly reported: W. Metlesics and L. H. Sternbach, *J. Am. Chem. Soc.*, **88**, 1077 (1966).

[2] A. Boris, personal communication, 1962; see also G. W. Duncan, S. C. Lyster, and J. B. Wright, *Proc. Soc. Exptl. Biol. Med.*, **120**, 725 (1965).

[3] W. Metlesics, T. Resnick, G. Silverman, R. Tavares, and L. H. Sternbach, *J. Med. Chem.*, **9**, 633 (1966).

taken at elevated temperatures. The additional bands disappear at 100–130° to form single peaks which have the expected intensities.[4] (See Figure 2.)

A mixture of the expected two diastereomeric tetrahydro derivatives (position of the phenyl groups either *cis* or *trans* to each other, compounds III and II, respectively) was formed on reduction of I with lithium aluminum hydride in tetrahydrofuran. On catalytic hydrogenation of I with acetic acid a mixture of III and V in an approximate ratio of 1:3 was obtained. The stereoisomeric tetrahydro derivative II was not found as a product of the catalytic hydrogenation. Since it is reasonable to predict that the hydrogen would add to the molecule from one side, the *cis* configuration was assigned to compound III (for unequivocal proof see below).

Reduction of I with lithium aluminum hydride in refluxing ether gave a mixture of II and III from which pure II was obtained in 73% yield by fractional crystallization.

The reduction of IV with lithium aluminum hydride in tetrahydrofuran gave predominately III and some II. Although II is the less soluble isomer, it was possible to obtain a 38% yield of pure III by recrystallization of the crude reduction product.

The fact that II and III constitute a pair of diastereomers was convincingly proved by rearranging pure II with sodium hydride to a mixture of II and III (ratio approximately 1:1). A similar mixture of II and III was obtained by heating pure III with sodium hydride. It is assumed that the hydride ion forms carbanions of II and III which then partially undergo inversion.

A partial inversion of II was also observed under conditions of vapor phase chromatography. Vapor phase chromatography of pure III gave a single peak, whereas, under the same conditions pure II was partially converted and gave two peaks of which one (area *ca.* 30%) had the same retention time as III. The second peak (area *ca.* 70%) was attributed to unrearranged II.

Compound III was readily oxidized to I by chromium trioxide in acetic acid, whereas II was oxidized only on using a solution of chromium trioxide in sulfuric acid and in low yield.

There are significant differences between the spectra of II and III which are obviously due to different conformations of the dibenzo[*b*,*f*][1,5]diazocine ring system. The ultraviolet spectrum of III shows no characteristic absorption maximum,[5] whereas II has a maximum at 256 mμ (ϵ 22,000).[6] Indications for NH–N bonding are found in the infrared spectrum of III which shows two bands (3335 and 3315 cm^{-1}), whereas II has only one band (3350 cm^{-1}) in the NH region. The presence of CH–NH coupling in the nmr spectra of compounds II and III was found to be dependent on the solvent used (singlets in DMF-d_7 and AB quartets in THF-d_8).

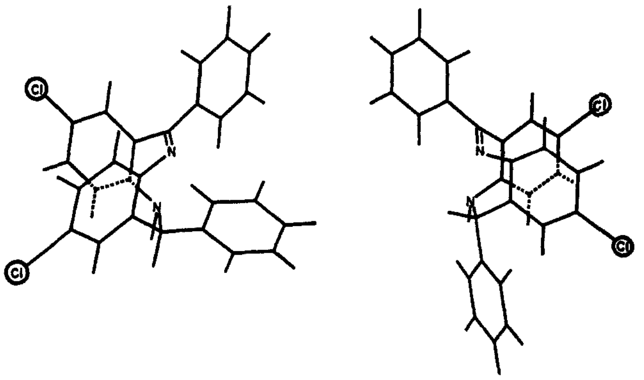

Figure 1.—Models of two preferred conformations of IV.

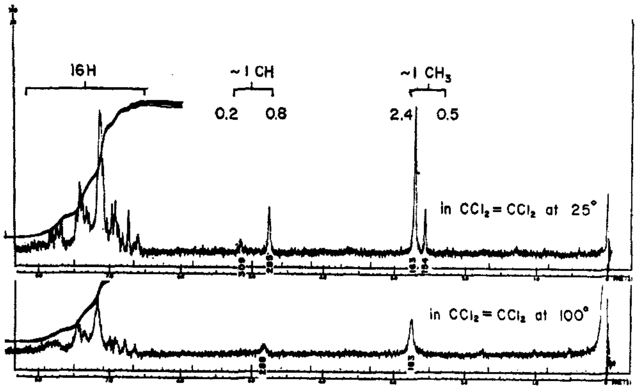

Figure 2.—Nmr spectra of XII.

Further reduction of the methyl derivative XII with lithium aluminum hydride gave predominately the isomer X to which the *cis* configuration was assigned in view of the uncharacteristic ultraviolet absorption (compare III). The main product of methylation of X was identical with the dimethyl derivative (VII) also obtained directly from the *cis* isomer (III).[7]

A small amount of the isomer (IX) was formed along with the main product (X) on reduction of XII with lithium aluminum hydride. Compound X, on treatment with sodium hydride, was rearranged to yield a mixture from which the *trans* isomer (IX) was isolated in 12% yield by chromatographic separation. Further methylation of IX gave a dimethyl derivative (VI) which was identical with the one obtained by direct methylation of II.[7]

The monomethylated tetrahydro derivatives (IX and X) could be reoxidized to XII with chromic acid. The nmr spectrum shows NH–CH splitting (AB quartet) for X but not for IX. (See Scheme I.)

The reduction of I with zinc in acetic acid gave a product to which structure V was ascribed. This structural assignment is based on compatible infrared and nmr spectra (no aliphatic protons, two NH groups) and the fact that V was stable to further reduction as well as to hydrolysis.[8] Hydrogenation of I with Adams catalyst in acetic acid containing hydrogen chloride gave V in approximately 90% yield. Since the measured uptake of hydrogen was close to 1 molar equiv this compound had to be a dihydro derivative of

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[4] The referees drew our attention to the description of a similar phenomenon by R. L. Winebolt, E. Wyss, and J. A. Moore, *J. Org. Chem.*, **31**, 48 (1966); see also E. Grunwald and E. Price, *J. Am. Chem. Soc.*, **87**, 3139 (1965), and H. Hart and J. L. Corbin, *ibid.*, **87**, 3135 (1965).

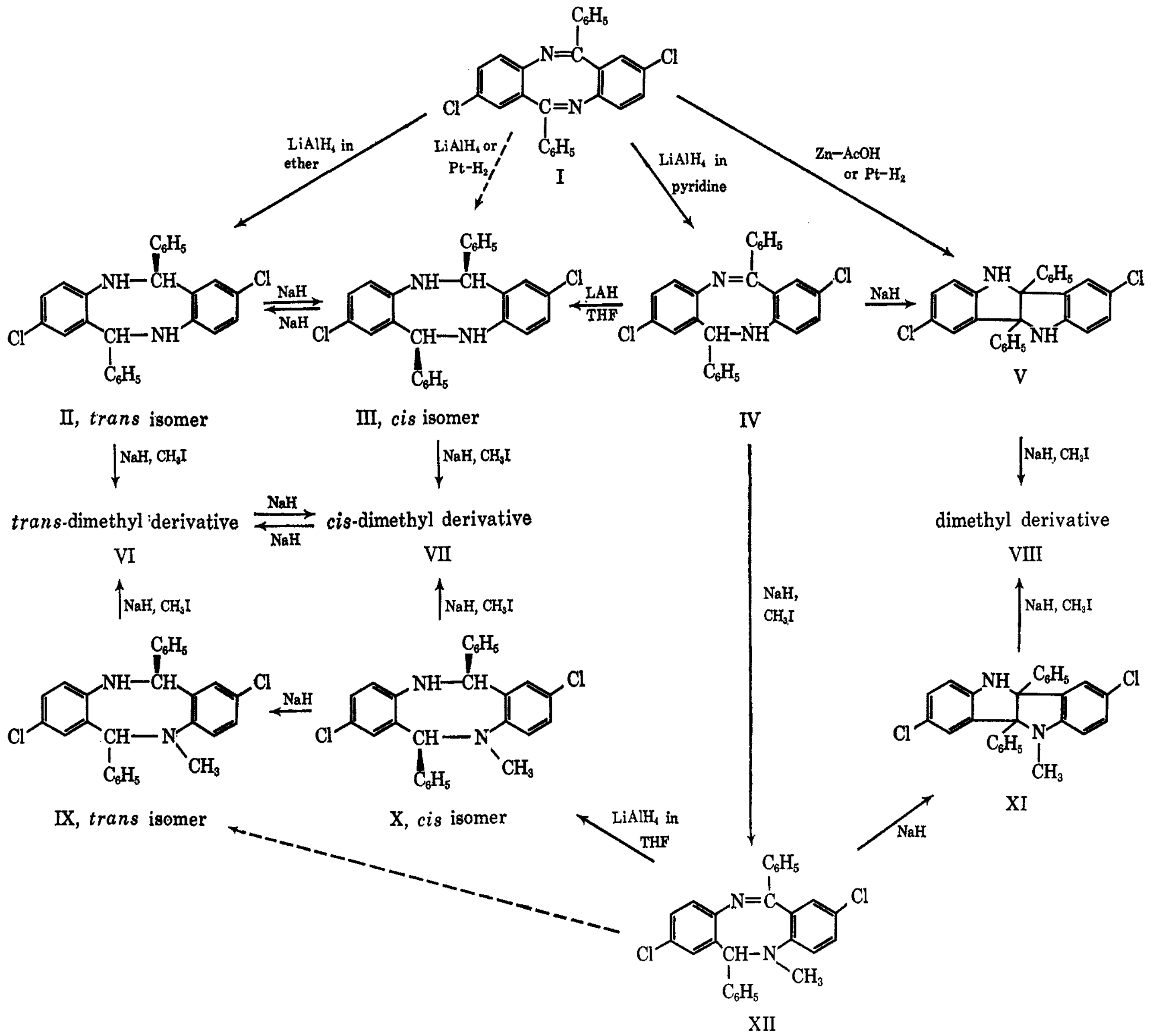
[5] The absence of the absorption maximum which would be characteristic for the *p*-chloroaniline part of the molecule shows the small extent of resonance between the nitrogen atoms and the aromatic rings. For comparison of ultraviolet spectra of Trögers base, see B. M. Wepster, *Rec. Trav. Chim.*, **72**, 661 (1953).

[6] Roughly equivalent to two units of *p*-chloroaniline [λ_{max} 242 mμ (ϵ 9000)].

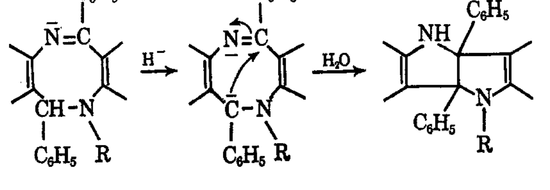
[7] Because sodium hydride causes partial inversions in this class of compounds at elevated temperatures, these methylations were carried out at room temperature where inversions were observed to be minimal.

[8] Transannular ring closures of eight-membered carbocycles have been described in the literature; see S. Wawzonek, *J. Am. Chem. Soc.*, **62**, 745 (1940), and M. Stiles, Abstracts of the 19th Organic Symposium of the American Chemical Society, Tempe, Ariz., June 1965, p 62.

SCHEME I



I. On oxidation, V was readily reconverted to the starting material I. Compound V was also obtained in excellent yield by treatment of IV with sodium hydride at elevated temperatures.[9] It is proposed that in the course of this reaction a carbanion is formed which undergoes a transannular rearrangement as indicated. This result at the same time confirms the assignment of structure V.



An analogous rearrangement was observed when the methylation product (XII)[10] was treated with sodium hydride at elevated temperatures to give XI. The structure of XI was proved by methylation to the dimethyl derivative (VIII) which was identical with the methylation product of V.

The assignment of the *cis* configuration for compound III originally based on the result of the catalytic hydrogenation of I (see above) could have been proved by resolution of III into optical antipodes.[11] However, the following approach was selected.

The condensation of formaldehyde with the tetrahydro derivatives (II and III) gave the three expected methanodibenzodiazocines XV, XVI, and XVII.[12] These compounds are analogs of Troeger's base (Cl instead of CH_3 and CHC_6H_5 instead of CH_2). Inspection of molecular models made it obvious that the *trans*-tetrahydro derivative II can give only one product (XV), whereas the *cis* isomer (III) would lead

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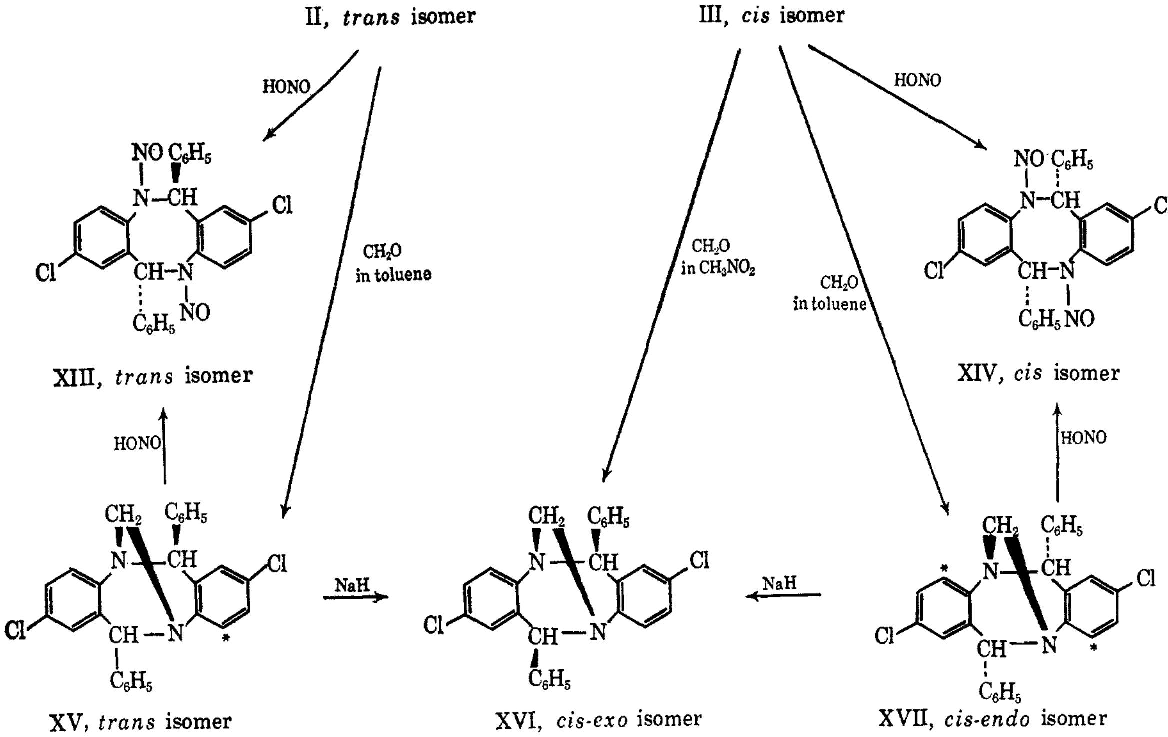
[9] Attempts to achieve a rearrangement using acidic catalysts were unsuccessful.

[10] A small amount of VIII was isolated as a by-product after methylating IV using sodium hydride as a base. Since transannular rearrangements of IV and XII were observed under these conditions VIII is the expected product from the rearranged precursors V or XI.

[11] This product would be racemic, whereas the *trans* isomer II which has a center of symmetry would be a *meso* compound.

[12] For analogy, see F. C. Cooper and M. W. Partridge, *J Chem. Soc.*, 2888 (1957).

Scheme II



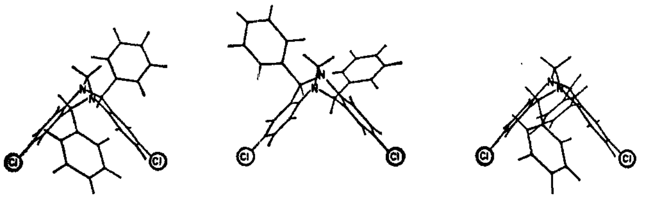


Figure 3.—Models of XV, XVI, and XVII.

to the formation of the two isomeric products (XVI and XVII) which differ in the orientation of the *cis*-phenyl groups to the methylene bridge.[13] We found that the condensation of formaldehyde with II did give only one methanodibenzodiazocine, while from the condensation of formaldehyde with III two isomeric methanodibenzodiazocines were isolated. This fact alone constitutes proof for the stereochemistry of compounds II and III. It is a further example of the known method for stereochemical assignment[14] which involves the addition of a new element of asymmetry[15] to the two isomers in question and counting the number of diastereomers formed.

All three isomers showed similar ultraviolet and infrared spectra. Compounds XV and XVII were quantitatively rearranged to XVI on treatment with sodium hydride but, in contrast to the partial rearrangement of II $\rightleftharpoons$ III with sodium hydride, compound XVI could not be rearranged to either compound XV or to compound XVII under these conditions. This shows that the *cis,exo* isomer (XVI) having the least crowded configuration (see models, Figure 3) is the most stable isomer. Compound XVI was also unchanged on treatment with nitrous acid, whereas the isomers XV and XVII were cleaved to give the corresponding *cis*- and *trans*-dinitrosodibenzodiazocines (XIII and XIV,[16] respectively). These compounds were shown to be identical with the products obtained from II and III by direct nitrosation.

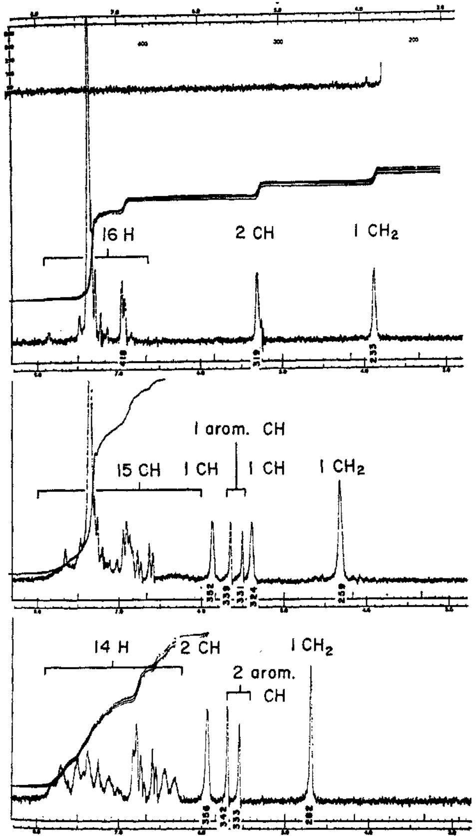


Figure 4.—Nmr spectra of XVI (*cis,exo* isomer), XV (*trans* isomer), and XVII (*cis,endo* isomer).

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[13] All three compounds lack molecular symmetry and are therefore racemates.

[14] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 184; see also G. W. Wheland, "Advanced Organic Chemistry," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1960, p 465.

[15] Generally a new asymmetric center, in this case molecular asymmetry.

[16] For cleavage of Troeger's base with nitrous acid see ref 12.

The remaining question of assigning the configurations of the two *cis* products (XVI and XVII) was solved by nmr spectroscopy. (See Figure 4.) Compound XVI showed two signals of equal intensity, one for the methylene bridge (233 cps) and the other for two equivalent benzyl protons (319 cps). It therefore had to be a *cis* isomer. The spectrum of XV had signals attributable to the methylene bridge (259 cps) and two different types of benzylic protons (324 and 352 cps). Compound XV, therefore, had to be the *trans* isomer. Two additional signals at 331 and 339 cps with the intensity of *ca.* one proton were recognized as a doublet due to an aromatic proton strongly shielded by a phenyl group.

Inspection of the model of XV shows that the phenyl substituent in the endo position (within the basket formed by the molecule and pointing away from the methylene bridge) lies above one of the protons of the benzo group.[17] The spectrum of XVII shows the signals for the methylene bridge and two equivalent benzyl protons. The additional doublet (333 and 342 cps) assigned to the shielded aromatic protons is twice as strong as in XV. This is expected since the effects discussed above are now due to two phenyl rings in the *endo* position. (See Scheme II.)

Experimental Section[18]

***trans*-2,8-Dichloro-5,6,11,12-tetrahydro-6,12-diphenyldibenzo-[*b,f*][1,5]diazocine** (II).—To a stirred solution of 50 g (0.117 mole) of I[3] in 2500 ml of ether was added 5.5 g (0.145 mole) of lithium aluminum hydride. The solution was heated to reflux for 16 hr and cooled in an ice bath, and 28 ml of 2 *N* sodium hydroxide was added dropwise. After stirring for 2 hr, the solids were filtered from the solution. The filter cake was extracted with 1000 ml of boiling tetrahydrofuran and the suspension was filtered hot. Ethyl acetate was added to the filtrate and the tetrahydrofuran was removed *in vacuo*. White prisms were obtained in 73% yield (37.1 g) melting at 244–247°. This compound held solvents tenaciously and had to be dried *in vacuo* at 160°: ultraviolet $\lambda_{\max}$ 256 mμ (ϵ 22,000) and 305 mμ (ϵ 4000); nmr (DMF-d_7) 2NHC*H* 353 cps (s),[19] (THF-d_8) 2 NHC*H* 350, 341 cps (d), part of AB quartet, 2N*H*CH 333, 324 (d), part of AB quartet; infrared (KBr) 3350 cm^{-1}.

Anal. Calcd for $C_{26}H_{20}Cl_2N_2$: C, 72.39; H, 4.67; Cl, 16.44; N, 6.50. Found: C, 72.67; H, 4.68; Cl, 16.34; N, 6.53.

Chromium trioxide dissolved in 8.5 *N* sulfuric acid oxidized II to I (25°, 2 hr).

Diacetyl Derivative of II.—A solution of 8 g (0.0185 mole) of II in 80 ml of acetic anhydride and 8 ml of pyridine was heated to reflux for 3 hr. On addition of ether to the cooled solution crystals were obtained which melted at 360–370°. The yield was 4.2 g (44%). A small sample of this very sparingly soluble compound was recrystallized from a mixture of methylene chloride and methanol to give white prisms: mp 370–372°, ultraviolet λ_{infl} 255 mμ (ϵ 1000).

Anal. Calcd for $C_{30}H_{24}Cl_2N_2O_2$: C, 69.91; H, 4.69; O, 6.21. Found: C, 69.82; H, 5.04; N, 6.23.

***cis*-2,8-Dichloro-5,6,11,12-tetrahydro-6,12-diphenyldibenzo-[*b,f*][1,5]diazocine** (III).—A solution of 85.8 g (0.2 mole) of IV in 700 ml of tetrahydrofuran was added dropwise to a stirred solution of 11.3 g (0.3 mole) of lithium aluminum hydride in 500 ml of tetrahydrofuran. Throughout the addition (*ca.* 45 min) the temperature was kept below 10° by an ice bath. The mixture was then heated to reflux for 16 hr and cooled, and after addition of 600 ml of wet ether and 25 ml of water, it was stirred for 2 hr. The solution was filtered through "Celite" and the filter cake was washed with 1000 ml of tetrahydrofuran. The solvent was removed *in vacuo* and the residue was repeatedly recrystallized from benzene to yield 33.2 g (38% of theory) of white prisms melting at 225–227°. This product was shown to be free of II[20] by thin layer chromatography (alumina, hexane). The highest melting point of III obtained after chromatography on alumina was 228–230°. In a single experiment a dimorphic form melting at 193–196° was obtained after recrystallization from ethanol: ultraviolet λ_{infl} 255 mμ (ϵ 8000) and λ_{infl} 283 mμ (ϵ 2600); nmr (THF-d_8) 2NHC*H* 333, 325 cps (d), part of AB quartet, 2N*H*CH 321, 313 cps (d), part of AB quartet (DMF-d_7) 2 NHC*H* 344 cps (s); infrared (KBr) 3335 and 3315 cm^{-1}.

Anal. Calcd for $C_{26}H_{20}Cl_2N_2$: C, 72.39; H, 4.67; Cl, 16.44; N, 6.50. Found: C, 72.24; H, 4.68; Cl, 16.39; N, 6.43.

Compound III was reoxidized to I with chromium trioxide in acetic acid (20 hr, 25°).

Diacetyl Derivative of III.—A solution of 10 g (0.0232 mole) of III in 50 ml of pyridine and 25 ml of acetic anhydride was heated to reflux for 5 hr. The mixture was poured into ice-water and the crystalline precipitate was filtered from the solution. Recrystallization from a mixture of methylene chloride and ethanol gave 7.6 g (63% of theory) of white prisms melting at 288–290°, ultraviolet λ_{infl} 260 mμ (ϵ 1500).

Anal. Calcd for $C_{30}H_{24}Cl_2N_2O_2$: C, 69.91; H, 4.69. Found: C, 69.61; H, 4.78.

Isomerization of II and III.—Treatment of pure II or III with sodium hydride in dimethylformamide (55°, 90 min) gave a mixture of II and III in the approximate ratio of 1:1 (±10%). The accuracy of the determination of this ratio by vapor phase chromatography was diminished by the fact that pure II was partly (*ca.* 30%) isomerized to III under the conditions of the chromatography (retention time 15–20 min at 225°). Pure III passed through the same column without noticeable isomerization.

2,8-Dichloro-5,6-dihydro-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (IV).—To a solution of 86.8 g (0.203 mole) of I[3] in 1000 ml of pyridine cooled to 10° in an ice bath was added 7.6 g (0.20 mole) of lithium aluminum hydride in small portions with stirring. The cooling was discontinued after 15–30 min and the dark brown solution was stirred at 25° for 16 hr. The solution was cooled in an ice bath, 1000 ml of wet ether and 30 g of ice were added in small portions, and the mixture was stirred for 1–2 hr at 25°. The solution was filtered through Celite and the solvent was removed *in vacuo* to give yellow needles which after recrystallization from a mixture of methylene chloride and ethanol melted at 200–208° (remainders up to 230°). The yield was 67.7 g (78% of theory): ultraviolet $\lambda_{\max}$ 257 mμ (ϵ 30,000) and 320 mμ (ϵ 5000); nmr ($CDCl_3$) 1NHC*H*, 368 and 359 cps (d), part of AB quartet and 331 and 322 cps (d), part of AB quartet, 1N*H*CH 255 and 247 cps (d), part of AB quartet.

Anal. Calcd for $C_{26}H_{18}Cl_2N_2$: C, 72.73; H, 4.22; N, 6.53; Cl, 16.52. Found: C, 72.92; H, 4.42; N, 6.49; Cl, 16.39.

The melting point of IV remained unsharp despite repeated purification by crystallization, high vacuum distillation, and chromatography. Vapor phase chromatography gave no indication of an impurity in IV. Thin layer chromatography (silica; chloroform–heptane, 3:2) showed the presence of II, III, and V in the recrystallization mother liquor of IV. R_f values were sufficiently different to ascertain that none of these compounds was a possible impurity in IV. Oxidation of IV with chromium trioxide in acetic acid (25°, 1 hr) gave I in good yield.

Acetyl Derivative of IV.—A solution of 11.9 g (0.028 mole) of IV in 75 ml of benzene and 25 ml of acetyl chloride was heated to reflux for 2.5 hr. Evaporation *in vacuo* gave a viscous residue which crystallized on addition of methanol. Recrystallization

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[17] The observed coupling constant of J = 8 cps requires the presence of a proton in the *ortho* position and the absence of a proton in *meta* position to the one producing the doublet. Only the proton (*) *meta* to the Cl atom meets these requirements.

[18] All melting points are corrected. The spectra were determined using a Beckman IR-9 spectrophotometer (infrared), a Carey 14 spectrophotometer (ultraviolet spectra in isopropyl alcohol), and a Varian A-60 spectrometer at 60 Mcps (nmr). Gas chromatography was performed with a Barber-Colman Model 10 instrument using columns with DCDS treated Gas Chrom P and 1% SE-30. N,N-Dimethylformamide used as solvent for reactions with sodium hydride was filtered through a column of alumina. The identity of compounds was established by comparison of spectral properties and mixture melting point.

[19] In the case of multiplets, the positions of the compound peaks are reported followed by the multiplicity expressed by s, d, t, and q for singlet, doublet, triplet, and quartet, respectively.

[20] Compound II is the minor product formed in the reduction. Since II is less soluble than III, the yield of pure III obtained by recrystallization was relatively low.

from a mixture of methylene chloride and methanol gave 11.0 g (84% of theory) of white prisms melting at 212–215°: ultraviolet λ_{max} 263 mμ (ε 23,500) and 331 mμ (ε 2000); nmr (DMF-d_7) at *ca.* 25° 1CH_3CO 118 (s) and 98 cps (s), at 130° 1CH_3CO 100 cps (s, broad).

Anal. Calcd for $C_{28}H_{20}Cl_2N_2O$: C, 71.34; H, 4.28; O, 3.39. Found: C, 71.39; H, 4.44; O, 3.82.

Hydrolysis of this compound in tetrahydrofuran with sodium methoxide (reflux for 18 hr) gave IV melting at 200–207°.

3,8-Dichloro-4b,5,9b,10-tetrahydro-4b,9b-diphenylindolo[3,2-*b*]indole (V). A. By Catalytic Reduction of I.—A solution of 85.4 g (0.2 mole) of I^3 in 1000 ml of acetic acid containing *ca.* 25 g of hydrogen chloride was hydrogenated at 25° and atmospheric pressure using 2 g of platinum oxide as catalyst. During the rapid uptake of hydrogen, a white salt precipitated from the solution and the consumption stopped after 5500 ml of hydrogen had been absorbed (0.2 mole, 4800 ml + 500 ml for the catalyst). The solution was filtered from the crystalline precipitate and the catalyst, and discarded. The solid part was suspended in ice water and made basic with aqueous ammonia, and the product was extracted with ether. The ether solution was washed with water, dried with sodium sulfate, and evaporated to dryness. The residue was recrystallized from a mixture of methylene chloride and methanol to give 75.1 g (88% of theory) of white prisms melting at 225–228°. A sample obtained by chromatography on basic alumina using benzene as eluent melted at 228–230°: ultraviolet λ_{max} 248 mμ (ε 25,000), λ_{infl} 260 mμ (ε 21,000), and λ_{max} 315 mμ (ε 5500); nmr (THF-d_8) 2NH 374 cps (s).

Anal. Calcd for $C_{26}H_{18}Cl_2N_2$: C, 72.73; H, 4.22; Cl, 16.52; mol wt, 429.3. Found: C, 72.62; H, 4.37; Cl, 16.30; mol wt, 379 (isothermal distillation in acetone).

Compound V was found to be stable to further catalytic hydrogenation (Pt, 25°, 1 atm), reduction with lithium aluminum hydride, and also to acidic hydrolysis.

Oxidation of compound V with chromium trioxide in acetic acid, gave a quantitative yield of starting material I, which was also obtained from V on prolonged standing in solutions (air oxidation).

When the hydrogenation was carried out using acetic acid as solvent (no hydrogen chloride added) a mixture resulted, which by chromatographic separation, was shown to contain III and V in a ratio of *ca.* 1:3.

B. By Chemical Reduction of I.—To a solution of 2 g of I in a mixture of 25 ml of methylene chloride, 50 ml of acetic acid, and 5 ml of water was added 7 g of zinc dust. The mixture was stirred for 2 hr at 25°, poured into ice–water, made alkaline with sodium hydroxide, and extracted with ether. Evaporation of the ether gave white prisms which after recrystallization from methanol melted at 227–229°. The yield was 1.2 g (60%).

C. By Rearrangement of IV.—A solution of 4.3 g (0.01 mole) of IV in 50 ml of dimethylformamide was prepared under nitrogen. On addition of 1 g of a 50% suspension of sodium hydride in mineral oil the color of the solution turned to green. On heating to 60° for 30 min the color of the solution had faded to yellow and the solution was poured into ice water. A yield of 3.8 g (88% of theory) of V was obtained.

Diacetyl Derivative of V.—To a stirred solution of 150 ml of acetic anhydride containing 1.5 ml of boron fluoride etherate was added 33 g of V in small portions. The solution was stirred for 30 min, poured into ice water, and stirred to decompose the acetic anhydride, and the crystalline precipitate was collected on a filter. Recrystallization from a mixture of methylene chloride and methanol gave 32.6 g (83% of theory) of white prisms melting at 299–301°: ultraviolet λ_{max} 262 mμ (ε 25,000) and λ_{infl} 290 mμ (ε 5500).

Anal. Calcd for $C_{30}H_{22}Cl_2N_2O_2$: C, 70.18; H, 4.32; N, 5.46; O, 6.23. Found: C, 69.91; H, 4.30; N, 5.55; O, 6.34.

On reduction of this compound with lithium aluminum hydride in tetrahydrofuran (6 hr, 25°) compound V was the main product.

***trans*-2,8-Dichloro-5,6,11,12-tetrahydro-5,11-dimethyl-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (VI).**—A solution of 4.3 g (0.01 mole) of II was prepared in 50 ml of dimethylformamide under nitrogen. The solution was cooled to 3° and 1.5 g of a 50% suspension of sodium hydride in mineral oil was added. Stirring was continued for 1.5 hr at a temperature of *ca.* 5–10°, then 10 ml of methyl iodide was added slowly and the stirring was continued for 1 hr at 25°. The mixture was poured into ice–water and extracted with ether. Evaporation of the ether left a crystalline residue which was dissolved in benzene, filtered through acidic alumina, and recrystallized from ether. White prisms (1.7 g, 37% of theory) were obtained which melted at 207–209°: ultraviolet λ_{max} 262 mμ (ε 12,000) and λ_{infl} 287 mμ (ε 7500); nmr (CDCl$_3$) 2NCH_3 152 (s) and 2CH 323 cps (s).

Anal. Calcd for $C_{28}H_{24}Cl_2N_2$: C, 73.20; H, 5.27. Found: C, 73.28; H, 5.24.

Treatment of this compound with sodium hydride in dimethylformamide (60°, 4 hr) gave a mixture which, according to vapor phase chromatography, consisted of VI and VII in a ratio of approximately 1:1. Compound VI was also obtained by methylation of IX according to the procedure described above.

***cis*-2,8-Dichloro-5,6,11,12-tetrahydro-5,11-dimethyl-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (VII).**—A solution of 4.3 g (0.01 mole) of III in 30 ml of dimethylformamide was prepared under nitrogen. After addition of 1 g of a 50% suspension of sodium hydride in mineral oil and 15 min of stirring at 25°, 1.5 ml (0.024 mole) of methyl iodide was added, and the stirring was continued for 15 min. This procedure was repeated (1 g of 50% sodium hydride, 15 min of stirring, 3 ml of methyl iodide, 30 min of stirring) and the resulting mixture was poured into ice water and extracted with ether. Evaporation of the ether left a crystalline residue which after recrystallization from a mixture of methylene chloride and ethanol gave 2.4 g (52%) of white prisms melting at 214–216°: ultraviolet λ_{infl} 225 mμ (ε 28,000), λ_{max} 275 mμ (ε 6000), and λ_{infl} 305 mμ (ε 2500); nmr (CDCl$_3$) 2NCH_3 157 (s) and 2CH 271 cps (s).

Anal. Calcd for $C_{28}H_{24}Cl_2N_2$:. C, 73.20; H, 5.27. Found: C, 72.93; H, 5.52.

Treatment of this compound with sodium hydride in dimethylformamide (60°, 4 hr) gave a mixture which according to vapor phase chromatography consisted of VI and VII in a ratio of approximately 1:9.

Compound VII was also obtained by methylation of X according to the procedure described above.

3,8-Dichloro-4b,5,9b,10-tetrahydro-5,10-dimethyl-4b,9b-diphenylindolo[3,2-*b*]indole (VIII).—To a solution of 8.6 g (0.02 mole) of V in 75 ml of dimethylformamide prepared under nitrogen was added 6.0 g of a 50% suspension of sodium hydride in mineral oil. The mixture was stirred and heated to 55° for 30 min and cooled in an ice bath. After the addition of 10 ml (0.16 mole) of methyl iodide, stirring was continued for 1 hr at 25° and the mixture was poured into ice–water. Extraction with methylene chloride and replacement of this solvent by ethanol gave 7.5 g (82%) of white prisms melting at 253–256°. Recrystallization from a mixture of benzene and hexane gave white prisms melting at 261–263°: ultraviolet λ_{max} 254 mμ (ε 22,000), λ_{infl} 280 mμ (ε 11,000), λ_{max} 337 mμ (ε 5000); nmr (CDCl$_3$) 2NCH_3, 168 cps (s).

Anal. Calcd for $C_{28}H_{22}Cl_2N_2$: C, 73.54; H, 4.85; N, 15.50. Found: C, 73.18; H, 5.16; N, 15.55.

Compound VIII was also obtained in 81% yield by methylation of XI according to the procedure described above.

***trans*-2,8-Dichloro-5,6,11,12-tetrahydro-5-methyl-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (IX).**—To a solution of 4 g (0.009 mole) of X in 75 ml of dimethylformamide prepared under nitrogen was added 4 g of a 50% suspension of sodium hydride in mineral oil. The mixture was stirred at 50° for 2 hr, poured into ice–water, and extracted with ether. The ether was dried and evaporated and the residue was chromatographed on 150 g of acidic alumina. With benzene a 24% yield (0.95 g) of X was obtained. Further elution with ethylacetate and methylene chloride (1:9) gave *ca.* 500 mg (12.5% of theory) of white prisms which after recrystallization from a mixture of benzene and hexane melted at 187–189° (IX): ultraviolet λ_{max} 258 mμ (ε 16,000) and λ_{infl} 310 mμ (ε 3000); nmr (CDCl$_3$) 1 NCH_3 172 (s), 1CH 355 (s), 1CH 311 (s), and 1NH 276 cps (s).

Anal. Calcd for $C_{27}H_{22}Cl_2N_2$: C, 72.81; H, 4.98. Found: C, 72.84; H, 4.97.

***cis*-2,8-Dichloro-5,6,11,12-tetrahydro-5-methyl-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (X).**—A solution of 8.6 g (0.019 mole) of XII in 120 ml of tetrahydrofuran containing 1.5 g (0.02 mole) of lithium aluminum hydride was heated to reflux for 16 hr. The solution was cooled and 7 ml of water was added. After filtration through Celite a clear solution was obtained which left a crystalline residue on evaporation. Recrystallization from a mixture of benzene and petroleum ether (bp 30–60°) gave 1.8 g (21% of theory) of white prisms melting at 183–184°: ultraviolet λ_{infl} 260 mμ (ε 6000) and λ_{infl} 290 mμ (ε 2000); nmr (CDCl$_3$) 1NCH_3 159 (s), 1CHNH 322 and 310 (d), part of AB quartet, 1CHN*H* 387, 375 (d), part of AB quartet, and 1C*H*NCH$_3$ 288 cps (s).

Anal. Calcd for $C_{27}H_{22}Cl_2N_2$: C, 72.81; H, 4.98; Found: C, 73.00; H, 5.12.

After chromatography of the mother liquor a small amount of the *trans* isomer IX was obtained. Oxidation of X with chromium trioxide and sulfuric acid in acetone gave XII which was isolated in substance after chromatography.

3,8-Dichloro-4b,5,9b,10-tetrahydro-5-methyl-4b,9b-diphenylindolo[3,2-*b*]indole (XI).—A solution of 4.4 g (0.01 mole) of XII in 75 ml of dimethylformamide was prepared under nitrogen. After adding 0.5 g. of a 50% suspension of sodium hydride in mineral oil, the temperature of the mixture was kept at 70–80° for 90 min. The solution was cooled and poured into ice–water. Extraction with ether gave a material which after recrystallization from a mixture of methylene chloride and methanol formed white prisms melting at 229–231°: ultraviolet λ_{max} 250 mμ (ϵ 23,000), λ_{infl} 273 mμ (ϵ 11,000), and λ_{max} 320 mμ (ϵ 5500; nmr (CDCl$_3$) 1NCH_3 171 (s) and 1N*H* 269 cps (s).

Anal. Calcd for $C_{27}H_{20}Cl_2N_2$: C, 73.14; H, 4.55. Found: C, 73.34; H, 4.69.

2,8-Dichloro-5,6-dihydro-5-methyl-6,12-diphenyldibenzo[*b,f*][1,5]diacocine (XII).—To a cooled solution of 4.3 g (0.01 mole) of IV in 35 ml of dimethylformamide, 3.0 g of a 50% suspension of sodium hydride in mineral oil was added. The mixture was stirred for 15 min at 25°, 5 ml of methyl iodide was added, and the stirring was continued for 5 min. The solution was poured into ice–water and extracted with ether. On concentrating the ether extract a small amount of VIII (0.2 g) was isolated. The main product XII melting at 177–180° was obtained on addition of hexane in *ca.* 60% yield (2.8 g). Recrystallization from a mixture of methylene chloride and ethanol gave pale yellow prisms melting at 181–184°: ultraviolet λ_{max} 259 mμ (ϵ 29,000) and 315 mμ (ϵ 4000); nmr (perchloroethylene) at *ca.* 25° 1CH_3 163 (s) and 154 (s), 1NC*H* 309 (s) and 285 cps (s), and at *ca.* 100° 1CH$_3$ 163 (s, broad) and 288 cps (s, broad).

Anal. Calcd for $C_{27}H_{20}Cl_2N_2$: C, 73.14; H, 4.55. Found: C, 73.48; H, 4.79.

***trans*-2,8-Dichloro-5,6,11,12-tetrahydro-5,11-dinitroso-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (XIII).**—To a stirred suspension of 4.3 g (0.01 mole) of II in 100 ml of acetic acid was added a solution of 2 g (0.029 mole) of sodium nitrite in 10 ml of water. The stirring was continued for 1 hr. The crystalline precipitate was collected on a filter, dried, and recrystallized from a mixture of tetrahydrofuran and ether. White prisms melting at 224° dec were obtained in 76% yield (3.7 g).

Anal. Calcd for $C_{26}H_{18}Cl_2N_4O_2$: C, 63.81; H, 3.71; N, 11.45. Found: C, 63.91; H, 3.74; H, 11.59.

***cis*-2,8-Dichloro-5,6,11,12-tetrahydro-5,11-dinitroso-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (XIV).**—To a solution of 4.3 g (0.01 mole) of III in 100 ml of acetic acid was added 1.72 g (0.025 mole) of sodium nitrite in 5 ml of water. A precipitate formed on standing for 16 hr and was collected on a filter. Recrystallization from benzene gave 3.9 g (80%) of white prisms melting at 240° dec.

Anal. Calcd for $C_{26}H_{18}Cl_2N_4O_2$: C, 63.81; H, 3.71; N, 11.45. Found: C, 63.94; H, 3.58; N, 11.28.

***trans*-2,8-Dichloro-6,12-diphenyl-6H,12H-5,11-methanodibenzo[*b,f*][1,5]diazocine (XV).**—To a solution of 20 g (0.046 mole) of II in 600 ml of toluene, 10 g of paraformaldehyde was added and the mixture was refluxed for 16 hr. Paraformaldehyde was filtered from the solution which was concentrated *in vacuo* to give white needles which after recrystallization from a mixture of methylene chloride and ethanol melted at 187–192° (incomplete melt to 220°): yield 18 g (88%), ultraviolet λ_{infl} 255 mμ (ϵ 10,000) and 295 mμ (ϵ 2000); nmr (CDCl$_3$) 1C*H* 352 (s), 1C*H* 324 (s), 1 *o-H* 339 and 331 (d), and 1CH_2 259 cps (s).

Anal. Calcd for $C_{27}H_{20}Cl_2N_2$: C, 73.14; H, 4.55; mol wt, 443. Found: C, 72.88; H, 4.84; mol wt, 427 (isothermal distillation in acetone).

The melting point of this compound remained unsharp despite numerous purifications by crystallization, high-vacuum distillation, and chromatography. Vapor phase chromatography gave no indication of an impurity in XV. In a column chromatography on acidic alumina 140 fractions were obtained. Spectral properties of these fractions were found to be constant.

Compound XV was dissolved in acetic acid and treated with nitrous acid (16 hr, 25°) to give XIII and was rearranged by sodium hydride in dimethylformamide (0.5 hr, 25°) to give an 80% yield of XVI.

***cis,exo*-2,8-Dichloro-6,12-diphenyl-6H,12H-5,11-methanodibenzo[*b,f*][1,5]diazocine (XVI).**—A suspension of 10.0 g (0.023 mole) of III in a mixture of 6.5 ml of 98% formic acid and 5.0 ml 37% of aqueous formaldehyde and 100 ml of nitromethane was heated on a steam bath for 6.5 hr and left at 25° for 16 hr. The precipitate was filtered and recrystallized from a mixture of methylene chloride and ethanol to give 8.8 g (85% of theory) of white needles melting at 279–281°: ultraviolet λ_{infl} 255 mμ (ϵ 10,000) and 296 mμ (ϵ 2000); nmr (CDCl$_3$) 2C*H* 319 (s) and NCH$_2$N 233 cps (s).

Anal. Calcd for $C_{27}H_{20}Cl_2N_2$: C, 73.14; H, 4.55; mol wt, 443. Found: C, 73.54; H, 4.37; mol wt, 432 (isothermal distillation in acetone).

***cis,endo*-2,8-Dichloro-6,12-diphenyl-6H,12H-5,11-methanodibenzo[*b,f*]1,5]diazocine (XVII).**—A solution of 6.5 g (0.015 mole) of III in 150 ml of toluene containing 3.3 g of paraformaldehyde was heated to reflux for 18 hr. After cooling the paraformaldehyde was filtered from the solution and the solvent was evaporated *in vacuo*. The residue crystallized on addition of ether to give 2.9 g of a fraction which according to thin layer chromatography contained mainly compound XVI and the starting material III. From the mother liquor another crystalline fraction was obtained which after recrystallization from a mixture of methylene chloride and methanol gave 1.3 g of white prisms melting at 214–230°. This fraction was chromatographed on 36 g of alumina (Woelm, No. I neutral) using benzene as eluent. The first fractions contained a small amount of XVI, later fractions gave white prisms which after recrystallization from a mixture of methylene chloride and methanol melted at 241–243°: yield 0.6 g; ultraviolet λ_{infl} 258 mμ (ϵ 7500) and λ_{infl} 295 mμ (ϵ 2000); nmr (CDCl$_3$) 2C*H* 356 (s), NCH$_2$N 282 (s), and 2 *o-H* 343, and 333 cps (d).

Anal. Calcd for $C_{27}H_{20}Cl_2N_2$: C, 73.14; H, 4.55; mol wt, 443. Found: C, 72.86; H, 4.28; mol wt, 394 (isothermal distillation in acetone).

Vapor phase chromatography of the crude reaction mixture showed it to contain the compounds III, XVI, and XVII in the ratio of approximately 2:1:1. In an experiment using twice the amount of paraformaldehyde a ratio of 2:3:5 was found.

Compound XVII on treatment with nitrous acid in acetic acid (3 hr, 25°) readily formed XIV, and sodium hydride in dimethylformamide (1 hr, 25°) gave compound XVI as the sole product.

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